1

Structure and Bonding

What is organic chemistry, and why should you study it? The answers to these questions are all around you. Every living organism is made of organic chemicals. The proteins that make up your hair, skin, and muscles; the DNA that controls your genetic heritage; the foods that nourish you; and the medicines that heal you are all organic chemicals. Anyone with a curiosity about life and living things, and anyone who wants to be a part of the many exciting developments now happening in medicine and the biological sciences, must first understand organic chemistry. Look at the following drawings for instance, which show the chemical structures of some molecules whose names might be familiar to you.
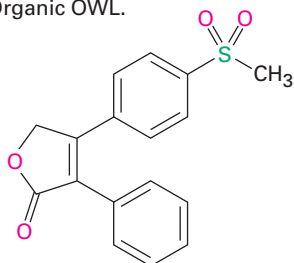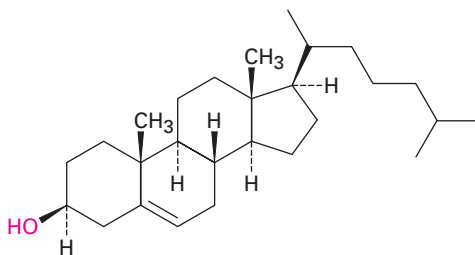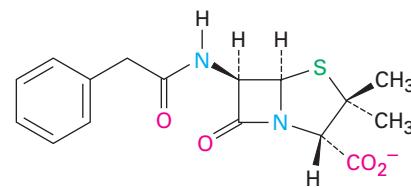
Rofecoxib
(Vioxx)
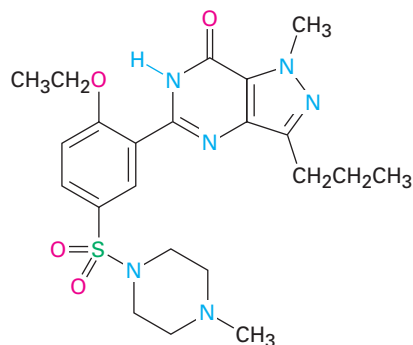
Sildenafil
(Viagra)
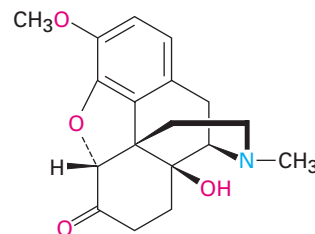
Oxycodone
(OxyContin)

Cholesterol

Benzylpenicillin

Although the drawings may appear unintelligible at this point, don't worry. Before long they'll make perfectly good sense and you'll be drawing similar structures for any substance you're interested in.

The foundations of organic chemistry date from the mid-1700s, when chemistry was evolving from an alchemist's art into a modern science. At that time, unexplainable differences were noted between substances obtained from living sources and those obtained from minerals. Compounds obtained from plants and animals were often difficult to isolate and purify. Even when pure, they were often difficult to work with, and they tended to decompose more easily than compounds obtained from minerals. The Swedish chemist Torbern Bergman in 1770 was the first to express this difference between "organic" and "inorganic" substances, and the term *organic chemistry* soon came to mean the chemistry of compounds found in living organisms.

To many chemists of the time, the only explanation for the differences in behavior between organic and inorganic compounds was that organic compounds must contain a peculiar "vital force" as a result of their origin in living sources. One consequence of this vital force, chemists believed, was that organic compounds could not be prepared and manipulated in the laboratory as could inorganic compounds. As early as 1816, however, this vitalistic theory received a heavy blow when Michel Chevreul found that soap, prepared by the reaction of alkali with animal fat, could be separated into several pure organic compounds, which he termed *fatty acids.* For the first time, one organic substance (fat) was converted into others (fatty acids plus glycerin) without the intervention of an outside vital force.

$$\text{Animal fat} \xrightarrow[\text{H}_2\text{O}]{\text{NaOH}} \text{Soap} + \text{Glycerin}$$

$$\text{Soap} \xrightarrow{\text{H}_3\text{O}^+} \text{"Fatty acids"}$$

Little more than a decade later, the vitalistic theory suffered still further when Friedrich Wöhler discovered in 1828 that it was possible to convert the "inorganic" salt ammonium cyanate into the "organic" substance urea, which had previously been found in human urine.

$$\text{NH}_4^+ \;{}^-\text{OCN} \xrightarrow{\text{Heat}} \underset{\textbf{Urea}}{\text{H}_2\text{N}-\overset{\overset{\textstyle \text{O}}{\|}}{\text{C}}-\text{NH}_2}$$

Ammonium cyanate

By the mid-1800s, the weight of evidence was clearly against the vitalistic theory. As William Brande wrote in 1848, "No definite line can be drawn between organic and inorganic chemistry. . . . Any distinctions . . . must for the present be merely considered as matters of practical convenience calculated to further the progress of students." Chemistry today is unified, and the same principles explain the behaviors of all substances, regardless of origin or complexity. The only distinguishing characteristic of organic chemicals is that *all contain the element carbon.*
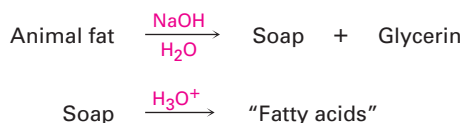
Michel-Eugène Chevreul

Michel-Eugène Chevreul (1786–1889) was born in Angers, France. After studies at the Collège de France in Paris, he became professor of physics at the Lycée Charlemagne in 1813 and professor of chemistry in 1830. Chevreul's studies of soaps and waxes led him to patent a method for manufacturing candles. He also published work on the psychology of color perception and of aging. All France celebrated his 100th birthday in 1886.
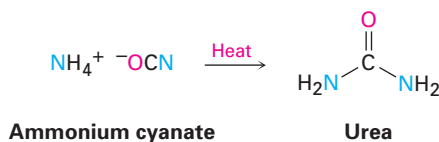
Friedrich Wöhler

Friedrich Wöhler (1800–1882) was born in Eschersheim, Germany, and studied at Heidelberg under Leopold Gmelin. From 1836 to 1882, he was professor of chemistry at Göttingen. Wöhler developed the first industrial method for preparing aluminum metal, and he discovered several new elements. In addition, he wrote textbooks about both inorganic and organic chemistry.

William Thomas Brande

William Thomas Brande (1788–1866) was born in London, England. Trained as an apothecary, he became a lecturer in chemistry at the University of London in 1808 and was a professor at the Royal Institution from 1813 to 1852. His scientific achievements were modest, although he was the first person to discover naphthalene, now used in mothballs.

Organic chemistry, then, is the study of carbon compounds. But why is carbon special? Why, of the more than 30 million presently known chemical compounds, do more than 99% of them contain carbon? The answers to these questions come from carbon's electronic structure and its consequent position in the periodic table (Figure 1.1). As a group 4A element, carbon can share four valence electrons and form four strong covalent bonds. Furthermore, carbon atoms can bond to one another, forming long chains and rings. Carbon, alone of all elements, is able to form an immense diversity of compounds, from the simple to the staggeringly complex—from methane, with one carbon atom, to DNA, which can have more than *100 hundred million* carbons.

Figure 1.1 The position of carbon in the periodic table. Other elements commonly found in organic compounds are shown in the colors typically used to represent them.

Not all carbon compounds are derived from living organisms, of course, and chemists over the years have developed a remarkably sophisticated ability to design and synthesize new organic compounds. Medicines, dyes, polymers, food additives, pesticides, and a host of other substances are now prepared in the laboratory. Organic chemistry touches the lives of everyone. Its study is a fascinating undertaking.

WHY THIS CHAPTER?

We'll ease into the study of organic chemistry by first reviewing some ideas about atoms, bonds, and molecular geometry that you may recall from your general chemistry course. Much of the material in this chapter and the next is likely to be familiar to you, but it's nevertheless a good idea to make sure you understand it before going on.

1.1 | Atomic Structure: The Nucleus

As you probably know, an atom consists of a dense, positively charged *nucleus* surrounded at a relatively large distance by negatively charged *electrons* (Figure 1.2). The nucleus consists of subatomic particles called *neutrons,* which are electrically neutral, and *protons,* which are positively charged. Because an atom is neutral

overall, the number of positive protons in the nucleus and the number of negative electrons surrounding the nucleus are the same.

Although extremely small—about 10^{-14} to 10^{-15} meter (m) in diameter—the nucleus nevertheless contains essentially all the mass of the atom. Electrons have negligible mass and circulate around the nucleus at a distance of approximately 10^{-10} m. Thus, the diameter of a typical atom is about 2×10^{-10} m, or 200 *picometers* (pm), where 1 pm = 10^{-12} m. To give you an idea of how small this is, a thin pencil line is about 3 million carbon atoms wide. Many organic chemists and biochemists, particularly in the United States, still use the unit *angstrom* (Å) to express atomic distances, where 1 Å = 10^{-10} m = 100 pm, but we'll stay with the SI unit picometer in this book.

Figure 1.2 A schematic view of an atom. The dense, positively charged nucleus contains most of the atom's mass and is surrounded by negatively charged electrons. The three-dimensional view on the right shows calculated electron-density surfaces. Electron density increases steadily toward the nucleus and is 40 times greater at the blue solid surface than at the gray mesh surface.

Nucleus (protons + neutrons)

Volume around nucleus occupied by orbiting electrons
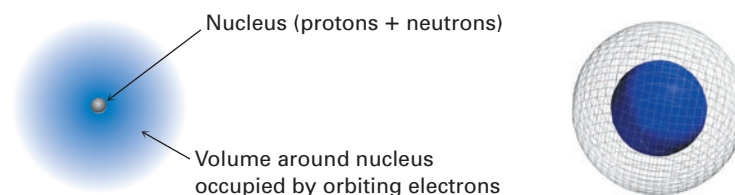
A specific atom is described by its *atomic number* (Z), which gives the number of protons in the atom's nucleus, and its *mass number* (A), which gives the total of protons plus neutrons in its nucleus. All the atoms of a given element have the same atomic number—1 for hydrogen, 6 for carbon, 15 for phosphorus, and so on—but they can have different mass numbers, depending on how many neutrons they contain. Atoms with the same atomic number but different mass numbers are called **isotopes**. The weighted average mass in atomic mass units (amu) of an element's naturally occurring isotopes is called the element's *atomic mass* (or *atomic weight*)—1.008 amu for hydrogen, 12.011 amu for carbon, 30.974 amu for phosphorus, and so on.

1.2 | Atomic Structure: Orbitals

How are the electrons distributed in an atom? You might recall from your general chemistry course that, according to the quantum mechanical model, the behavior of a specific electron in an atom can be described by a mathematical expression called a *wave equation*—the same sort of expression used to describe the motion of waves in a fluid. The solution to a wave equation is called a *wave function,* or **orbital**, and is denoted by the Greek letter psi, ψ.

By plotting the square of the wave function, ψ^2, in three-dimensional space, the orbital describes the volume of space around a nucleus that an electron is most likely to occupy. You might therefore think of an orbital as looking like a photograph of the electron taken at a slow shutter speed. The orbital would appear as a blurry cloud indicating the region of space around the nucleus where the electron has been. This electron cloud doesn't have a sharp boundary, but for practical purposes we can set the limits by saying that an orbital represents the space where an electron spends most (90%–95%) of its time.

What do orbitals look like? There are four different kinds of orbitals, denoted *s*, *p*, *d*, and *f*, each with a different shape. Of the four, we'll be concerned primarily with *s* and *p* orbitals because these are the most common in organic and biological chemistry. The *s* orbitals are spherical, with the nucleus at their center; *p* orbitals are dumbbell-shaped; and four of the five *d* orbitals are cloverleaf-shaped, as shown in Figure 1.3. The fifth *d* orbital is shaped like an elongated dumbbell with a doughnut around its middle.

Figure 1.3 Representations of *s*, *p*, and *d* orbitals. The *s* orbitals are spherical, the *p* orbitals are dumbbell-shaped, and four of the five *d* orbitals are cloverleaf-shaped. Different lobes of *p* orbitals are often drawn for convenience as teardrops, but their true shape is more like that of a doornob, as indicated.

An *s* orbital   **A *p* orbital**   **A *d* orbital**
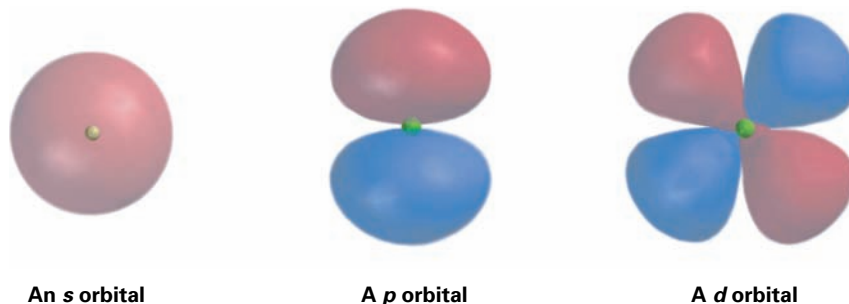
The orbitals in an atom are organized into different layers, or **electron shells**, of successively larger size and energy. Different shells contain different numbers and kinds of orbitals, and each orbital within a shell can be occupied by two electrons. The first shell contains only a single *s* orbital, denoted 1*s*, and thus holds only 2 electrons. The second shell contains one 2*s* orbital and three 2*p* orbitals and thus holds a total of 8 electrons. The third shell contains a 3*s* orbital, three 3*p* orbitals, and five 3*d* orbitals, for a total capacity of 18 electrons. These orbital groupings and their energy levels are shown in Figure 1.4.

Figure 1.4 The energy levels of electrons in an atom. The first shell holds a maximum of 2 electrons in one 1*s* orbital; the second shell holds a maximum of 8 electrons in one 2*s* and three 2*p* orbitals; the third shell holds a maximum of 18 electrons in one 3*s*, three 3*p*, and five 3*d* orbitals; and so on. The two electrons in each orbital are represented by up and down arrows, ↑↓. Although not shown, the energy level of the 4*s* orbital falls between 3*p* and 3*d*.
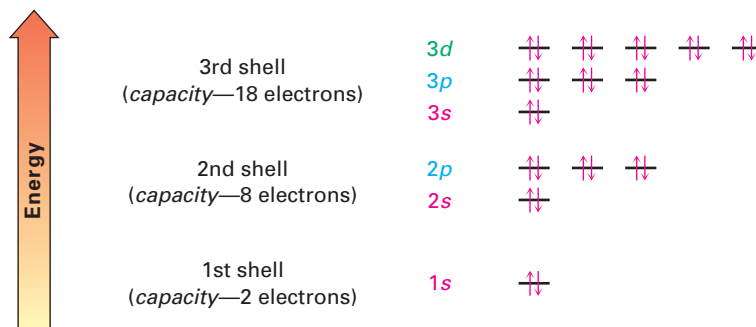
The three different *p* orbitals within a given shell are oriented in space along mutually perpendicular directions, denoted p_x, p_y, and p_z. As shown in Figure 1.5, the two lobes of each *p* orbital are separated by a region of zero electron density called a **node**. Furthermore, the two orbital regions separated by the node have different algebraic signs, $+$ and $-$, in the wave function. As we'll see in Section 1.11, the algebraic signs of the different orbital lobes have important consequences with respect to chemical bonding and chemical reactivity.

Figure 1.5 Shapes of the 2p orbitals. Each of the three mutually perpendicular, dumbbell-shaped orbitals has two lobes separated by a node. The two lobes have different algebraic signs in the corresponding wave function, as indicated by the different colors.

A 2p_x orbital   A 2p_y orbital   A 2p_z orbital
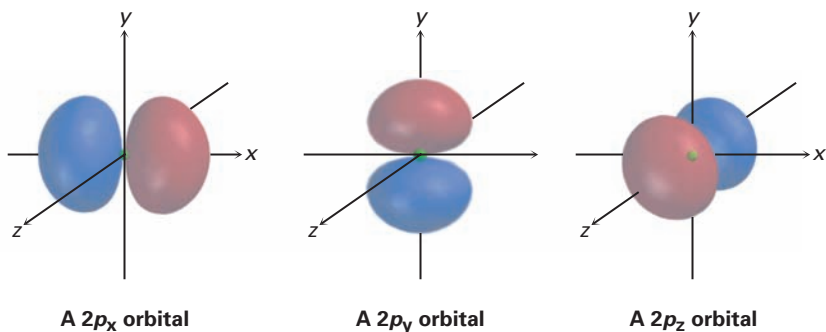
1.3 | Atomic Structure: Electron Configurations

The lowest-energy arrangement, or **ground-state electron configuration**, of an atom is a listing of the orbitals occupied by its electrons. We can predict this arrangement by following three rules.

Rule 1   The lowest-energy orbitals fill up first, according to the order $1s \rightarrow 2s \rightarrow 2p \rightarrow 3s \rightarrow 3p \rightarrow 4s \rightarrow 3d$, a statement called the *aufbau principle.* Note that the 4s orbital lies between the 3p and 3d orbitals in energy.

Rule 2   Electrons act as if they were spinning around an axis, in much the same way that the earth spins. This spin can have two orientations, denoted as up ↑ and down ↓. Only two electrons can occupy an orbital, and they must be of opposite spin, a statement called the *Pauli exclusion principle.*

Rule 3   If two or more empty orbitals of equal energy are available, one electron occupies each with spins parallel until all orbitals are half-full, a statement called *Hund's rule.*

Some examples of how these rules apply are shown in Table 1.1. Hydrogen, for instance, has only one electron, which must occupy the lowest-energy orbital. Thus, hydrogen has a 1s ground-state configuration. Carbon has six electrons and the ground-state configuration $1s^2\, 2s^2\, 2p_x{}^1\, 2p_y{}^1$, and so forth. Note that a superscript is used to represent the number of electrons in a particular orbital.

Table 1.1 | Ground-State Electron Configurations of Some Elements

Element	Atomic number	Configuration				Element	Atomic number	Configuration			
Hydrogen	1	1s	↿			Phosphorus	15	3p	↿	↿	↿
								3s	⇅		
Carbon	6	2p	↿	↿	—			2p	⇅	⇅	⇅
		2s	⇅					2s	⇅		
		1s	⇅					1s	⇅		

Problem 1.1 | Give the ground-state electron configuration for each of the following elements:
(a) Oxygen   (b) Silicon   (c) Sulfur

Problem 1.2 | How many electrons does each of the following elements have in its outermost electron shell?
(a) Magnesium   (b) Molybdenum   (c) Selenium

1.4 | Development of Chemical Bonding Theory

Friedrich August Kekulé

Friedrich August Kekulé (1829–1896) was born in Darmstadt, Germany. He entered the University of Giessen in 1847 intending to become an architect but soon switched to chemistry. After receiving his doctorate under Liebig and doing further study in Paris, Kekulé became a lecturer at Heidelberg in 1855 and a professor of chemistry at Ghent (1858) and Bonn (1867). His realization that carbon can form rings of atoms is said to have come to him in a dream in which he saw a snake biting its tail.

By the mid-1800s, the new science of chemistry was developing rapidly and chemists had begun to probe the forces holding compounds together. In 1858, August Kekulé and Archibald Couper independently proposed that, in all its compounds, carbon is *tetravalent*—it always forms four bonds when it joins other elements to form stable compounds. Furthermore, said Kekulé, carbon atoms can bond to one another to form extended chains of linked atoms.

Shortly after the tetravalent nature of carbon was proposed, extensions to the Kekulé–Couper theory were made when the possibility of *multiple* bonding between atoms was suggested. Emil Erlenmeyer proposed a carbon–carbon triple bond for acetylene, and Alexander Crum Brown proposed a carbon–carbon double bond for ethylene. In 1865, Kekulé provided another major advance when he suggested that carbon chains can double back on themselves to form *rings* of atoms.

Although Kekulé and Couper were correct in describing the tetravalent nature of carbon, chemistry was still viewed in a two-dimensional way until 1874. In that year, Jacobus van't Hoff and Joseph Le Bel added a third dimension to our ideas about organic compounds when they proposed that the four bonds of carbon are not oriented randomly but have specific spatial directions. Van't Hoff went even further and suggested that the four atoms to

| Archibald Scott Couper	Richard A. C. E. Erlenmeyer	Alexander Crum Brown	Jacobus Hendricus van't Hoff
Archibald Scott Couper (1831–1892) was born in Kirkintilloch, Scotland, and studied at the universities of Glasgow, Edinburgh, and Paris. Although his scientific paper about the ability of carbon to form four bonds was submitted prior to a similar paper by Kekulé, Couper never received credit for his work. His health began to decline after the rejection of his achievements, and he suffered a nervous breakdown in 1858. He then retired from further scientific work and spent the last 30 years of his life in the care of his mother.	**Richard A. C. E. Erlenmeyer** (1825–1909) was born in Wehen, Germany. He studied in Giessen and in Heidelberg, intending originally to be a pharmacist, and was professor of chemistry at Munich Polytechnicum from 1868 to 1883. Much of his work was carried out with biological molecules, and he was the first to prepare the amino acid tyrosine.	**Alexander Crum Brown** (1838–1922) was born in Edinburgh, the son of a Presbyterian minister. He studied at Edinburgh, Heidelberg, and Marburg and was professor of chemistry at Edinburgh from 1869 to 1908. Crum Brown's interests were many. He studied the physiology of the canals in the inner ear, he was proficient in Japanese, and he had a lifelong interest in knitting.	**Jacobus Hendricus van't Hoff** (1852–1911) was born in Rotterdam, Netherlands, and studied at Delft, Leyden, Bonn, Paris, and Utrecht. Widely educated, he served as professor of chemistry, mineralogy, and geology at the University of Amsterdam from 1878 to 1896 and later became professor at Berlin. In 1901, he received the first Nobel Prize in chemistry for his work on chemical equilibrium and osmotic pressure.

Joseph Achille Le Bel

Joseph Achille Le Bel (1847–1930) was born in Péchelbronn, France, and studied at the École Polytechnique and the Sorbonne in Paris. Freed by his family's wealth from the need to earn a living, he established his own private laboratory.

which carbon is bonded sit at the corners of a regular tetrahedron, with carbon in the center.

A representation of a tetrahedral carbon atom is shown in Figure 1.6. Note the conventions used to show three-dimensionality: solid lines represent bonds in the plane of the page, the heavy wedged line represents a bond coming out of the page toward the viewer, and the dashed line represents a bond receding back behind the page, away from the viewer. These representations will be used throughout the text.

Figure 1.6 A representation of Van't Hoff's tetrahedral carbon atom. The solid lines are in the plane of the paper, the heavy wedged line comes out of the plane of the page, and the dashed line goes back behind the plane of the page.
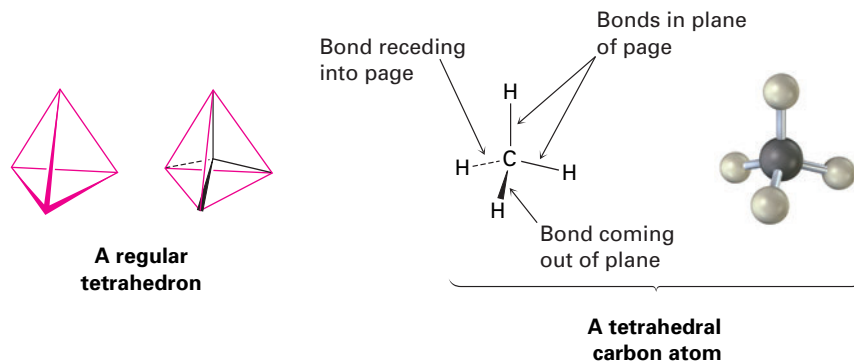
Why, though, do atoms bond together, and how can bonds be described electronically? The *why* question is relatively easy to answer. Atoms bond together because the compound that results is lower in energy, and thus more stable, than the separate atoms. Energy (usually as heat) always flows out of the chemical system when a chemical bond forms. Conversely, energy must be put into the system to break a chemical bond. Making bonds always releases energy, and breaking bonds always absorbs energy. The *how* question is more difficult. To answer it, we need to know more about the electronic properties of atoms.

We know through observation that eight electrons (an electron *octet*) in an atom's outermost shell, or **valence shell**, impart special stability to the noble-gas elements in group 8A of the periodic table: Ne (2 + 8); Ar (2 + 8 + 8); Kr (2 + 8 + 18 + 8). We also know that the chemistry of main-group elements is governed by their tendency to take on the electron configuration of the nearest noble gas. The alkali metals in group 1A, for example, achieve a noble-gas configuration by losing the single *s* electron from their valence shell to form a cation, while the halogens in group 7A achieve a noble-gas configuration by gaining a *p* electron to fill their valence shell, thereby forming an anion. The resultant ions are held together in compounds like Na$^+$ Cl$^-$ by an electrostatic attraction that we call an *ionic bond*.

But how do elements closer to the middle of the periodic table form bonds? Look at methane, CH_4, the main constituent of natural gas, for example. The bonding in methane is not ionic because it would take too much energy for carbon ($1s^2 2s^2 2p^2$) either to gain or lose four electrons to achieve a noble-gas configuration. As a result, carbon bonds to other atoms, not by gaining or losing electrons, but by sharing them. Such a shared-electron bond, first proposed in 1916 by G. N. Lewis, is called a **covalent bond**. The neutral collection of atoms held together by covalent bonds is called a **molecule**.

Gilbert Newton Lewis

Gilbert Newton Lewis (1875–1946) was born in Weymouth, Massachusetts, and received his Ph.D. at Harvard in 1899. After a short time as professor of chemistry at the Massachusetts Institute of Technology (1905–1912), he spent the rest of his career at the University of California at Berkeley (1912–1946). In addition to his work on structural theory, Lewis was the first to prepare "heavy water," D_2O, in which the two hydrogens of water are the ^2H isotope, deuterium.

A simple way of indicating the covalent bonds in molecules is to use what are called *Lewis structures,* or **electron-dot structures**, in which the valence electrons of an atom are represented as dots. Thus, hydrogen has one dot representing its $1s$ electron, carbon has four dots ($2s^2\ 2p^2$), oxygen has six dots ($2s^2\ 2p^4$), and so on. A stable molecule results whenever a noble-gas configuration is achieved for all the atoms—eight dots (an octet) for main-group atoms or two dots for hydrogen. Simpler still is the use of *Kekulé structures,* or **line-bond structures**, in which a two-electron covalent bond is indicated as a line drawn between atoms.

Electron-dot structures (Lewis structures)				
Line-bond structures (Kekulé structures)	Methane (CH_4)	Ammonia (NH_3)	Water (H_2O)	Methanol (CH_3OH)
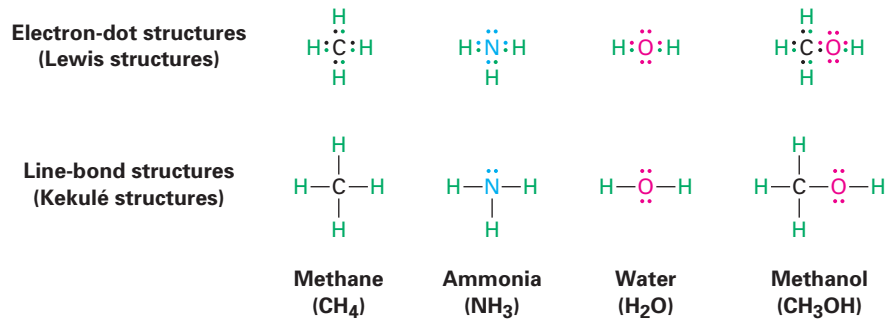
The number of covalent bonds an atom forms depends on how many additional valence electrons it needs to reach a noble-gas configuration. Hydrogen has one valence electron ($1s$) and needs one more to reach the helium configuration ($1s^2$), so it forms one bond. Carbon has four valence electrons ($2s^2\ 2p^2$) and needs four more to reach the neon configuration ($2s^2\ 2p^6$), so it forms four bonds. Nitrogen has five valence electrons ($2s^2\ 2p^3$), needs three more, and forms three bonds; oxygen has six valence electrons ($2s^2\ 2p^4$), needs two more, and forms two bonds; and the halogens have seven valence electrons, need one more, and form one bond.

H—	—C—	—N—	—O—	:F— :Cl— :Br— :I—
One bond	**Four bonds**	**Three bonds**	**Two bonds**	**One bond**
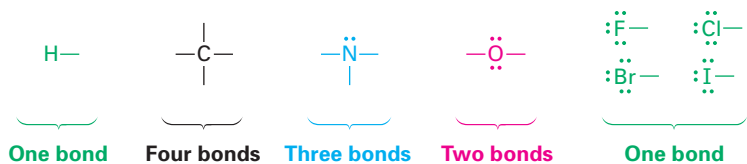
Valence electrons that are not used for bonding are called **lone-pair electrons**, or *nonbonding electrons.* The nitrogen atom in ammonia, for instance, shares six valence electrons in three covalent bonds and has its remaining two valence electrons in a nonbonding lone pair. As a time-saving shorthand, nonbonding electrons are often omitted when drawing line-bond structures, but you still have to keep them in mind since they're often crucial in chemical reactions.

Nonbonding, lone-pair electrons

H:N:H or H—N—H [or H—N—H]

Ammonia
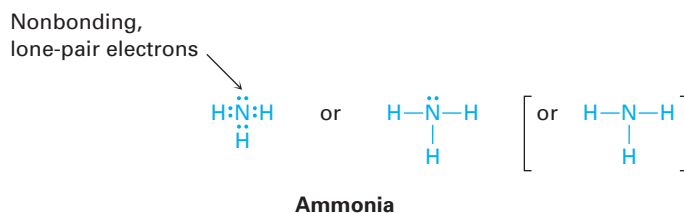
| WORKED EXAMPLE 1.1	***Predicting the Number of Bonds Formed by Atoms in a Molecule***
	How many hydrogen atoms does phosphorus bond to in forming phosphine, $PH_?$?
Strategy	Identify the periodic group of phosphorus, and tell from that how many electrons (bonds) are needed to make an octet.
Solution	Phosphorus is in group 5A of the periodic table and has five valence electrons. It thus needs to share three more electrons to make an octet and therefore bonds to three hydrogen atoms, giving PH_3.

Problem 1.3 Draw a molecule of chloroform, $CHCl_3$, using solid, wedged, and dashed lines to show its tetrahedral geometry.

Problem 1.4 Convert the following representation of ethane, C_2H_6, into a conventional drawing that uses solid, wedged, and dashed lines to indicate tetrahedral geometry around each carbon (gray = C, ivory = H).
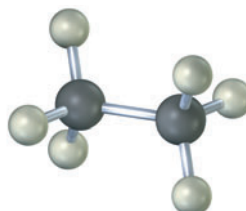
Ethane

Problem 1.5 What are likely formulas for the following substances?
(a) $GeCl_?$ (b) $AlH_?$ (c) $CH_?Cl_2$ (d) $SiF_?$ (e) $CH_3NH_?$

Problem 1.6 Write line-bond structures for the following substances, showing all nonbonding electrons:
(a) $CHCl_3$, chloroform (b) H_2S, hydrogen sulfide
(c) CH_3NH_2, methylamine (d) CH_3Li, methyllithium

Problem 1.7 Why can't an organic molecule have the formula C_2H_7?

1.5 | The Nature of Chemical Bonds: Valence Bond Theory

How does electron sharing lead to bonding between atoms? Two models have been developed to describe covalent bonding: *valence bond theory* and *molecular orbital theory.* Each model has its strengths and weaknesses, and chemists tend

to use them interchangeably depending on the circumstances. Valence bond theory is the more easily visualized of the two, so most of the descriptions we'll use in this book derive from that approach.

According to **valence bond theory**, a covalent bond forms when two atoms approach each other closely and a singly occupied orbital on one atom *overlaps* a singly occupied orbital on the other atom. The electrons are now paired in the overlapping orbitals and are attracted to the nuclei of both atoms, thus bonding the atoms together. In the H_2 molecule, for example, the H–H bond results from the overlap of two singly occupied hydrogen 1s orbitals.

The overlapping orbitals in the H_2 molecule have the elongated egg shape we might get by pressing two spheres together. If a plane were to pass through the middle of the bond, the intersection of the plane and the overlapping orbitals would be a circle. In other words, the H–H bond is *cylindrically symmetrical,* as shown in Figure 1.7. Such bonds, which are formed by the head-on overlap of two atomic orbitals along a line drawn between the nuclei, are called **sigma (σ) bonds**.

During the bond-forming reaction 2 H· → H_2, 436 kJ/mol (104 kcal/mol) of energy is released. Because the product H_2 molecule has 436 kJ/mol less energy than the starting 2 H· atoms, we say that the product is more stable than the reactant and that the H–H bond has a **bond strength** of 436 kJ/mol. In other words, we would have to put 436 kJ/mol of energy *into* the H–H bond to break the H_2 molecule apart into H atoms (Figure 1.8.) [For convenience, we'll generally give energies in both kilocalories (kcal) and the SI unit kilojoules (kJ): 1 kJ = 0.2390 kcal; 1 kcal = 4.184 kJ.]

Figure 1.7 The cylindrical symmetry of the H–H σ bond in an H_2 molecule. The intersection of a plane cutting through the σ bond is a circle.

Figure 1.8 Relative energy levels of H atoms and the H_2 molecule. The H_2 molecule has 436 kJ/mol (104 kcal/mol) less energy than the two H atoms, so 436 kJ/mol of energy is released when the H–H bond forms. Conversely, 436 kJ/mol must be added to the H_2 molecule to break the H–H bond.
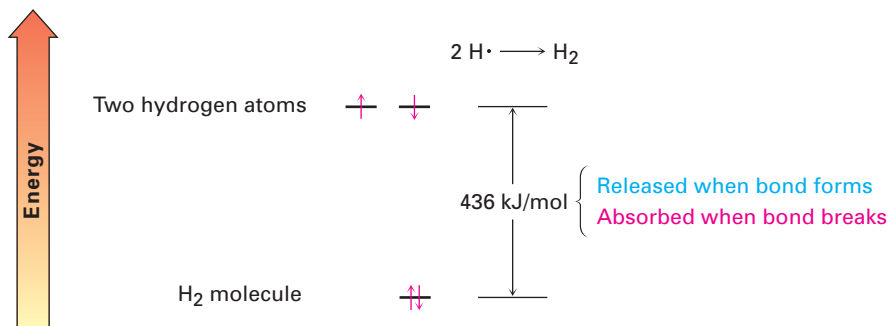
How close are the two nuclei in the H_2 molecule? If they are too close, they will repel each other because both are positively charged, yet if they're too far apart, they won't be able to share the bonding electrons. Thus, there is an optimum distance between nuclei that leads to maximum stability (Figure 1.9). Called the **bond length**, this distance is 74 pm in the H_2 molecule. Every covalent bond has both a characteristic bond strength and bond length.

Figure 1.9 A plot of energy versus internuclear distance for two hydrogen atoms. The distance between nuclei at the minimum energy point is the bond length.
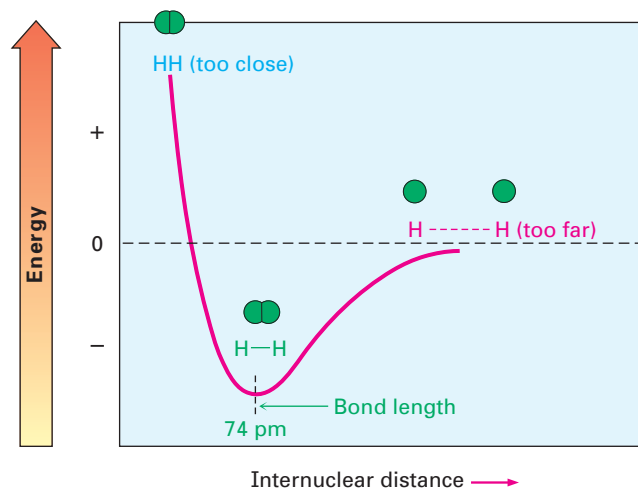
1.6 | sp^3 Hybrid Orbitals and the Structure of Methane

Linus Carl Pauling

Linus Carl Pauling (1901–1994) was born in Portland, Oregon, the son of a pharmacist. After obtaining a B.S. degree at Oregon State University, he received a Ph.D. from the California Institute of Technology in 1925. He was professor of chemistry from 1925 to 1967 at the California Institute of Technology and then from 1974 to 1994 at the University of California in San Diego and Stanford University. Pauling was a scientific giant, who made fundamental discoveries in fields ranging from chemical bonding to molecular biology to medicine. A lifelong pacifist, Pauling is the only solo winner of two Nobel Prizes in different fields: the first in 1954 for chemistry and the second in 1963 for peace.

The bonding in the hydrogen molecule is fairly straightforward, but the situation is more complicated in organic molecules with tetravalent carbon atoms. Take methane, CH_4, for instance. As we've seen, carbon has four valence electrons ($2s^2\,2p^2$) and forms four bonds. Because carbon uses two kinds of orbitals for bonding, $2s$ and $2p$, we might expect methane to have two kinds of C–H bonds. In fact, though, all four C–H bonds in methane are identical and are spatially oriented toward the corners of a regular tetrahedron (Figure 1.6). How can we explain this?

An answer was provided in 1931 by Linus Pauling, who showed how an s orbital and three p orbitals on an atom can combine mathematically, or *hybridize,* to form four equivalent atomic orbitals with tetrahedral orientation. Shown in Figure 1.10, these tetrahedrally oriented orbitals are called sp^3 **hybrids**. Note that the superscript 3 in the name sp^3 tells how many of each type of atomic orbital combine to form the hybrid, not how many electrons occupy it.

The concept of hybridization explains *how* carbon forms four equivalent tetrahedral bonds but not *why* it does so. The shape of the hybrid orbital suggests the answer. When an s orbital hybridizes with three p orbitals, the resultant sp^3 hybrid orbitals are unsymmetrical about the nucleus. One of the two
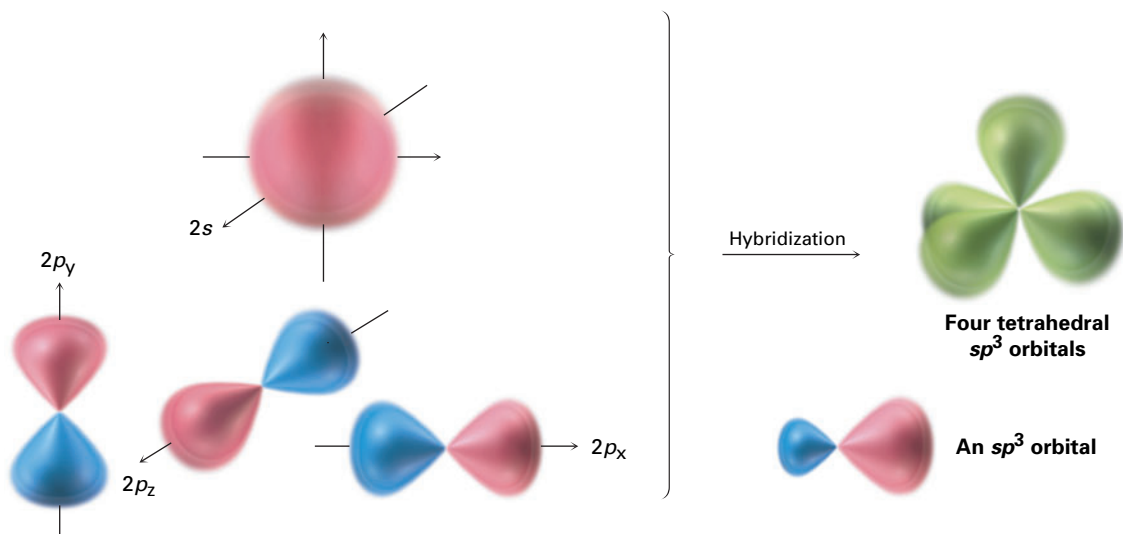
Active Figure 1.10 Four *sp*³ hybrid orbitals (green), oriented to the corners of a regular tetrahedron, are formed by combination of an *s* orbital (red) and three *p* orbitals (red/blue). The *sp*³ hybrids have two lobes and are unsymmetrical about the nucleus, giving them a directionality and allowing them to form strong bonds to other atoms. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*

lobes is much larger than the other and can therefore overlap more effectively with an orbital from another atom when it forms a bond. As a result, *sp*³ hybrid orbitals form stronger bonds than do unhybridized *s* or *p* orbitals.

The asymmetry of *sp*³ orbitals arises because, as noted previously, the two lobes of a *p* orbital have different algebraic signs, + and −. Thus, when a *p* orbital hybridizes with an *s* orbital, the positive *p* lobe adds to the *s* orbital but the negative *p* lobe subtracts from the *s* orbital. The resultant hybrid orbital is therefore unsymmetrical about the nucleus and is strongly oriented in one direction.

When each of the four identical *sp*³ hybrid orbitals of a carbon atom overlaps with the 1*s* orbital of a hydrogen atom, four identical C−H bonds are formed and methane results. Each C−H bond in methane has a strength of 436 kJ/mol (104 kcal/mol) and a length of 109 pm. Because the four bonds have a specific geometry, we also can define a property called the **bond angle**. The angle formed by each H−C−H is 109.5°, the so-called tetrahedral angle. Methane thus has the structure shown in Figure 1.11.

Active Figure 1.11 The structure of methane, showing its 109.5° bond angles. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*
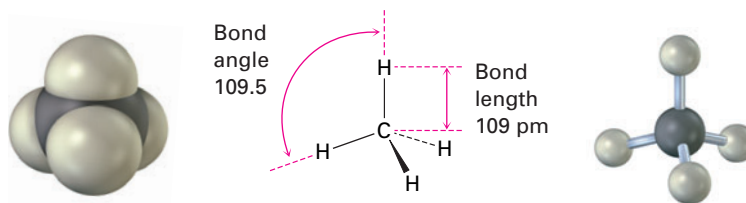
1.7 | sp^3 Hybrid Orbitals and the Structure of Ethane

The same kind of orbital hybridization that accounts for the methane structure also accounts for the bonding together of carbon atoms into chains and rings to make possible many millions of organic compounds. Ethane, C_2H_6, is the simplest molecule containing a carbon–carbon bond.

H H
H:C:C:H   H—C—C—H CH_3CH_3
H H

Some representations of ethane
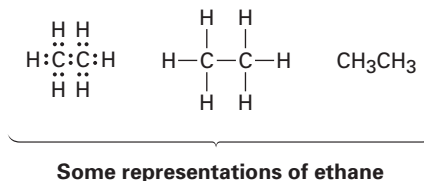
We can picture the ethane molecule by imagining that the two carbon atoms bond to each other by σ overlap of an sp^3 hybrid orbital from each (Figure 1.12). The remaining three sp^3 hybrid orbitals of each carbon overlap with the 1*s* orbitals of three hydrogens to form the six C—H bonds. The C—H bonds in ethane are similar to those in methane, although a bit weaker—423 kJ/mol (101 kcal/mol) for ethane versus 436 kJ/mol for methane. The C—C bond is 154 pm long and has a strength of 376 kJ/mol (90 kcal/mol). All the bond angles of ethane are near, although not exactly at, the tetrahedral value of 109.5°.

Figure 1.12 The structure of ethane. The carbon–carbon bond is formed by σ overlap of two carbon sp^3 hybrid orbitals. For clarity, the smaller lobes of the sp^3 hybrid orbitals are not shown.

sp^3 **carbon** sp^3 **carbon** sp^3–sp^3 σ **bond**

Ethane
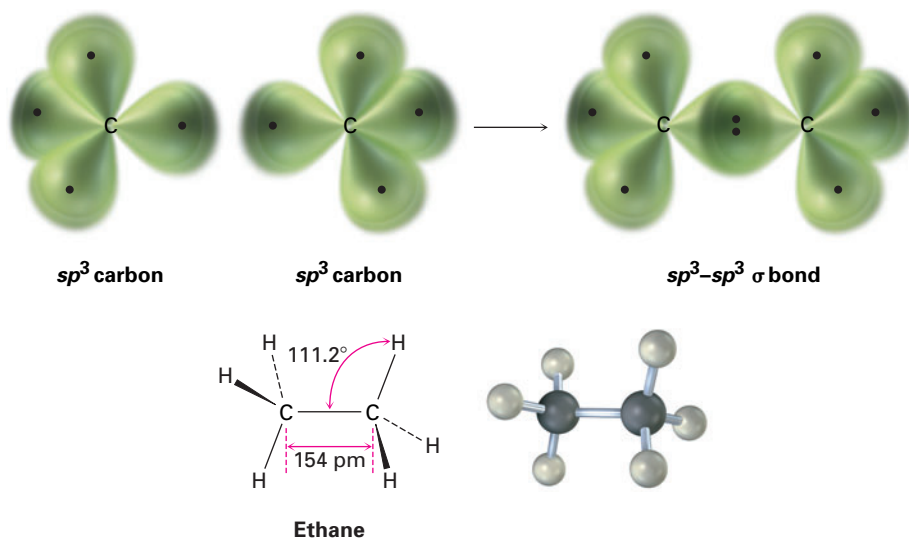
Problem 1.8 | Draw a line-bond structure for propane, $CH_3CH_2CH_3$. Predict the value of each bond angle, and indicate the overall shape of the molecule.

Problem 1.9 | Convert the following molecular model of hexane, a component of gasoline, into a line-bond structure (gray = C, ivory = H).
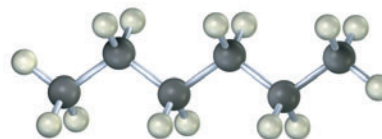
Hexane

1.8 | *sp²* **Hybrid Orbitals and the Structure of Ethylene**

Although sp^3 hybridization is the most common electronic state of carbon, it's not the only possibility. Look at ethylene, C_2H_4, for example. It was recognized more than 100 years ago that ethylene carbons can be tetravalent only if they share *four* electrons and are linked by a *double* bond. Furthermore, ethylene is planar (flat) and has bond angles of approximately 120° rather than 109.5°.

$H_2C=CH_2$

Top view   Side view
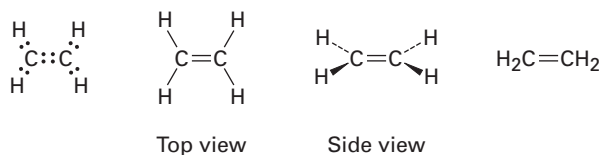
Some representations of ethylene

When we discussed sp^3 hybrid orbitals in Section 1.6, we said that the four valence-shell atomic orbitals of carbon combine to form four equivalent sp^3 hybrids. Imagine instead that the 2*s* orbital combines with only *two* of the three available 2*p* orbitals. Three **sp^2 hybrid orbitals** result, and one 2*p* orbital remains unchanged. The three sp^2 orbitals lie in a plane at angles of 120° to one another, with the remaining *p* orbital perpendicular to the sp^2 plane, as shown in Figure 1.13.

Figure 1.13 An *sp²*-hybridized carbon. The three equivalent *sp²* hybrid orbitals (green) lie in a plane at angles of 120° to one another, and a single unhybridized *p* orbital (red/blue) is perpendicular to the *sp²* plane.

Side view   Top view
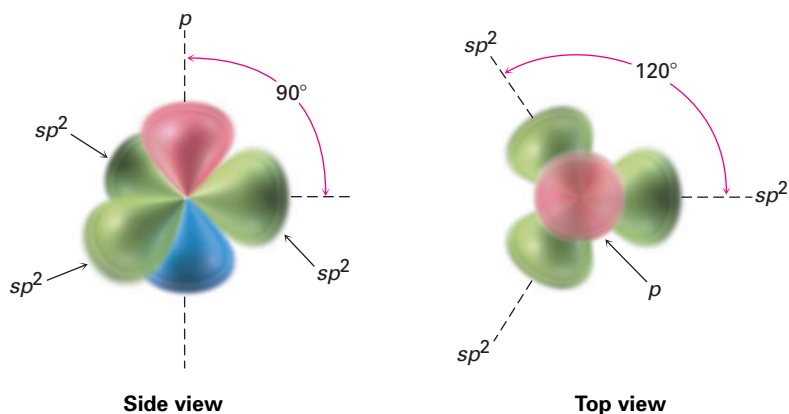
When two sp^2-hybridized carbons approach each other, they form a σ bond by sp^2–sp^2 head-on overlap. At the same time, the unhybridized p orbitals approach with the correct geometry for *sideways* overlap, leading to the formation of what is called a **pi (π) bond**. The combination of an sp^2–sp^2 σ bond and a $2p$–$2p$ π bond results in the sharing of four electrons and the formation of a carbon–carbon double bond (Figure 1.14). Note that the electrons in the σ bond occupy the region centered between nuclei, while the electrons in the π bond occupy regions on either side of a line drawn between nuclei.

To complete the structure of ethylene, four hydrogen atoms form σ bonds with the remaining four sp^2 orbitals. Ethylene thus has a planar structure, with H−C−H and H−C−C bond angles of approximately 120°. (The actual values are 117.4° for the H−C−H bond angle and 121.3° for the H−C−C bond angle.) Each C−H bond has a length of 108.7 pm and a strength of 465 kJ/mol (111 kcal/mol).

Figure 1.14 The structure of ethylene. Orbital overlap of two sp^2-hybridized carbons forms a carbon–carbon double bond. One part of the double bond results from σ (head-on) overlap of sp^2 orbitals (green), and the other part results from π (sideways) overlap of unhybridized p orbitals (red/blue). The π bond has regions of electron density on either side of a line drawn between nuclei.
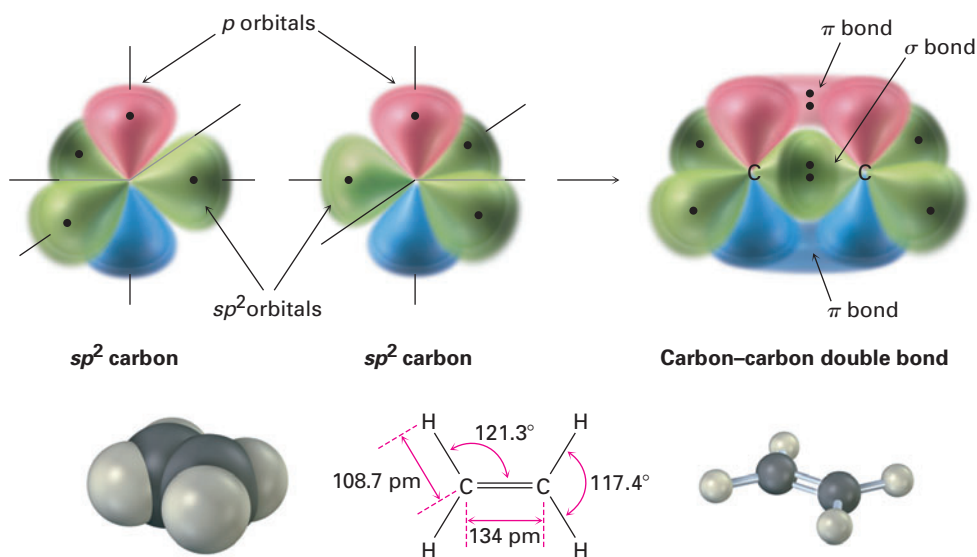
As you might expect, the carbon–carbon double bond in ethylene is both shorter and stronger than the single bond in ethane because it has four electrons bonding the nuclei together rather than two. Ethylene has a C=C bond length of 134 pm and a strength of 728 kJ/mol (174 kcal/mol) versus a C−C length of 154 pm and a strength of 376 kJ/mol for ethane. Note that the carbon–carbon double bond is less than twice as strong as a single bond because the overlap in the π part of the double bond is not as effective as the overlap in the σ part.

WORKED EXAMPLE 1.2

Predicting the Structures of Simple Organic Molecules from Their Formulas

Commonly used in biology as a tissue preservative, formaldehyde, CH_2O, contains a carbon–*oxygen* double bond. Draw the line-bond structure of formaldehyde, and indicate the hybridization of the carbon atom.

Strategy   We know that hydrogen forms one covalent bond, carbon forms four, and oxygen forms two. Trial and error, combined with intuition, is needed to fit the atoms together.

**Solution**   There is only one way that two hydrogens, one carbon, and one oxygen can combine:

$$\ddot{\text{O}}:$$

Formaldehyde

Like the carbon atoms in ethylene, the carbon atom in formaldehyde is in a double bond and therefore sp^2-hybridized.

Problem 1.10   Draw a line-bond structure for propene, $CH_3CH{=}CH_2$; indicate the hybridization of each carbon; and predict the value of each bond angle.

Problem 1.11   Draw a line-bond structure for 1,3-butadiene, $H_2C{=}CH{-}CH{=}CH_2$; indicate the hybridization of each carbon; and predict the value of each bond angle.

Problem 1.12   Following is a molecular model of aspirin (acetylsalicylic acid). Identify the hybridization of each carbon atom in aspirin, and tell which atoms have lone pairs of electrons (gray = C, red = O, ivory = H).

**Aspirin
(acetylsalicylic acid)**
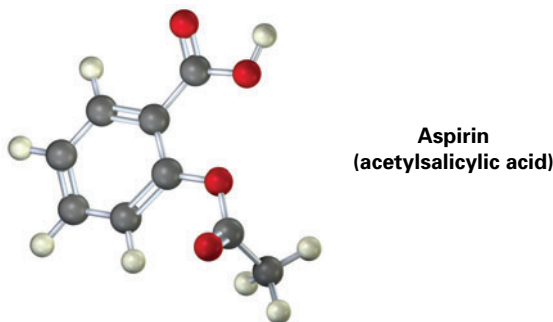
1.9   *sp* Hybrid Orbitals and the Structure of Acetylene

In addition to forming single and double bonds by sharing two and four electrons, respectively, carbon also can form a *triple* bond by sharing six electrons. To account for the triple bond in a molecule such as acetylene, $H{-}C{\equiv}C{-}H$, we need a third kind of hybrid orbital, an ***sp* hybrid**. Imagine that, instead of combining with two or three *p* orbitals, a carbon 2*s* orbital hybridizes with only a single *p* orbital. Two *sp* hybrid orbitals result, and two *p* orbitals remain unchanged. The two *sp* orbitals are oriented 180° apart on the *x*-axis, while the

remaining two *p* orbitals are perpendicular on the *y*-axis and the *z*-axis, as shown in Figure 1.15.

Figure 1.15 An *sp*-hybridized carbon atom. The two *sp* hybrid orbitals (green) are oriented 180° away from each other, perpendicular to the two remaining *p* orbitals (red/blue).

One *sp* hybrid   Another *sp* hybrid
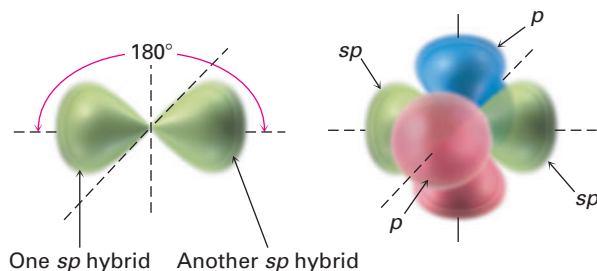
When two *sp*-hybridized carbon atoms approach each other, *sp* hybrid orbitals on each carbon overlap head-on to form a strong *sp–sp* σ bond. In addition, the p_z orbitals from each carbon form a p_z–p_z π bond by sideways overlap and the p_y orbitals overlap similarly to form a p_y–p_y π bond. The net effect is the sharing of six electrons and formation of a carbon–carbon triple bond. The two remaining *sp* hybrid orbitals each form a σ bond with hydrogen to complete the acetylene molecule (Figure 1.16).

Figure 1.16 The structure of acetylene. The two *sp*-hybridized carbon atoms are joined by one *sp–sp* σ bond and two *p–p* π bonds.

Carbon–carbon triple bond
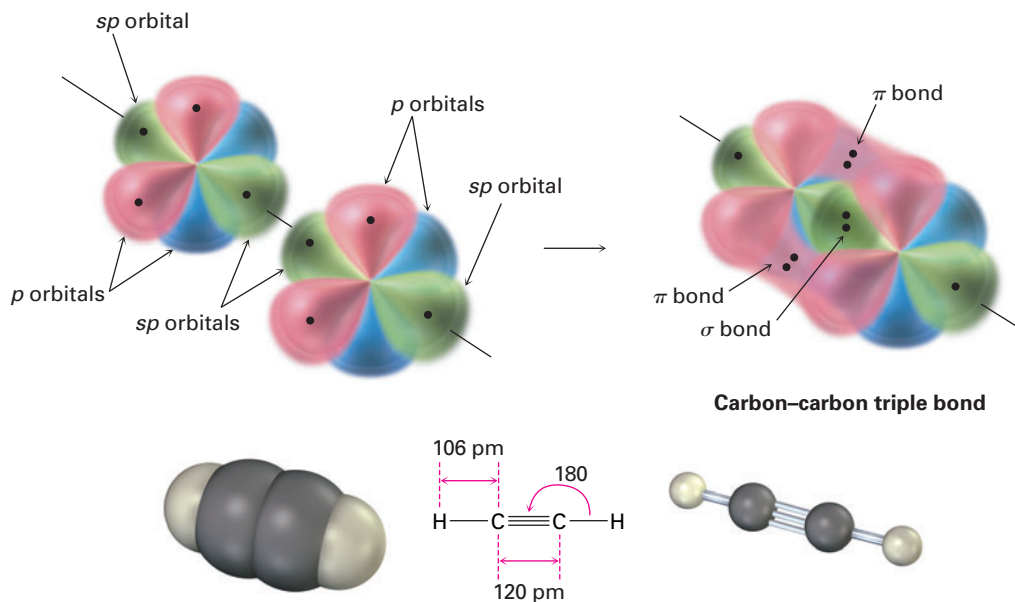
As suggested by *sp* hybridization, acetylene is a linear molecule with H−C−C bond angles of 180°. The C−H bonds have a length of 106 pm and a strength of 556 kJ/mol (133 kcal/mol). The C−C bond length in acetylene is 120 pm, and its strength is about 965 kJ/mol (231 kcal/mol), making it the shortest and strongest of any carbon–carbon bond. A comparison of *sp*, sp^2, and sp^3 hybridization is given in Table 1.2.

Table 1.2	Comparison of C—C and C—H Bonds in Methane, Ethane, Ethylene, and Acetylene			
		Bond strength		
Molecule	Bond	(kJ/mol)	(kcal/mol)	Bond length (pm)
Methane, CH_4	(sp^3) C—H	436	104	109
Ethane, CH_3CH_3	(sp^3) C—C (sp^3)	376	90	154
	(sp^3) C—H	423	101	109
Ethylene, $H_2C{=}CH_2$	(sp^2) C—C (sp^2)	728	174	134
	(sp^2) C—H	465	111	109
Acetylene, $HC{\equiv}CH$	(sp) C≡C (sp)	965	231	120
	(sp) C—H	556	133	106

Problem 1.13 Draw a line-bond structure for propyne, $CH_3C{\equiv}CH$; indicate the hybridization of each carbon; and predict a value for each bond angle.

1.10 | Hybridization of Nitrogen, Oxygen, Phosphorus, and Sulfur

The valence-bond concept of orbital hybridization described in the previous four sections is not limited to carbon compounds. Covalent bonds formed by other elements can also be described using hybrid orbitals. Look, for instance, at the nitrogen atom in methylamine, CH_3NH_2, an organic derivative of ammonia (NH_3) and the substance responsible for the odor of rotting fish.

The experimentally measured H—N—H bond angle in methylamine is 107.1° and the C—N—H bond angle is 110.3°, both of which are close to the 109.5° tetrahedral angle found in methane. We therefore assume that nitrogen hybridizes to form four sp^3 orbitals, just as carbon does. One of the four sp^3 orbitals is occupied by two nonbonding electrons, and the other three hybrid orbitals have one electron each. Overlap of these half-filled nitrogen orbitals with half-filled orbitals from other atoms (C or H) gives methylamine. Note that the unshared lone pair of electrons in the fourth sp^3 hybrid orbital of nitrogen occupies as much space as an N—H bond does and is very important to the chemistry of methylamine and other nitrogen-containing organic molecules.
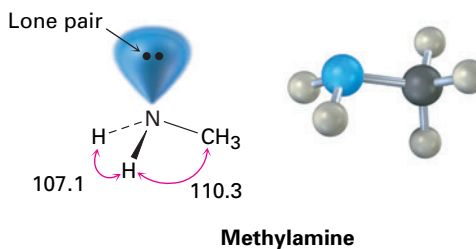
Methylamine

Like the carbon atom in methane and the nitrogen atom in methylamine, the oxygen atom in methanol (methyl alcohol) and many other organic molecules can also be described as sp^3-hybridized. The C—O—H bond angle in methanol is 108.5°, very close to the 109.5° tetrahedral angle. Two of the four sp^3 hybrid

orbitals on oxygen are occupied by nonbonding electron lone pairs, and two are used to form bonds.

**Methanol
(methyl alcohol)**
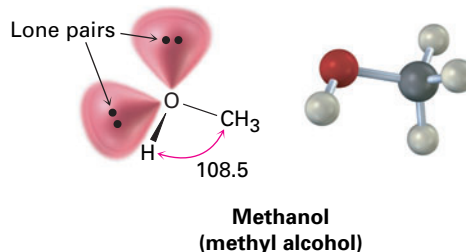
Phosphorus and sulfur are the third-row analogs of nitrogen and oxygen, and the bonding in both can be described using hybrid orbitals. Because of their positions in the third row, however, both phosphorus and sulfur can expand their outer-shell octets and form more than the typical number of covalent bonds. Phosphorus, for instance, often forms five covalent bonds, and sulfur occasionally forms four.

Phosphorus is most commonly encountered in biological molecules in *organophosphates,* compounds that contain a phosphorus atom bonded to four oxygens, with one of the oxygens also bonded to carbon. Methyl phosphate, $CH_3OPO_3{}^{2-}$ is the simplest example. The $O-P-O$ bond angle in such compounds is typically in the range 110 to 112°, implying sp^3 hybridization for the phosphorus.

**Methyl phosphate
(an organophosphate)**
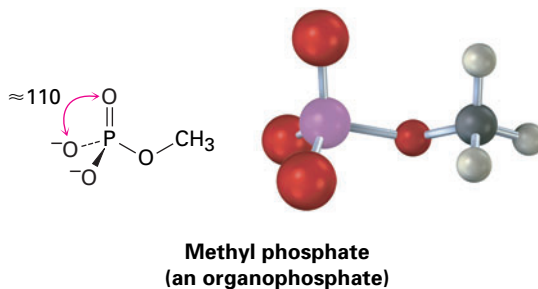
Sulfur is most commonly encountered in biological molecules either in compounds called *thiols,* which have a sulfur atom bonded to one hydrogen and one carbon, or in *sulfides,* which have a sulfur atom bonded to two carbons. Produced by some bacteria, methanethiol (CH_3SH) is the simplest example of a thiol, and dimethyl sulfide [$(CH_3)_2S$] is the simplest example of a sulfide. Both can be described by approximate sp^3 hybridization around sulfur, although both have significant deviation from the 109.5° tetrahedral angle.

ThomsonNOW™ Click *Organic Interactive* to learn how to **identify hybridization in a variety of organic molecules**.

Methanethiol

Dimethyl sulfide

Problem 1.14 | Identify all nonbonding lone pairs of electrons in the following molecules, and tell what geometry you expect for each of the indicated atoms.

(a) The oxygen atom in dimethyl ether, CH_3—O—CH_3

(b) The nitrogen atom in trimethylamine, H_3C—N—CH_3
$|$
CH_3

(c) The phosphorus atom in phosphine, PH_3

(d) The sulfur atom in the amino acid methionine, CH_3—S—CH_2CH_2CHCOH
$\overset{\displaystyle O}{\overset{\|}{}}$
$|$
NH_2

1.11 | The Nature of Chemical Bonds: Molecular Orbital Theory

We said in Section 1.5 that chemists use two models for describing covalent bonds: valence bond theory and molecular orbital theory. Having now seen the valence bond approach, which uses hybrid atomic orbitals to account for geometry and assumes the overlap of atomic orbitals to account for electron sharing, let's look briefly at the molecular orbital approach to bonding. We'll return to the topic in Chapters 14 and 15 for a more in-depth discussion.

Molecular orbital (MO) theory describes covalent bond formation as arising from a mathematical combination of atomic orbitals (wave functions) on different atoms to form *molecular orbitals,* so called because they belong to the entire *molecule* rather than to an individual atom. Just as an *atomic* orbital, whether unhybridized or hybridized, describes a region of space around an *atom* where an electron is likely to be found, so a *molecular* orbital describes a region of space in a *molecule* where electrons are most likely to be found.

Like an atomic orbital, a molecular orbital has a specific size, shape, and energy. In the H_2 molecule, for example, two singly occupied 1s atomic orbitals combine to form two molecular orbitals. There are two ways for the orbital combination to occur—an additive way and a subtractive way. The additive combination leads to formation of a molecular orbital that is lower in energy and roughly egg-shaped, while the subtractive combination leads to formation of a molecular orbital that is higher in energy and has a node between nuclei (Figure 1.17). Note that the additive combination is a *single,* egg-shaped, molecular orbital; it is not the same as the two overlapping 1s atomic orbitals of the valence bond description. Similarly, the subtractive combination is a single molecular orbital with the shape of an elongated dumbbell.

Figure 1.17 Molecular orbitals of H_2. Combination of two hydrogen 1s atomic orbitals leads to two H_2 molecular orbitals. The lower-energy, bonding MO is filled, and the higher-energy, antibonding MO is unfilled.

Node

σ Antibonding MO (unfilled)

Combine

Two 1s orbitals

σ Bonding MO (filled)

Energy

The additive combination is lower in energy than the two hydrogen 1*s* atomic orbitals and is called a **bonding MO** because electrons in this MO spend most of their time in the region between the two nuclei, thereby bonding the atoms together. The subtractive combination is higher in energy than the two hydrogen 1*s* orbitals and is called an **antibonding MO** because any electrons it contains *can't* occupy the central region between the nuclei, where there is a node, and can't contribute to bonding. The two nuclei therefore repel each other.

Just as bonding and antibonding σ molecular orbitals result from the combination of two *s* atomic orbitals in H_2, so bonding and antibonding π molecular orbitals result from the combination of two *p* atomic orbitals in ethylene. As shown in Figure 1.18, the lower-energy, π bonding MO has no node between nuclei and results from combination of *p* orbital lobes with the same algebraic sign. The higher-energy, π antibonding MO has a node between nuclei and results from combination of lobes with opposite algebraic signs. Only the bonding MO is occupied; the higher-energy, antibonding MO is vacant. We'll see in Chapters 14 and 15 that molecular orbital theory is particularly useful for describing π bonds in compounds that have more than one double bond.
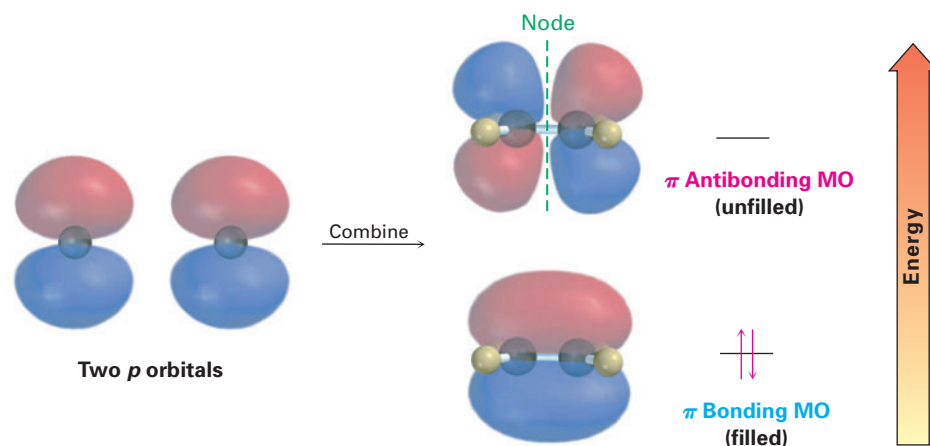
Figure 1.18 A molecular orbital description of the C=C π bond in ethylene. The lower-energy, π bonding MO results from a combination of *p* orbital lobes with the same algebraic sign and is filled. The higher-energy, π antibonding MO results from a combination of *p* orbital lobes with the opposite algebraic signs and is unfilled.

1.12 | Drawing Chemical Structures

Let's cover one more point before ending this introductory chapter. In the structures we've been drawing until now, a line between atoms has represented the two electrons in a covalent bond. Drawing every bond and every atom is tedious, however, so chemists have devised several shorthand ways for writing structures. In **condensed structures**, carbon–hydrogen and carbon–carbon single bonds aren't shown; instead, they're understood. If a carbon has three hydrogens bonded to it, we write CH_3; if a carbon has two hydrogens bonded to

it, we write CH_2; and so on. The compound called 2-methylbutane, for example, is written as follows:
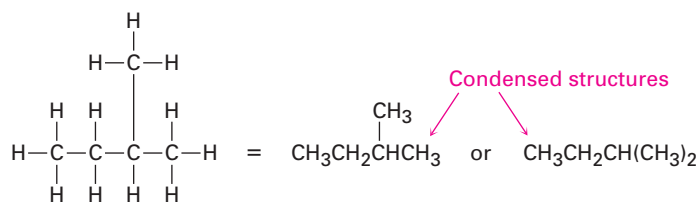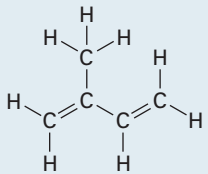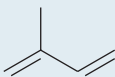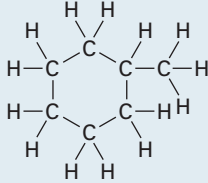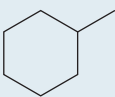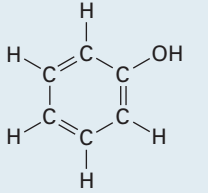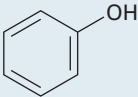
2-Methylbutane

Notice that the horizontal bonds between carbons aren't shown in condensed structures—the CH_3, CH_2, and CH units are simply placed next to each other—but the vertical carbon–carbon bond in the first of the condensed structures drawn above is shown for clarity. Notice also in the second of the condensed structures that the two CH_3 units attached to the CH carbon are grouped together as $(CH_3)_2$.

Even simpler than condensed structures is the use of **skeletal structures** such as those shown in Table 1.3. The rules for drawing skeletal structures are straightforward.

Rule 1 Carbon atoms aren't usually shown. Instead, a carbon atom is assumed to be at each intersection of two lines (bonds) and at the end of each line. Occasionally, a carbon atom might be indicated for emphasis or clarity.

Rule 2 Hydrogen atoms bonded to carbon aren't shown. Since carbon always has a valence of 4, we mentally supply the correct number of hydrogen atoms for each carbon.

Rule 3 Atoms other than carbon and hydrogen *are* shown.

Table 1.3 Kekulé and Skeletal Structures for Some Compounds

Compound	Kekulé structure	Skeletal structure
Isoprene, C_5H_8		
Methylcyclohexane, C_7H_{14}		
Phenol, C_6H_6O		

One further comment: although such groupings as $-CH_3$, $-OH$, and $-NH_2$ are usually written with the C, O, or N atom first and the H atom second, the order of writing is sometimes inverted to H_3C-, $HO-$, and H_2N- if needed to make the bonding connections in a molecule clearer. Larger units such as $-CH_2CH_3$ are not inverted, though; we don't write H_3CH_2C- because it would be confusing. There are, however, no well-defined rules that cover all cases; it's largely a matter of preference.

ThomsonNOW™ Click *Organic Interactive* to learn how to **interconvert skeletal structures, condensed structures, and molecular models.**
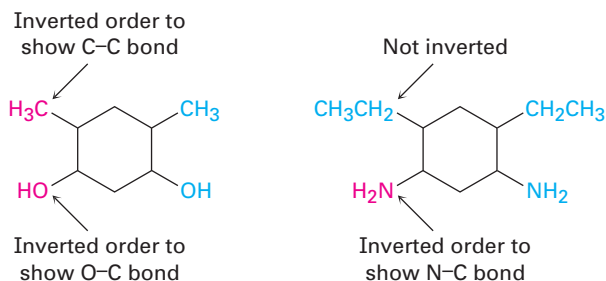
WORKED EXAMPLE 1.3   *Interpreting Line-Bond Structures*

Carvone, a substance responsible for the odor of spearmint, has the following structure. Tell how many hydrogens are bonded to each carbon, and give the molecular formula of carvone.

Carvone
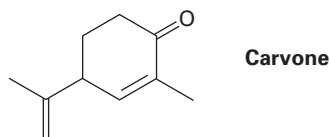
Strategy   The end of a line represents a carbon atom with 3 hydrogens, CH_3; a two-way intersection is a carbon atom with 2 hydrogens, CH_2; a three-way intersection is a carbon atom with 1 hydrogen, CH; and a four-way intersection is a carbon atom with no attached hydrogens.

Solution

Carvone, $C_{10}H_{14}O$
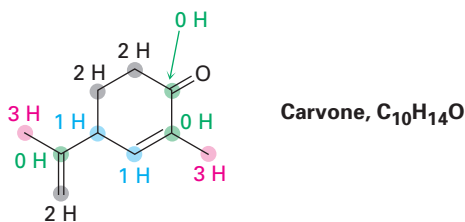
Problem 1.15   Tell how many hydrogens are bonded to each carbon in the following compounds, and give the molecular formula of each substance:

(a)

Adrenaline

(b)
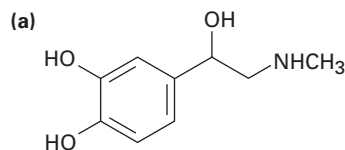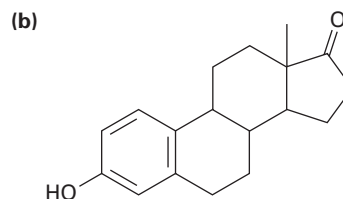
Estrone (a hormone)

Problem 1.16   Propose skeletal structures for compounds that satisfy the following molecular formulas. There is more than one possibility in each case.
(a) C_5H_{12} **(b)** C_2H_7N **(c)** C_3H_6O **(d)** C_4H_9Cl

Problem 1.17   The following molecular model is a representation of *para*-aminobenzoic acid (PABA), the active ingredient in many sunscreens. Indicate the positions of the multiple bonds, and draw a skeletal structure (gray = C, red = O, blue = N, ivory = H).
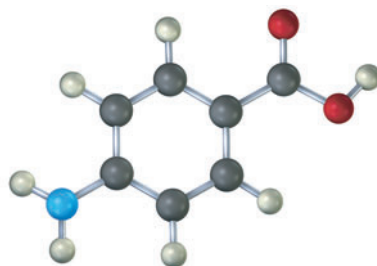
para-**Aminobenzoic acid**
(PABA)

Focus On . . .

Chemicals, Toxicity, and Risk

We all take many risks each day, some much more dangerous than others.

We hear and read a lot these days about the dangers of "chemicals"—about pesticide residues on our food, toxic wastes on our land, unsafe medicines, and so forth. What's a person to believe?

Life is not risk-free; we all take many risks each day. We decide to ride a bike rather than drive, even though there is a ten times greater likelihood per mile of dying in a bicycling accident than in a car. We decide to walk down stairs rather than take an elevator, even though 7000 people die from falls each year in the United States. We decide to smoke cigarettes, even though it increases our chance of getting cancer by 50%. Making decisions that affect our health is something we do routinely without even thinking about it.

What about risks from chemicals? Risk evaluation of chemicals is carried out by exposing test animals (usually rats) to the chemical and then monitoring for signs of harm. To limit the expense and time needed, the amounts administered are hundreds or thousands of times greater than those a person might normally encounter. Data are then reduced to a single number called an LD_{50}, the amount of a substance per kilogram body weight that is lethal to

(continued)

50% of the test animals. The LD_{50}'s of some common substances are shown in Table 1.4. The lower the value, the more toxic the substance.

Table 1.4   **Some LD_{50} Values**

Substance	LD_{50} (g/kg)	Substance	LD_{50} (g/kg)
Strychnine	0.005	Iron(II) sulfate	1.5
Arsenic trioxide	0.015	Chloroform	3.2
DDT	0.115	Ethyl alcohol	10.6
Aspirin	1.1	Sodium cyclamate	17

Even with animal data available, risk is still hard to assess. If a substance is harmful to animals, is it necessarily harmful to humans? How can a large dose for a small animal be translated into a small dose for a large human? All substances are toxic to some organisms to some extent, and the difference between help and harm is often a matter of degree. Vitamin A, for example, is necessary for vision, yet it can promote cancer at high dosages. Arsenic tri-oxide is the most classic of poisons, yet recent work has shown it to be effec-tive at inducing remissions in some types of leukemia. Even water can be toxic if drunk in large amounts because it dilutes the salt in body fluids and causes a potentially life-threatening condition called *hyponatremia*. Furthermore, how we evaluate risk is strongly influenced by familiarity. Many foods contain natural ingredients far more toxic than synthetic additives or pesticide residues, but the ingredients are ignored because the foods are familiar.

All decisions involve tradeoffs. Does the benefit of increased food pro-duction outweigh possible health risks of a pesticide? Do the beneficial effects of a new drug outweigh a potentially dangerous side effect in a small fraction of users? The answers are rarely obvious, but we should at least try to base our responses on facts.

SUMMARY AND KEY WORDS

Organic chemistry is the study of carbon compounds. Although a division into organic and inorganic chemistry occurred historically, there is no scientific rea-son for the division.

An atom consists of a positively charged nucleus surrounded by one or more negatively charged electrons. The electronic structure of an atom can be described by a quantum mechanical wave equation, in which electrons are con-sidered to occupy **orbitals** around the nucleus. Different orbitals have different energy levels and different shapes. For example, *s* orbitals are spherical and *p* orbitals are dumbbell-shaped. The **ground-state electron configuration** of an

atom can be found by assigning electrons to the proper orbitals, beginning with the lowest-energy ones.

A **covalent bond** is formed when an electron pair is shared between atoms. According to **valence bond theory**, electron sharing occurs by overlap of two atomic orbitals. According to **molecular orbital (MO) theory**, bonds result from the mathematical combination of atomic orbitals to give molecular orbitals, which belong to the entire molecule. Bonds that have a circular cross-section and are formed by head-on interaction are called **sigma (σ) bonds**; bonds formed by sideways interaction of *p* orbitals are called **pi (π) bonds**.

In the valence bond description, carbon uses hybrid orbitals to form bonds in organic molecules. When forming only single bonds with tetrahedral geometry, carbon uses four equivalent *sp*^{3} **hybrid orbitals**. When forming a double bond with planar geometry, carbon uses three equivalent *sp*^{2} **hybrid orbitals** and one unhybridized *p* orbital. When forming a triple bond with linear geometry, carbon uses two equivalent *sp* **hybrid orbitals** and two unhybridized *p* orbitals. Other atoms such as nitrogen, phosphorus, oxygen, and sulfur also use hybrid orbitals to form strong, oriented bonds.

Organic molecules are usually drawn using either condensed structures or skeletal structures. In **condensed structures**, carbon–carbon and carbon–hydrogen bonds aren't shown. In **skeletal structures**, only the bonds and not the atoms are shown. A carbon atom is assumed to be at the ends and at the junctions of lines (bonds), and the correct number of hydrogens is mentally supplied.

Working Problems

There is no surer way to learn organic chemistry than by working problems. Although careful reading and rereading of this text are important, reading alone isn't enough. You must also be able to use the information you've read and be able to apply your knowledge in new situations. Working problems gives you practice at doing this.

Each chapter in this book provides many problems of different sorts. The in-chapter problems are placed for immediate reinforcement of ideas just learned, while end-of-chapter problems provide additional practice and are of several types. They begin with a short section called "Visualizing Chemistry," which helps you "see" the microscopic world of molecules and provides practice for working in three dimensions. After the visualizations are many "Additional Problems." Early problems are primarily of the drill type, providing an opportunity for you to practice your command of the fundamentals. Later problems tend to be more thought-provoking, and some are real challenges.

As you study organic chemistry, take the time to work the problems. Do the ones you can, and ask for help on the ones you can't. If you're stumped by a particular problem, check the accompanying *Study Guide and Solutions Manual* for an explanation that will help clarify the difficulty. Working problems takes effort, but the payoff in knowledge and understanding is immense.

EXERCISES

Organic **KNOWLEDGE TOOLS**

ThomsonNOW™ Sign in at **www.thomsonedu.com** to assess your knowledge of this chapter's topics by taking a pre-test. The pre-test will link you to interactive organic chemistry resources based on your score in each concept area.

Online homework for this chapter may be assigned in Organic OWL.

■ indicates problems assignable in Organic OWL.

VISUALIZING CHEMISTRY

(Problems 1.1–1.17 appear within the chapter.)

1.18 ■ Convert each of the following molecular models into a skeletal structure, and give the formula of each. Only the connections between atoms are shown; multiple bonds are not indicated (gray = C, red = O, blue = N, ivory = H).

(a)

(b)
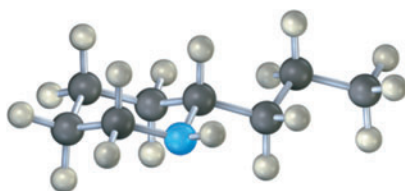
Coniine (the toxic substance
in poison hemlock)
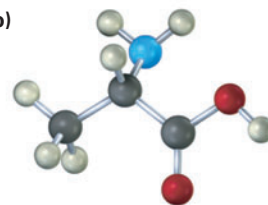
Alanine (an amino acid)

1.19 ■ The following model is a representation of citric acid, the key substance in the so-called citric acid cycle by which food molecules are metabolized in the body. Only the connections between atoms are shown; multiple bonds are not indicated. Complete the structure by indicating the positions of multiple bonds and lone-pair electrons (gray = C, red = O, ivory = H).
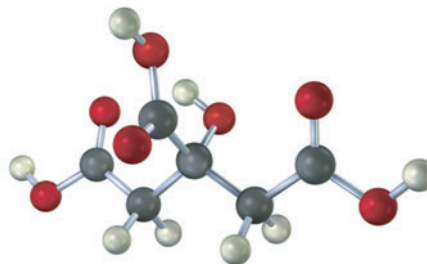
1.20 ■ The following model is a representation of acetaminophen, a pain reliever sold in drugstores as Tylenol. Identify the hybridization of each carbon atom in acetaminophen, and tell which atoms have lone pairs of electrons (gray = C, red = O, blue = N, ivory = H).
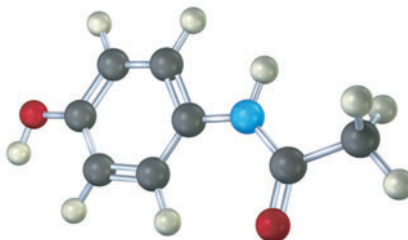
1.21 The following model is a representation of aspartame, $C_{14}H_{18}N_2O_5$, known commercially as NutraSweet. Only the connections between atoms are shown; multiple bonds are not indicated. Complete the structure by indicating the positions of multiple bonds (gray = C, red = O, blue = N, ivory = H).
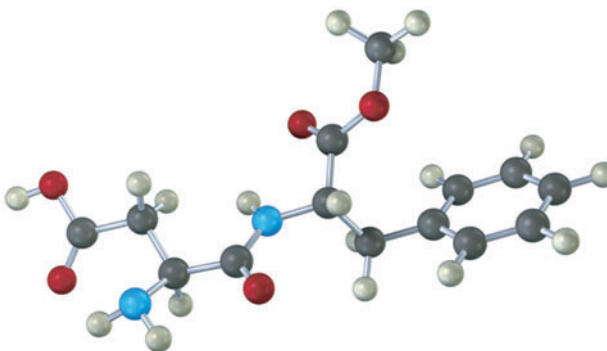
ADDITIONAL PROBLEMS

1.22 ■ How many valence electrons does each of the following dietary trace elements have?
  (a) Zinc   (b) Iodine   (c) Silicon   (d) Iron

1.23 ■ Give the ground-state electron configuration for each of the following elements:
  (a) Potassium   (b) Arsenic   (c) Aluminum   (d) Germanium

1.24 ■ What are likely formulas for the following molecules?
  (a) NH$_?$OH   (b) AlCl$_?$ (c) CF$_2$Cl$_?$ (d) CH$_?$O

1.25 Draw an electron-dot structure for acetonitrile, C_2H_3N, which contains a carbon–nitrogen triple bond. How many electrons does the nitrogen atom have in its outer shell? How many are bonding, and how many are non-bonding?

1.26 What is the hybridization of each carbon atom in acetonitrile (Problem 1.25)?

1.27 ■ Draw a line-bond structure for vinyl chloride, C_2H_3Cl, the starting material from which PVC [poly(vinyl chloride)] plastic is made.

■ Assignable in OWL

1.28 ■ Fill in any nonbonding valence electrons that are missing from the following structures:

(a)
H₃C–S–S–CH₃

Dimethyl disulfide

(b)

H₃C–C(=O)–NH₂

Acetamide

(c)

H₃C–C(=O)–O⁻
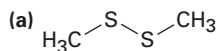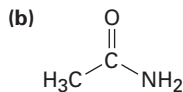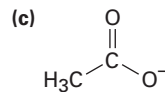
Acetate ion

1.29 Convert the following line-bond structures into molecular formulas:

(a)

Aspirin
(acetylsalicylic acid)

(b)

Vitamin C
(ascorbic acid)

(c)

Nicotine

(d)
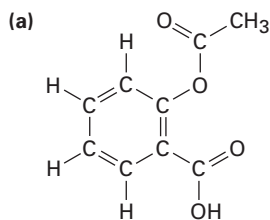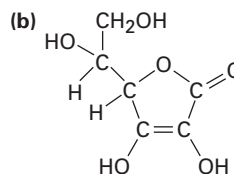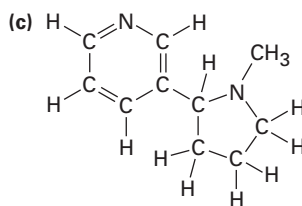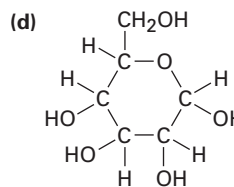
Glucose

1.30 Convert the following molecular formulas into line-bond structures that are consistent with valence rules:
(a) C_3H_8
(b) CH_5N
(c) C_2H_6O (2 possibilities)
(d) C_3H_7Br (2 possibilities)
(e) C_2H_4O (3 possibilities)
(f) C_3H_9N (4 possibilities)
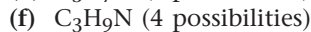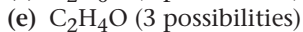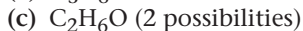
1.31 ■ What kind of hybridization do you expect for each carbon atom in the following molecules?

(a) Propane, $CH_3CH_2CH_3$

(b) 2-Methylpropene,
CH_3
$CH_3C=CH_2$

(c) 1-Butene-3-yne, $H_2C=CH–C≡CH$

(d) Acetic acid,
O
‖
CH_3COH

■ Assignable in OWL
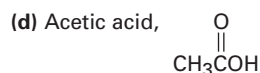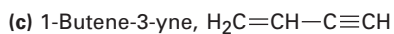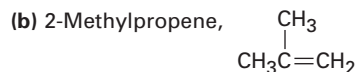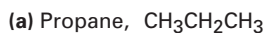
1.32 What is the shape of benzene, and what hybridization do you expect for each carbon?

Benzene
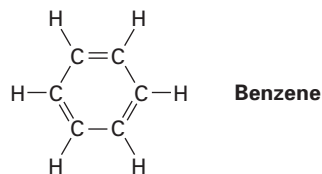
1.33 ■ What bond angles do you expect for each of the following, and what kind of hybridization do you expect for the central atom in each?

(a)

H_2N-CH_2-C-OH
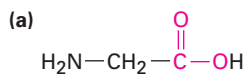
Glycine
(an amino acid)

(b)

Pyridine

(c)

$CH_3-CH-C-OH$
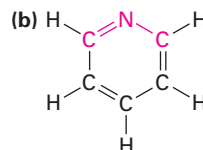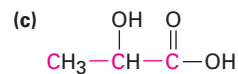
Lactic acid
(in sour milk)

1.34 ■ Convert the following structures into skeletal drawings:

(a)

Indole

(b)

1,3-Pentadiene

(c)

1,2-Dichlorocyclopentane

(d)
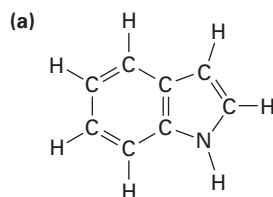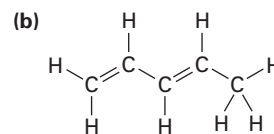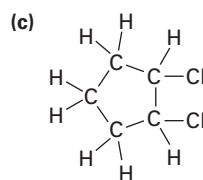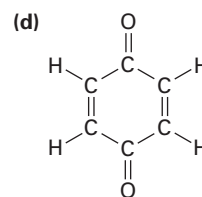
Benzoquinone

1.35 ■ Tell the number of hydrogens bonded to each carbon atom in the following substances, and give the molecular formula of each:

(a)

(b)

(c)

■ Assignable in OWL
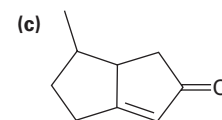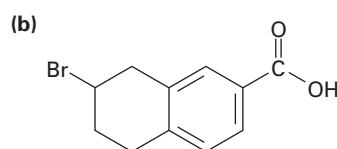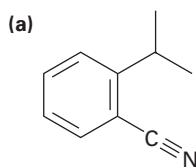
1.36 Propose structures for molecules that meet the following descriptions:
    (a) Contains two sp^2-hybridized carbons and two sp^3-hybridized carbons
    (b) Contains only four carbons, all of which are sp^2-hybridized
    (c) Contains two sp-hybridized carbons and two sp^2-hybridized carbons

1.37 ■ Why can't molecules with the following formulas exist?
    (a) CH_5 (b) C_2H_6N (c) $C_3H_5Br_2$

1.38 Draw a three-dimensional representation of the oxygen-bearing carbon atom in ethanol, CH_3CH_2OH, using the standard convention of solid, wedged, and dashed lines.

1.39 Oxaloacetic acid, an important intermediate in food metabolism, has the formula $C_4H_4O_5$ and contains three C=O bonds and two O—H bonds. Propose two possible structures.

1.40 ■ Draw structures for the following molecules, showing lone pairs:
    (a) Acrylonitrile, C_3H_3N, which contains a carbon–carbon double bond and a carbon–nitrogen triple bond
    (b) Ethyl methyl ether, C_3H_8O, which contains an oxygen atom bonded to two carbons
    (c) Butane, C_4H_{10}, which contains a chain of four carbon atoms
    (d) Cyclohexene, C_6H_{10}, which contains a ring of six carbon atoms and one carbon–carbon double bond

1.41 Potassium methoxide, $KOCH_3$, contains both covalent and ionic bonds. Which do you think is which?

1.42 What kind of hybridization do you expect for each carbon atom in the following molecules?
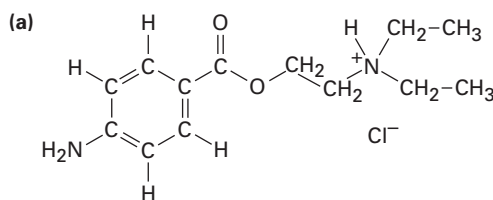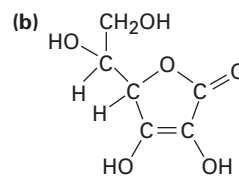
Procaine   **Vitamin C (ascorbic acid)**

1.43 Pyridoxal phosphate, a close relative of vitamin B_6, is involved in a large number of metabolic reactions. Tell the hybridization, and predict the bond angles for each nonterminal atom.


Pyridoxal phosphate
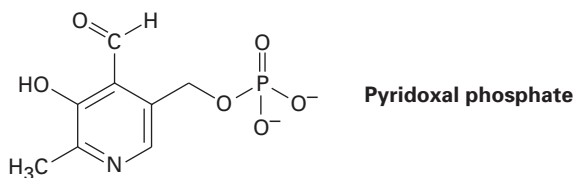
1.44 Why do you suppose no one has ever been able to make cyclopentyne as a stable molecule?


**Cyclopentyne**

■ Assignable in OWL

1.45 What is wrong with the following sentence? "The π bonding molecular orbital in ethylene results from sideways overlap of two p atomic orbitals."

1.46 Allene, $H_2C{=}C{=}CH_2$, is somewhat unusual in that it has two adjacent double bonds. Draw a picture showing the orbitals involved in the σ and π bonds of allene. Is the central carbon atom sp^2- or sp-hybridized? What about the hybridization of the terminal carbons? What shape do you predict for allene?

1.47 Allene (see Problem 1.46) is related structurally to carbon dioxide, CO_2. Draw a picture showing the orbitals involved in the σ and π bonds of CO_2, and identify the likely hybridization of carbon.

1.48 Complete the electron-dot structure of caffeine, showing all lone-pair electrons, and identify the hybridization of the indicated atoms.

Caffeine
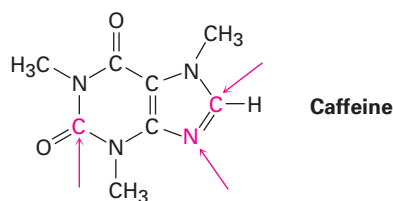
1.49 Almost all stable organic species have tetravalent carbon atoms, but species with trivalent carbon atoms also exist. *Carbocations* are one such class of compounds.
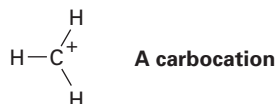
A carbocation

(a) How many valence electrons does the positively charged carbon atom have?
(b) What hybridization do you expect this carbon atom to have?
(c) What geometry is the carbocation likely to have?

1.50 A *carbanion* is a species that contains a negatively charged, trivalent carbon.
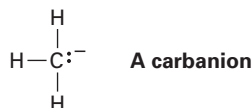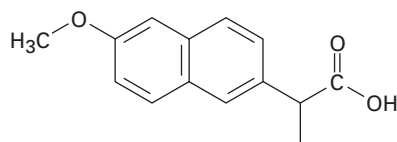

A carbanion

(a) What is the electronic relationship between a carbanion and a trivalent nitrogen compound such as NH_3?
(b) How many valence electrons does the negatively charged carbon atom have?
(c) What hybridization do you expect this carbon atom to have?
(d) What geometry is the carbanion likely to have?

1.51 Divalent carbon species called *carbenes* are capable of fleeting existence. For example, methylene, $:CH_2$, is the simplest carbene. The two unshared electrons in methylene can be either spin-paired in a single orbital or unpaired in different orbitals. Predict the type of hybridization you expect carbon to adopt in singlet (spin-paired) methylene and triplet (spin-unpaired) methylene. Draw a picture of each, and identify the valence orbitals on carbon.

1.52 There are two different substances with the formula C_4H_{10}. Draw both, and tell how they differ.
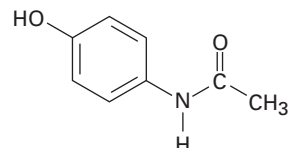

■ Assignable in OWL

1.53 There are two different substances with the formula C_3H_6. Draw both, and tell how they differ.

1.54 There are two different substances with the formula C_2H_6O. Draw both, and tell how they differ.

1.55 There are three different substances that contain a carbon–carbon double bond and have the formula C_4H_8. Draw them, and tell how they differ.

1.56 Among the most common over-the-counter drugs you might find in a medicine cabinet are mild pain relievers such ibuprofen (Advil, Motrin), naproxen (Aleve), and acetaminophen (Tylenol).
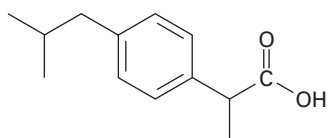
Ibuprofen   **Naproxen**   **Acetaminophen**

(a) How many sp^3-hybridized carbons does each molecule have?
(b) How many sp^2-hybridized carbons does each molecule have?
(c) Can you spot any similarities in their structures?

2

Polar Covalent Bonds;
Acids and Bases

We saw in the last chapter how covalent bonds between atoms are described, and we looked at the valence bond model, which uses hybrid orbitals to account for the observed shapes of organic molecules. Before going on to a systematic study of organic chemistry, however, we still need to review a few fundamental topics. In particular, we need to look more closely at how electrons are distributed in covalent bonds and at some of the consequences that arise when the electrons in a bond are not shared equally between atoms.

WHY THIS CHAPTER?

Understanding organic chemistry means knowing not just what happens but also why and how it happens. In this chapter, we'll look some of the basic ways chemists use to describe and account for chemical reactivity, thereby providing a foundation for understanding the specific reactions discussed in subsequent chapters.

2.1 | Polar Covalent Bonds: Electronegativity

Up to this point, we've treated chemical bonds as either ionic or covalent. The bond in sodium chloride, for instance, is ionic. Sodium transfers an electron to chlorine to give Na^+ and Cl^- ions, which are held together in the solid by electrostatic attractions. The C$-$C bond in ethane, however, is covalent. The two bonding electrons are shared equally by the two equivalent carbon atoms, resulting in a symmetrical electron distribution in the bond. Most bonds, however, are neither fully ionic nor fully covalent but are somewhere between the two extremes. Such bonds are called **polar covalent bonds**, meaning that the bonding electrons are attracted more strongly by one atom than the other so that the electron distribution between atoms in not symmetrical (Figure 2.1).

Sean Duggan

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Figure 2.1 The continuum in bonding from covalent to ionic is a result of an unequal distribution of bonding electrons between atoms. The symbol δ (lowercase Greek delta) means *partial* charge, either partial positive ($\delta+$) for the electron-poor atom or partial negative ($\delta-$) for the electron-rich atom.
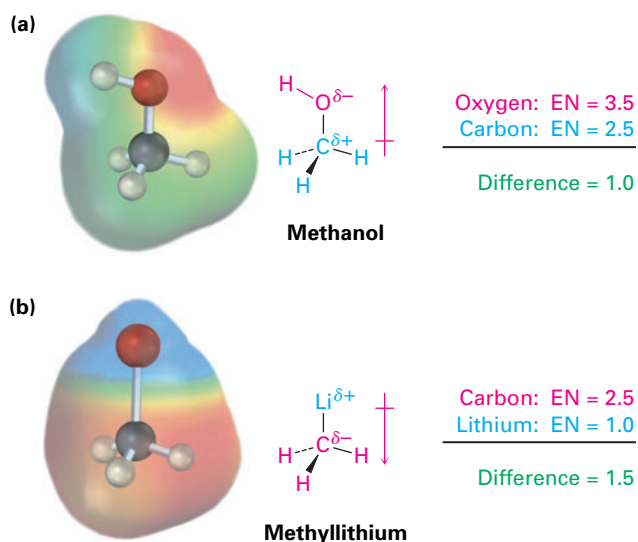

Ionic character

$\delta+$ $\delta-$

X : X   X : Y   X⁺ :Y⁻

Covalent bond   **Polar covalent bond**   **Ionic bond**
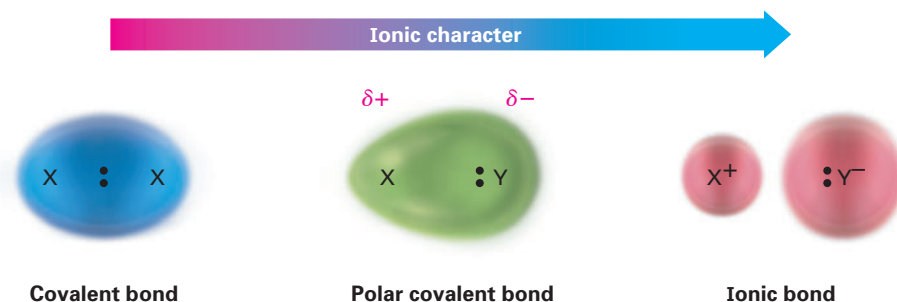
Bond polarity is due to differences in **electronegativity (EN)**, the intrinsic ability of an atom to attract the shared electrons in a covalent bond. As shown in Figure 2.2, electronegativities are based on an arbitrary scale, with fluorine being the most electronegative (EN = 4.0) and cesium, the least (EN = 0.7). Metals on the left side of the periodic table attract electrons weakly and have lower electronegativities, whereas the halogens and other reactive nonmetals on the right side of the periodic table attract electrons strongly and have higher electronegativities. Carbon, the most important element in organic compounds, has an electronegativity value of 2.5.

Figure 2.2 Electronegativity values and trends. Electronegativity generally increases from left to right across the periodic table and decreases from top to bottom. The values are on an arbitrary scale, with F = 4.0 and Cs = 0.7. Elements in orange are the most electronegative, those in yellow are medium, and those in green are the least electronegative.

As a loose guide, bonds between atoms whose electronegativities differ by less than 0.5 are nonpolar covalent, bonds between atoms whose electronegativities differ by 0.5 to 2 are polar covalent, and bonds between atoms whose electronegativities differ by more than 2 are largely ionic. Carbon–hydrogen bonds, for example, are relatively nonpolar because carbon (EN = 2.5) and hydrogen (EN = 2.1) have similar electronegativities. Bonds between carbon and *more* electronegative elements such as oxygen (EN = 3.5) and nitrogen (EN = 3.0), by contrast, are polarized so that the bonding electrons are drawn away from carbon toward the electronegative atom. This leaves carbon with a partial positive charge, denoted by $\delta+$, and the electronegative atom with a partial negative charge, $\delta-$. An example is the C–O bond in methanol, CH_3OH (Figure 2.3a). Bonds between carbon and *less* electronegative elements are polarized so that carbon bears a partial negative charge and the other atom bears a partial positive charge. An example is methyllithium, CH_3Li (Figure 2.3b).

Figure 2.3 **(a)** Methanol, CH_3OH, has a polar covalent C—O bond, and **(b)** methyllithium, CH_3Li, has a polar covalent C—Li bond. The computer-generated representations, called electrostatic potential maps, use color to show calculated charge distributions, ranging from red (electron-rich; $\delta-$) to blue (electron-poor; $\delta+$).

(a)

Oxygen: EN = 3.5
Carbon: EN = 2.5

Difference = 1.0

Methanol

(b)

Carbon: EN = 2.5
Lithium: EN = 1.0

Difference = 1.5

Methyllithium

Note in the representations of methanol and methyllithium in Figure 2.3 that a crossed arrow $+\!\!\longrightarrow$ is used to indicate the direction of bond polarity. By convention, *electrons are displaced in the direction of the arrow.* The tail of the arrow (which looks like a plus sign) is electron-poor ($\delta+$), and the head of the arrow is electron-rich ($\delta-$).

Note also in Figure 2.3 that calculated charge distributions in molecules can be displayed visually using so-called electrostatic potential maps, which use color to indicate electron-rich (red; $\delta-$) and electron-poor (blue; $\delta+$) regions. In methanol, oxygen carries a partial negative charge and is colored red, while the carbon and hydrogen atoms carry partial positive charges and are colored blue-green. In methyllithium, lithium carries a partial positive charge (blue), while carbon and the hydrogen atoms carry partial negative charges (red). Electro-static potential maps are useful because they show at a glance the electron-rich and electron-poor atoms in molecules. We'll make frequent use of these maps throughout the text and will see numerous examples of how electronic structure correlates with chemical reactivity.

When speaking of an atom's ability to polarize a bond, we often use the term *inductive effect.* An **inductive effect** is simply the shifting of electrons in a σ bond in response to the electronegativity of nearby atoms. Metals, such as lithium and magnesium, inductively donate electrons, whereas reactive non-metals, such as oxygen and nitrogen, inductively withdraw electrons. Inductive effects play a major role in understanding chemical reactivity, and we'll use them many times throughout this text to explain a variety of chemical phenomena.

Problem 2.1 Which element in each of the following pairs is more electronegative?
(a) Li or H   **(b)** B or Br   **(c)** Cl or I   **(d)** C or H

Problem 2.2 Use the $\delta+/\delta-$ convention to show the direction of expected polarity for each of the bonds indicated.
(a) H_3C—Cl   **(b)** H_3C—NH_2 **(c)** H_2N—H
(d) H_3C—SH   **(e)** H_3C—MgBr   **(f)** H_3C—F

Problem 2.3 | Use the electronegativity values shown in Figure 2.2 to rank the following bonds from least polar to most polar: H_3C-Li, H_3C-K, H_3C-F, $H_3C-MgBr$, H_3C-OH.

Problem 2.4 | Look at the following electrostatic potential map of chloromethane, and tell the direction of polarization of the C−Cl bond:

Chloromethane
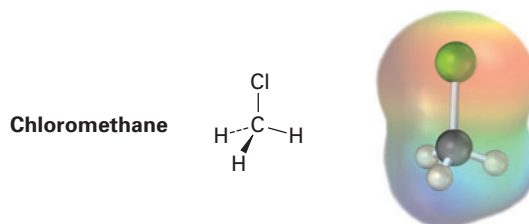
2.2 | Polar Covalent Bonds: Dipole Moments

Just as individual bonds are often polar, molecules as a whole are often polar also. Molecular polarity results from the vector summation of all individual bond polarities and lone-pair contributions in the molecule. As a practical matter, strongly polar substances are often soluble in polar solvents like water, whereas nonpolar substances are insoluble in water.

Net molecular polarity is measured by a quantity called the *dipole moment* and can be thought of in the following way: assume that there is a center of mass of all positive charges (nuclei) in a molecule and a center of mass of all negative charges (electrons). If these two centers don't coincide, then the molecule has a net polarity.

The **dipole moment**, μ (Greek mu), is defined as the magnitude of the charge Q at either end of the molecular dipole times the distance r between the charges, $\mu = Q \times r$. Dipole moments are expressed in *debyes* (D), where 1 D = 3.336×10^{-30} coulomb meter (C · m) in SI units. For example, the unit charge on an electron is 1.60×10^{-19} C. Thus, if one positive charge and one negative charge were separated by 100 pm (a bit less than the length of a typical covalent bond), the dipole moment would be 1.60×10^{-29} C · m, or 4.80 D.

$$\mu = Q \times r$$

$$\mu = (1.60 \times 10^{-19} \text{ C})(100 \times 10^{-12} \text{ m})\left(\frac{1 \text{ D}}{3.336 \times 10^{-30} \text{ C} \cdot \text{m}}\right) = 4.80 \text{ D}$$

It's relatively easy to measure dipole moments in the laboratory, and values for some common substances are given in Table 2.1. Of the compounds shown in the table, sodium chloride has the largest dipole moment (9.00 D) because it is ionic. Even small molecules like water ($\mu = 1.85$ D), methanol (CH_3OH; $\mu = 1.70$ D), and ammonia ($\mu = 1.47$ D) have substantial dipole moments, however, both because they contain strongly electronegative atoms (oxygen and nitrogen) and because all three molecules have lone-pair electrons. The lone-pair electrons on oxygen and nitrogen atom stick out into space away from

the positively charged nuclei, giving rise to a considerable charge separation and making a large contribution to the dipole moment.
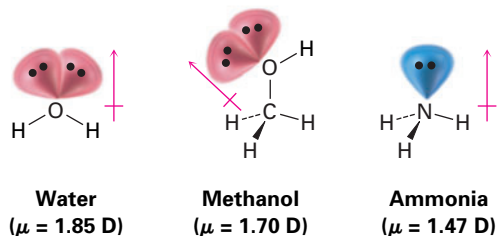

Water	Methanol	Ammonia
(μ = 1.85 D)	(μ = 1.70 D)	(μ = 1.47 D)

Table 2.1 Dipole Moments of Some Compounds

Compound	Dipole moment (D)	Compound	Dipole moment (D)
NaCl	9.00	NH_3	1.47
CH_2O	2.33	CH_3NH_2	1.31
CH_3Cl	1.87	CO_2	0
H_2O	1.85	CH_4	0
CH_3OH	1.70	CH_3CH_3	0
CH_3CO_2H	1.70		0
CH_3SH	1.52	Benzene	

In contrast with water, methanol, ammonia, and other substances in Table 2.1, carbon dioxide, methane, ethane, and benzene have zero dipole moments. Because of the symmetrical structures of these molecules, the individual bond polarities and lone-pair contributions exactly cancel.

Carbon dioxide	Methane	Ethane	Benzene
(μ = 0)	(μ = 0)	(μ = 0)	(μ = 0)
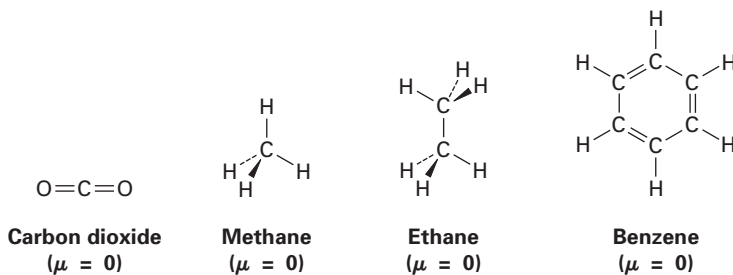
WORKED EXAMPLE 2.1

Predicting the Direction of a Dipole Moment

Make a three-dimensional drawing of methylamine, CH_3NH_2, a substance responsible for the odor of rotting fish, and show the direction of its dipole moment (μ = 1.31).

Strategy   Look for any lone-pair electrons, and identify any atom with an electronegativity substantially different from that of carbon. (Usually, this means O, N, F, Cl, or Br.) Electron density will be displaced in the general direction of the electronegative atoms and the lone pairs.

Solution   Methylamine contains an electronegative nitrogen atom with two lone-pair electrons. The dipole moment thus points generally from $-CH_3$ toward $-NH_2$.
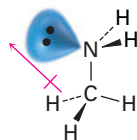
Methylamine
(μ = 1.31)

Problem 2.5   Ethylene glycol, $HOCH_2CH_2OH$, has zero dipole moment even though carbon–oxygen bonds are strongly polarized. Explain.

Problem 2.6   Make three-dimensional drawings of the following molecules, and predict whether each has a dipole moment. If you expect a dipole moment, show its direction.
(a) $H_2C=CH_2$ (b) $CHCl_3$ (c) CH_2Cl_2 (d) $H_2C=CCl_2$

2.3 | Formal Charges

Closely related to the ideas of bond polarity and dipole moment is the concept of assigning *formal charges* to specific atoms within a molecule, particularly atoms that have an apparently "abnormal" number of bonds. Look at dimethyl sulfoxide (CH_3SOCH_3), for instance, a solvent commonly used for preserving biological cell lines at low temperatures. The sulfur atom in dimethyl sulfoxide has three bonds rather than the usual two and has a formal positive charge. The oxygen atom, by contrast, has one bond rather than the usual two and has a formal negative charge. Note that an electrostatic potential map of dimethyl sulfoxide shows the oxygen as negative (red) and the sulfur as relatively positive (blue), in accord with the formal charges.

Formal negative charge on oxygen

Formal positive charge on sulfur
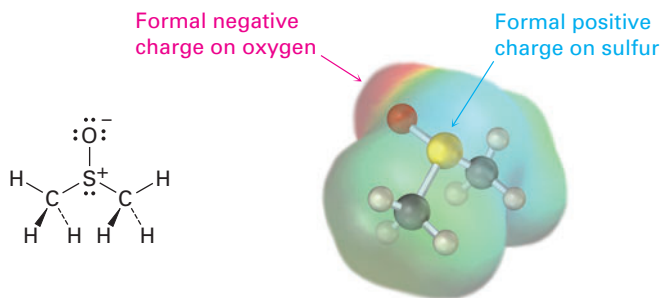
Dimethyl sulfoxide

Formal charges, as the name suggests, are a formalism and don't imply the presence of actual ionic charges in a molecule. Instead, they're a device for electron "bookkeeping" and can be thought of in the following way: a typical covalent bond is formed when each atom donates one electron. Although the bonding electrons are shared by both atoms, each atom can still be considered to "own" one electron for bookkeeping purposes. In methane, for instance, the carbon atom owns one electron in each of the four C−H bonds, for a total of four. Because a neutral, isolated carbon atom has four valence electrons, and because the carbon atom in methane still owns four, the methane carbon atom is neutral and has no formal charge.

An isolated carbon atom owns 4 valence electrons.

·C·

This carbon atom also owns $\frac{8}{2}$ = 4 valence electrons.

H
H:C:H
H
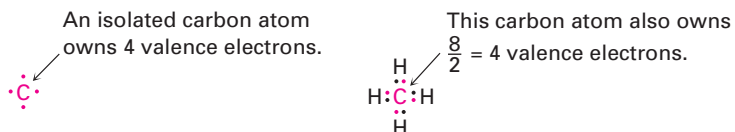
The same is true for the nitrogen atom in ammonia, which has three covalent N−H bonds and two nonbonding electrons (a lone pair). Atomic nitrogen has five valence electrons, and the ammonia nitrogen also has five—one in each of three shared N−H bonds plus two in the lone pair. Thus, the nitrogen atom in ammonia has no formal charge.

An isolated nitrogen atom owns 5 valence electrons.

·N·

This nitrogen atom also owns $\frac{6}{2}$ + 2 = 5 valence electrons.

H:N:H
H
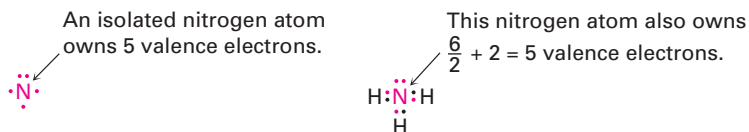
The situation is different in dimethyl sulfoxide. Atomic sulfur has six valence electrons, but the dimethyl sulfoxide sulfur owns only *five*—one in each of the two S−C single bonds, one in the S−O single bond, and two in a lone pair. Thus, the sulfur atom has formally lost an electron and therefore has a positive charge. A similar calculation for the oxygen atom shows that it has formally gained an electron and has a negative charge. Atomic oxygen has six valence electrons, but the oxygen in dimethyl sulfoxide has seven—one in the O−S bond and two in each of three lone pairs.

:Ö:⁻
H   H
  C S⁺ C
H H H H
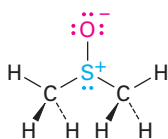
For sulfur:

Sulfur valence electrons   = 6
Sulfur bonding electrons   = 6
Sulfur nonbonding electrons = 2

Formal charge = 6 − 6/2 − 2 = +1

For oxygen:

Oxygen valence electrons   = 6
Oxygen bonding electrons   = 2
Oxygen nonbonding electrons = 6

Formal charge = 6 − 2/2 − 6 = −1

To express the calculations in a general way, the **formal charge** on an atom is equal to the number of valence electrons in a neutral, isolated atom minus the number of electrons owned by that atom in a molecule. The number of electrons in the bonded atom, in turn, is equal to half the number of bonding electrons plus the nonbonding, lone-pair electrons.

$$\textbf{Formal charge} = \left(\begin{array}{c} \text{Number of} \\ \text{valence electrons} \\ \text{in free atom} \end{array} \right) - \left(\begin{array}{c} \text{Number of} \\ \text{valence electrons} \\ \text{in bonded atom} \end{array} \right)$$

$$= \left(\begin{array}{c} \text{Number of} \\ \text{valence electrons} \\ \text{in free atom} \end{array} \right) - \left(\begin{array}{c} \text{Number of} \\ \text{bonding electrons} \\ \hline 2 \end{array} \right) - \left(\begin{array}{c} \text{Number of} \\ \text{nonbonding} \\ \text{electrons} \end{array} \right)$$

A summary of commonly encountered formal charges and the bonding situations in which they occur is given in Table 2.2. Although only a bookkeeping device, formal charges often give clues about chemical reactivity, so it's helpful to be able to identify and calculate them correctly.

Table 2.2 | A Summary of Common Formal Charges

Atom	C			N		O		S		P
Structure	—Ċ—	—C⁺—	—C̈⁻—	—N⁺—	—N̈⁻—	—Ö⁺—	—Ö⁻	—S̈⁺—	—S̈⁻	—P⁺—
Valence electrons	4	4	4	5	5	6	6	6	6	5
Number of bonds	3	3	3	4	2	3	1	3	1	4
Number of nonbonding electrons	1	0	2	0	4	2	6	2	6	0
Formal charge	0	+1	−1	+1	−1	+1	−1	+1	−1	+1

Problem 2.7 | Nitromethane has the structure indicated. Explain why it must have formal charges on N and O.
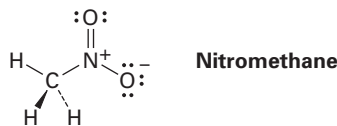
Nitromethane

Problem 2.8 | Calculate formal charges for the nonhydrogen atoms in the following molecules:

(a) Diazomethane, $H_2C{=}N{=}\ddot{N}{:}$ **(b)** Acetonitrile oxide, $H_3C{-}C{\equiv}N{-}\ddot{O}{:}$

(c) Methyl isocyanide, $H_3C{-}N{\equiv}C{:}$

Problem 2.9 | Organic phosphate groups occur commonly in biological molecules. Calculate formal charges on the four O atoms in the methyl phosphate dianion.


Methyl phosphate
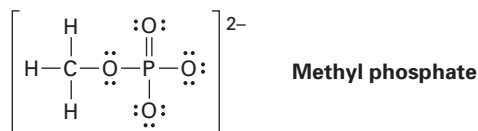
2.4 | Resonance

Most substances can be represented without difficulty by the Kekulé line-bond structures we've been using up to this point, but an interesting problem sometimes arises. Look at the acetate ion, for instance. When we draw a line-bond structure for acetate, we need to show a double bond to one oxygen and a single bond to the other. But which oxygen is which? Should we draw a double bond to the "top" oxygen and a single bond to the "bottom" oxygen or vice versa?

Double bond to this oxygen?

Acetate ion   **Or to this oxygen?**
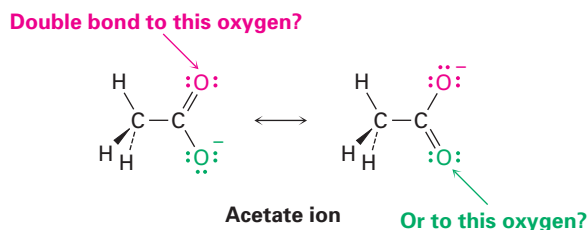
Although the two oxygen atoms in the acetate ion appear different in line-bond structures, experiments show that they are equivalent. Both carbon–oxygen bonds, for example, are 127 pm in length, midway between the length of a typical $C-O$ bond (135 pm) and a typical $C=O$ bond (120 pm). In other words, *neither* of the two structures for acetate is correct by itself. The true structure is intermediate between the two, and an electrostatic potential map shows that both oxygen atoms share the negative charge and have equal electron densities (red).

Acetate ion—two resonance forms
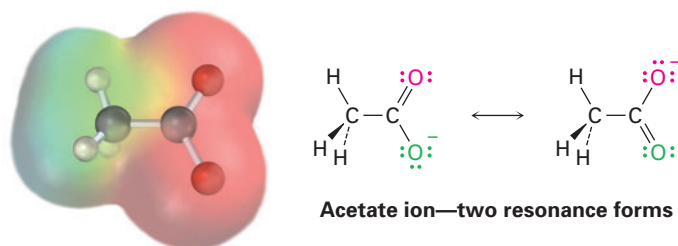
The two individual line-bond structures for acetate are called **resonance forms**, and their special resonance relationship is indicated by the double-headed arrow between them. *The only difference between resonance forms is the placement of the π and nonbonding valence electrons.* The atoms themselves occupy exactly the same place in both resonance forms, the connections between atoms are the same, and the three-dimensional shapes of the resonance forms are the same.

A good way to think about resonance forms is to realize that a substance like the acetate ion is no different from any other. Acetate doesn't jump back and forth between two resonance forms, spending part of the time looking like one and part of the time looking like the other. Rather, acetate has a single

unchanging structure that is a **resonance hybrid** of the two individual forms and has characteristics of both. The only "problem" with acetate is that we can't draw it accurately using a familiar line-bond structure. Line-bond structures just don't work well for resonance hybrids. The difficulty, however, lies with the *representation* of acetate on paper, not with acetate itself.

Resonance is an extremely useful concept that we'll return to on numerous occasions throughout the rest of this book. We'll see in Chapter 15, for instance, that the six carbon–carbon bonds in so-called *aromatic* compounds, such as benzene, are equivalent and that benzene is best represented as a hybrid of two resonance forms. Although an individual resonance form seems to imply that benzene has alternating single and double bonds, neither form is correct by itself. The true benzene structure is a hybrid of the two individual forms, and all six carbon–carbon bonds are equivalent. This symmetrical distribution of electrons around the molecule is evident in an electrostatic potential map.

Benzene (two resonance forms)
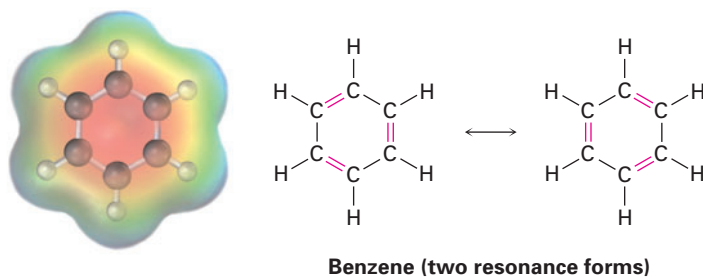
2.5 | Rules for Resonance Forms

When first dealing with resonance forms, it's useful to have a set of guidelines that describe how to draw and interpret them.

Rule 1   **Individual resonance forms are imaginary, not real.** The real structure is a composite, or resonance hybrid, of the different forms. Species such as the acetate ion and benzene are no different from any other. They have single, unchanging structures, and they do not switch back and forth between resonance forms. The only difference between these and other substances is in the way they must be represented on paper.

Rule 2   **Resonance forms differ only in the placement of their π or nonbonding electrons.** Neither the position nor the hybridization of any atom changes from one resonance form to another. In the acetate ion, for example, the carbon atom is sp^2-hybridized and the oxygen atoms remain in exactly the same place in both resonance forms. Only the positions of the π electrons in the C=O bond and the lone-pair electrons on oxygen differ from one form to another. This movement of electrons from one resonance structure to another can be indicated by using curved arrows. *A curved arrow always indicates the movement of electrons, not the movement of atoms.* An arrow shows that a pair of electrons moves *from* the atom or bond at the tail of the arrow *to* the atom or bond at the head of the arrow.
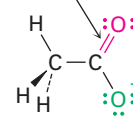
The red curved arrow indicates that a lone pair of electrons moves from the top oxygen atom to become part of a C=O bond.
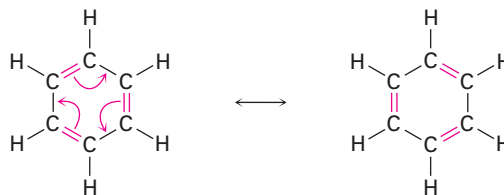
The new resonance form has a double bond here…
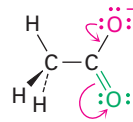
Simultaneously, two electrons from the C=O bond move onto the bottom oxygen atom to become a lone pair.

and has a lone pair of electrons here.

The situation with benzene is similar to that with acetate. The π electrons in the double bonds move, as shown with curved arrows, but the carbon and hydrogen atoms remain in place.


Rule 3 **Different resonance forms of a substance don't have to be equivalent.** For example, we'll see in Chapter 22 that a compound such as acetone, which contains a C=O bond, can be converted into its anion by reaction with a strong base. The resultant anion has two resonance forms. One form contains a carbon–*oxygen* double bond and has a negative charge on *carbon;* the other contains a carbon–*carbon* double bond and has a negative charge on *oxygen.* Even though the two resonance forms aren't equivalent, both contribute to the overall resonance hybrid.

This resonance form has the negative charge on carbon.

This resonance form has the negative charge on oxygen.

Acetone

Acetone anion
(two resonance forms)
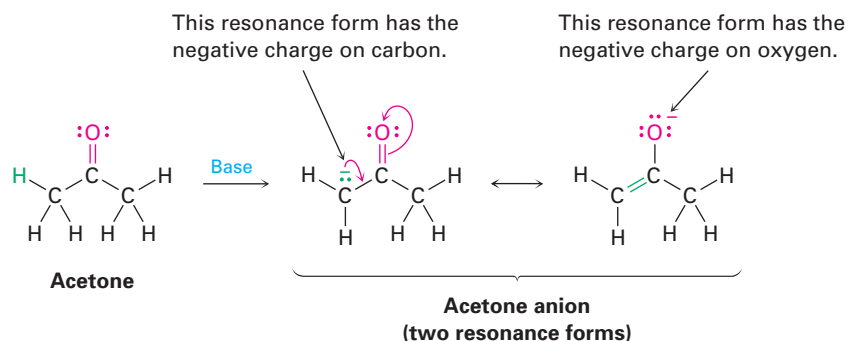
When two resonance forms are nonequivalent, the actual structure of the resonance hybrid is closer to the more stable form than to the less stable form. Thus, we might expect the true structure of the acetone anion to be closer to the resonance form that places the negative charge on an electronegative oxygen atom than to the form that places the charge on a carbon atom.

Rule 4   **Resonance forms obey normal rules of valency.** A resonance form is like any other structure: the octet rule still applies to main-group atoms. For example, one of the following structures for the acetate ion is not a valid resonance form because the carbon atom has five bonds and ten valence electrons:

Acetate ion   **NOT a valid resonance form**
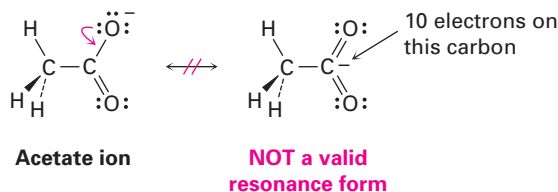
Rule 5   **The resonance hybrid is more stable than any individual resonance form.** In other words, resonance leads to stability. Generally speaking, the larger the number of resonance forms, the more stable a substance is because electrons are spread out over a larger part of the molecule and are closer to more nuclei. We'll see in Chapter 15, for instance, that a benzene ring is more stable because of resonance than might otherwise be expected.

2.6 | Drawing Resonance Forms

Look back at the resonance forms of the acetate ion and the acetone anion shown in the previous section. The pattern seen there is a common one that leads to a useful technique for drawing resonance forms. In general, *any three-atom grouping with a p orbital on each atom has two resonance forms.*
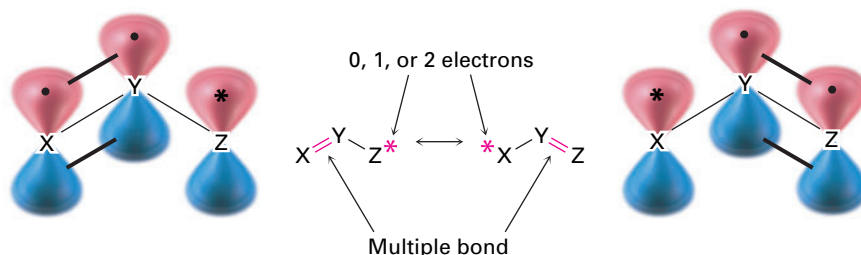
The atoms X, Y, and Z in the general structure might be C, N, O, P, or S, and the asterisk (*) might mean that the *p* orbital on atom Z is vacant, that it contains a single electron, or that it contains a lone pair of electrons. The two resonance forms differ simply by an exchange in position of the multiple bond and the asterisk from one end to the other.

By learning to recognize such three-atom groupings within larger structures, resonance forms can be systematically generated. Look, for instance, at the anion produced when H^+ is removed from 2,4-pentanedione by reaction with a base. How many resonance structures does the resultant anion have?
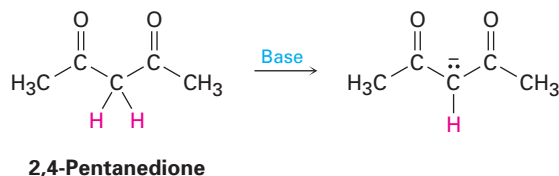
2,4-Pentanedione

The 2,4-pentanedione anion has a lone pair of electrons and a formal negative charge on the central carbon atom, next to a C=O bond on the left. The O=C−C:⁻ grouping is a typical one for which two resonance structures can be drawn.
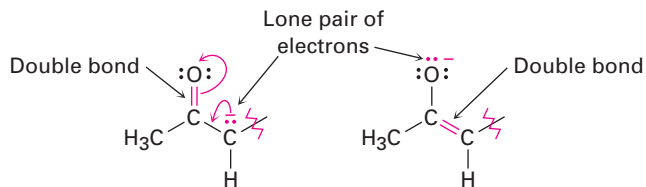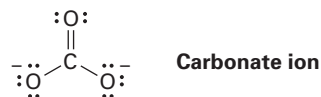

Just as there is a C=O bond to the left of the lone pair, there is a second C=O bond to the right. Thus, we can draw a total of three resonance structures for the 2,4-pentanedione anion.
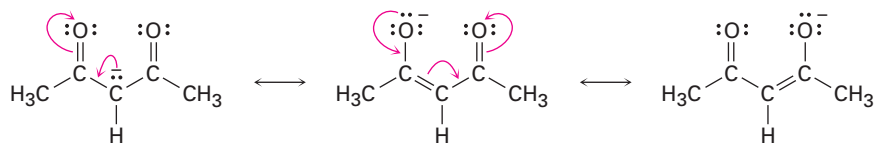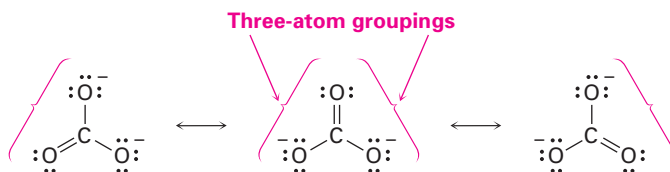

WORKED EXAMPLE 2.2   *Drawing Resonance Forms for an Anion*

Draw three resonance forms for the carbonate ion, $CO_3{}^{2-}$.

Carbonate ion

Strategy   Look for one or more three-atom groupings that contain a multiple bond next to an atom with a p orbital. Then exchange the positions of the multiple bond and the electrons in the p orbital. In the carbonate ion, each of the singly bonded oxygen atoms with its lone pairs and negative charge is next to the C=O bond, giving the grouping O=C−O:⁻.

Solution   Exchanging the position of the double bond and an electron lone pair in each grouping generates three resonance structures.

Three-atom groupings

WORKED EXAMPLE 2.3   *Drawing Resonance Forms for a Radical*

Draw three resonance forms for the pentadienyl radical. A *radical* is a substance that contains a single, unpaired electron in one of its orbitals, denoted by a dot (·).

Unpaired electron

Pentadienyl radical
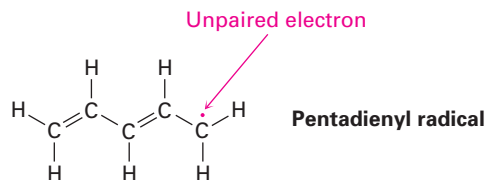
Strategy   Find the three-atom groupings that contain a multiple bond next to a *p* orbital.

Solution   The unpaired electron is on a carbon atom next to a C=C bond, giving a typical three-atom grouping that has two resonance forms.

Three-atom grouping
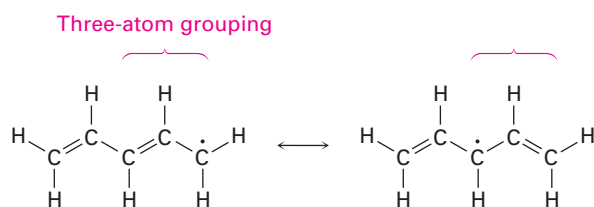
In the second resonance form, the unpaired electron is next to another double bond, giving another three-atom grouping and leading to another resonance form.

Three-atom grouping
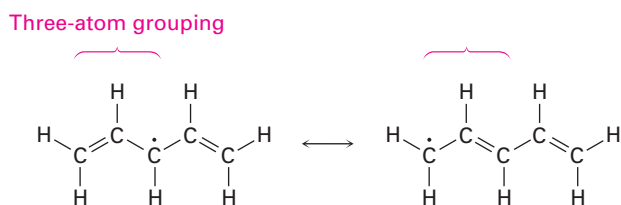
Thus, the three resonance forms for the pentadienyl radical are:
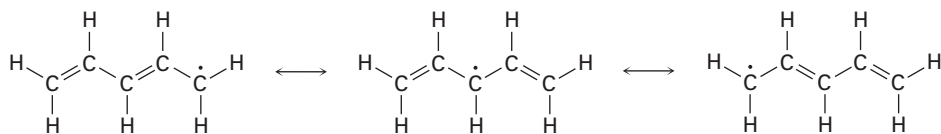
Problem 2.10   Draw the indicated number of resonance forms for each of the following species:
(a) The methyl phosphate anion, $CH_3OPO_3^{2-}$ (3)
(b) The nitrate anion, NO_3^- (3)
(c) The allyl cation, $H_2C=CH-CH_2^+$ (2)
(d) The benzoate anion (4)
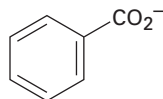
| # Acids and Bases: The Brønsted–Lowry Definition

A further important concept related to electronegativity and polarity is that of *acidity* and *basicity.* We'll see, in fact, that much of the chemistry of organic molecules can be explained by their acid–base behavior. You may recall from a course in general chemistry that there are two frequently used definitions of acidity: the *Brønsted–Lowry definition* and the *Lewis definition.* We'll look at the Brønsted–Lowry definition in this and the next three sections and then discuss the Lewis definition in Section 2.11.

A **Brønsted–Lowry acid** is a substance that donates a proton (H^+), and a **Brønsted–Lowry base** is a substance that accepts a proton. (The name *proton* is often used as a synonym for hydrogen ion, H^+, because loss of the valence electron from a neutral hydrogen atom leaves only the hydrogen nucleus— a proton.) When gaseous hydrogen chloride dissolves in water, for example, a polar HCl molecule acts as an acid and donates a proton, while a water molecule acts as a base and accepts the proton, yielding hydronium ion (H_3O^+) and chloride ion (Cl^-).

| H—Cl	+	H—O—H	⟶	H—O⁺—H (H)	+	Cl⁻
Acid		**Base**		**Conjugate acid**		**Conjugate base**
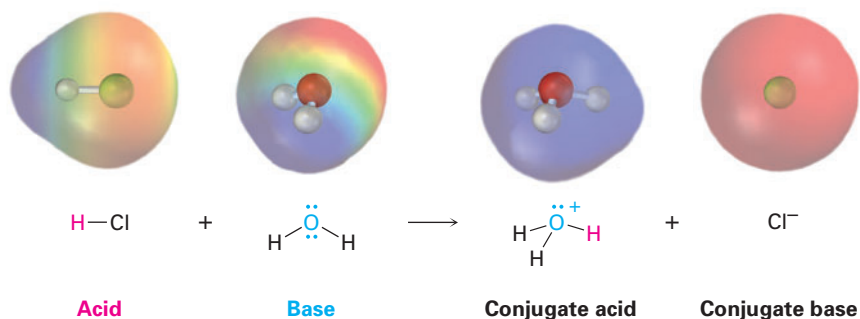
Hydronium ion, the product that results when the base H_2O gains a proton, is called the **conjugate acid** of the base, and chloride ion, the product that results when the acid HCl loses a proton, is called the **conjugate base** of the acid. Other common mineral acids such as H_2SO_4 and HNO_3 behave similarly, as do organic acids such as acetic acid, CH_3CO_2H.

In a general sense,

H—A	+	:B	⇌	:A⁻	+	H—B⁺
Acid		**Base**		**Conjugate base**		**Conjugate acid**

For example:

|						
Acid		**Base**		**Conjugate base**		**Conjugate acid**
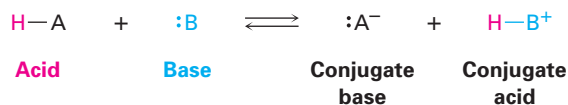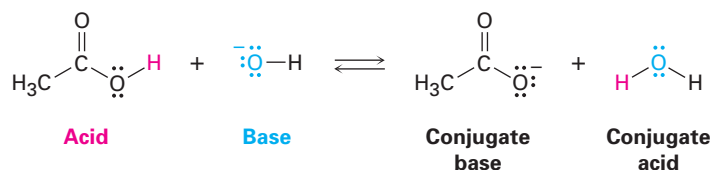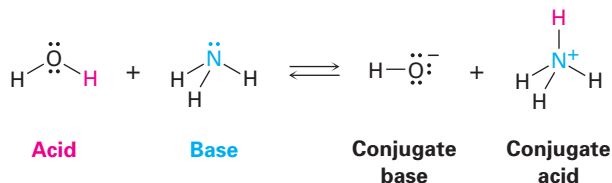
Notice that water can act *either* as an acid or as a base, depending on the circumstances. In its reaction with HCl, water is a base that accepts a proton to give the hydronium ion, H_3O^+. In its reaction with amide ion, $^-NH_2$, however, water is an acid that donates a proton to give ammonia, NH_3, and hydroxide ion, HO^-.

Problem 2.11 | Nitric acid (HNO_3) reacts with ammonia (NH_3) to yield ammonium nitrate. Write the reaction, and identify the acid, the base, the conjugate acid product, and the conjugate base product.

2.8 | Acid and Base Strength

Acids differ in their ability to donate H^+. Stronger acids such as HCl react almost completely with water, whereas weaker acids such as acetic acid (CH_3CO_2H) react only slightly. The exact strength of a given acid, HA, in water solution is described using the equilibrium constant K_{eq} for the acid-dissociation equilibrium. Remember from general chemistry that brackets [ ] around a substance mean that the concentration of the enclosed species is given in moles per liter, M.

$$HA + H_2O \rightleftharpoons A^- + H_3O^+$$

$$K_{eq} = \frac{[H_3O^+][A^-]}{[HA][H_2O]}$$
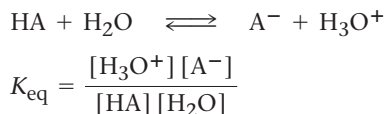
In the dilute aqueous solution normally used for measuring acidity, the concentration of water, $[H_2O]$, remains nearly constant at approximately 55.4 M at 25 °C. We can therefore rewrite the equilibrium expression using a new quantity called the **acidity constant**, K_a. The acidity constant for any acid HA is simply the equilibrium constant for the acid dissociation multiplied by the molar concentration of pure water.

$$HA + H_2O \rightleftharpoons A^- + H_3O^+$$

$$K_a = K_{eq}[H_2O] = \frac{[H_3O^+][A^-]}{[HA]}$$
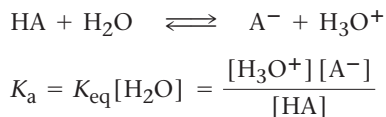
Stronger acids have their equilibria toward the right and thus have larger acidity constants, whereas weaker acids have their equilibria toward the left and have smaller acidity constants. The range of K_a values for different acids is enormous, running from about 10^{15} for the strongest acids to about 10^{-60} for the

weakest. The common inorganic acids such as H_2SO_4, HNO_3, and HCl have K_a's in the range of 10^2 to 10^9, while organic acids generally have K_a's in the range of 10^{-5} to 10^{-15}. As you gain more experience, you'll develop a rough feeling for which acids are "strong" and which are "weak" (always remembering that the terms are relative).

For convenience, acid strengths are normally expressed using pK_a values rather than K_a values, where the **pK_a** is the negative common logarithm of the K_a.

$$pK_a = -\log K_a$$

A *stronger* acid (larger K_a) has a *smaller* pK_a, and a *weaker* acid (smaller K_a) has a *larger* pK_a. Table 2.3 lists the pK_a's of some common acids in order of their strength. A more comprehensive table is given in Appendix B.

Table 2.3 | **Relative Strengths of Some Common Acids and Their Conjugate Bases**

	Acid	Name	pK_a	Conjugate base	Name	
Weaker acid	CH_3CH_2OH	Ethanol	16.00	$CH_3CH_2O^-$	Ethoxide ion	**Stronger base**
	H_2O	Water	15.74	HO^-	Hydroxide ion	
	HCN	Hydrocyanic acid	9.31	CN^-	Cyanide ion	
	$H_2PO_4^-$	Dihydrogen phosphate ion	7.21	HPO_4^{2-}	Hydrogen phosphate ion	
	CH_3CO_2H	Acetic acid	4.76	$CH_3CO_2^-$	Acetate ion	
	H_3PO_4	Phosphoric acid	2.16	$H_2PO_4^-$	Dihydrogen phosphate ion	
	HNO_3	Nitric acid	−1.3	NO_3^-	Nitrate ion	
	HCl	Hydrochloric acid	−7.0	Cl^-	Chloride ion	
Stronger acid						**Weaker base**

Notice that the pK_a value shown in Table 2.3 for water is 15.74, which results from the following calculation: the K_a for any acid in water is the equilibrium constant K_{eq} for the acid dissociation multiplied by 55.4, the molar concentration of pure water. For the acid dissociation of water, we have

$$H_2O + H_2O \;\rightleftharpoons\; OH^- + H_3O^+$$

$$K_{eq} = \frac{[H_3O^+][OH^-]}{[H_2O]^2} \quad \text{and} \quad K_a = K_{eq} \times [H_2O] = \frac{[H_3O^+][OH^-]}{[H_2O]}$$
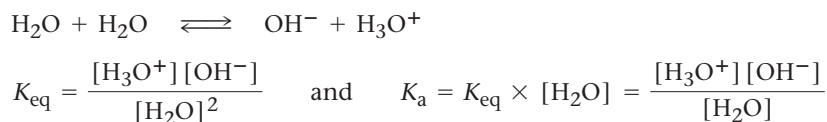
The numerator in this expression, $[H_3O^+][OH^-]$, is the so-called ion-product constant for water, $K_w = 1.00 \times 10^{-14}$, and the denominator is $[H_2O] = 55.4$ M at 25 °C. Thus, we have

$$K_a = \frac{1.0 \times 10^{-14}}{55.4} = 1.8 \times 10^{-16} \quad \text{and} \quad pK_a = 15.74$$

Notice also in Table 2.3 that there is an inverse relationship between the acid strength of an acid and the base strength of its conjugate base. That is, a *strong* acid has a *weak* conjugate base, and a *weak* acid has a *strong* conjugate base. To understand this relationship, think about what happens to the acidic hydrogen in an acid–base reaction. A strong acid is one that loses an H^+ easily, meaning that its conjugate base holds on to the H^+ weakly and is therefore a weak base. A weak acid is one that loses an H^+ with difficulty, meaning that its conjugate base holds on to the H^+ strongly and is therefore a strong base. HCl, for instance, is a strong acid, meaning that Cl^- holds on to the H^+ weakly and is thus a weak base. Water, on the other hand, is a weak acid, meaning that OH^- holds on to the H^+ strongly and is a strong base.

Problem 2.12 | The amino acid phenylalanine has $pK_a = 1.83$, and tryptophan has $pK_a = 2.83$. Which is the stronger acid?

Phenylalanine
(pK_a = 1.83)

Tryptophan
(pK_a = 2.83)
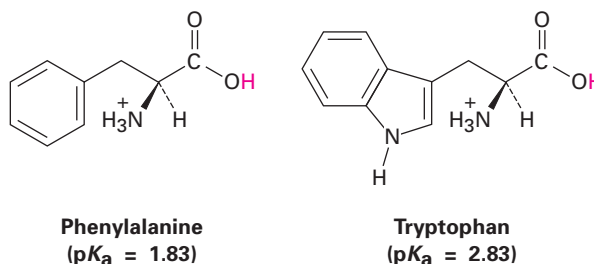
Problem 2.13 | Amide ion, H_2N^-, is a much stronger base than hydroxide ion, HO^-. Which is the stronger acid, NH_3 or H_2O? Explain.

2.9 | Predicting Acid–Base Reactions from pK_a Values

Compilations of pK_a values like those in Table 2.2 and Appendix B are useful for predicting whether a given acid–base reaction will take place because H^+ will always go *from* the stronger acid *to* the stronger base. That is, an acid will donate a proton to the conjugate base of a weaker acid, and the conjugate base of a weaker acid will remove the proton from a stronger acid. For example, since water ($pK_a = 15.74$) is a weaker acid than acetic acid ($pK_a = 4.76$), hydroxide ion holds a proton more tightly than acetate ion does. Hydroxide ion will therefore react with acetic acid, CH_3CO_2H, to yield acetate ion and H_2O.

Acetic acid
(pK_a = 4.76)   **Hydroxide ion**   **Acetate ion**   **Water**
(pK_a = 15.74)
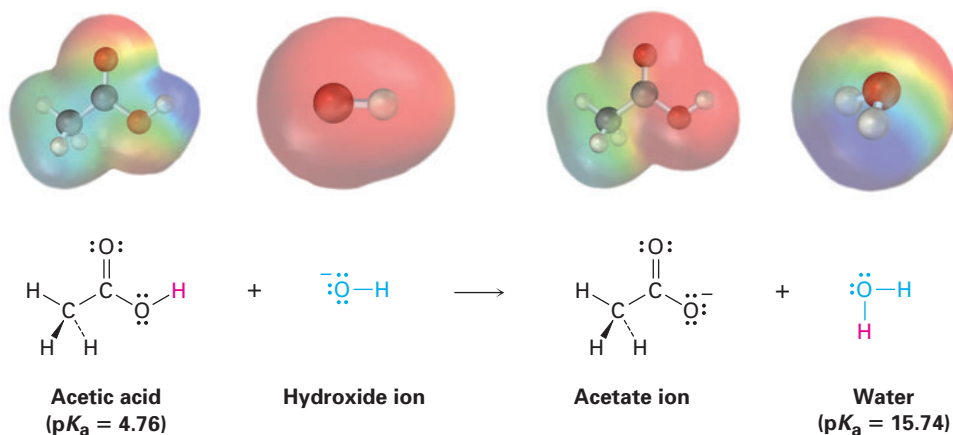
Another way to predict acid–base reactivity is to remember that the product conjugate acid in an acid–base reaction must be weaker and less reactive than the starting acid and the product conjugate base must be weaker and less reactive than the starting base. In the reaction of acetic acid with hydroxide ion, for example, the product conjugate acid (H_2O) is weaker than the starting acid (CH_3CO_2H) and the product conjugate base ($CH_3CO_2^-$) is weaker than the starting base (OH^-).

Stronger   **Stronger**   **Weaker**   **Weaker**
acid   **base**   **acid**   **base**
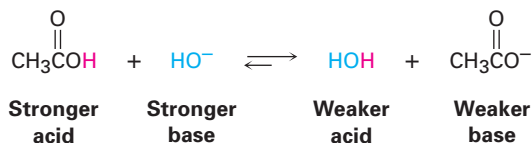
WORKED EXAMPLE 2.4

Predicting Acid Strengths from pK_a Values

Water has pK_a = 15.74, and acetylene has pK_a = 25. Which is the stronger acid? Does hydroxide ion react with acetylene?
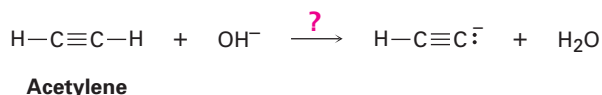
Acetylene

Strategy   In comparing two acids, the one with the lower pK_a is stronger. Thus, water is a stronger acid than acetylene and gives up H^+ more easily.

Solution   Because water is a stronger acid and gives up H^+ more easily than acetylene does, the HO^- ion must have less affinity for H^+ than the $HC\equiv C:^-$ ion has. In other words, the anion of acetylene is a stronger base than hydroxide ion, and the reaction will not proceed as written.

WORKED EXAMPLE 2.5   *Calculating K_a from pK_a*

According to the data in Table 2.3, acetic acid has $pK_a = 4.76$. What is its K_a?

Strategy   Since pK_a is the negative logarithm of K_a, it's necessary to use a calculator with an ANTILOG or INV LOG function. Enter the value of the pK_a (4.76), change the sign (-4.76), and then find the antilog (1.74×10^{-5}).

Solution $K_a = 1.74 \times 10^{-5}$.

Problem 2.14   Will either of the following reactions take place as written, according to the data in Table 2.3?

(a) $HCN \ + \ CH_3CO_2^- \ Na^+ \ \xrightarrow{?} \ Na^+ \ {}^-CN \ + \ CH_3CO_2H$

(b) $CH_3CH_2OH \ + \ Na^+ \ {}^-CN \ \xrightarrow{?} \ CH_3CH_2O^- \ Na^+ \ + \ HCN$
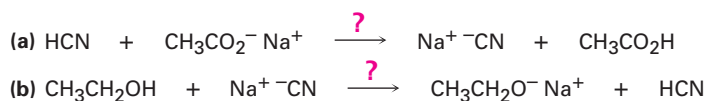
Problem 2.15   Ammonia, NH_3, has $pK_a \approx 36$, and acetone has pK_a 19. Will the following reaction take place?

Acetone
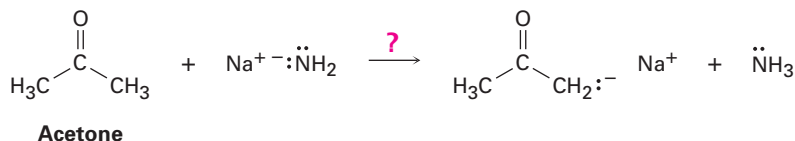
Problem 2.16   What is the K_a of HCN if its $pK_a = 9.31$?

2.10 Organic Acids and Organic Bases

Many of the reactions we'll be seeing in future chapters involve organic acids and organic bases. Although it's too early to go into the details of these processes now, you might keep the following generalities in mind as your study progresses.

Organic Acids

Organic acids are characterized by the presence of a positively polarized hydrogen atom (blue in electrostatic potential maps) and are of two main kinds: those acids such as methanol and acetic acid that contain a hydrogen atom bonded to an electronegative oxygen atom (O—H) and those such as acetone (Section 2.5) that contain a hydrogen atom bonded to a carbon atom next to a C=O bond (O=C—C—H).

Some organic acids

Methanol
(pK_a = 15.54)

Acetic acid
(pK_a = 4.76)

Acetone
(pK_a = 19.3)
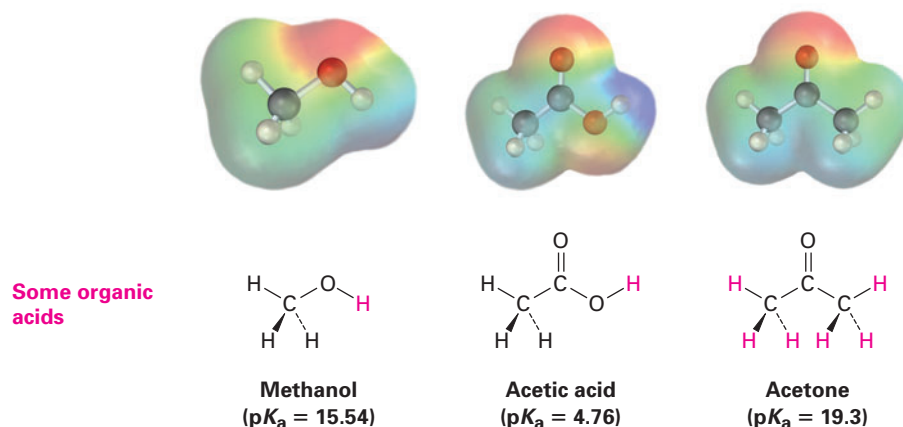
Methanol contains an O−H bond and is a weak acid; acetic acid also contains an O−H bond and is a somewhat stronger acid. In both cases, acidity is due to the fact that the conjugate base resulting from loss of H$^+$ is stabilized by having its negative charge on a strongly electronegative oxygen atom. In addition, the conjugate base of acetic acid is stabilized by resonance (Sections 2.4 and 2.5).

Anion is stabilized by having negative charge on a highly electronegative atom.

Anion is stabilized both by having negative charge on a highly electronegative atom and by resonance.
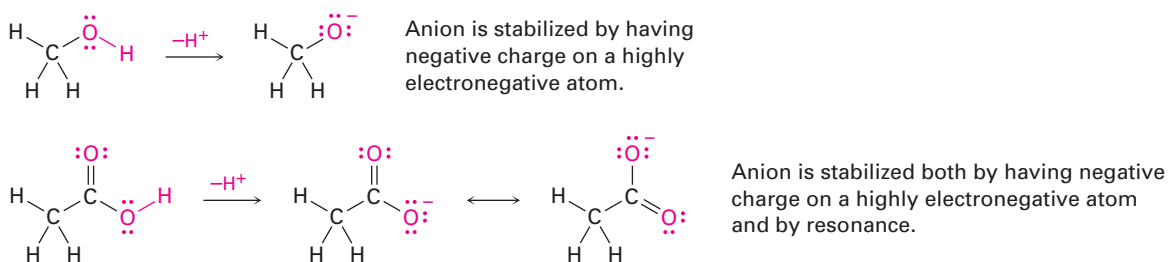
The acidity of acetone and other compounds with C=O bonds is due to the fact that the conjugate base resulting from loss of H$^+$ is stabilized by resonance. In addition, one of the resonance forms stabilizes the negative charge by placing it on an electronegative oxygen atom.

Anion is stabilized both by resonance and by having negative charge on a highly electronegative atom.
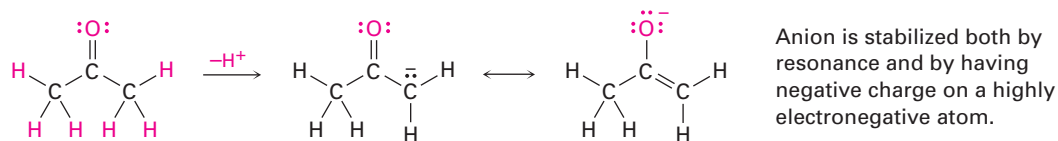
Electrostatic potential maps of the conjugate bases from methanol, acetic acid, and acetone are shown in Figure 2.4. As you might expect, all three show a substantial amount of negative charge (red) on oxygen.

Figure 2.4 Electrostatic potential maps of the conjugate bases of **(a)** methanol, **(b)** acetic acid, and **(c)** acetone. The electronegative oxygen atoms stabilize the negative charge in all three.

(a)

(b)

(c)

CH_3O^-

$CH_3\overset{O}{\overset{\|}{C}}O^-$

$CH_3\overset{O}{\overset{\|}{C}}CH_2^-$
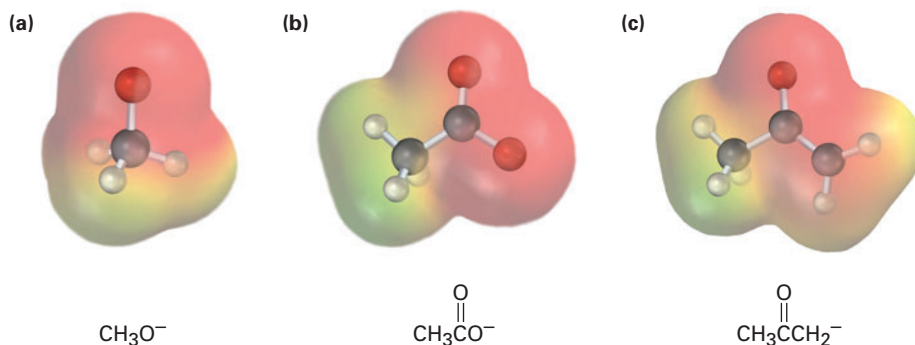
Compounds called *carboxylic acids,* which contain the $-CO_2H$ grouping, occur abundantly in all living organisms and are involved in almost all metabolic pathways. Acetic acid, pyruvic acid, and citric acid are examples.

Acetic acid   **Pyruvic acid**   **Citric acid**
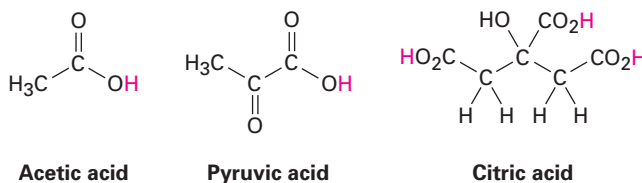
Organic Bases

Organic bases are characterized by the presence of an atom (reddish in electrostatic potential maps) with a lone pair of electrons that can bond to H^+. Nitrogen-containing compounds such as trimethylamine are the most common organic bases, but oxygen-containing compounds can also act as bases when reacting with a sufficiently strong acid. Note that some oxygen-containing compounds can act both as acids and as bases depending on the circumstances, just as water can. Methanol and acetone, for instance, act as *acids* when they donate a proton but as *bases* when their oxygen atom accepts a proton.

Some organic bases

Methylamine   **Methanol**   **Acetone**
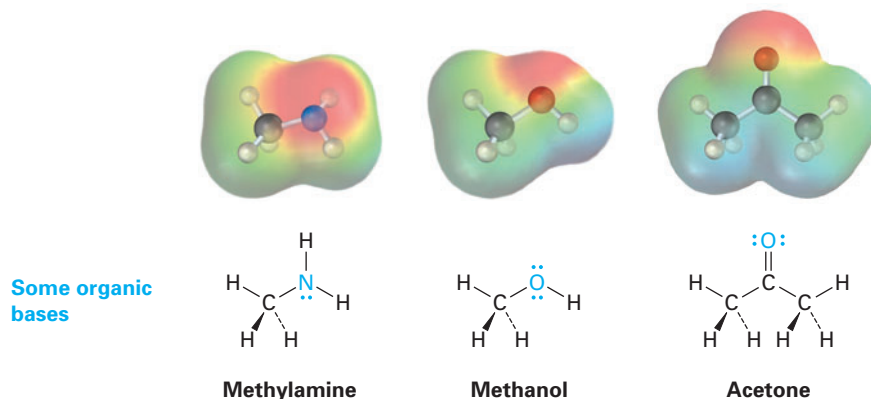
We'll see in Chapter 26 that substances called *amino acids,* so-named because they are both amines ($-NH_2$) and carboxylic acids ($-CO_2H$), are the building

blocks from which the proteins present in all living organisms arise. Twenty different amino acids go into making up proteins; alanine is an example.

Alanine
(uncharged form)   **Alanine**
(zwitterion form)
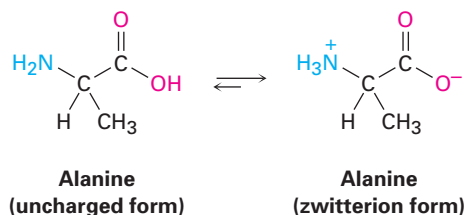
Interestingly, alanine and other amino acids exist primarily in a doubly charged form called a *zwitterion* rather than in the uncharged form. The zwitterion form arises because amino acids have both acidic and basic sites within the same molecule and therefore undergo an *internal* acid–base reaction.

2.11 | Acids and Bases: The Lewis Definition

The *Lewis definition* of acids and bases is broader and more encompassing than the Brønsted–Lowry definition because it's not limited to substances that donate or accept just protons. A **Lewis acid** is a substance that *accepts an electron pair,* and a **Lewis base** is a substance that *donates an electron pair.* The donated electron pair is shared between the acid and the base in a covalent bond.

Filled orbital   Vacant orbital

B   +   A   ⟶   B—A

Lewis base   **Lewis acid**
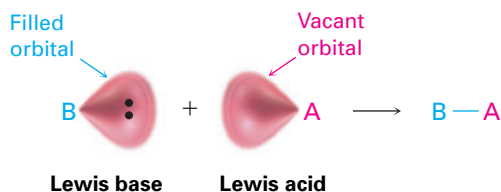
Lewis Acids and the Curved Arrow Formalism

The fact that a Lewis acid is able to accept an electron pair means that it must have either a vacant, low-energy orbital or a polar bond to hydrogen so that it can donate H^+ (which has an empty $1s$ orbital). Thus, the Lewis definition of acidity includes many species in addition to H^+. For example, various metal cations, such as Mg^{2+}, are Lewis acids because they accept a pair of electrons when they form a bond to a base. We'll also see in later chapters that certain metabolic reactions begin with an acid–base reaction between Mg^{2+} as a Lewis acid and an organic diphosphate or triphosphate ion as the Lewis base.

Mg^{2+} +

Lewis acid   **Lewis base**
(an organodiphosphate ion)   **Acid–base complex**
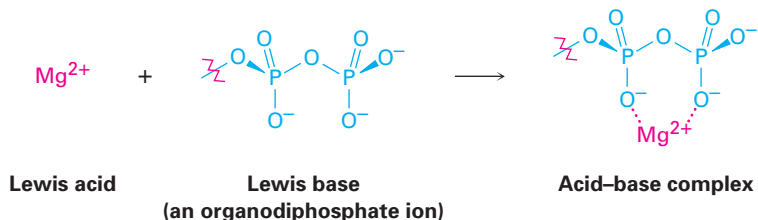
In the same way, compounds of group 3A elements, such as BF_3 and $AlCl_3$, are Lewis acids because they have unfilled valence orbitals and can accept electron

pairs from Lewis bases, as shown in Figure 2.5. Similarly, many transition-metal compounds, such as $TiCl_4$, $FeCl_3$, $ZnCl_2$, and $SnCl_4$, are Lewis acids.

Active Figure 2.5 The reaction of boron trifluoride, a Lewis acid, with dimethyl ether, a Lewis base. The Lewis acid accepts a pair of electrons, and the Lewis base donates a pair of nonbonding electrons. Note how the movement of electrons *from* the Lewis base *to* the Lewis acid is indicated by a curved arrow. Note also how, in electrostatic potential maps, the boron becomes more negative (red) after reaction because it has gained electrons and the oxygen atom becomes more positive (blue) because it has donated electrons. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*

Boron trifluoride (Lewis acid)   **Dimethyl ether (Lewis base)**   **Acid–base complex**
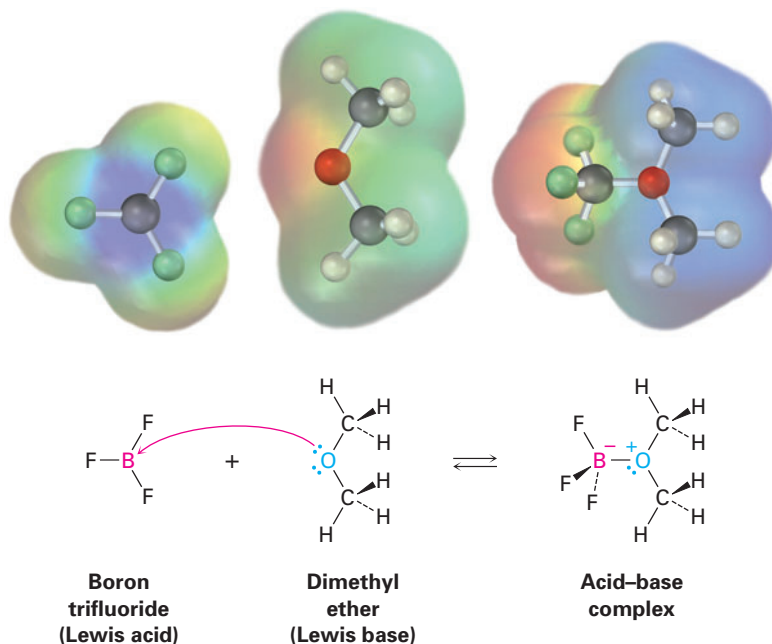
Look closely at the acid–base reaction in Figure 2.5, and note how it is shown. Dimethyl ether, the Lewis base, donates an electron pair to a vacant valence orbital of the boron atom in BF_3, a Lewis acid. The direction of electron-pair flow from the base to acid is shown using curved arrows, just as the direction of electron flow in going from one resonance structure to another was shown using curved arrows in Section 2.5. *A curved arrow always means that a pair of electrons moves* from *the atom at the tail of the arrow to the atom at the head of the arrow.* We'll use this curved-arrow notation throughout the remainder of this text to indicate electron flow during reactions.

Some further examples of Lewis acids follow:

Some neutral proton donors:

H_2O HCl   HBr HNO_3 H_2SO_4

Some Lewis acids

A carboxylic acid   **A phenol**   **An alcohol**

Some cations:

Li^+ Mg^{2+}

Some metal compounds:

$AlCl_3$ $TiCl_4$ $FeCl_3$ $ZnCl_2$
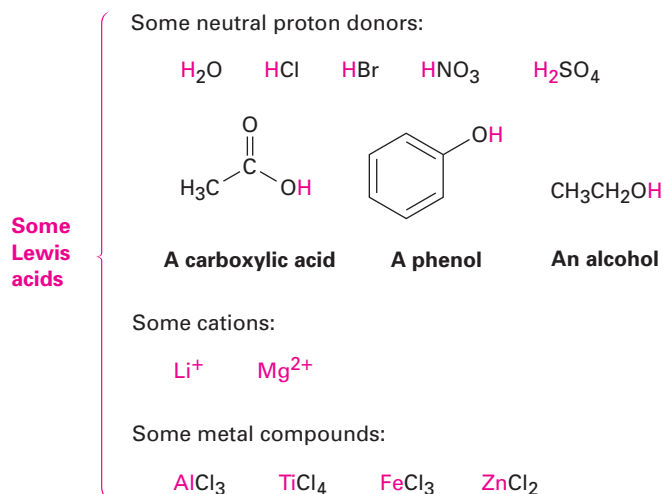
Lewis Bases

The Lewis definition of a base as a compound with a pair of nonbonding electrons that it can use to bond to a Lewis acid is similar to the Brønsted–Lowry definition. Thus, H_2O, with its two pairs of nonbonding electrons on oxygen, acts as a Lewis base by donating an electron pair to an H^+ in forming the hydronium ion, H_3O^+.

| Acid | Base | Hydronium ion |
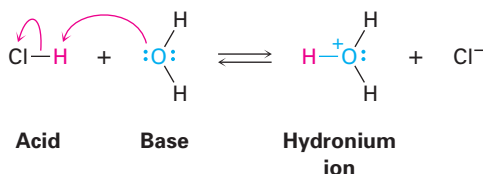
In a more general sense, most oxygen- and nitrogen-containing organic compounds can act as Lewis bases because they have lone pairs of electrons. A divalent oxygen compound has two lone pairs of electrons, and a trivalent nitrogen compound has one lone pair. Note in the following examples that some compounds can act as both acids and bases, just as water can. Alcohols and carboxylic acids, for instance, act as acids when they donate an H^+ but as bases when their oxygen atom accepts an H^+.

Some Lewis bases

CH₃CH₂ÖH — **An alcohol**

CH₃ÖCH₃ — **An ether**

CH₃CH (with :O: double bond) — **An aldehyde**

CH₃CCH₃ (with :O: double bond) — **A ketone**

CH₃CCl (with :O: double bond) — **An acid chloride**

CH₃CÖH (with :O: double bond) — **A carboxylic acid**

CH₃CÖCH₃ (with :O: double bond) — **An ester**

CH₃CNH₂ (with :O: double bond) — **An amide**

CH₃ÑCH₃ with CH₃ — **An amine**

CH₃SCH₃ — **A sulfide**

CH₃O—P—O—P—O—P—Ö (with O double bonds and :O:⁻ groups) — **An organotriphosphate ion**

Notice in the list of Lewis bases just given that some compounds, such as carboxylic acids, esters, and amides, have more than one atom with a lone pair of electrons and can therefore react at more than one site. Acetic acid, for example, can be protonated either on the doubly bonded oxygen atom or on the singly bonded oxygen atom. Reaction normally occurs only once in such instances, and the more stable of the two possible protonation products is formed. For acetic acid, protonation by reaction with sulfuric acid occurs on

the doubly bonded oxygen because that product is stabilized by two reso-
nance forms.

**Acetic acid
(base)**

Not formed
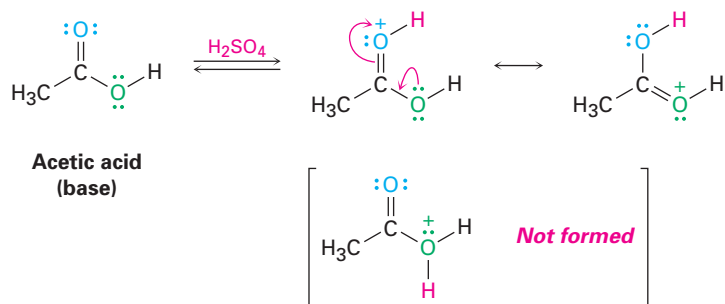
WORKED EXAMPLE 2.6   *Using Curved Arrows to Show Electron Flow*

Using curved arrows, show how acetaldehyde, CH_3CHO, can act as a Lewis base.

Strategy   A Lewis base donates an electron pair to a Lewis acid. We therefore need to locate the
electron lone pairs on acetaldehyde and use a curved arrow to show the movement
of a pair toward the H atom of the acid.

Solution

Acetaldehyde
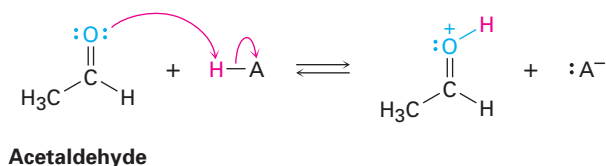
Problem 2.17   Using curved arrows, show how the species in part (a) can act as Lewis bases in their
reactions with HCl, and show how the species in part (b) can act as Lewis acids in
their reaction with OH^-.
(a) CH_3CH_2OH, $HN(CH_3)_2$, $P(CH_3)_3$ (b) H_3C^+, $B(CH_3)_3$, $MgBr_2$

Problem 2.18   Imidazole forms part of the structure of the amino acid histidine and can act as both
an acid and a base.

Imidazole   **Histidine**
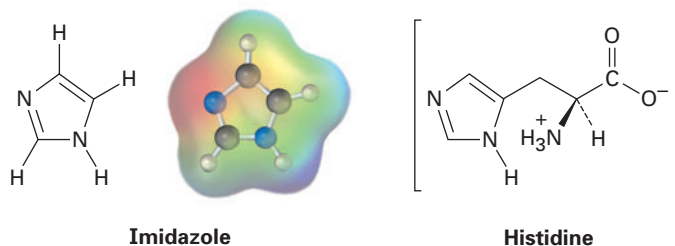
(a) Look at the electrostatic potential map of imidazole, and identify the most
    acidic hydrogen atom and the most basic nitrogen atom.
(b) Draw structures for the resonance forms of the products that result when imid-
    azole is protonated by an acid and deprotonated by a base.

2.12 | Molecular Models

Because organic chemistry is a three-dimensional science, molecular shape is often critical in determining the chemistry a compound undergoes, both in the laboratory and in living organisms. Learning to visualize molecular shapes is therefore an important skill to develop. One helpful technique, particularly when dealing with large biomolecules, is to use one of the many computer programs that are available for rotating and manipulating molecules on the screen. Another technique is to use molecular models. With practice, you can learn to see many spatial relationships even when viewing two-dimensional drawings, but there's no substitute for building a molecular model and turning it in your hands to get different perspectives.

Many kinds of models are available, some at relatively modest cost, and it's a good idea to have access to a set of models while studying this book. *Space-filling models* are better for examining the crowding within a molecule, but *ball-and-stick models* are generally the least expensive and most durable for student use. Figure 2.6 shows two kinds of models of acetic acid, CH_3CO_2H.

Figure 2.6 Molecular models of acetic acid, CH_3CO_2H. **(a)** Space-filling; **(b)** ball-and-stick.

(a)

(b)

Laurie Campbell/Getty Images

Laurie Campbell/Getty Images
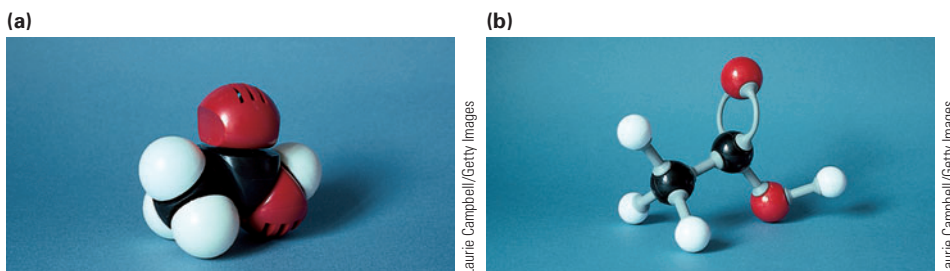
2.13 | Noncovalent Interactions

When thinking about chemical reactivity, chemists usually focus their attention on bonds, the covalent interactions between atoms *within* individual molecules. Also important, however, particularly in large biomolecules like proteins and nucleic acids, are a variety of interactions *between* molecules that strongly affect molecular properties. Collectively called either *intermolecular forces, van der Waals forces,* or **noncovalent interactions**, they are of several different types: dipole–dipole forces, dispersion forces, and hydrogen bonds.

Dipole–dipole forces occur between polar molecules as a result of electrostatic interactions among dipoles. The forces can be either attractive or repulsive depending on the orientation of the molecules—attractive when unlike charges are together and repulsive when like charges are together. The attractive geometry is lower in energy and therefore predominates (Figure 2.7).

Figure 2.7 Dipole–dipole forces cause polar molecules **(a)** to attract one another when they orient with unlike charges together but **(b)** to repel one another when they orient with like charges together.
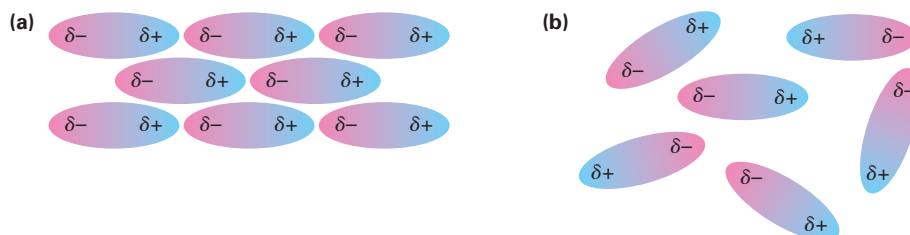
Dispersion forces occur between all neighboring molecules and arise because the electron distribution within molecules is constantly changing. Although uniform on a time-averaged basis, the electron distribution even in nonpolar molecules is likely to be nonuniform at any given instant. One side of a molecule may, by chance, have a slight excess of electrons relative to the opposite side, giving the molecule a temporary dipole. This temporary dipole in one molecule causes a nearby molecule to adopt a temporarily opposite dipole, with the result that a tiny attraction is induced between the two (Figure 2.8). Temporary molecular dipoles have only a fleeting existence and are constantly changing, but their cumulative effect is often strong enough to cause a substance to be liquid or solid rather than gaseous.

Figure 2.8 Attractive dispersion forces in nonpolar molecules are caused by temporary dipoles, as shown in these models of pentane, C_5H_{12}.
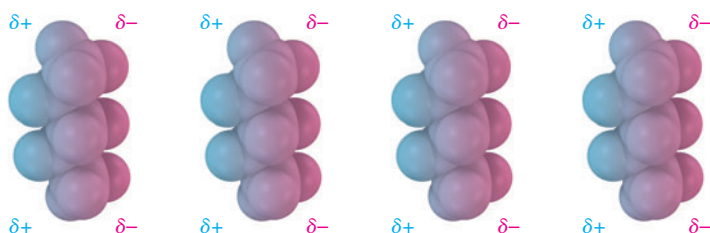
Perhaps the most important noncovalent interaction in biological molecules is the **hydrogen bond**, an attractive interaction between a hydrogen bonded to an electronegative O or N atom and an unshared electron pair on another O or N atom. In essence, a hydrogen bond is a strong dipole–dipole interaction involving polarized O−H and N−H bonds. Electrostatic potential maps of water and ammonia clearly show the positively polarized hydrogens (blue) and the negatively polarized oxygens and nitrogens (red).
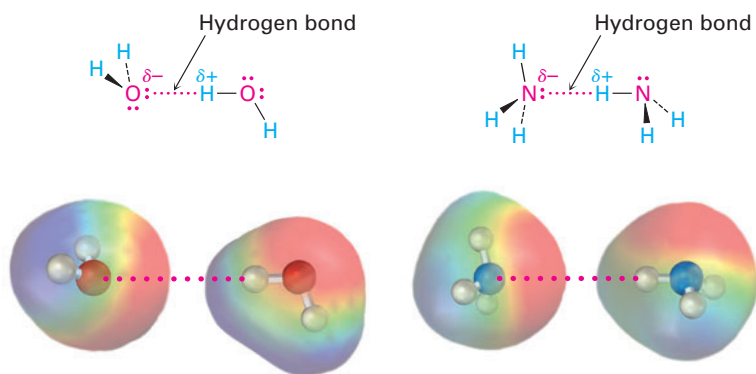
Hydrogen-bonding has enormous consequences for living organisms. Hydrogen bonds cause water to be a liquid rather than a gas at ordinary temperatures,

they hold enzymes in the shapes necessary for catalyzing biological reactions, and they cause strands of deoxyribonucleic acid (DNA) to pair up and coil into the double helix that stores genetic information.

Hydrogen bonds between DNA strands
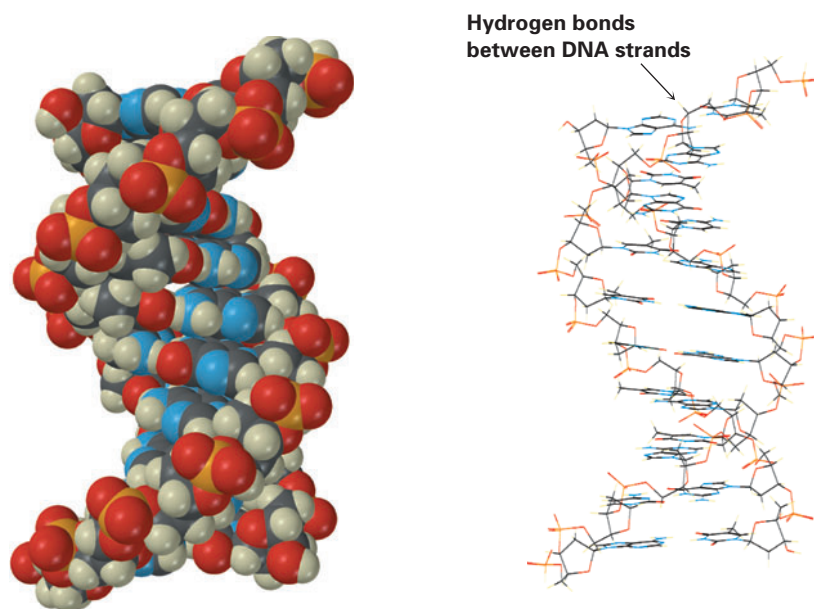
A deoxyribonucleic acid segment

One further point before leaving the subject of noncovalent interactions: chemists frequently use the terms **hydrophilic**, meaning "water-loving," to describe a substance that dissolves in water and **hydrophobic**, meaning "water-fearing," to describe a substance that does not dissolve in water. Hydrophilic substances, such as table sugar, usually have a number of ionic charges or polar −OH groups in their structure, so they are strongly attracted to water. Hydrophobic substances, such as vegetable oil, do not have groups that form hydrogen bonds, so their attraction to water is weak.

Problem 2.19 | Of the two vitamins A and C, one is hydrophilic and water-soluble while the other is hydrophobic and fat-soluble. Which is which?
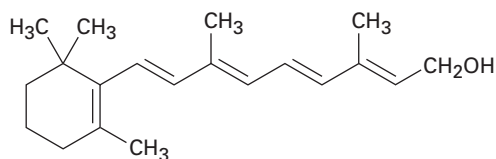
Vitamin A
(retinol)
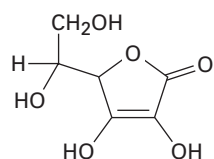
Vitamin C
(ascorbic acid)

Focus On . . .

Alkaloids: Naturally Occurring Bases

The coca bush *Erythroxylon coca,* native to upland rain forest areas of Colombia, Ecuador, Peru, Bolivia, and western Brazil, is the source of the alkaloid cocaine.

Just as ammonia is a weak base, there are a large number of nitrogen-containing organic compounds called *amines* that are also weak bases. In the early days of organic chemistry, basic amines derived from natural sources were known as *vegetable alkali,* but they are now called *alkaloids*. The study of alkaloids provided much of the impetus for the growth of organic chemistry in the 19th century and remains today an active and fascinating area of research.

Alkaloids vary widely in structure, from the simple to the enormously complex. The odor of rotting fish, for example, is caused largely by methylamine, CH_3NH_2, a simple relative of ammonia in which one of the NH_3 hydrogens has been replaced by an organic CH_3 group. In fact, the use of lemon juice to mask fish odors is simply an acid–base reaction of the citric acid in lemons with methylamine base in the fish.

Many alkaloids have pronounced biological properties, and a substantial number of the pharmaceutical agents used today are derived from naturally occurring amines. As a few examples, morphine, an analgesic agent, is obtained from the opium poppy *Papaver somniferum.* Cocaine, both an anesthetic and a central nervous system stimulant, is obtained from the coca bush *Erythroxylon coca,* endemic to upland rain forest areas of Colombia, Ecuador, Peru, Bolivia, and western Brazil. Reserpine, a tranquilizer and antihypertensive, comes from powdered roots of the semitropical plant *Rauwolfia serpentina.* Ephedrine, a bronchodilator and decongestant, is obtained from the Chinese plant *Ephedra sinica.*

Morphine

Cocaine
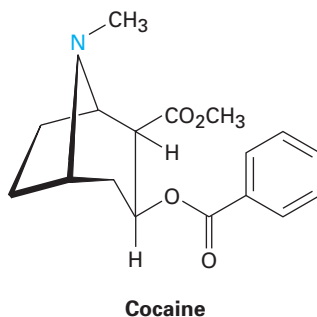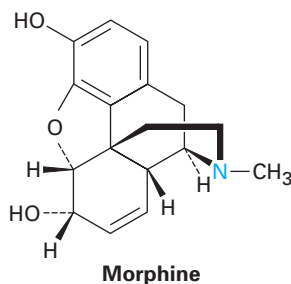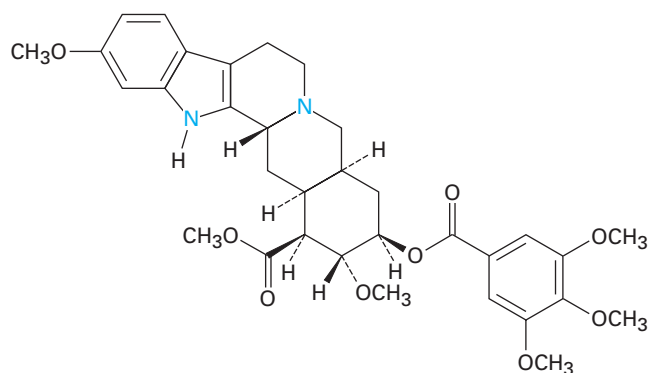
Reserpine
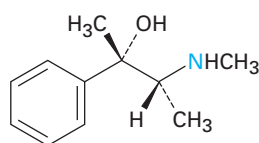
Ephedrine

A recent report from the U.S. National Academy of Sciences estimates than less than 1% of all living species have been characterized. Thus, alkaloid chemistry remains today an active area of research, and innumerable substances with potentially useful properties remain to be discovered.

SUMMARY AND KEY WORDS

acidity constant (K_a), 50
Brønsted–Lowry acid, 49
Brønsted–Lowry base, 49
conjugate acid, 49
conjugate base, 49
dipole moment (μ), 38
electronegativity (EN), 36
formal charge, 41
hydrogen bond, 62
hydrophilic, 63
hydrophobic, 63
inductive effect, 37
Lewis acid, 57
Lewis base, 57
noncovalent interaction, 61

Organic molecules often have **polar covalent bonds** as a result of unsymmetrical electron sharing caused by differences in the **electronegativity** of atoms. A carbon–oxygen bond is polar, for example, because oxygen attracts the shared electrons more strongly than carbon does. Carbon–hydrogen bonds are relatively nonpolar. Many molecules as a whole are also polar owing to the vector summation of individual polar bonds and electron lone pairs. The polarity of a molecule is measured by its **dipole moment**, μ.

Plus (+) and minus (−) signs are often used to indicate the presence of **formal charges** on atoms in molecules. Assigning formal charges to specific atoms is a bookkeeping technique that makes it possible to keep track of the valence electrons around an atom and offers some clues about chemical reactivity.

Some substances, such as acetate ion and benzene, can't be represented by a single line-bond structure and must be considered as a **resonance hybrid** of two or more structures, neither of which is correct by itself. The only difference between two **resonance forms** is in the location of their π and nonbonding electrons. The nuclei remain in the same places in both structures, and the hybridization of the atoms remains the same.

Acidity and basicity are closely related to the ideas of polarity and electronegativity. A **Brønsted–Lowry acid** is a compound that can donate a proton (hydrogen ion, H^+), and a **Brønsted–Lowry base** is a compound that can accept a proton. The strength of a Brønsted–Lowry acid or base is expressed by its **acidity constant, K_a,** or by the negative logarithm of the acidity constant, **pK_a**. The larger the pK_a, the weaker the acid. More useful is the Lewis definition of acids and bases. A **Lewis acid** is a compound that has a low-energy empty orbital that can accept an electron pair; Mg^{2+}, BF_3, $AlCl_3$, and H^+ are examples. A **Lewis base** is a compound that can donate an unshared electron pair; NH_3 and H_2O are examples. Most organic molecules that contain oxygen and nitrogen can act as Lewis bases toward sufficiently strong acids.

A variety of **noncovalent interactions** have a significant effect on the properties of large biomolecules. **Hydrogen-bonding**—the attractive interaction between a positively polarized hydrogen atom bonded to an oxygen or nitrogen atom with an unshared electron pair on another O or N atom, is particularly important in giving proteins and nucleic acids their shapes.

EXERCISES

Organic **KNOWLEDGE TOOLS**

ThomsonNOW™ Sign in at **www.thomsonedu.com** to assess your knowledge of this chapter's topics by taking a pre-test. The pre-test will link you to interactive organic chemistry resources based on your score in each concept area.

Online homework for this chapter may be assigned in Organic OWL.

■ indicates problems assignable in Organic OWL.

▲ denotes problems linked to Key Ideas of this chapter and testable in ThomsonNOW.

VISUALIZING CHEMISTRY

(Problems 2.1–2.19 appear within the chapter.)

2.20 Fill in the multiple bonds in the following model of naphthalene, $C_{10}H_8$ (gray = C, ivory = H). How many resonance structures does naphthalene have?

■ Assignable in OWL   ▲ Key Idea Problems
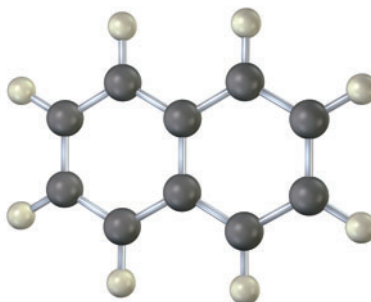
2.21 ■ The following model is a representation of ibuprofen, a common over-the-counter pain reliever. Indicate the positions of the multiple bonds, and draw a skeletal structure (gray = C, red = O, ivory = H).
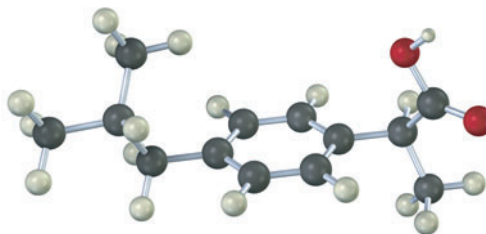
2.22 *cis*-1,2-Dichloroethylene and *trans*-dichloroethylene are *isomers,* compounds with the same formula but different chemical structures. Look at the following electrostatic potential maps, and tell whether either compound has a dipole moment.


cis-1,2-Dichloroethylene   **trans-1,2-Dichloroethylene**
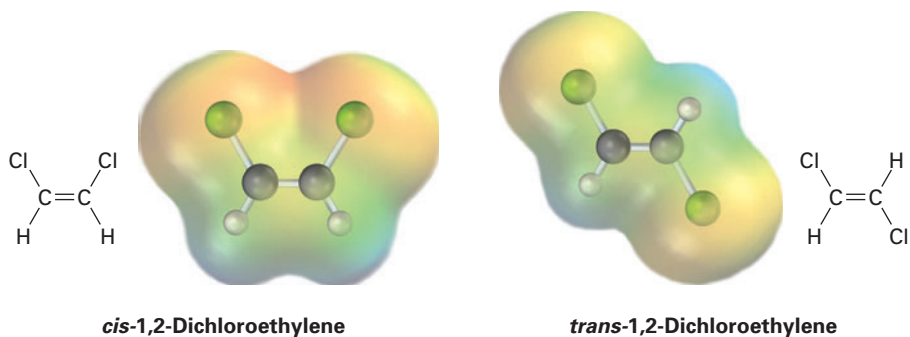
2.23 ■ The following molecular models are representations of **(a)** adenine and **(b)** cytosine, constituents of DNA. Indicate the positions of multiple bonds and lone pairs for both, and draw skeletal structures (gray = C, red = O, blue = N, ivory = H).

(a)   **(b)**

Adenine   **Cytosine**

■ Assignable in OWL   ▲ Key Idea Problems
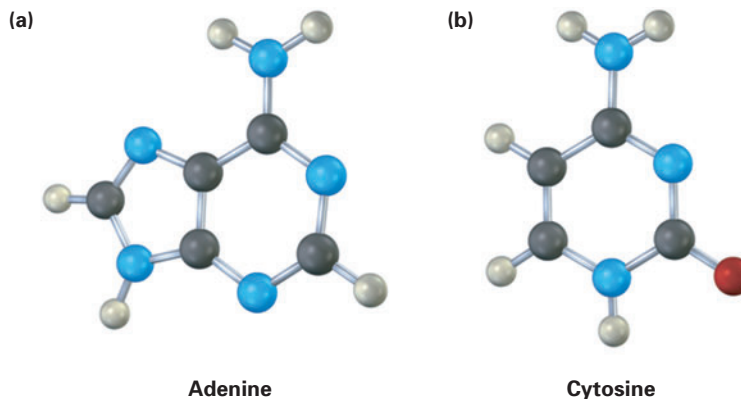
ADDITIONAL PROBLEMS

2.24 Tell the number of hydrogens bonded to each carbon atom in the following substances, and give the molecular formula of each:

(a)

Ephedrine

(b)

Cocaine
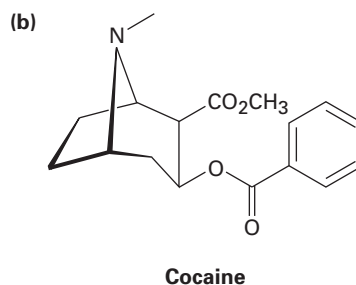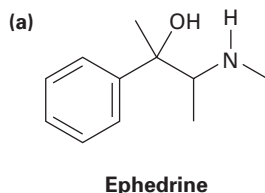
2.25 ■ Identify the most electronegative element in each of the following molecules:
(a) CH_2FCl (b) $FCH_2CH_2CH_2Br$
(c) $HOCH_2CH_2NH_2$ (d) CH_3OCH_2Li

2.26 ■ Use the electronegativity table (Figure 2.2) to predict which bond in each of the following sets is more polar, and indicate the direction of bond polarity for each compound.
(a) H_3C-Cl or $Cl-Cl$ (b) H_3C-H or $H-Cl$
(c) $HO-CH_3$ or $(CH_3)_3Si-CH_3$ (d) H_3C-Li or $Li-OH$
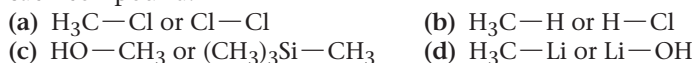
2.27 ■ Which of the following molecules has a dipole moment? Indicate the expected direction of each.
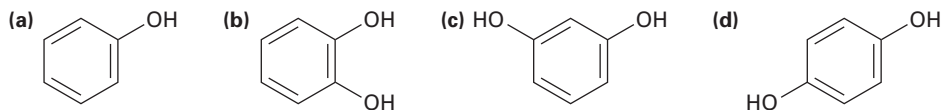
2.28 (a) The H−Cl bond length is 136 pm. What would the dipole moment of HCl be if the molecule were 100% ionic, $H^+ Cl^-$?
(b) The actual dipole moment of HCl is 1.08 D. What is the percent ionic character of the H−Cl bond?

2.29 Phosgene, $Cl_2C=O$, has a smaller dipole moment than formaldehyde, $H_2C=O$, even though it contains electronegative chlorine atoms in place of hydrogen. Explain.

2.30 Fluoromethane (CH_3F, $\mu = 1.81$ D) has a smaller dipole moment than chloromethane (CH_3Cl, $\mu = 1.87$ D) even though fluorine is more electronegative than chlorine. Explain.

2.31 Methanethiol, CH_3SH, has a substantial dipole moment ($\mu = 1.52$) even though carbon and sulfur have identical electronegativities. Explain.

2.32 ■ Calculate the formal charges on the atoms shown in red.

■ Assignable in OWL   ▲ Key Idea Problems
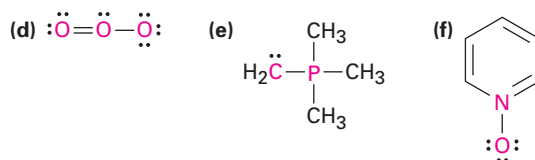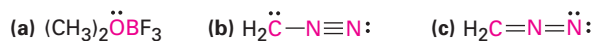
2.33 ■ Which of the following pairs of structures represent resonance forms?
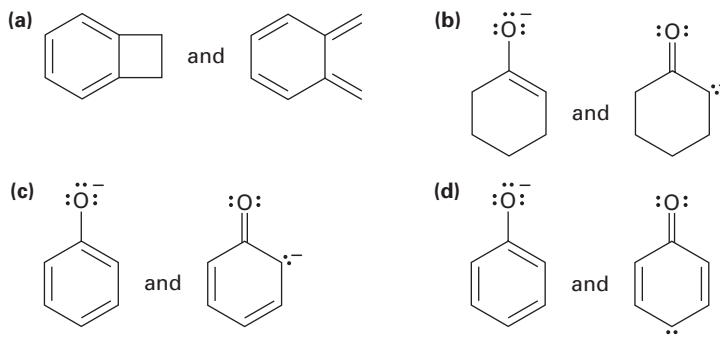
(a)

 and

(b) :Ö:⁻   :O:

 and

(c) :Ö:⁻   :O:

 and

(d) :Ö:⁻   :O:

 and

2.34 ■ ▲ Draw as many resonance structures as you can for the following species:

(a)

$$:O:$$
$$H_3C-C-\overset{\cdot\cdot}{C}H_2^-$$

(b)

(c)

$$:NH_2$$
$$H_2\overset{\cdot\cdot}{N}-C\overset{+}{=}NH_2$$

(d) $H_3C-\overset{\cdot\cdot}{\underset{\cdot\cdot}{S}}-\overset{+}{C}H_2$

(e) $H_2C=CH-CH=CH-\overset{+}{C}H-CH_3$
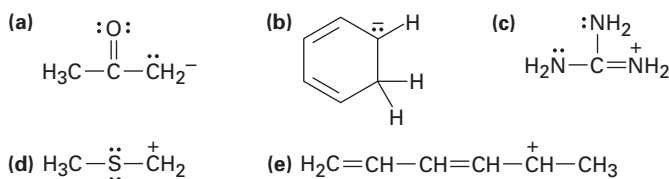
2.35 Cyclobutadiene is a rectangular molecule with two shorter double bonds and two longer single bonds. Why do the following structures *not* represent resonance forms?

2.36 Alcohols can act either as weak acids or as weak bases, just as water can. Show the reaction of methanol, CH_3OH, with a strong acid such as HCl and with a strong base such as $Na^+\ ^-NH_2$.

2.37 ▲ The O–H hydrogen in acetic acid is much more acidic than any of the C–H hydrogens. Explain this result using resonance structures.

Acetic acid
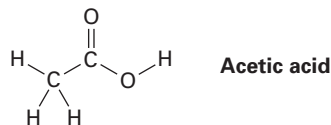
2.38 ■ Which of the following are likely to act as Lewis acids and which as Lewis bases?
(a) $AlBr_3$ (b) $CH_3CH_2NH_2$ (c) BH_3
(d) HF   (e) CH_3SCH_3 (f) $TiCl_4$
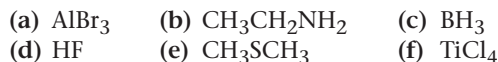
2.39 Draw an electron-dot structure for each of the molecules in Problem 2.38, indicating any unshared electron pairs.

2.40 ■ Write the products of the following acid–base reactions:
(a) $CH_3OH + H_2SO_4 \rightleftarrows ?$
(b) $CH_3OH + NaNH_2 \rightleftarrows ?$
(c) $CH_3NH_3^+\ Cl^- + NaOH \rightleftarrows ?$

■ Assignable in OWL   ▲ Key Idea Problems
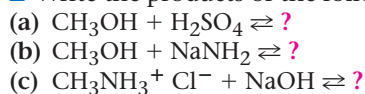
2.41 ■ Assign formal charges to the atoms in each of the following molecules:

(a)

$$H_3C-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{N}}-\ddot{\overset{..}{\underset{..}{O}}}:$$

(b) $H_3C-\overset{..}{\underset{..}{N}}-N\equiv N:$

(c) $H_3C-\overset{..}{N}=N=\ddot{\underset{..}{N}}:$
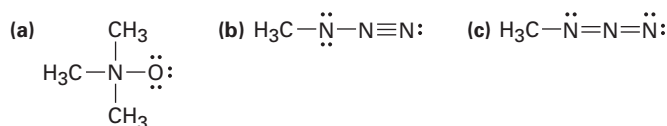
2.42 Maleic acid has a dipole moment, but the closely related fumaric acid, a substance involved in the citric acid cycle by which food molecules are metabolized, does not. Explain.
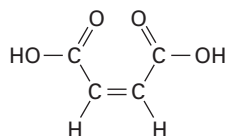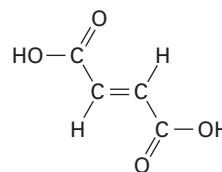
Maleic acid   **Fumaric acid**

2.43 ■ Rank the following substances in order of increasing acidity:

$$\underset{\textbf{Acetone}}{\underset{\textbf{(p}K_a\textbf{ = 19.3)}}{CH_3\overset{\overset{\displaystyle O}{\|}}{C}CH_3}}$$

$$\underset{\textbf{2,4-Pentanedione}}{\underset{\textbf{(p}K_a\textbf{ = 9)}}{CH_3\overset{\overset{\displaystyle O}{\|}}{C}CH_2\overset{\overset{\displaystyle O}{\|}}{C}CH_3}}$$
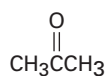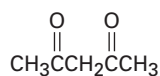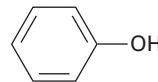
$$\underset{\textbf{Phenol}}{\underset{\textbf{(p}K_a\textbf{ = 9.9)}}{\text{—OH}}}$$
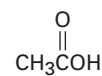
$$\underset{\textbf{Acetic acid}}{\underset{\textbf{(p}K_a\textbf{ = 4.76)}}{CH_3\overset{\overset{\displaystyle O}{\|}}{C}OH}}$$

2.44 Which, if any, of the four substances in Problem 2.43 is a strong enough acid to react almost completely with NaOH? (The pK_a of H_2O is 15.74.)

2.45 The ammonium ion ($NH_4{}^+$, pK_a = 9.25) has a lower pK_a than the methylammonium ion ($CH_3NH_3{}^+$, pK_a = 10.66). Which is the stronger base, ammonia (NH_3) or methylamine (CH_3NH_2)? Explain.

2.46 Is *tert*-butoxide anion a strong enough base to react with water? In other words, can a solution of potassium *tert*-butoxide be prepared in water? The pK_a of *tert*-butyl alcohol is approximately 18.
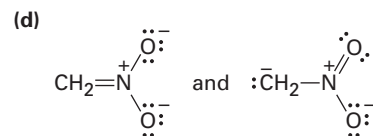
$$K^+ \ {}^-O-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH_3 \qquad \textbf{Potassium }\textit{tert}\textbf{-butoxide}$$
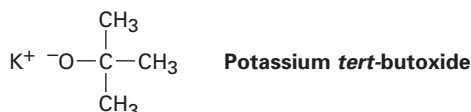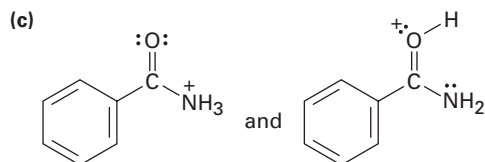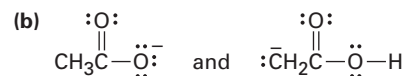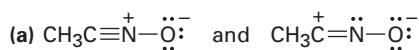
2.47 Predict the structure of the product formed in the reaction of the organic base pyridine with the organic acid acetic acid, and use curved arrows to indicate the direction of electron flow.
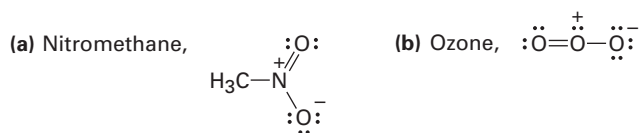
Pyridine   **Acetic acid**

■ Assignable in OWL   ▲ Key Idea Problems
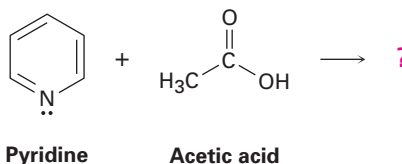
2.48 ■ Calculate K_a values from the following pK_a's:
    (a) Acetone, $pK_a = 19.3$ **(b)** Formic acid, $pK_a = 3.75$

2.49 ■ Calculate pK_a values from the following K_a's:
    (a) Nitromethane, $K_a = 5.0 \times 10^{-11}$ **(b)** Acrylic acid, $K_a = 5.6 \times 10^{-5}$

2.50 What is the pH of a 0.050 M solution of formic acid, $pK_a = 3.75$?

2.51 Sodium bicarbonate, $NaHCO_3$, is the sodium salt of carbonic acid (H_2CO_3), $pK_a = 6.37$. Which of the substances shown in Problem 2.43 will react with sodium bicarbonate?

2.52 Assume that you have two unlabeled bottles, one of which contains phenol ($pK_a = 9.9$) and one of which contains acetic acid ($pK_a = 4.76$). In light of your answer to Problem 2.51, suggest a simple way to determine what is in each bottle.

2.53 ■ Identify the acids and bases in the following reactions:

(a) CH_3OH + H^+ $\longrightarrow$ $CH_3\overset{+}{O}H_2$

(b)

(c)

(d)
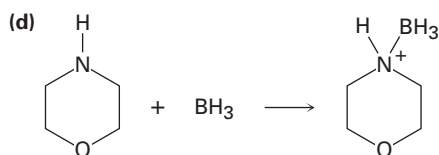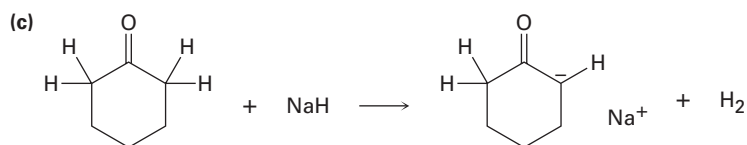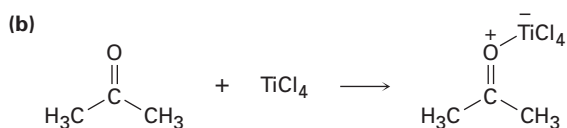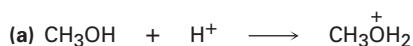
2.54 ■ ▲ Which of the following pairs represent resonance structures?

(a) $CH_3C\equiv\overset{+}{N}-\overset{..}{\underset{..}{O}}\overset{-}{:}$ and $CH_3\overset{+}{C}=\overset{..}{N}-\overset{..}{\underset{..}{O}}\overset{-}{:}$ **(b)**


(c)

(d)

2.55 ▲ Draw as many resonance structures as you can for the following species, adding appropriate formal charges to each:

(a) Nitromethane,

**(b)** Ozone, $:\overset{..}{O}=\overset{+}{\overset{..}{O}}-\overset{..}{\underset{..}{O}}:^-$

(c) Diazomethane, $H_2C=\overset{+}{N}=\overset{..}{\underset{..}{N}}:$

2.56 Carbocations, ions that contain a trivalent, positively charged carbon atom, react with water to give alcohols:


A carbocation   **An alcohol**
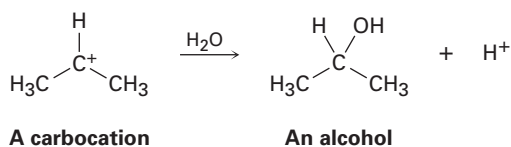
How can you account for the fact that the following carbocation gives a mixture of *two* alcohols on reaction with water?
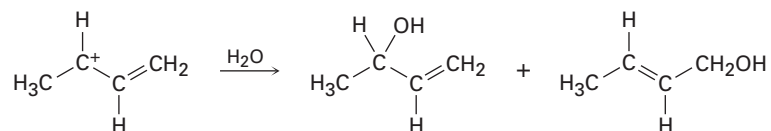
2.57 We'll see in the next chapter that organic molecules can be classified according to the *functional groups* they contain, where a functional group is a collection of atoms with a characteristic chemical reactivity. Use the electronegativity values given in Figure 2.2 to predict the direction of polarization of the following functional groups.

(a)

(b)

(c)

(d) $-C\equiv N$

Ketone   **Alcohol**   **Amide**   **Nitrile**
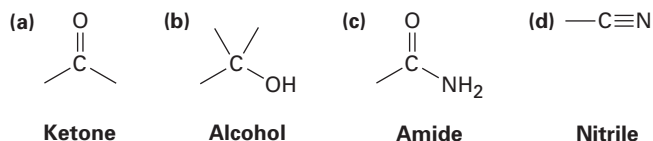
2.58 Phenol, C_6H_5OH, is a stronger acid than methanol, CH_3OH, even though both contain an O–H bond. Draw the structures of the anions resulting from loss of H^+ from phenol and methanol, and use resonance structures to explain the difference in acidity.

Phenol (pK_a = 9.89)   **Methanol (pK_a = 15.54)**

■ Assignable in OWL   ▲ Key Idea Problems
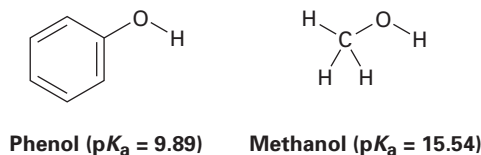
3

Organic Compounds: Alkanes and Their Stereochemistry

Sean Duggan

Organic KNOWLEDGE TOOLS

ThomsonNOW™ Throughout this chapter, sign in at **www.thomsonedu.com** for online self-study and interactive tutorials based on your level of understanding.

Online homework for this chapter may be assigned in Organic OWL.

According to _Chemical Abstracts,_ the publication that abstracts and indexes the chemical literature, there are more than 30 million known organic compounds. Each of these compounds has its own physical properties, such as melting point and boiling point, and each has its own chemical reactivity.

Chemists have learned through many years of experience that organic compounds can be classified into families according to their structural features and that the members of a given family often have similar chemical behavior. Instead of 30 million compounds with random reactivity, there are a few dozen families of organic compounds whose chemistry is reasonably predictable. We'll study the chemistry of specific families throughout much of this book, beginning in this chapter with a look at the simplest family, the _alkanes._

WHY THIS CHAPTER?

Alkanes are relatively unreactive, but they nevertheless provide a useful vehicle for introducing some important general ideas. In this chapter, we'll use alkanes for discussing the basic approach to naming organic compounds and for taking an initial look at some of the three-dimensional aspects of molecules, a topic of particular importance in understanding biological organic chemistry.

3.1 Functional Groups

ThomsonNOW™ Click _Organic Interactive_ to learn how to **recognize functional groups in organic molecules**.

The structural features that make it possible to classify compounds into families are called _functional groups._ A **functional group** is a group of atoms that has a characteristic chemical behavior in every molecule where it occurs. For example, compare ethylene, a plant hormone that causes fruit to ripen, with menthene, a much more complicated molecule. Both substances contain a carbon–carbon double-bond functional group, and both therefore react with Br_2 in the same way to give products in which a Br atom has added to each of the double-bond carbons (Figure 3.1). This example is typical: _the chemistry of every organic molecule, regardless of size and complexity, is determined by the functional groups it contains._
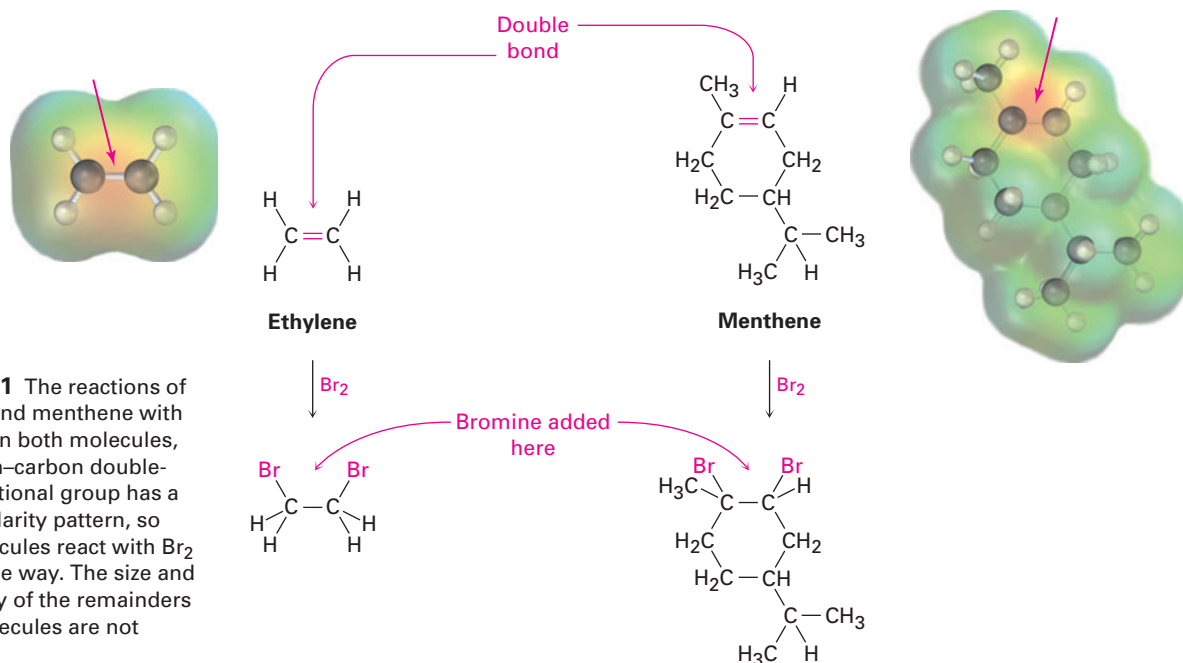
Figure 3.1 The reactions of ethylene and menthene with bromine. In both molecules, the carbon–carbon double-bond functional group has a similar polarity pattern, so both molecules react with Br_2 in the same way. The size and complexity of the remainders of the molecules are not important.

Look carefully at Table 3.1 on pages 76 and 77, which lists many of the common functional groups and gives simple examples of their occurrence. Some functional groups have only carbon–carbon double or triple bonds; others have halogen atoms; and still others contain oxygen, nitrogen, or sulfur. Much of the chemistry you'll be studying is the chemistry of these functional groups.

Functional Groups with Carbon–Carbon Multiple Bonds

Alkenes, alkynes, and arenes (aromatic compounds) all contain carbon–carbon multiple bonds. *Alkenes* have a double bond, *alkynes* have a triple bond, and *arenes* have alternating double and single bonds in a six-membered ring of carbon atoms. Because of their structural similarities, these compounds also have chemical similarities.

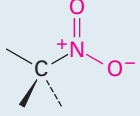Alkene

Alkyne

Arene
(aromatic ring)
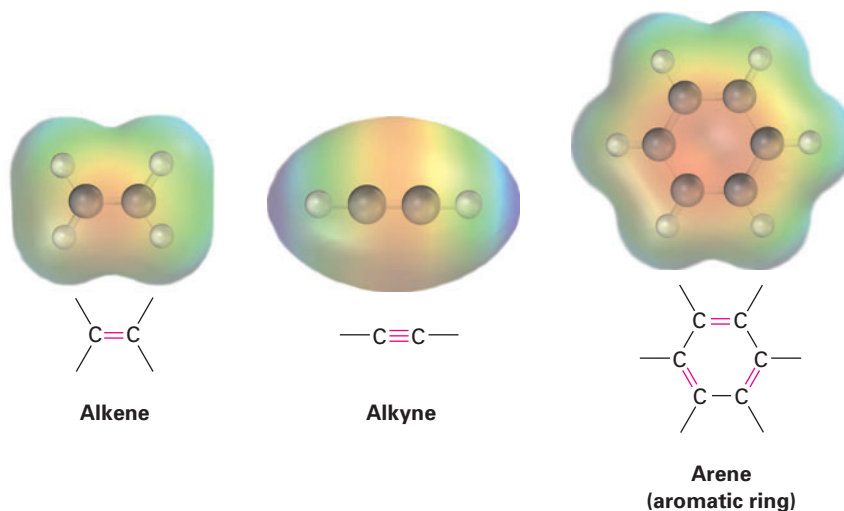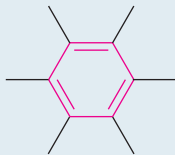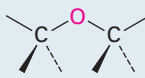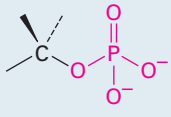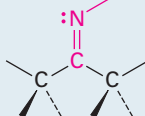
Functional Groups with Carbon Singly Bonded to an Electronegative Atom Alkyl halides (haloalkanes), alcohols, ethers, amines, thiols, sulfides, and disulfides all have a carbon atom singly bonded to an electronegative atom—halogen, oxygen, nitrogen, or sulfur. *Alkyl halides* have a carbon atom bonded to halogen ($-X$), *alcohols* have a carbon atom bonded to the oxygen of a hydroxyl group ($-OH$), *ethers* have two carbon atoms bonded to the same oxygen, *organophosphates* have a carbon atom bonded to the oxygen of a phosphate group ($-OPO_3^{2-}$), *amines* have a carbon atom bonded to a nitrogen, *thiols* have a carbon atom bonded to an $-SH$ group, *sulfides* have two carbon atoms bonded to the same sulfur, and *disulfides* have carbon atoms bonded to two sulfurs that are joined together. In all cases, the bonds are polar, with the carbon atom bearing a partial positive charge ($\delta+$) and the electronegative atom bearing a partial negative charge ($\delta-$).

Alkyl halide (haloalkane) Alcohol Ether Phosphate

Amine Thiol Sulfide Disulfide
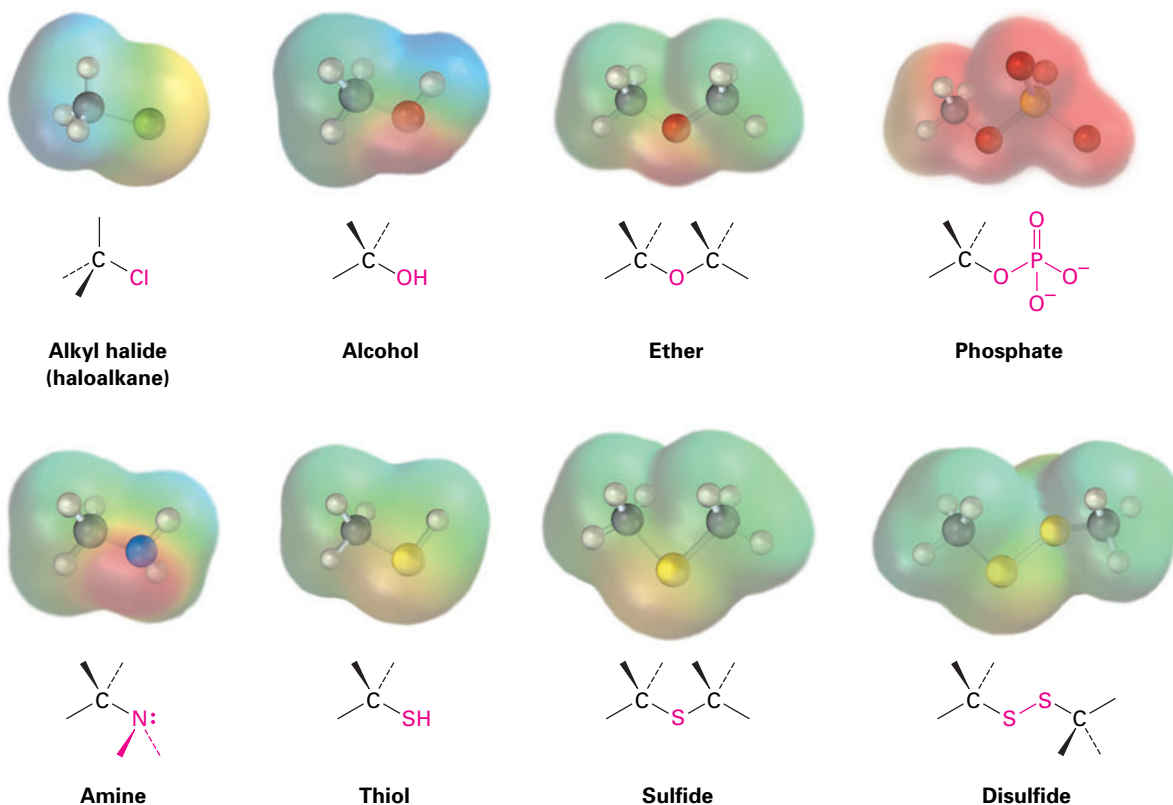
Functional Groups with a Carbon–Oxygen Double Bond (Carbonyl Groups) Note particularly the last seven entries in Table 3.1, which list different families of compounds that contain the *carbonyl group,* C=O (pronounced car-bo-**neel**). Functional groups with a carbon–oxygen double bond are present in the great majority of organic compounds and in practically all biological molecules. These compounds behave similarly in many respects but differ depending on the identity of the atoms bonded to the carbonyl-group carbon. *Aldehydes* have at least one hydrogen bonded to the C=O, *ketones* have two carbons bonded to the C=O, *carboxylic acids* have an $-OH$ group bonded to the C=O, *esters* have an ether-like oxygen bonded to the C=O, *amides* have an amine-like nitrogen

Table 3.1 | **Structures of Some Common Functional Groups**

Name	Structure*	Name ending	Example
Alkene (double bond)	$\text{C}=\text{C}$	-ene	$H_2C=CH_2$ Ethene
Alkyne (triple bond)	$-C\equiv C-$	-yne	$HC\equiv CH$ Ethyne
Arene (aromatic ring)		None	Benzene
Halide	$\text{C}-\text{X}$ (X = F, Cl, Br, I)	None	CH_3Cl Chloromethane
Alcohol	$\text{C}-\text{OH}$	-ol	CH_3OH Methanol
Ether	$\text{C}-\text{O}-\text{C}$	ether	CH_3OCH_3 Dimethyl ether
Monophosphate	$\text{C}-\text{O}-\overset{O}{\underset{O^-}{P}}-O^-$	phosphate	$CH_3OPO_3{}^{2-}$ Methyl phosphate
Amine	$\text{C}-\text{N:}$	-amine	CH_3NH_2 Methylamine
Imine (Schiff base)	$\text{C}-\overset{:N}{\underset{}{C}}-\text{C}$	None	$\overset{NH}{\underset{}{\|}}$ CH_3CCH_3 Acetone imine
Nitrile	$-C\equiv N$	-nitrile	$CH_3C\equiv N$ Ethanenitrile
Nitro	$\text{C}-\overset{O}{\underset{}{\overset{+}{N}}}-O^-$	None	CH_3NO_2 Nitromethane
Thiol	$\text{C}-\text{SH}$	-thiol	CH_3SH Methanethiol

*The bonds whose connections aren't specified are assumed to be attached to carbon or hydrogen atoms in the rest of the molecule.

(continued)

**Table 3.1** | **Structures of Some Common Functional Groups** *(continued)*

Name	Structure*	Name ending	Example
Sulfide		*sulfide*	CH_3SCH_3 Dimethyl sulfide
Disulfide		*disulfide*	CH_3SSCH_3 Dimethyl disulfide
Carbonyl			
Aldehyde		*-al*	CH_3CH (with O double bond) Ethanal
Ketone		*-one*	CH_3CCH_3 (with O double bond) Propanone
Carboxylic acid		*-oic acid*	CH_3COH (with O double bond) Ethanoic acid
Ester		*-oate*	CH_3COCH_3 (with O double bond) Methyl ethanoate
Amide		*-amide*	CH_3CNH_2 (with O double bond) Ethanamide
Carboxylic acid anhydride		*-oic anhydride*	CH_3COCCH_3 (with two O double bonds) Ethanoic anhydride
Carboxylic acid chloride		*-oyl chloride*	CH_3CCl (with O double bond) Ethanoyl chloride

*The bonds whose connections aren't specified are assumed to be attached to carbon or hydrogen atoms in the rest of the molecule.

bonded to the C=O, *acid chlorides* have a chlorine bonded to the C=O, and so on. The carbonyl carbon atom bears a partial positive charge ($\delta+$), and the oxygen bears a partial negative charge ($\delta-$).
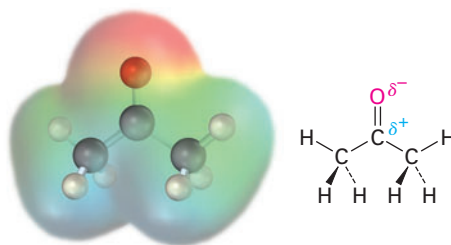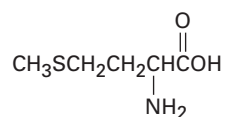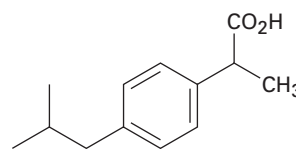

Acetone—a typical carbonyl compound

Aldehyde   Ketone   Carboxylic acid   Ester

Thioester   Amide   Acid chloride
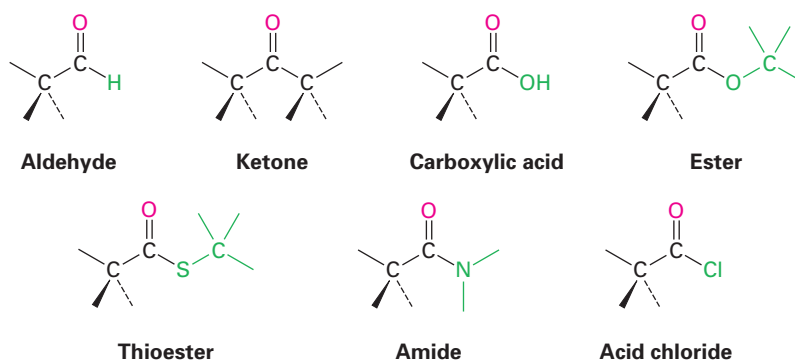
Problem 3.1 Identify the functional groups in each of the following molecules:

(a) Methionine, an amino acid:

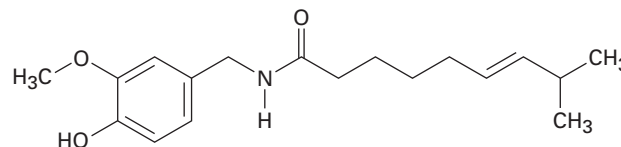$$CH_3SCH_2CH_2\underset{\underset{NH_2}{|}}{\overset{\overset{O}{\|}}{C}}HCOH$$

**(b)** Ibuprofen, a pain reliever:

(c) Capsaicin, the pungent substance in chili peppers:

Problem 3.2 Propose structures for simple molecules that contain the following functional groups:
(a) Alcohol   **(b)** Aromatic ring   **(c)** Carboxylic acid
(d) Amine   **(e)** Both ketone and amine   **(f)** Two double bonds

Problem 3.3 | Identify the functional groups in the following model of arecoline, a veterinary drug used to control worms in animals. Convert the drawing into a line-bond structure and a molecular formula (red = O, blue = N).
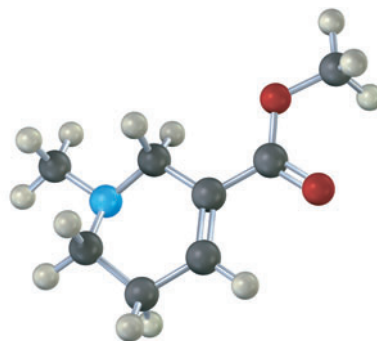

3.2 | Alkanes and Alkane Isomers

Before beginning a systematic study of the different functional groups, let's look first at the simplest family of molecules—the *alkanes*—to develop some general ideas that apply to all families. We saw in Section 1.7 that the carbon–carbon single bond in ethane results from σ (head-on) overlap of carbon sp^3 orbitals. If we imagine joining three, four, five, or even more carbon atoms by C−C single bonds, we can generate the large family of molecules called **alkanes**.

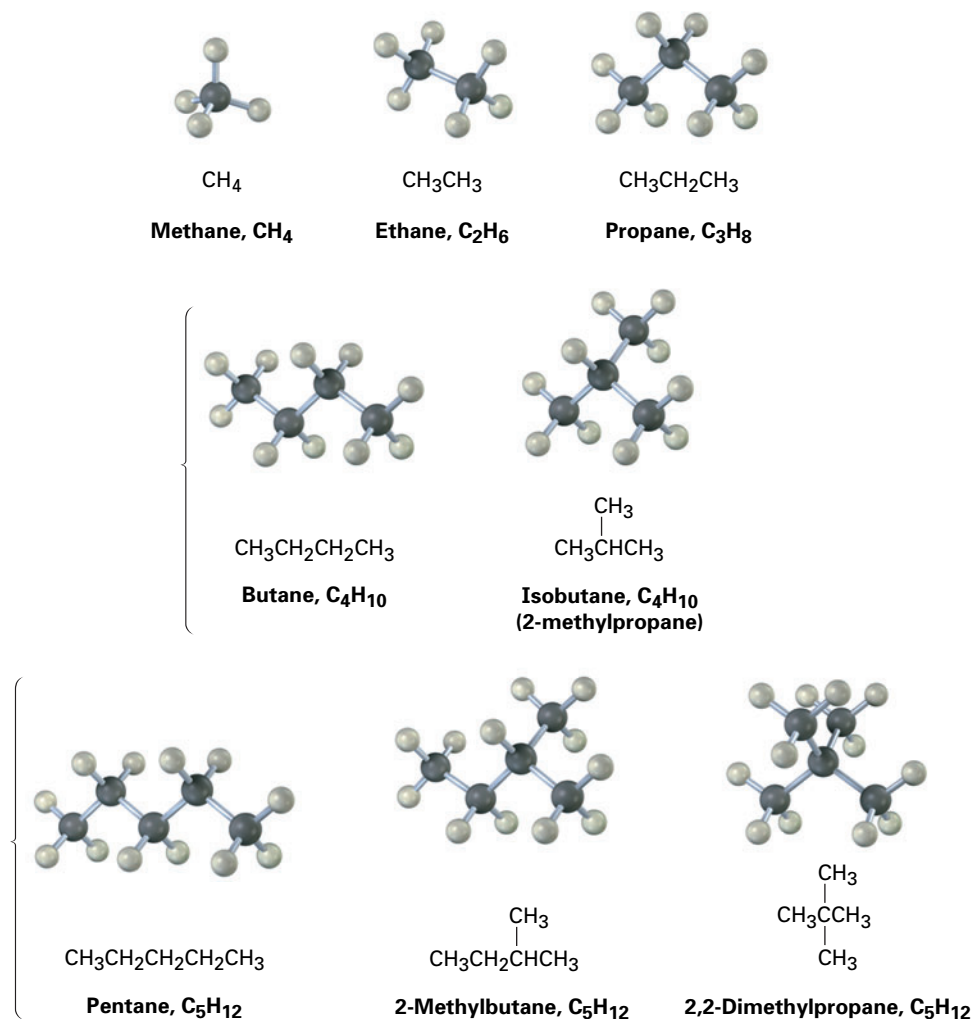**Methane** **Ethane** **Propane** **Butane**
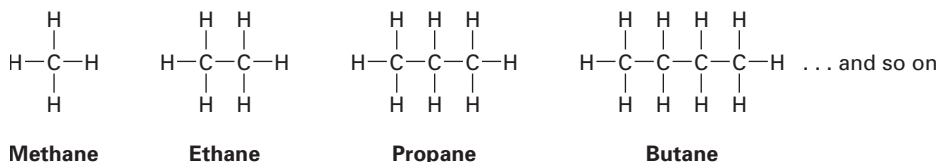
Alkanes are often described as *saturated hydrocarbons*—**hydrocarbons** because they contain only carbon and hydrogen; **saturated** because they have only C−C and C−H single bonds and thus contain the maximum possible number of hydrogens per carbon. They have the general formula C_nH_{2n+2}, where n is an integer. Alkanes are also occasionally referred to as **aliphatic** compounds, a name derived from the Greek *aleiphas,* meaning "fat." We'll see in Section 27.1 that many animal fats contain long carbon chains similar to alkanes.
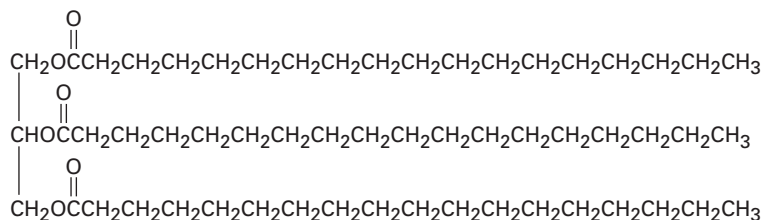
A typical animal fat

Think about the ways that carbon and hydrogen might combine to make alkanes. With one carbon and four hydrogens, only one structure is possible: methane, CH_4. Similarly, there is only one combination of two carbons with six hydrogens (ethane, CH_3CH_3) and only one combination of three carbons with eight hydrogens (propane, $CH_3CH_2CH_3$). If larger numbers of carbons and hydrogens combine, however, more than one structure is possible. For example, there are *two* substances with the formula C_4H_{10}: the four carbons can all be in a row (butane), or they can branch (isobutane). Similarly, there are three C_5H_{12} molecules, and so on for larger alkanes.

CH_4　　　　CH_3CH_3　　　　$CH_3CH_2CH_3$

Methane, CH_4　　　**Ethane, C_2H_6**　　　**Propane, C_3H_8**

$CH_3CH_2CH_2CH_3$

$$CH_3CHCH_3$$
$$\overset{\displaystyle CH_3}{|}$$

Butane, C_4H_{10}　　　**Isobutane, C_4H_{10}**
(2-methylpropane)

$CH_3CH_2CH_2CH_2CH_3$

$$CH_3CH_2CHCH_3$$
with CH_3

$$CH_3CCH_3$$
with CH_3 above and CH_3 below

Pentane, C_5H_{12}　　　**2-Methylbutane, C_5H_{12}**　　　**2,2-Dimethylpropane, C_5H_{12}**

Compounds like butane and pentane, whose carbons are all connected in a row, are called **straight-chain alkanes**, or *normal alkanes.* Compounds like 2-methylpropane (isobutane), 2-methylbutane, and 2,2-dimethylpropane, whose carbon chains branch, are called **branched-chain alkanes**. The difference between the two is that you can draw a line connecting all the carbons of a straight-chain alkane without retracing your path or lifting your pencil from
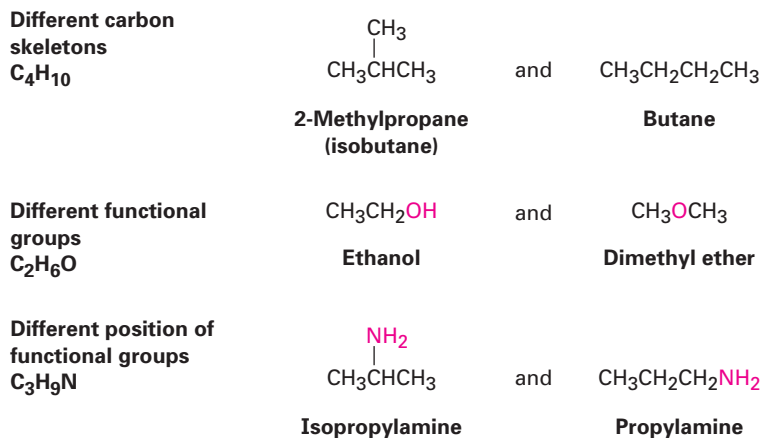
Table 3.2	Number of Alkane Isomers
Formula	**Number of isomers**
C_6H_{14}	5
C_7H_{16}	9
C_8H_{18}	18
C_9H_{20}	35
$C_{10}H_{22}$	75
$C_{15}H_{32}$	4,347
$C_{20}H_{42}$	366,319
$C_{30}H_{62}$	4,111,846,763

the paper. For a branched-chain alkane, however, you either have to retrace your path or lift your pencil from the paper to draw a line connecting all the carbons.

Compounds like the two C_4H_{10} molecules and the three C_5H_{12} molecules, which have the same formula but different structures, are called *isomers,* from the Greek *isos + meros,* meaning "made of the same parts." **Isomers** are compounds that have the same numbers and kinds of atoms but differ in the way the atoms are arranged. Compounds like butane and isobutane, whose atoms are connected differently, are called **constitutional isomers**. We'll see shortly that other kinds of isomers are also possible, even among compounds whose atoms are connected in the same order. As Table 3.2 shows, the number of possible alkane isomers increases dramatically as the number of carbon atoms increases.

Constitutional isomerism is not limited to alkanes—it occurs widely throughout organic chemistry. Constitutional isomers may have different carbon skeletons (as in isobutane and butane), different functional groups (as in ethanol and dimethyl ether), or different locations of a functional group along the chain (as in isopropylamine and propylamine). Regardless of the reason for the isomerism, constitutional isomers are always different compounds with different properties, but with the same formula.

Different carbon skeletons
C_4H_{10}

$$CH_3CHCH_3 \overset{\displaystyle CH_3}{|} \quad \text{and} \quad CH_3CH_2CH_2CH_3$$

2-Methylpropane (isobutane)   **Butane**

Different functional groups
C_2H_6O

$$CH_3CH_2OH \quad \text{and} \quad CH_3OCH_3$$

Ethanol   **Dimethyl ether**

Different position of functional groups
C_3H_9N

$$CH_3CHCH_3 \overset{\displaystyle NH_2}{|} \quad \text{and} \quad CH_3CH_2CH_2NH_2$$

Isopropylamine   **Propylamine**

A given alkane can be drawn arbitrarily in many ways. For example, the straight-chain, four-carbon alkane called butane can be represented by any of the structures shown in Figure 3.2. These structures don't imply any particular three-dimensional geometry for butane; they indicate only the connections among atoms. In practice, as noted in Section 1.12, chemists rarely draw all the bonds in a molecule and usually refer to butane by the condensed structure, $CH_3CH_2CH_2CH_3$ or $CH_3(CH_2)_2CH_3$. Still more simply, butane can even be represented as $n\text{-}C_4H_{10}$, where n denotes *normal* (straight-chain) butane.

Figure 3.2 Some representations of butane, C_4H_{10}. The molecule is the same regardless of how it's drawn. These structures imply only that butane has a continuous chain of four carbon atoms; they do not imply any specific geometry.

$$CH_3-CH_2-CH_2-CH_3 \qquad CH_3CH_2CH_2CH_3 \qquad CH_3(CH_2)_2CH_3$$
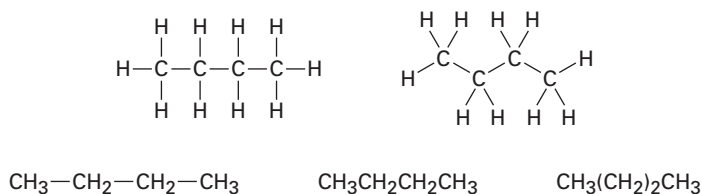
Straight-chain alkanes are named according to the number of carbon atoms they contain, as shown in Table 3.3. With the exception of the first four compounds—methane, ethane, propane, and butane—whose names have historical roots, the alkanes are named based on Greek numbers. The suffix -ane is added to the end of each name to indicate that the molecule identified is an alkane. Thus, pentane is the five-carbon alkane, hexane is the six-carbon alkane, and so on. We'll soon see that these alkane names form the basis for naming all other organic compounds, so at least the first ten should be memorized.

Table 3.3   Names of Straight-Chain Alkanes

Number of carbons (n)	Name	Formula (C_nH_{2n+2})
1	Methane	CH_4
2	Ethane	C_2H_6
3	Propane	C_3H_8
4	Butane	C_4H_{10}
5	Pentane	C_5H_{12}
6	Hexane	C_6H_{14}
7	Heptane	C_7H_{16}
8	Octane	C_8H_{18}
9	Nonane	C_9H_{20}
10	Decane	$C_{10}H_{22}$
11	Undecane	$C_{11}H_{24}$
12	Dodecane	$C_{12}H_{26}$
13	Tridecane	$C_{13}H_{28}$
20	Icosane	$C_{20}H_{42}$
30	Triacontane	$C_{30}H_{62}$

WORKED EXAMPLE 3.1

Drawing the Structures of Isomers

Propose structures for two isomers with the formula C_2H_7N.

Strategy   We know that carbon forms four bonds, nitrogen forms three, and hydrogen forms one. Write down the carbon atoms first, and then use a combination of trial and error plus intuition to put the pieces together.

Solution   There are two isomeric structures. One has the connection $C-C-N$, and the other has the connection $C-N-C$.
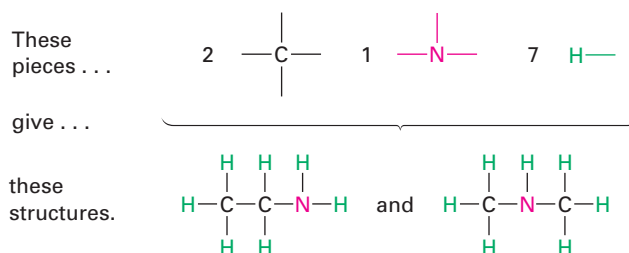
Problem 3.4 | Draw structures of the five isomers of C_6H_{14}.

Problem 3.5 | Propose structures that meet the following descriptions:
(a) Two isomeric esters with the formula $C_5H_{10}O_2$
(b) Two isomeric nitriles with the formula C_4H_7N
(c) Two isomeric disulfides with the formula $C_4H_{10}S_2$

Problem 3.6 | How many isomers are there with the following descriptions?
(a) Alcohols with the formula C_3H_8O
(b) Bromoalkanes with the formula C_4H_9Br

3.3 | Alkyl Groups

If you imagine removing a hydrogen atom from an alkane, the partial structure that remains is called an **alkyl group**. Alkyl groups are not stable compounds themselves, they are simply parts of larger compounds. Alkyl groups are named by replacing the -*ane* ending of the parent alkane with an -*yl* ending. For example, removal of a hydrogen from methane, CH_4, generates a *methyl* group, $-CH_3$, and removal of a hydrogen from ethane, CH_3CH_3, generates an *ethyl* group, $-CH_2CH_3$. Similarly, removal of a hydrogen atom from the end carbon of any straight-chain alkane gives the series of straight-chain alkyl groups shown in Table 3.4. Combining an alkyl group with any of the functional groups listed earlier makes it possible to generate and name many thousands of compounds. For example:

Methane	**A methyl group**	**Methyl alcohol (methanol)**	**Methylamine**
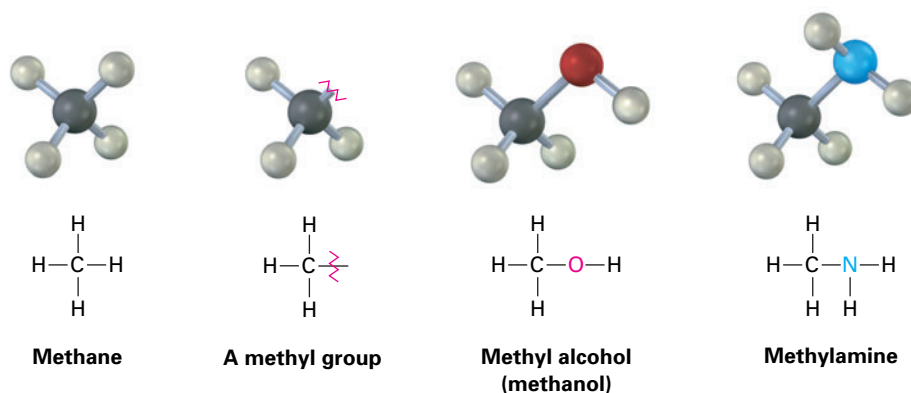
Table 3.4 | **Some Straight-Chain Alkyl Groups**

Alkane	Name	Alkyl group	Name (abbreviation)
CH_4	Methane	$-CH_3$	Methyl (Me)
CH_3CH_3	Ethane	$-CH_2CH_3$	Ethyl (Et)
$CH_3CH_2CH_3$	Propane	$-CH_2CH_2CH_3$	Propyl (Pr)
$CH_3CH_2CH_2CH_3$	Butane	$-CH_2CH_2CH_2CH_3$	Butyl (Bu)
$CH_3CH_2CH_2CH_2CH_3$	Pentane	$-CH_2CH_2CH_2CH_2CH_3$	Pentyl, or amyl

Just as straight-chain alkyl groups are generated by removing a hydrogen from an *end* carbon, branched alkyl groups are generated by removing a hydrogen atom from an *internal* carbon. Two 3-carbon alkyl groups and four 4-carbon alkyl groups are possible (Figure 3.3).

**Figure 3.3** Alkyl groups generated from straight-chain alkanes.

C_3

$CH_3CH_2CH_3$	$CH_3CH_2CH_2-$	CH_3CHCH_3
Propane	**Propyl**	**Isopropyl**

C_4

$CH_3CH_2CH_2CH_3$	$CH_3CH_2CH_2CH_2-$	$CH_3CH_2CHCH_3$
Butane	**Butyl**	*sec*-**Butyl**

		CH_3
CH_3	CH_3	CH_3-C-
CH_3CHCH_3	CH_3CHCH_2-	CH_3
Isobutane	**Isobutyl**	*tert*-**Butyl**
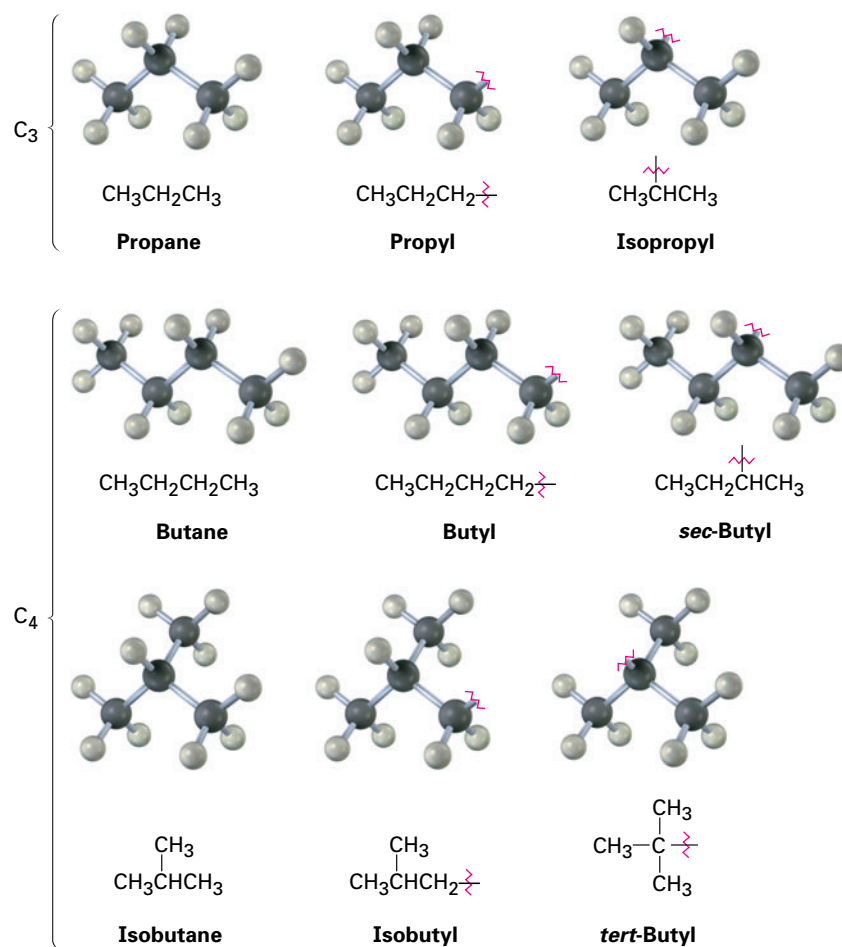
One further word about naming alkyl groups: the prefixes *sec-* (for secondary) and *tert-* (for tertiary) used for the C_4 alkyl groups in Figure 3.3 refer to *the number of other carbon atoms attached to the branching carbon atom.* There are four possibilities: primary (1°), secondary (2°), tertiary (3°), and quaternary (4°).

Primary carbon (1°) is bonded to one other carbon.	*Secondary* carbon (2°) is bonded to two other carbons.	*Tertiary* carbon (3°) is bonded to three other carbons.	*Quaternary* carbon (4°) is bonded to four other carbons.
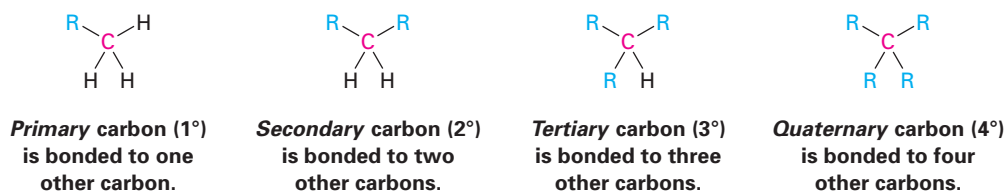
The symbol **R** is used in organic chemistry to represent a *generalized* organic group. The R group can be methyl, ethyl, propyl, or any of a multitude of others.

You might think of **R** as representing the **R**est of the molecule, which we aren't bothering to specify.

The terms *primary, secondary, tertiary,* and *quaternary* are routinely used in organic chemistry, and their meanings need to become second nature. For example, if we were to say, "Citric acid is a tertiary alcohol," we would mean that it has an alcohol functional group ($-OH$) bonded to a carbon atom that is itself bonded to three other carbons. (These other carbons may in turn connect to other functional groups).

General class of tertiary
alcohols, R_3COH

Citric acid—a specific
tertiary alcohol
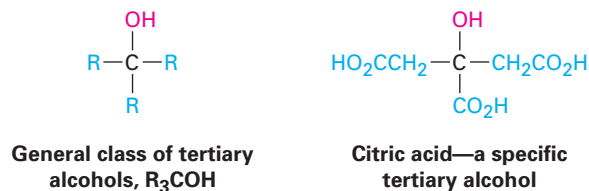
In addition, we also speak about hydrogen atoms as being primary, secondary, or tertiary. Primary hydrogen atoms are attached to primary carbons (RCH_3), secondary hydrogens are attached to secondary carbons (R_2CH_2), and tertiary hydrogens are attached to tertiary carbons (R_3CH). There is, of course, no such thing as a quaternary hydrogen. (Why?)
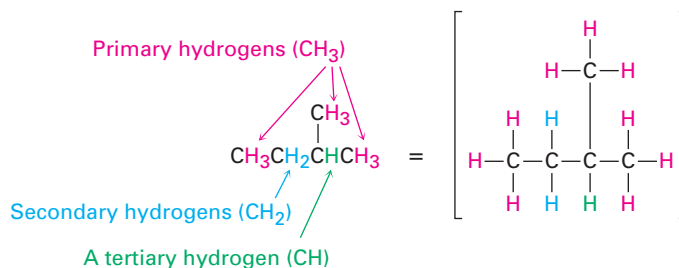
Problem 3.7 Draw the eight 5-carbon alkyl groups (pentyl isomers).

Problem 3.8 Identify the carbon atoms in the following molecules as primary, secondary, tertiary, or quaternary:

(a)
$$CH_3$$
$$CH_3CHCH_2CH_2CH_3$$

(b)
$$CH_3CHCH_3$$
$$CH_3CH_2CHCH_2CH_3$$

(c)
$$CH_3 \quad CH_3$$
$$CH_3CHCH_2CCH_3$$
$$CH_3$$
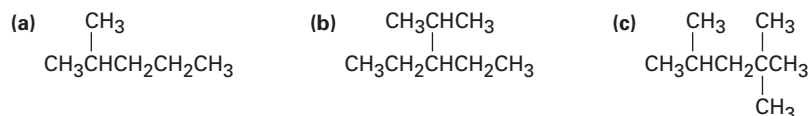
Problem 3.9 Identify the hydrogen atoms on the compounds shown in Problem 3.8 as primary, secondary, or tertiary.

Problem 3.10 Draw structures of alkanes that meet the following descriptions:
(a) An alkane with two tertiary carbons
(b) An alkane that contains an isopropyl group
(c) An alkane that has one quaternary and one secondary carbon

3.4 | Naming Alkanes

In earlier times, when relatively few pure organic chemicals were known, new compounds were named at the whim of their discoverer. Thus, urea (CH_4N_2O) is a crystalline substance isolated from urine; morphine ($C_{17}H_{19}NO_3$) is an analgesic (painkiller) named after Morpheus, the Greek god of dreams; and barbituric acid is a tranquilizing agent said to be named by its discoverer in honor of his friend Barbara.

As the science of organic chemistry slowly grew in the 19th century, so too did the number of known compounds and the need for a systematic method of naming them. The system of nomenclature we'll use in this book is that devised by the International Union of Pure and Applied Chemistry (IUPAC, usually spoken as **eye**-you-pac).

A chemical name typically has four parts in the IUPAC system of nomenclature: prefix, locant, parent, and suffix. The prefix specifies the location and identity of various **substituent** groups in the molecule, the locant gives the location of the primary functional group, the parent selects a main part of the molecule and tells how many carbon atoms are in that part, and the suffix identifies the primary functional group.

<div align="center">

Prefix—**Locant**—**Parent**—**Suffix**

| Where and what are the substituents? | Where is the primary functional group? | How many carbons? | What is the primary functional group? |

</div>

As we cover new functional groups in later chapters, the applicable IUPAC rules of nomenclature will be given. In addition, Appendix A at the back of this book gives an overall view of organic nomenclature and shows how compounds that contain more than one functional group are named. For the present, let's see how to name branched-chain alkanes and learn some general naming rules that are applicable to all compounds.

All but the most complex branched-chain alkanes can be named by following four steps. For a very few compounds, a fifth step is needed.

Step 1   **Find the parent hydrocarbon.**

(a) Find the longest continuous chain of carbon atoms in the molecule, and use the name of that chain as the parent name. The longest chain may not always be apparent from the manner of writing; you may have to "turn corners."

<div align="center">

CH₂CH₃
|
CH₃CH₂CH₂CH—CH₃   Named as a substituted hexane

CH₃
|
CH₂
|
CH₃—CHCH—CH₂CH₃   Named as a substituted heptane
|
CH₂CH₂CH₃

</div>
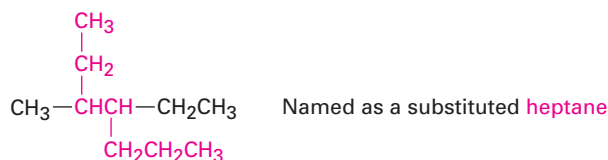
(b) If two different chains of equal length are present, choose the one with the larger number of branch points as the parent.

$$CH_3$$
$$|$$
$$CH_3CHCHCH_2CH_2CH_3$$
$$|$$
$$CH_2CH_3$$
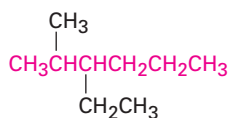
Named as a hexane with *two* substituents

NOT

$$CH_3$$
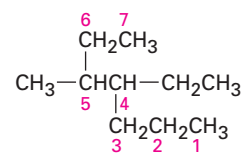$$|$$
$$CH_3CH-CHCH_2CH_2CH_3$$
$$|$$
$$CH_2CH_3$$
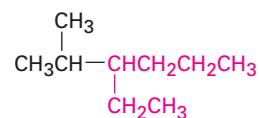
as a hexane with *one* substituent

Step 2   **Number the atoms in the main chain.**

(a) Beginning at the end nearer the first branch point, number each carbon atom in the parent chain.

$$\overset{2}{C}H_2\overset{1}{C}H_3$$
$$|$$
$$CH_3-\overset{3}{C}H\overset{4}{C}H-CH_2CH_3$$
$$|$$
$$\underset{5}{C}H_2\underset{6}{C}H_2\underset{7}{C}H_3$$

NOT

$$\overset{6}{C}H_2\overset{7}{C}H_3$$
$$|$$
$$CH_3-\overset{5}{C}H\overset{4}{C}H-CH_2CH_3$$
$$|$$
$$\underset{3}{C}H_2\underset{2}{C}H_2\underset{1}{C}H_3$$
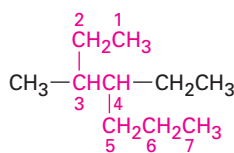
The first branch occurs at C3 in the proper system of numbering, not at C4.

(b) If there is branching an equal distance away from both ends of the parent chain, begin numbering at the end nearer the second branch point.

$$\overset{8}{C}H_2\overset{9}{C}H_3 \quad CH_3 \quad CH_2CH_3$$
$$| \qquad\qquad | \qquad |$$
$$CH_3-\underset{7}{C}H\underset{6}{C}H_2\underset{5}{C}H_2\underset{4}{C}H-\underset{3}{C}H\underset{2}{C}H_2\underset{1}{C}H_3$$

NOT

$$\overset{2}{C}H_2\overset{1}{C}H_3 \quad CH_3 \quad CH_2CH_3$$
$$| \qquad\qquad | \qquad |$$
$$CH_3-\underset{3}{C}H\underset{4}{C}H_2\underset{5}{C}H_2\underset{6}{C}H-\underset{7}{C}H\underset{8}{C}H_2\underset{9}{C}H_3$$
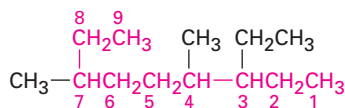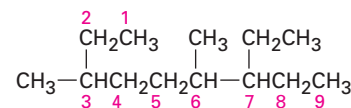
Step 3   **Identify and number the substituents.**

(a) Assign a number, called a *locant,* to each substituent to locate its point of attachment to the parent chain.

$$\overset{9}{C}H_3\overset{8}{C}H_2 \qquad H_3C \quad CH_2CH_3$$
$$| \qquad\qquad\quad | \quad\; |$$
$$CH_3-\underset{7}{C}H\underset{6}{C}H_2\underset{5}{C}H_2\underset{4}{C}H\underset{3}{C}H\underset{2}{C}H_2\underset{1}{C}H_3$$
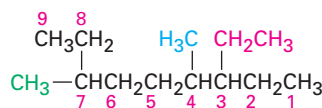
Named as a nonane

Substituents: On C3, CH_2CH_3 (3-ethyl)
On C4, CH_3 (4-methyl)
On C7, CH_3 (7-methyl)

(b) If there are two substituents on the same carbon, give both the same number. There must be as many numbers in the name as there are substituents.

$$CH_3 \quad CH_3$$
$$\overset{4}{|} \qquad\; |$$
$$CH_3CH_2\overset{}{C}CH_2CHCH_3$$
$$\underset{6}{\;}\;\underset{5}{\;}\;|\underset{3}{\;}\;\underset{2}{\;}\;\underset{1}{\;}$$
$$CH_2CH_3$$
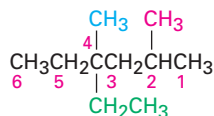
Named as a hexane

Substituents: On C2, CH_3 (2-methyl)
On C4, CH_3 (4-methyl)
On C4, CH_2CH_3 (4-ethyl)

**Step 4**   **Write the name as a single word.**

Use hyphens to separate the different prefixes, and use commas to separate numbers. If two or more different substituents are present, cite them in alphabetical order. If two or more identical substituents are present, use one of the multiplier prefixes *di-*, *tri-*, *tetra-*, and so forth, but don't use these prefixes for alphabetizing. Full names for some of the examples we have been using follow.
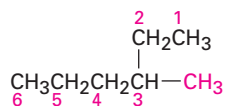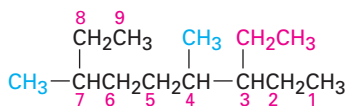
3-Methylhexane   **3-Ethyl-4,7-dimethylnonane**   **3-Ethyl-2-methylhexane**
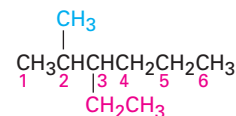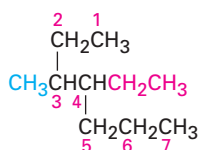
4-Ethyl-3-methylheptane   **4-Ethyl-2,4-dimethylhexane**
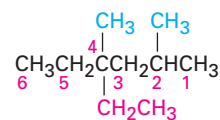
Step 5   **Name a complex substituent as though it were itself compound.**

In some particularly complex cases, a fifth step is necessary. It occasionally happens that a substituent on the main chain has sub-branching. In the following case, for instance, the substituent at C6 is a three-carbon chain with a methyl sub-branch. To name the compound fully, the complex substituent must first be named.
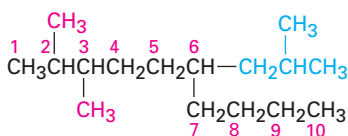
Named as a 2,3,6-   **A 2-methylpropyl group**
trisubstituted decane
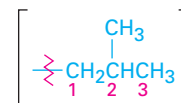
Begin numbering the branched substituent at its point of its attachment to the main chain, and identify it as a 2-methylpropyl group. The substituent is alphabetized according to the first letter of its complete name, including any numerical prefix, and is set off in parentheses when naming the entire molecule.
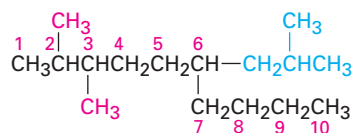
2,3-Dimethyl-6-(2-methylpropyl)decane

As a further example:

5-(1,2-Dimethylpropyl)-2-methylnonane   **A 1,2-dimethylpropyl group**
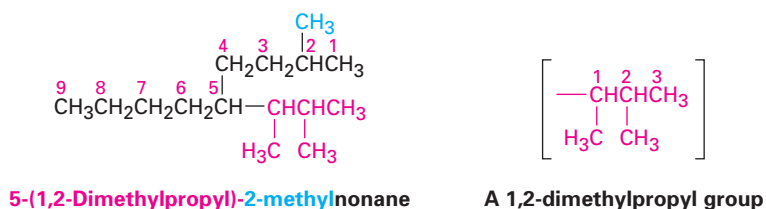
For historical reasons, some of the simpler branched-chain alkyl groups also have nonsystematic, common names, as noted earlier.

1. Three-carbon alkyl group:

Isopropyl (*i*-Pr)
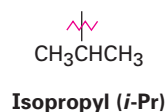
2. Four-carbon alkyl groups:
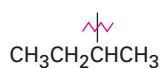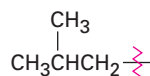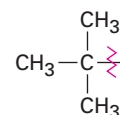
sec-Butyl   **Isobutyl**   **tert-Butyl**
(sec-Bu)   **(t-butyl or t-Bu)**

3. Five-carbon alkyl groups:
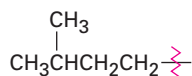
Isopentyl, also called   **Neopentyl**   **tert-Pentyl, also called**
isoamyl (i-amyl)   **tert-amyl (t-amyl)**

The common names of these simple alkyl groups are so well entrenched in the chemical literature that IUPAC rules make allowance for them. Thus, the following compound is properly named either 4-(1-methylethyl)heptane or 4-isopropylheptane. There is no choice but to memorize these common names; fortunately, there are only a few of them.
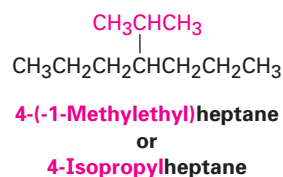
4-(-1-Methylethyl)heptane
or
4-Isopropylheptane

When writing an alkane name, the nonhyphenated prefix iso- is considered part of the alkyl-group name for alphabetizing purposes, but the hyphenated and italicized prefixes *sec*- and *tert*- are not. Thus, isopropyl and isobutyl are listed alphabetically under *i*, but *sec*-butyl and *tert*-butyl are listed under *b*.

WORKED EXAMPLE 3.2   *Practice in Naming Alkanes*

What is the IUPAC name of the following alkane?

$$CH_3CHCH_2CH_2CH_2CHCH_3$$

(substituents: CH_2CH_3 and CH_3)
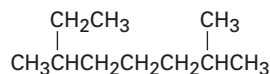
Strategy   Find the longest continuous carbon chain in the molecule, and use that as the parent name. This molecule has a chain of eight carbons—octane—with two methyl substituents. (You have to turn corners to see it.) Numbering from the end nearer the first methyl substituent indicates that the methyls are at C2 and C6

Solution

$$\underset{6\ \ \ 5\ \ \ \ 4\ \ \ \ 3\ \ \ \ 2\ \ \ 1}{CH_3CHCH_2CH_2CH_2CHCH_3}$$

(substituents: $\overset{7\ \ \ 8}{CH_2CH_3}$ and CH_3)

2,6-Dimethyloctane
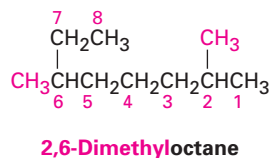
WORKED EXAMPLE 3.3   *Converting a Chemical Name into a Structure*

Draw the structure of 3-isopropyl-2-methylhexane.

Strategy   This is the reverse of Worked Example 3.2 and uses a reverse strategy. Look at the parent name (hexane), and draw its carbon structure.

$$C-C-C-C-C-C \qquad \textbf{Hexane}$$
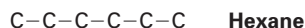
Next, find the substituents (3-isopropyl and 2-methyl), and place them on the proper carbons.

$$\underset{1\ \ \ 2|\ \ \ 3\ \ \ 4\ \ \ 5\ \ \ 6}{C-C-C-C-C-C}$$

CH₃CHCH₃ ←——— **An isopropyl group at C3**

CH₃ ←——— **A methyl group at C2**
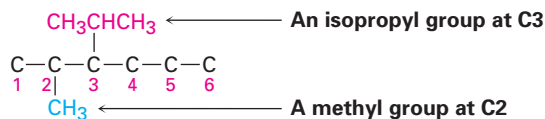
Finally, add hydrogens to complete the structure.

Solution

$$CH_3CHCHCH_2CH_2CH_3$$

(substituents: CH_3CHCH_3 and CH_3)

3-Isopropyl-2-methylhexane
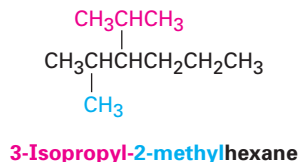
Problem 3.11 | Give IUPAC names for the following compounds:

(a) The three isomers of C_5H_{12}

(b)

$$CH_3CH_2\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}HCHCH_3$$

(c)

$$(CH_3)_2CHCH_2\underset{}{\overset{\overset{CH_3}{|}}{C}}HCH_3$$

(d)

$$(CH_3)_3CCH_2CH_2\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}H$$
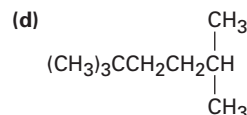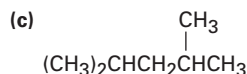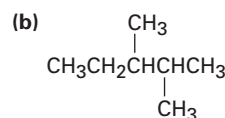
Problem 3.12 | Draw structures corresponding to the following IUPAC names:
(a) 3,4-Dimethylnonane   **(b)** 3-Ethyl-4,4-dimethylheptane
(c) 2,2-Dimethyl-4-propyloctane   **(d)** 2,2,4-Trimethylpentane

Problem 3.13 | Name the eight 5-carbon alkyl groups you drew in Problem 3.7.

Problem 3.14 | Give the IUPAC name for the following hydrocarbon, and convert the drawing into a skeletal structure.
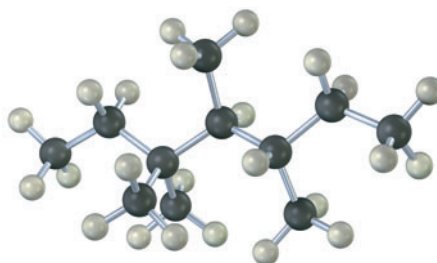
3.5 | **Properties of Alkanes**

Alkanes are sometimes referred to as *paraffins,* a word derived from the Latin *parum affinis,* meaning "little affinity." This term aptly describes their behavior, for alkanes show little chemical affinity for other substances and are chemically inert to most laboratory reagents. They are also relatively inert biologically and are not often involved in the chemistry of living organisms. Alkanes do, however, react with oxygen, halogens, and a few other substances under appropriate conditions.

Reaction with oxygen occurs during combustion in an engine or furnace when the alkane is used as a fuel. Carbon dioxide and water are formed as products, and a large amount of heat is released. For example, methane (natural gas) reacts with oxygen according to the equation

$$CH_4 + 2\,O_2 \qquad CO_2 + 2\,H_2O + \text{890 kJ/mol (213 kcal/mol)}$$
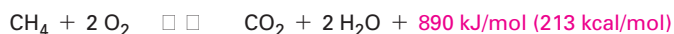
The reaction of an alkane with Cl_2 occurs when a mixture of the two is irradiated with ultraviolet light (denoted $h\nu$, where ν is the Greek letter nu).

Depending on the relative amounts of the two reactants and on the time allowed, a sequential substitution of the alkane hydrogen atoms by chlorine occurs, leading to a mixture of chlorinated products. Methane, for instance, reacts with Cl_2 to yield a mixture of CH_3Cl, CH_2Cl_2, $CHCl_3$, and CCl_4. We'll look at this reaction in more detail in Section 5.3.

$$CH_4 \ + \ Cl_2 \ \xrightarrow{\ h\nu\ } \ CH_3Cl \ + \ HCl$$
$$\xrightarrow[\;]{Cl_2} \ CH_2Cl_2 \ + \ HCl$$
$$\xrightarrow[\;]{Cl_2} \ CHCl_3 \ + \ HCl$$
$$\xrightarrow[\;]{Cl_2} \ CCl_4 \ + \ HCl$$

Alkanes show regular increases in both boiling point and melting point as molecular weight increases (Figure 3.4), an effect due to the presence of weak dispersion forces between molecules (Section 2.13). Only when sufficient energy is applied to overcome these forces does the solid melt or liquid boil. As you might expect, dispersion forces increase as molecular size increases, accounting for the higher melting and boiling points of larger alkanes.

Active Figure 3.4 A plot of melting and boiling points versus number of carbon atoms for the C_1–C_{14} alkanes. There is a regular increase with molecular size. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*

Another interesting effect seen in alkanes is that increased branching lowers an alkane's boiling point. Thus, pentane has no branches and boils at 36.1 °C, isopentane (2-methylbutane) has one branch and boils at 27.85 °C, and neopentane (2,2-dimethylpropane) has two branches and boils at 9.5 °C. Similarly, octane boils at 125.7 °C, whereas isooctane (2,2,4-trimethylpentane) boils at 99.3 °C. Branched-chain alkanes are lower-boiling because they are more nearly spherical than straight-chain alkanes, have smaller surface areas, and consequently have smaller dispersion forces.

3.6 | Conformations of Ethane

Up to this point, we've viewed molecules primarily in a two-dimensional way and have given little thought to any consequences that might arise from the spatial arrangement of atoms in molecules. Now it's time to add a third dimension to our study. **Stereochemistry** is the branch of chemistry concerned with the three-dimensional aspects of molecules. We'll see on many occasions in future chapters that the exact three-dimensional structure of a molecule is often crucial to determining its properties and biological behavior.

We know from Section 1.5 that σ bonds are cylindrically symmetrical. In other words, the intersection of a plane cutting through a carbon–carbon single-bond orbital looks like a circle. Because of this cylindrical symmetry, *rotation* is possible around carbon–carbon bonds in open-chain molecules. In ethane, for instance, rotation around the C–C bond occurs freely, constantly changing the spatial relationships between the hydrogens on one carbon and those on the other (Figure 3.5).

Active Figure 3.5 Rotation occurs around the carbon–carbon single bond in ethane because of σ bond cylindrical symmetry. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*
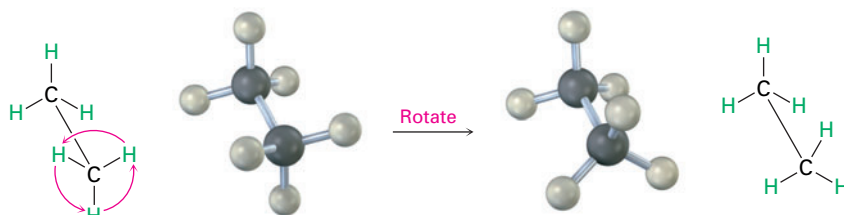
Melvin S. Newman

Melvin S. Newman (1908–1993) was born in New York and received his Ph.D. in 1932 from Yale University. He was professor of chemistry at the Ohio State University (1936–1973), where he was active in both research and chemical education.

The different arrangements of atoms that result from bond rotation are called **conformations**, and molecules that have different arrangements are called conformational isomers, or **conformers**. Unlike constitutional isomers, however, different conformers can't usually be isolated because they interconvert too rapidly.

Conformational isomers are represented in two ways, as shown in Figure 3.6. A *sawhorse representation* views the carbon–carbon bond from an oblique angle and indicates spatial orientation by showing all C–H bonds. A **Newman projection** views the carbon–carbon bond directly end-on and represents the two carbon atoms by a circle. Bonds attached to the front carbon are represented by lines to the center of the circle, and bonds attached to the rear carbon are represented by lines to the edge of the circle.

Figure 3.6 A sawhorse representation and a Newman projection of ethane. The sawhorse representation views the molecule from an oblique angle, while the Newman projection views the molecule end-on. Note that the molecular model of the Newman projection appears at first to have six atoms attached to a single carbon. Actually, the front carbon, with three attached green atoms, is directly in front of the rear carbon, with three attached red atoms.

Sawhorse representation

Newman projection
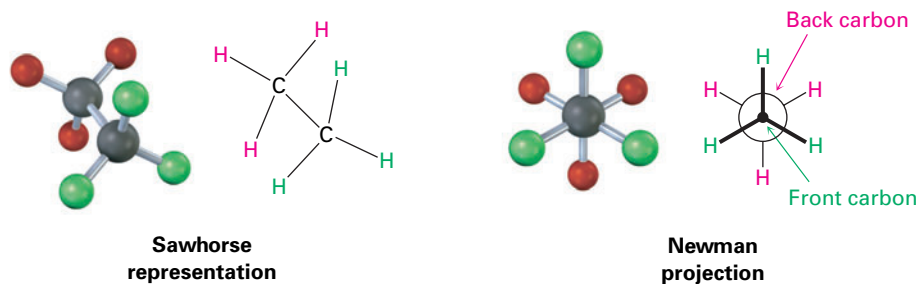
Despite what we've just said, we actually don't observe *perfectly* free rotation in ethane. Experiments show that there is a small (12 kJ/mol; 2.9 kcal/mol) barrier to rotation and that some conformers are more stable than others. The lowest-energy, most stable conformer is the one in which all six C−H bonds are as far away from one another as possible—**staggered** when viewed end-on in a Newman projection. The highest-energy, least stable conformer is the one in which the six C−H bonds are as close as possible—**eclipsed** in a Newman projection. At any given instant, about 99% of ethane molecules have an approximately staggered conformation and only about 1% are near the eclipsed conformation.

4.0 kJ/mol

4.0 kJ/mol   4.0 kJ/mol

Rotate rear carbon 60°

Ethane—staggered conformation

Ethane—eclipsed conformation
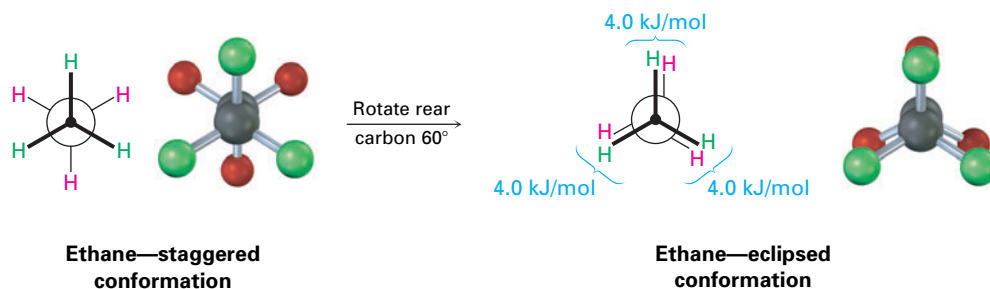
The extra 12 kJ/mol of energy present in the eclipsed conformer of ethane is called **torsional strain**. Its cause has been the subject of controversy, but the major factor is an interaction between C−H bonding orbitals on one carbon with antibonding orbitals on the adjacent carbon, which stabilizes the staggered conformer relative to the eclipsed conformer. Because the total strain of 12 kJ/mol arises from three equal hydrogen–hydrogen eclipsing interactions, we can assign a value of approximately 4.0 kJ/mol (1.0 kcal/mol) to each single interaction. The barrier to rotation that results can be represented on a graph of potential energy versus degree of rotation in which the angle between C−H bonds on front and back carbons as viewed end-on (the *dihedral angle*) goes full circle from 0° to 360°. Energy minima occur at staggered conformations, and energy maxima occur at eclipsed conformations, as shown in Figure 3.7.

Figure 3.7 A graph of potential energy versus bond rotation in ethane. The staggered conformers are 12 kJ/mol lower in energy than the eclipsed conformers.

Eclipsed conformations

Energy

12 kJ/mol

0°   60°   120°   180°   240°   300°   360°
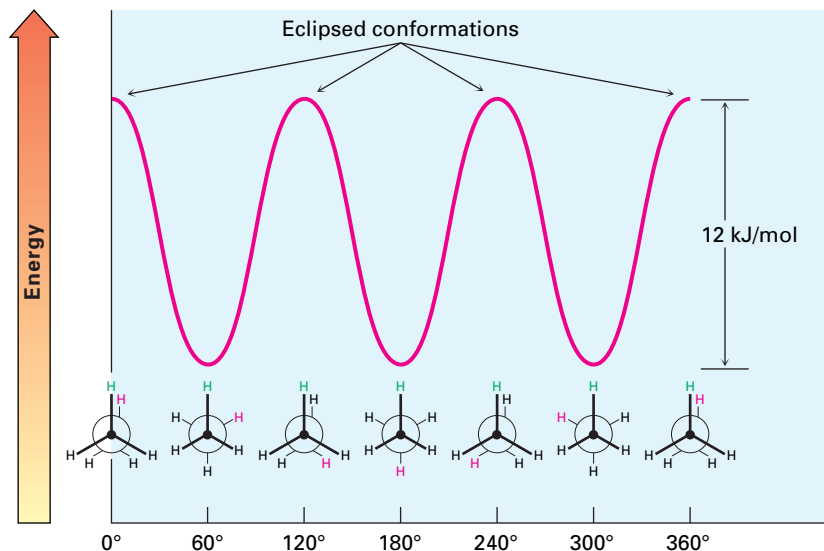
3.7 | Conformations of Other Alkanes

Propane, the next higher member in the alkane series, also has a torsional barrier that results in hindered rotation around the carbon–carbon bonds. The barrier is slightly higher in propane than in ethane—a total of 14 kJ/mol (3.4 kcal/mol) versus 12 kJ/mol.

The eclipsed conformer of propane has three interactions—two ethane-type hydrogen–hydrogen interactions and one additional hydrogen–methyl interaction. Since each eclipsing H   H interaction is the same as that in ethane and thus has an energy "cost" of 4.0 kJ/mol, we can assign a value of $14 - (2 \times 4.0) = 6.0$ kJ/mol (1.4 kcal/mol) to the eclipsing H CH_3 interaction (Figure 3.8).

Figure 3.8 Newman projections of propane showing staggered and eclipsed conformations. The staggered conformer is lower in energy by 14 kJ/mol.

Staggered propane   **Eclipsed propane**
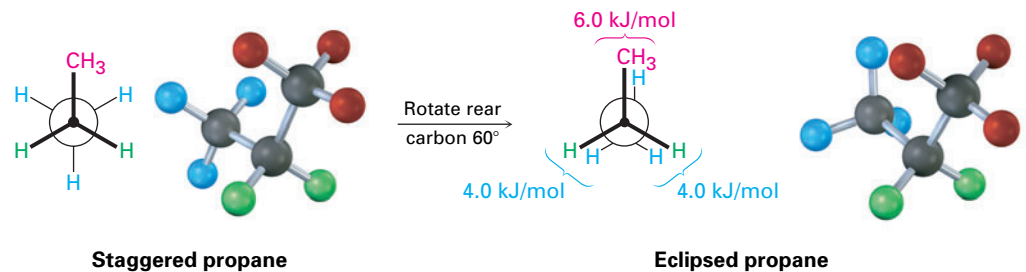
The conformational situation becomes more complex for larger alkanes because not all staggered conformations have the same energy and not all eclipsed conformations have the same energy. In butane, for instance, the lowest-energy arrangement, called the **anti conformation**, is the one in which the two methyl groups are as far apart as possible—180° away from each other. As rotation around the C2–C3 bond occurs, an eclipsed conformation is reached in which there are two CH_3 H interactions and one H   H interaction. Using the energy values derived previously from ethane and propane, this eclipsed conformation is more strained than the anti conformation by 2×6.0 kJ/mol + 4.0 kJ/mol (two CH_3 H interactions plus one H   H interaction), for a total of 16 kJ/mol (3.8 kcal/mol).

Butane—anti conformation (0 kJ/mol)   **Butane—eclipsed conformation (16 kJ/mol)**
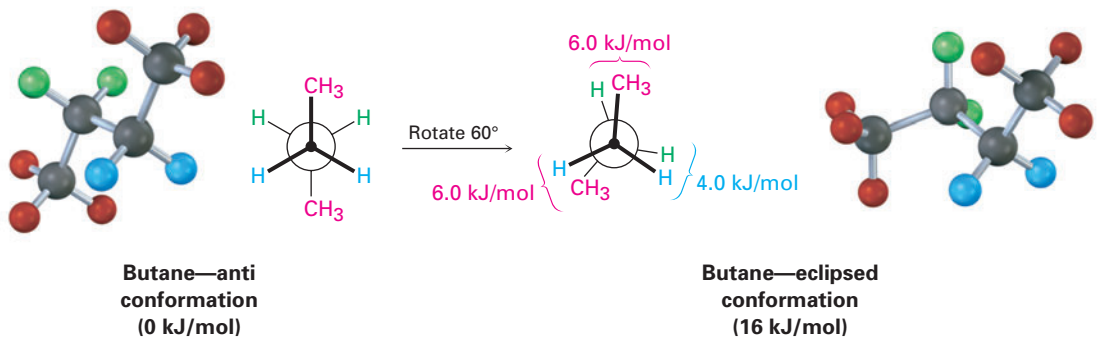
As bond rotation continues, an energy minimum is reached at the staggered conformation where the methyl groups are 60° apart. Called the **gauche**

conformation, it lies 3.8 kJ/mol (0.9 kcal/mol) higher in energy than the anti conformation *even though it has no eclipsing interactions.* This energy difference occurs because the hydrogen atoms of the methyl groups are near one another in the gauche conformation, resulting in what is called *steric strain.* **Steric strain** is the repulsive interaction that occurs when atoms are forced closer together than their atomic radii allow. It's the result of trying to force two atoms to occupy the same space.

Butane—eclipsed
conformation
(16 kJ/mol)

Butane—gauche
conformation
(3.8 kJ/mol)
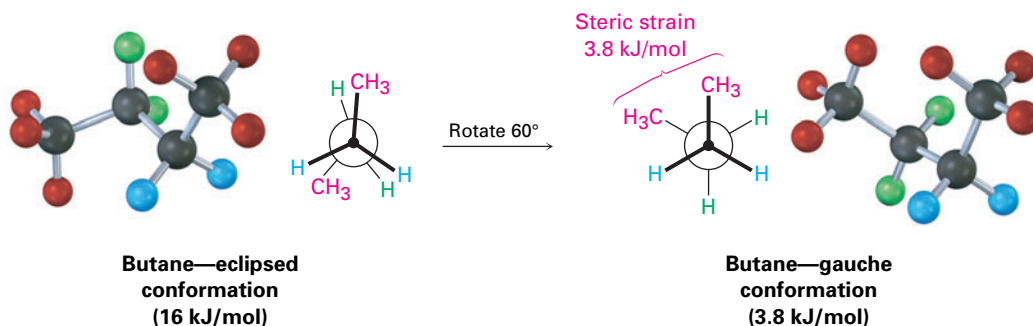
As the dihedral angle between the methyl groups approaches 0°, an energy maximum is reached at a second eclipsed conformation. Because the methyl groups are forced even closer together than in the gauche conformation, both torsional strain and steric strain are present. A total strain energy of 19 kJ/mol (4.5 kcal/mol) has been estimated for this conformation, making it possible to calculate a value of 11 kJ/mol (2.6 kcal/mol) for the CH_3 CH_3 eclipsing interaction: total strain of 19 kJ/mol less the strain of two H   H eclipsing interactions (2 × 4.0 kcal/mol) equals 11 kJ/mol.

Butane—gauche
conformation
(3.8 kJ/mol)

Butane—eclipsed
conformation
(19 kJ/mol)
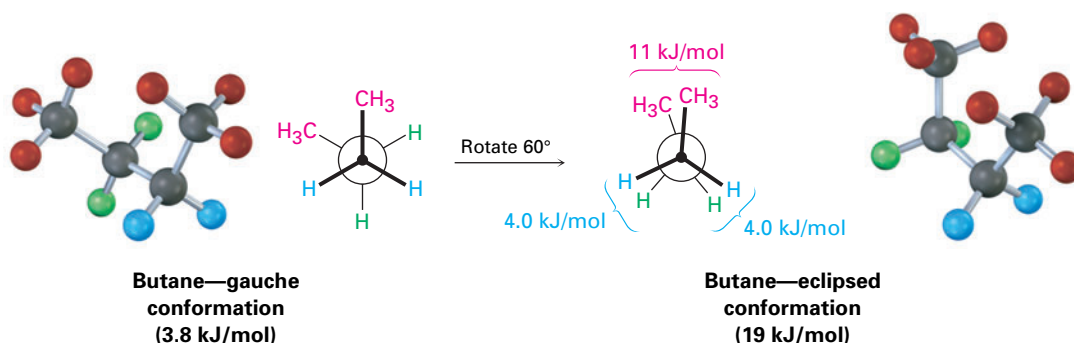
After 0°, the rotation becomes a mirror image of what we've already seen: another gauche conformation is reached, another eclipsed conformation, and finally a return to the anti conformation. A plot of potential energy versus rotation about the C2–C3 bond is shown in Figure 3.9.
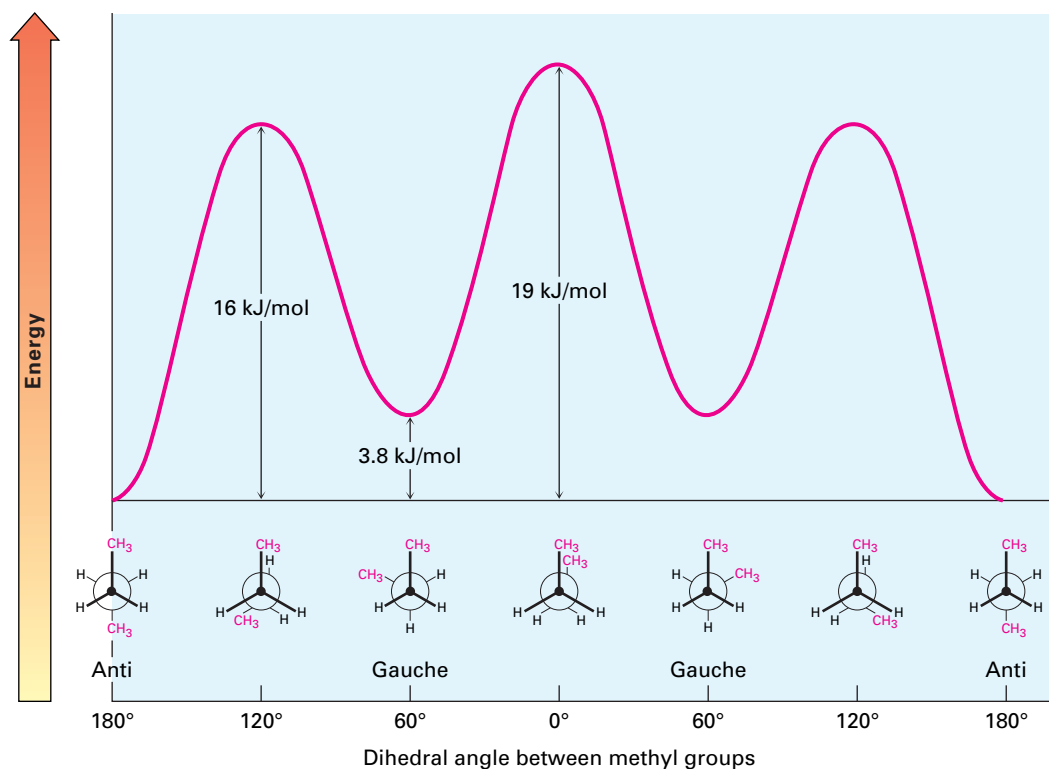
Figure 3.9 A plot of potential energy versus rotation for the C2–C3 bond in butane. The energy maximum occurs when the two methyl groups eclipse each other, and the energy minimum occurs when the two methyl groups are 180° apart (anti).

The notion of assigning definite energy values to specific interactions within a molecule is a very useful one that we'll return to in the next chapter. A summary of what we've seen thus far is given in Table 3.5.

Table 3.5 | Energy Costs for Interactions in Alkane Conformers

Interaction	Cause	Energy cost (kJ/mol)	(kcal/mol)
H H eclipsed	Torsional strain	4.0	1.0
H CH_3 eclipsed	Mostly torsional strain	6.0	1.4
CH_3 CH_3 eclipsed	Torsional and steric strain	11	2.6
CH_3 CH_3 gauche	Steric strain	3.8	0.9

The same principles just developed for butane apply to pentane, hexane, and all higher alkanes. The most favorable conformation for any alkane has the carbon–carbon bonds in staggered arrangements, with large substituents arranged anti to one another. A generalized alkane structure is shown in Figure 3.10.

Figure 3.10 The most stable alkane conformation is the one in which all substituents are staggered and the carbon–carbon bonds are arranged anti, as shown in this model of decane.
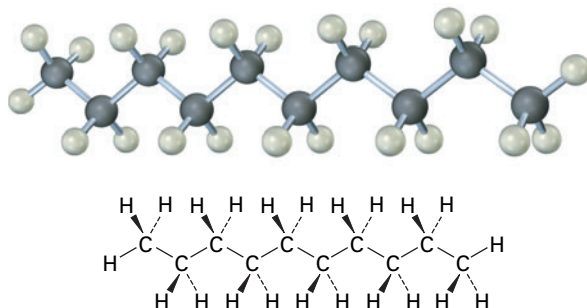
One final point: saying that one particular conformer is "more stable" than another doesn't mean the molecule adopts and maintains only the more stable conformation. At room temperature, rotations around σ bonds occur so rapidly that all conformers are in equilibrium. At any given instant, however, a larger percentage of molecules will be found in a more stable conformation than in a less stable one.

WORKED EXAMPLE 3.4

Drawing Newman Projections

Sighting along the C1–C2 bond of 1-chloropropane, draw Newman projections of the most stable and least stable conformations.

Strategy   The most stable conformation of a substituted alkane is generally a staggered one in which large groups have an anti relationship. The least stable conformation is generally an eclipsed one in which large groups are as close as possible.

Solution
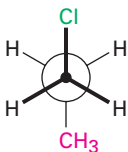
Most stable (staggered)   **Least stable (eclipsed)**
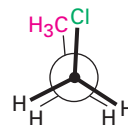
Problem 3.15   Make a graph of potential energy versus angle of bond rotation for propane, and assign values to the energy maxima.

Problem 3.16   Consider 2-methylpropane (isobutane). Sighting along the C2–C1 bond:
(a) Draw a Newman projection of the most stable conformation.
(b) Draw a Newman projection of the least stable conformation.
(c) Make a graph of energy versus angle of rotation around the C2–C1 bond.
(d) Since an H   H eclipsing interaction costs 4.0 kJ/mol and an H CH_3 eclipsing interaction costs 6.0 kJ/mol, assign relative values to the maxima and minima in your graph.

Problem 3.17   Sight along the C2–C3 bond of 2,3-dimethylbutane, and draw a Newman projection of the most stable conformation.

Problem 3.18   Draw a Newman projection along the C2–C3 bond of the following conformation of 2,3-dimethylbutane, and calculate a total strain energy:
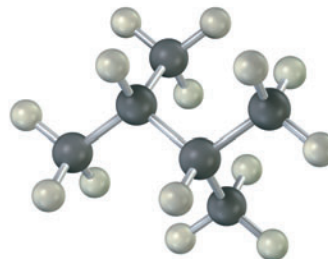
Focus On . . .

Gasoline

Gasoline is a finite resource; it won't be around forever.

British Foreign Minister Ernest Bevin once said that "The Kingdom of Heaven runs on righteousness, but the Kingdom of Earth runs on alkanes." Well, actually he said "runs on oil" not "runs on alkanes," but they're essentially the same. By far, the major sources of alkanes are the world's natural gas and petroleum deposits. Laid down eons ago, these deposits are thought to be derived from the decomposition of plant and animal matter, primarily of marine origin. *Natural gas* consists chiefly of methane but also contains ethane, propane, and butane. *Petroleum* is a complex mixture of hydrocarbons that must be separated into fractions and then further refined before it can be used.

The petroleum era began in August 1859, when the world's first oil well was drilled near Titusville, Pennsylvania. The petroleum was distilled into fractions according to boiling point, but it was high-boiling kerosene, or lamp oil, rather than gasoline that was primarily sought. Literacy was becoming widespread at the time, and people wanted better light for reading than was available from candles. Gasoline was too volatile for use in lamps and was initially considered a waste by-product. The world has changed greatly since those early days, however, and it is now gasoline rather than lamp oil that is prized.

Petroleum refining begins by fractional distillation of crude oil into three principal cuts according to boiling point (bp): straight-run gasoline (bp 30–200 °C), kerosene (bp 175–300 °C), and heating oil, or diesel fuel (bp 275–400 °C). Further distillation under reduced pressure then yields

(continued)

lubricating oils and waxes and leaves a tarry residue of asphalt. The distillation of crude oil is only the first step in gasoline production, however. Straight-run gasoline turns out to be a poor fuel in automobiles because of *engine knock,* an uncontrolled combustion that can occur in a hot engine.

The *octane number* of a fuel is the measure by which its antiknock properties are judged. It was recognized long ago that straight-chain hydrocarbons are far more prone to induce engine knock than are highly branched compounds. Heptane, a particularly bad fuel, is assigned a base value of 0 octane number, and 2,2,4-trimethylpentane, commonly known as isooctane, has a rating of 100.

$$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$$

$$CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}CH_2\overset{\displaystyle CH_3}{C}HCH_3$$

Heptane
(octane number = 0)

2,2,4-Trimethylpentane
(octane number = 100)
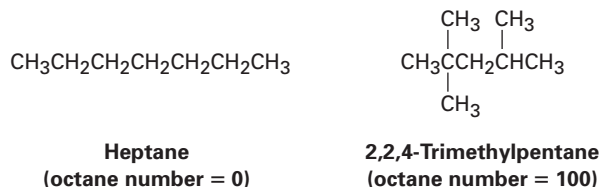
Because straight-run gasoline burns so poorly in engines, petroleum chemists have devised numerous methods for producing higher-quality fuels. One of these methods, *catalytic cracking,* involves taking the high-boiling kerosene cut (C_{11}–C_{14}) and "cracking" it into smaller branched molecules suitable for use in gasoline. Another process, called *reforming,* is used to convert C_6–C_8 alkanes to aromatic compounds such as benzene and toluene, which have substantially higher octane numbers than alkanes. The final product that goes in your tank has an approximate composition of 15% C_4–C_8 straight-chain alkanes, 25% to 40% C_4–C_{10} branched-chain alkanes, 10% cyclic alkanes, 10% straight-chain and cyclic alkenes, and 25% arenes (aromatics).

SUMMARY AND KEY WORDS

A **functional group** is a group of atoms within a larger molecule that has a characteristic chemical reactivity. Because functional groups behave in approximately the same way in all molecules where they occur, the chemical reactions of an organic molecule are largely determined by its functional groups.

Alkanes are a class of **saturated hydrocarbons** with the general formula C_nH_{2n+2}. They contain no functional groups, are relatively inert, and can be either **straight-chain** *(normal)* or **branched**. Alkanes are named by a series of IUPAC rules of nomenclature. Compounds that have the same chemical formula but different structures are called **isomers**. More specifically, compounds such as butane and isobutane, which differ in their connections between atoms, are called **constitutional isomers**.

Carbon–carbon single bonds in alkanes are formed by σ overlap of carbon sp^3 hybrid orbitals. Rotation is possible around σ bonds because of their cylindrical

symmetry, and alkanes therefore exist in a large number of rapidly interconverting **conformations**. **Newman projections** make it possible to visualize the spatial consequences of bond rotation by sighting directly along a carbon–carbon bond axis. Not all alkane conformations are equally stable. The **staggered** conformation of ethane is 12 kJ/mol (2.9 kcal/mol) more stable than the **eclipsed** conformation because of **torsional strain**. In general, any alkane is most stable when all its bonds are staggered.

EXERCISES

Organic KNOWLEDGE TOOLS

ThomsonNOW™ Sign in at **www.thomsonedu.com** to assess your knowledge of this chapter's topics by taking a pre-test. The pre-test will link you to interactive organic chemistry resources based on your score in each concept area.

Online homework for this chapter may be assigned in Organic OWL.

■ indicates problems assignable in Organic OWL.

VISUALIZING CHEMISTRY

(Problems 3.1–3.18 appear within the chapter.)

3.19 ■ Identify the functional groups in the following substances, and convert each drawing into a molecular formula (red = O, blue = N):

(a)

Phenylalanine

(b)
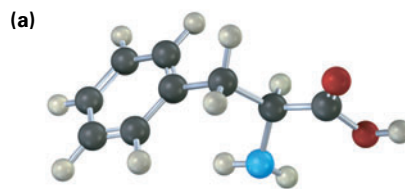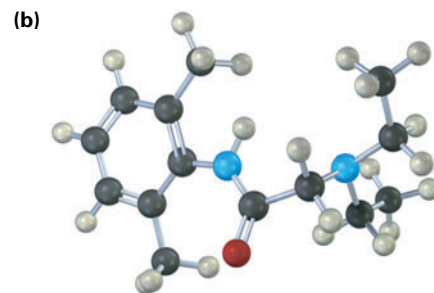
Lidocaine

3.20 ■ Give IUPAC names for the following alkanes, and convert each drawing into a skeletal structure:

(a)

(b)

(c)

(d)
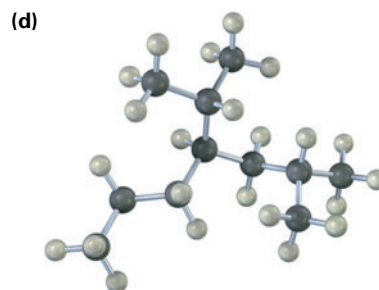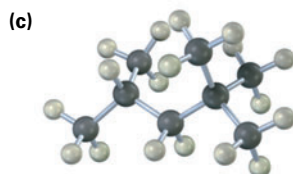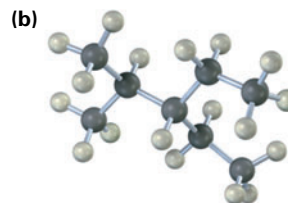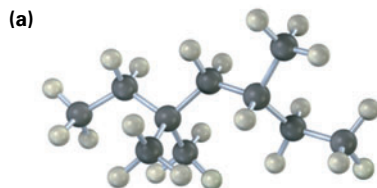
ADDITIONAL PROBLEMS

3.21 ■ Locate and identify the functional groups in the following molecules. In these representations, each intersection of lines and the end of each line represents a carbon atom with the appropriate number of hydrogens attached.

(a) CH_2OH ... $NHCH_3$

(b) O

(c) H ... N ... C=O ... CH_3

(d) O ... CH_3CHCOH ... NH_2

(e)

(f) Cl ... O
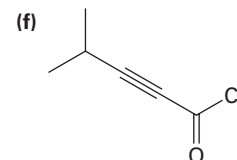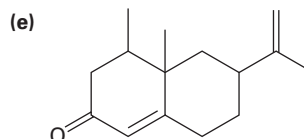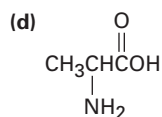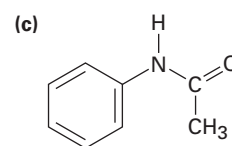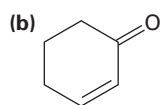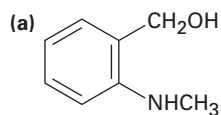
3.22 Draw structures that meet the following descriptions (there are many possibilities):
(a) Three isomers with the formula C_8H_{18}
(b) Two isomers with the formula $C_4H_8O_2$

3.23 Draw structures of the nine isomers of C_7H_{16}.

3.24 ■ In each of the following sets, which structures represent the same compound and which represent different compounds?

(a)

$$\underset{\substack{|\\ CH_3}}{\overset{\substack{Br\\|}}{CH_3CHCHCH_3}}$$
$$\underset{\substack{|\\ Br}}{\overset{\substack{CH_3\\|}}{CH_3CHCHCH_3}}$$
$$\underset{\substack{|\\ Br}}{\overset{\substack{CH_3\\|}}{CH_3CHCHCH_3}}$$

(b)

(c)

$$\underset{\substack{|\\ CH_2OH}}{\overset{\substack{CH_3\\|}}{CH_3CH_2CHCH_2CHCH_3}}$$
$$\underset{\substack{|\\ CH_3}}{\overset{\substack{CH_2CH_3\\|}}{HOCH_2CHCH_2CHCH_3}}$$
$$\overset{\substack{CH_3 \quad CH_3\\| \qquad |}}{CH_3CH_2CHCH_2CHCH_2OH}$$
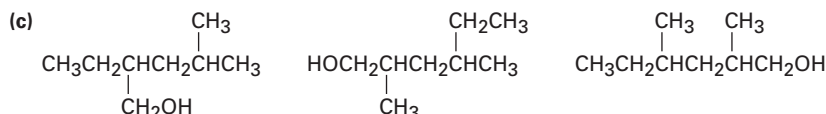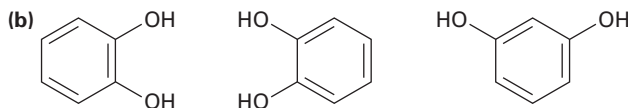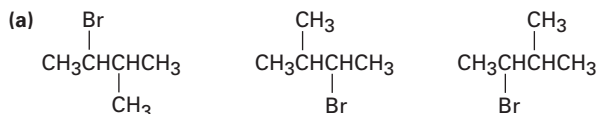
3.25 There are seven constitutional isomers with the formula $C_4H_{10}O$. Draw as many as you can.

3.26 ■ Propose structures that meet the following descriptions:
   (a) A ketone with five carbons   (b) A four-carbon amide
   (c) A five-carbon ester   (d) An aromatic aldehyde
   (e) A keto ester   (f) An amino alcohol

3.27 ■ Propose structures for the following:
   (a) A ketone, C_4H_8O (b) A nitrile, C_5H_9N
   (c) A dialdehyde, $C_4H_6O_2$ (d) A bromoalkene, $C_6H_{11}Br$
   (e) An alkane, C_6H_{14} (f) A *cyclic* saturated hydrocarbon, C_6H_{12}
   (g) A diene (dialkene), C_5H_8 (h) A keto alkene, C_5H_8O

3.28 Draw as many compounds as you can that fit the following descriptions:
   (a) Alcohols with formula $C_4H_{10}O$ (b) Amines with formula $C_5H_{13}N$
   (c) Ketones with formula $C_5H_{10}O$ (d) Aldehydes with formula $C_5H_{10}O$
   (e) Esters with formula $C_4H_8O_2$ (f) Ethers with formula $C_4H_{10}O$

3.29 ■ Draw compounds that contain the following:
   (a) A primary alcohol   (b) A tertiary nitrile
   (c) A secondary thiol   (d) Both primary and secondary alcohols
   (e) An isopropyl group   (f) A quaternary carbon

3.30 Draw and name all monobromo derivatives of pentane, $C_5H_{11}Br$.

3.31 Draw and name all monochloro derivatives of 2,5-dimethylhexane, $C_8H_{17}Cl$.

3.32 Predict the hybridization of the carbon atom in each of the following functional groups:
   (a) Ketone   (b) Nitrile   (c) Carboxylic acid

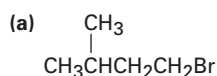**3.33** ■ Draw the structures of the following molecules:
   (a) *Biacetyl,* $C_4H_6O_2$, a substance with the aroma of butter; it contains no rings or carbon–carbon multiple bonds.
   (b) *Ethylenimine,* C_2H_5N, a substance used in the synthesis of melamine polymers; it contains no multiple bonds.
   (c) *Glycerol,* $C_3H_8O_3$, a substance isolated from fat and used in cosmetics; it has an −OH group on each carbon.

■ Assignable in OWL

3.34 ■ Draw structures for the following:
(a) 2-Methylheptane   (b) 4-Ethyl-2,2-dimethylhexane
(c) 4-Ethyl-3,4-dimethyloctane   (d) 2,4,4-Trimethylheptane
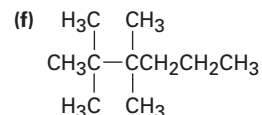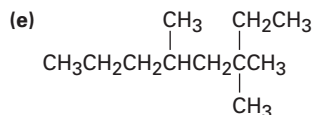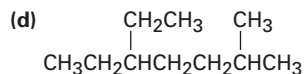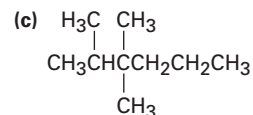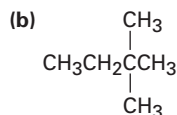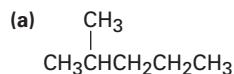(e) 3,3-Diethyl-2,5-dimethylnonane   (f) 4-Isopropyl-3-methylheptane

3.35 Draw a compound that:
(a) Has only primary and tertiary carbons
(b) Has no secondary or tertiary carbons
(c) Has four secondary carbons

3.36 Draw a compound that:
(a) Has nine primary hydrogens
(b) Has only primary hydrogens

3.37 For each of the following compounds, draw an isomer that has the same functional groups. Each intersection of lines represents a carbon atom with the appropriate number of hydrogens attached.

(a) CH_3
          |
    $CH_3CHCH_2CH_2Br$

(b)   ⬠—OCH_3

(c) $CH_3CH_2CH_2C{\equiv}N$

(d)   ⬡—OH

(e) CH_3CH_2CHO

(f)   (benzene ring)—CH_2CO_2H

3.38 ■ Give IUPAC names for the following compounds:

(a) CH_3
          |
    $CH_3CHCH_2CH_2CH_3$

(b) CH_3
          |
    $CH_3CH_2CCH_3$
          |
          CH_3

(c) H_3C CH_3
       | |
    $CH_3CHCCH_2CH_2CH_3$
              |
              CH_3

(d) CH_2CH_3 CH_3
          | |
    $CH_3CH_2CHCH_2CH_2CHCH_3$

(e) CH_3 CH_2CH_3
                | |
    $CH_3CH_2CH_2CHCH_2CCH_3$
                         |
                         CH_3

(f) H_3C CH_3
       | |
    $CH_3C{-}CCH_2CH_2CH_3$
       | |
       H_3C CH_3
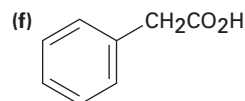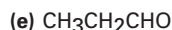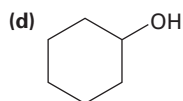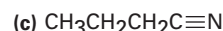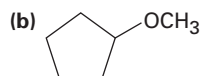
3.39 Name the five isomers of C_6H_{14}.

3.40 Explain why each of the following names is incorrect:
(a) 2,2-Dimethyl-6-ethylheptane   (b) 4-Ethyl-5,5-dimethylpentane
(c) 3-Ethyl-4,4-dimethylhexane   (d) 5,5,6-Trimethyloctane
(e) 2-Isopropyl-4-methylheptane

3.41 Propose structures and give IUPAC names for the following:
(a) A diethyldimethylhexane   (b) A (3-methylbutyl)-substituted alkane

3.42 ■ Consider 2-methylbutane (isopentane). Sighting along the C2–C3 bond:
(a) Draw a Newman projection of the most stable conformation.
(b) Draw a Newman projection of the least stable conformation.
(c) Since a CH_3 CH_3 eclipsing interaction costs 11 kJ/mol (2.5 kcal/mol) and a CH_3 CH_3 gauche interaction costs 3.8 kJ/mol (0.9 kcal/mol), make a quantitative plot of energy versus rotation about the C2–C3 bond.

3.43 ■ What are the relative energies of the three possible staggered conformations around the C2–C3 bond in 2,3-dimethylbutane? (See Problem 3.42.)

■ Assignable in OWL

3.44 Construct a qualitative potential-energy diagram for rotation about the C−C bond of 1,2-dibromoethane. Which conformation would you expect to be more stable? Label the anti and gauche conformations of 1,2-dibromoethane.

3.45 Which conformation of 1,2-dibromoethane (Problem 3.44) would you expect to have the larger dipole moment? The observed dipole moment of 1,2-dibromoethane is μ = 1.0 D. What does this tell you about the actual structure of the molecule?

3.46 ■ The barrier to rotation about the C−C bond in bromoethane is 15 kJ/mol (3.6 kcal/mol).
(a) What energy value can you assign to an H−Br eclipsing interaction?
(b) Construct a quantitative diagram of potential energy versus bond rotation for bromoethane.

3.47 Draw the most stable conformation of pentane, using wedges and dashes to represent bonds coming out of the paper and going behind the paper, respectively.

3.48 Draw the most stable conformation of 1,4-dichlorobutane, using wedges and dashes to represent bonds coming out of the paper and going behind the paper, respectively.

3.49 Malic acid, $C_4H_6O_5$, has been isolated from apples. Because this compound reacts with 2 molar equivalents of base, it is a dicarboxylic acid.
(a) Draw at least five possible structures.
(b) If malic acid is a secondary alcohol, what is its structure?

3.50 ■ Formaldehyde, $H_2C=O$, is known to all biologists because of its usefulness as a tissue preservative. When pure, formaldehyde *trimerizes* to give trioxane, $C_3H_6O_3$, which, surprisingly enough, has no carbonyl groups. Only one monobromo derivative ($C_3H_5BrO_3$) of trioxane is possible. Propose a structure for trioxane.

3.51 ■ Increased substitution around a bond leads to increased strain. Take the four substituted butanes listed below, for example. For each compound, sight along the C2–C3 bond and draw Newman projections of the most stable and least stable conformations. Use the data in Table 3.5 to assign strain energy values to each conformation. Which of the eight conformations is most strained? Which is least strained?
(a) 2-Methylbutane   (b) 2,2-Dimethylbutane
(c) 2,3-Dimethylbutane   (d) 2,2,3-Trimethylbutane

3.52 The cholesterol-lowering agents called *statins,* such as simvastatin (Zocor) and pravastatin (Pravachol), are among the most widely prescribed drugs in the world. Identify the functional groups in both, and tell how the two substances differ.
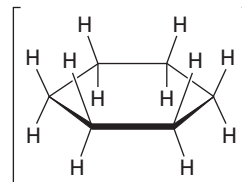

Simvastatin
(Zocor)

Pravastatin
(Pravachol)
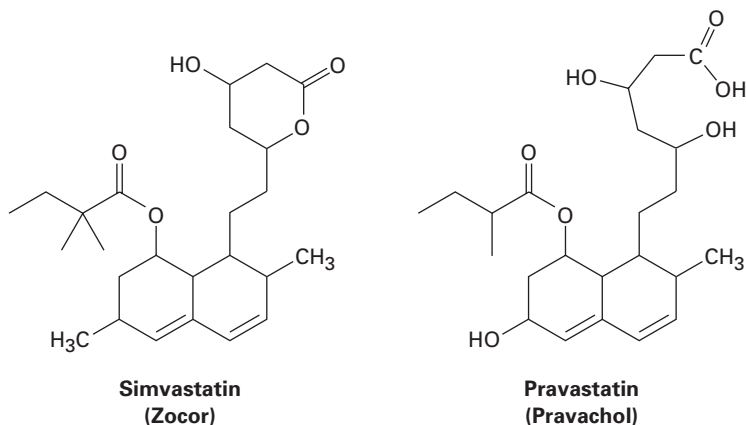
■ Assignable in OWL

3.53 We'll look in the next chapter at *cycloalkanes*—saturated cyclic hydrocarbons—and we'll see that the molecules generally adopt puckered, nonplanar conformations. Cyclohexane, for instance, has a puckered shape like a lounge chair rather than a flat shape. Why?
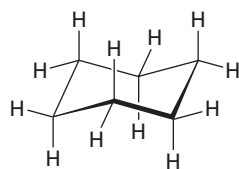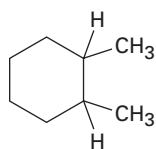
Nonplanar cyclohexane   **Planar cyclohexane**

3.54 We'll see in the next chapter that there are two isomeric substances both named 1,2-dimethylcyclohexane. Explain.

1,2-Dimethylcyclohexane

4

Organic Compounds: Cycloalkanes and Their Stereochemistry

We've discussed only open-chain compounds up to this point, but most organic compounds contain *rings* of carbon atoms. Chrysanthemic acid, for instance, whose esters occur naturally as the active insecticidal constituents of chrysanthemum flowers, contains a three-membered (cyclopropane) ring.
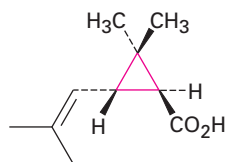
Chrysanthemic acid

Prostaglandins, potent hormones that control an extraordinary variety of physiological functions in humans, contain a five-membered (cyclopentane) ring.
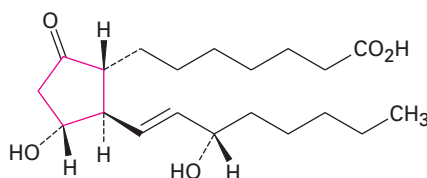
Prostaglandin E₁

Steroids, such as cortisone, contain four rings joined together—3 six-membered (cyclohexane) and 1 five-membered. We'll discuss steroids and their properties in more detail in Sections 27.6 and 27.7.

Cortisone

Sean Duggan

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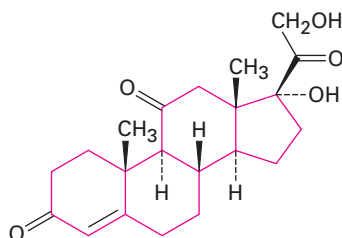
WHY THIS CHAPTER?

We'll see numerous instances in future chapters where the chemistry of a given functional group is strongly affected by being in a ring rather than an open chain. Because cyclic molecules are so commonly encountered in all classes of biomolecules, including proteins, lipids, carbohydrates, and nucleic acids, it's important that the effects of their cyclic structures be understood.

4.1 Naming Cycloalkanes

Saturated cyclic hydrocarbons are called **cycloalkanes**, or **alicyclic** compounds (**ali**phatic **cyclic**). Because cycloalkanes consist of rings of $-CH_2-$ units, they have the general formula $(CH_2)_n$, or C_nH_{2n}, and can be represented by polygons in skeletal drawings.

Cyclopropane   **Cyclobutane**   **Cyclopentane**   **Cyclohexane**
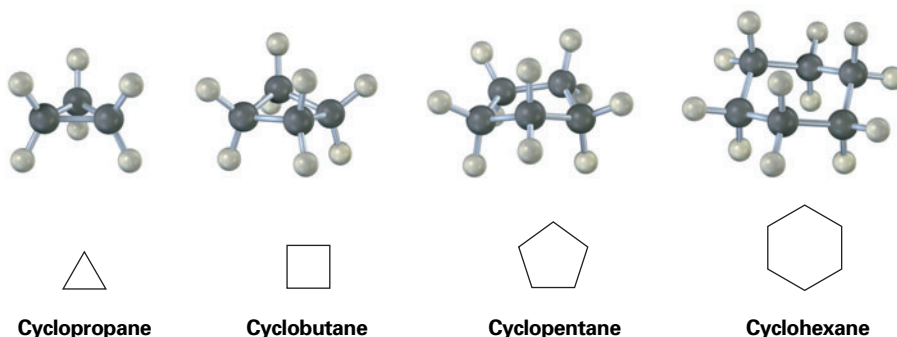
Substituted cycloalkanes are named by rules similar to those we saw in the previous chapter for open-chain alkanes (Section 3.4). For most compounds, there are only two steps.

Rule 1   **Find the parent.**

Count the number of carbon atoms in the ring and the number in the largest substituent chain. If the number of carbon atoms in the ring is equal to or greater than the number in the substituent, the compound is named as an alkyl-substituted cycloalkane. If the number of carbon atoms in the largest substituent is greater than the number in the ring, the compound is named as a cycloalkyl-substituted alkane. For example:

3 carbons   4 carbons

Methylcyclopentane   **1-Cyclopropylbutane**
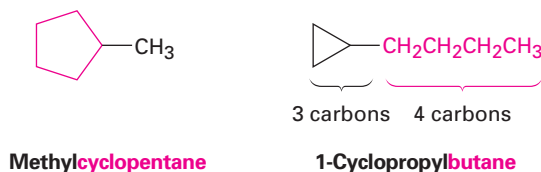
Rule 2   **Number the substituents, and write the name.**

For an alkyl- or halo-substituted cycloalkane, choose a point of attachment as carbon 1 and number the substituents on the ring so that the *second* substituent
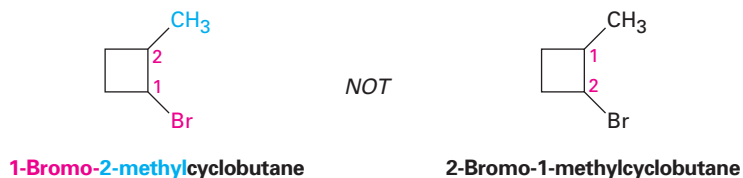
has as low a number as possible. If ambiguity still exists, number so that the third or fourth substituent has as low a number as possible, until a point of difference is found.
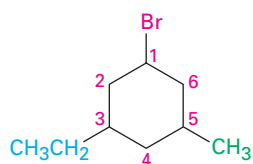

1,3-Dimethylcyclohexane
Lower

1,5-Dimethylcyclohexane
Higher

NOT

2-Ethyl-1,4-dimethylcyclohepTane
Lower   Lower

NOT

1-Ethyl-2,6-dimethylcycloheptane
Higher

3-Ethyl-1,4-dimethylcycloheptane
Higher
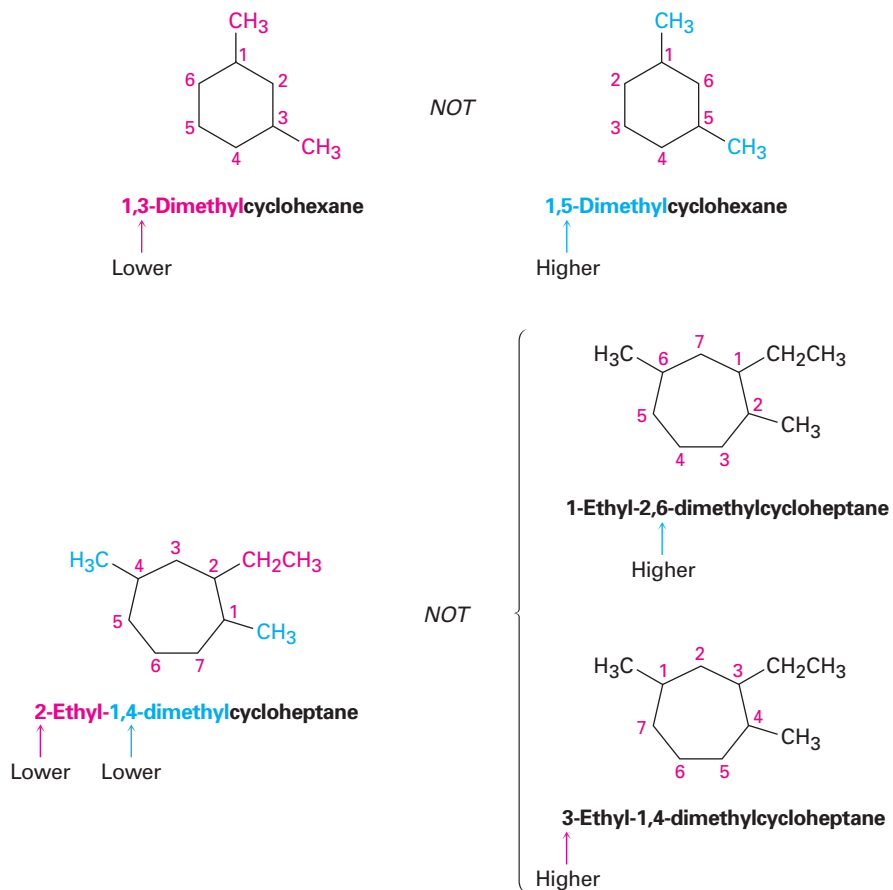
(a) When two or more different alkyl groups that could potentially receive the same numbers are present, number them by alphabetical priority.

1-Ethyl-2-methylcyclopentane

NOT

2-Ethyl-1-methylcyclopentane

(b) If halogens are present, treat them just like alkyl groups.

1-Bromo-2-methylcyclobutane

NOT

2-Bromo-1-methylcyclobutane

Some additional examples follow:
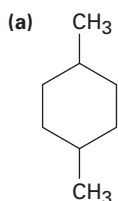
1-Bromo-3-ethyl-5-methyl-cyclohexane
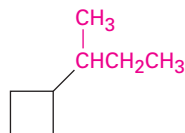
(1-Methylpropyl)cyclobutane or *sec*-butylcyclobutane
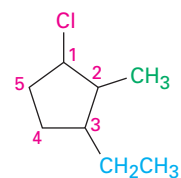
1-Chloro-3-ethyl-2-methyl-cyclopentane

Problem 4.1 | Give IUPAC names for the following cycloalkanes:

(a) CH₃ ... CH₃

(b) CH₂CH₂CH₃ ... CH₃

(c)

(d) CH₂CH₃ ... Br

(e) CH₃ ... CH(CH₃)₂

(f) Br ... CH₃ ... C(CH₃)₃
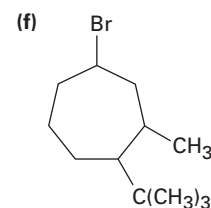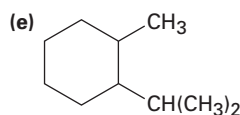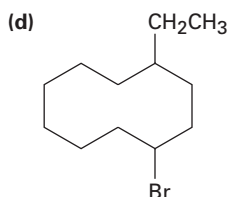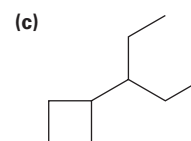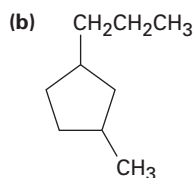
Problem 4.2 | Draw structures corresponding to the following IUPAC names:
(a) 1,1-Dimethylcyclooctane   (b) 3-Cyclobutylhexane
(c) 1,2-Dichlorocyclopentane   (d) 1,3-Dibromo-5-methylcyclohexane

Problem 4.3 | Name the following cycloalkane:
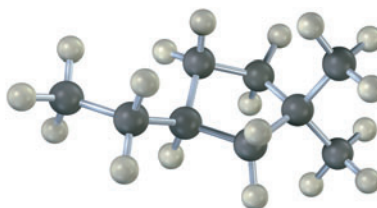
4.2 | Cis–Trans Isomerism in Cycloalkanes

In many respects, the chemistry of cycloalkanes is like that of open-chain alkanes: both are nonpolar and fairly inert. There are, however, some important differences. One difference is that cycloalkanes are less flexible than open-chain alkanes. In contrast with the relatively free rotation around single bonds in open-chain alkanes (Sections 3.6 and 3.7), there is much less freedom in cycloalkanes.

Cyclopropane, for example, must be a rigid, planar molecule because three points (the carbon atoms) define a plane. No bond rotation can take place around a cyclopropane carbon–carbon bond without breaking open the ring (Figure 4.1).
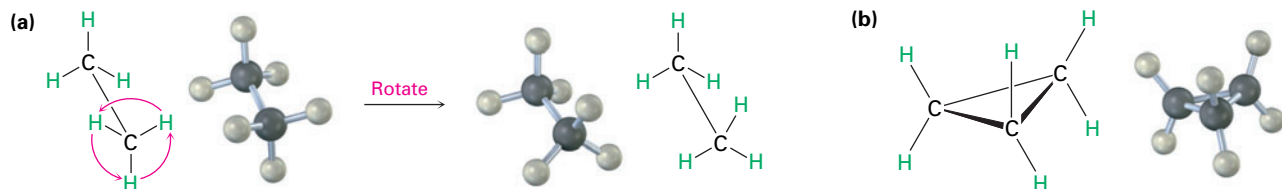

Figure 4.1 (a) Rotation occurs around the carbon–carbon bond in ethane, but **(b)** no rotation is possible around the carbon–carbon bonds in cyclopropane without breaking open the ring.

Larger cycloalkanes have increasing rotational freedom, and the very large rings (C_{25} and up) are so floppy that they are nearly indistinguishable from open-chain alkanes. The common ring sizes (C_3–C_7), however, are severely restricted in their molecular motions.

Because of their cyclic structures, cycloalkanes have two faces as viewed edge-on, a "top" face and a "bottom" face. As a result, isomerism is possible in substituted cycloalkanes. For example, there are two different 1,2-dimethyl-cyclopropane isomers, one with the two methyl groups on the same face of the ring and one with the methyls on opposite faces (Figure 4.2). Both isomers are stable compounds, and neither can be converted into the other without breaking and reforming chemical bonds. Make molecular models to prove this to yourself.
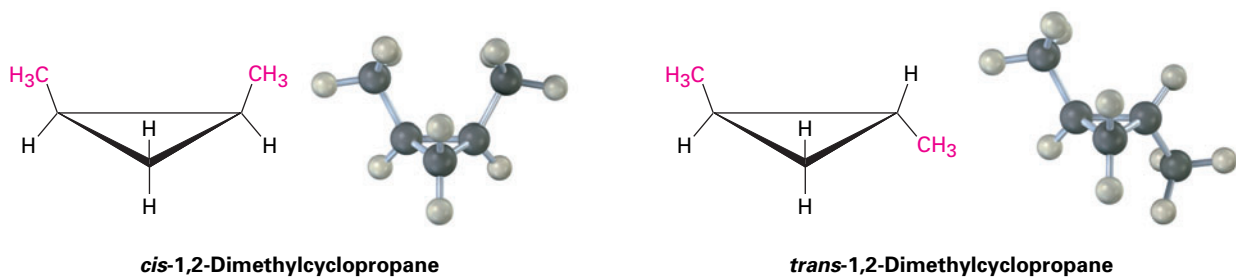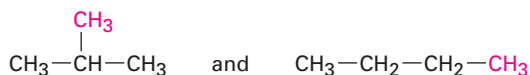

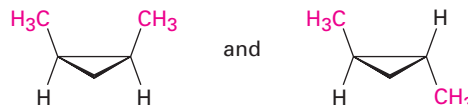*cis*-1,2-Dimethylcyclopropane   *trans*-1,2-Dimethylcyclopropane

Figure 4.2 There are two different 1,2-dimethylcyclopropane isomers, one with the methyl groups on the same face of the ring (cis) and the other with the methyl groups on opposite faces of the ring (trans). The two isomers do not interconvert.

Unlike the constitutional isomers butane and isobutane (Section 3.2), which have their atoms connected in a different order, the two 1,2-dimethyl-cyclopropanes have the same order of connections but differ in the spatial orientation of the atoms. Such compounds, which have their atoms connected in the same order but differ in three-dimensional orientation, are called stereo-chemical isomers, or **stereoisomers**.

Constitutional isomers (different connections between atoms)

Stereoisomers (same connections but different three-dimensional geometry)

The 1,2-dimethylcyclopropanes are members of a subclass of stereoisomers called **cis–trans isomers**. The prefixes *cis-* (Latin "on the same side") and *trans-* (Latin "across") are used to distinguish between them. Cis–trans isomerism is a common occurrence in substituted cycloalkanes.

***cis*-1,3-Dimethylcyclobutane**   ***trans*-1-Bromo-3-ethylcyclopentane**

WORKED EXAMPLE 4.1

Thomson**NOW** Click *Organic Interactive* to learn to **write IUPAC names for simple cycloalkanes**.

Thomson**NOW** Click *Organic Interactive* to **use an online palette to draw cycloalkane structures from their IUPAC names**.

Naming Cycloalkanes

Name the following substances, including the *cis-* or *trans-* prefix:
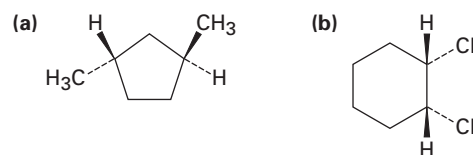

Strategy In these views, the ring is roughly in the plane of the page, a wedged bond protrudes out of the page, and a dashed bond recedes into the page. Two substituents are cis if they are both out of or both into the page, and they are trans if one is out of and one is into.

Solution (a) *trans*-1,3-Dimethylcyclopentane   (b) *cis*-1,2-Dichlorocyclohexane

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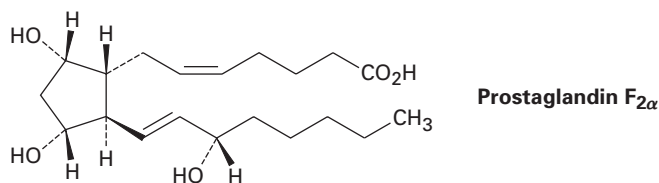**Problem 4.4** Name the following substances, including the *cis-* or *trans-* prefix:
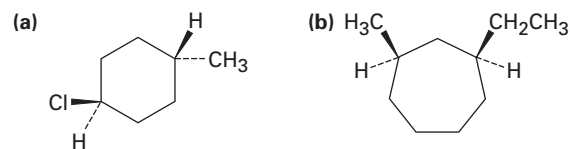
Problem 4.5 Draw the structures of the following molecules:
(a) *trans*-1-Bromo-3-methylcyclohexane   (b) *cis*-1,2-Dimethylcyclobutane
(c) *trans*-1-*tert*-Butyl-2-ethylcyclohexane

Problem 4.6 Prostaglandin $F_{2\alpha}$, a hormone that causes uterine contraction during childbirth, has the following structure. Are the two hydroxyl groups (−OH) on the cyclopentane ring cis or trans to each other? What about the two carbon chains attached to the ring?

Prostaglandin $F_{2\alpha}$

Problem 4.7 | Name the following substances, including the *cis-* or *trans-* prefix (red-brown = Br):

(a)

(b)
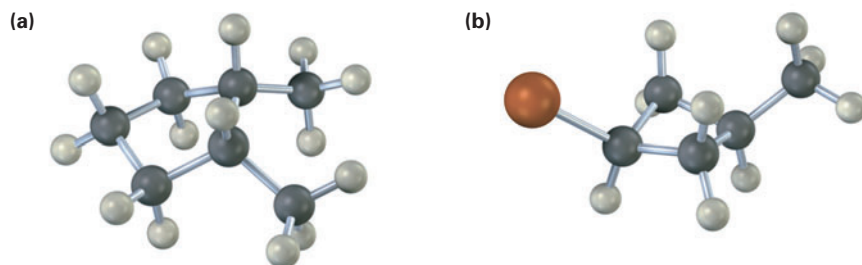
4.3 | Stability of Cycloalkanes: Ring Strain

Adolf von Baeyer

Adolf von Baeyer (1835–1917) was born in Berlin, Germany, and received his Ph.D. at the University of Berlin in 1858, working with Robert Bunsen and August Kekulé. After holding positions at Berlin and Strasbourg, he was a professor at Munich from 1875 to 1917. He was the first to synthesize the blue dye indigo and was also discoverer of the first barbiturate sedative, which he named after his friend Barbara. Baeyer was awarded the Nobel Prize in chemistry in 1905.

Chemists in the late 1800s knew that cyclic molecules existed, but the limitations on ring size were unclear. Although numerous compounds containing five- and six-membered rings were known, smaller and larger ring sizes had not been prepared, despite many efforts.

A theoretical interpretation of this observation was proposed in 1885 by Adolf von Baeyer, who suggested that small and large rings might be unstable due to **angle strain**—the strain induced in a molecule when bond angles are forced to deviate from the ideal 109° tetrahedral value. Baeyer based his suggestion on the simple geometric notion that a three-membered ring (cyclopropane) should be an equilateral triangle with bond angles of 60° rather than 109°, a four-membered ring (cyclobutane) should be a square with bond angles of 90°, a five-membered ring should be a regular pentagon with bond angles of 108°, and so on. Continuing this argument, large rings should be strained by having bond angles that are much greater than 109°.
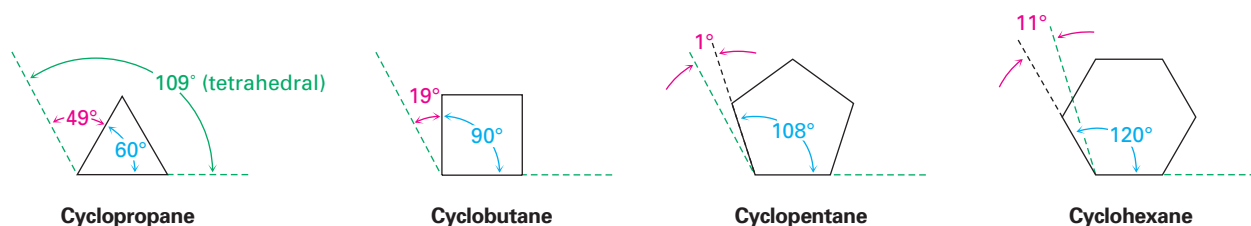

What are the facts? To measure the amount of strain in a compound, we have to measure the total energy of the compound and then subtract the energy of a strain-free reference compound. The difference between the two values should represent the amount of extra energy in the molecule due to strain. The simplest way to do this for a cycloalkane is to measure its *heat of combustion,* the amount of heat released when the compound burns completely with oxygen. The more energy (strain) the compound contains, the more energy (heat) is released on combustion.

$$(CH_2)_n + 3n/2\ O_2 \qquad n\ CO_2 + n\ H_2O + \textbf{Heat}$$

Because the heat of combustion of a cycloalkane depends on size, we need to look at heats of combustion per CH_2 unit. Subtracting a reference value derived from a strain-free acyclic alkane and then multiplying by the number of CH_2 units in the ring gives the overall strain energy. Figure 4.3 shows the results.

Figure 4.3 Cycloalkane strain energies, calculated by taking the difference between cycloalkane heat of combustion per CH_2 and acyclic alkane heat of combustion per CH_2, and multiplying by the number of CH_2 units in a ring. Small and medium rings are strained, but cyclohexane rings are strain-free.
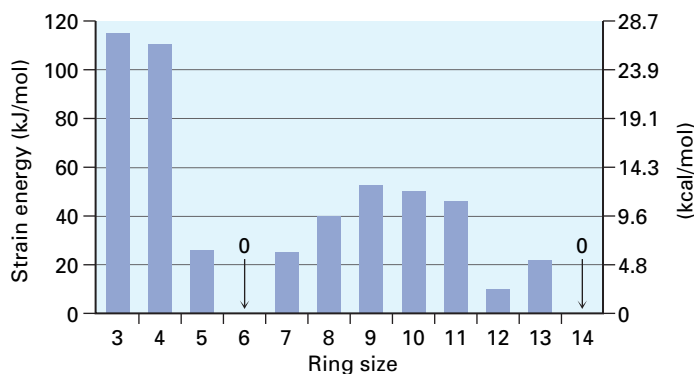
The data in Figure 4.3 show that Baeyer's theory is only partially correct. Cyclopropane and cyclobutane are indeed strained, just as predicted, but cyclopentane is more strained than predicted, and cyclohexane is strain-free. Cycloalkanes of intermediate size have only modest strain, and rings of 14 carbons or more are strain-free. Why is Baeyer's theory wrong?

Baeyer's theory is wrong for the simple reason that he assumed all cycloalkanes to be flat. In fact, as we'll see shortly, most cycloalkanes are *not* flat; they adopt puckered three-dimensional conformations that allow bond angles to be nearly tetrahedral. As a result, angle strain occurs only in three- and four-membered rings that have little flexibility. For most ring sizes, particularly the medium-ring (C_7–C_{11}) cycloalkanes, torsional strain caused by H   H eclipsing interactions on adjacent carbons (Section 3.6) and steric strain caused by the repulsion between nonbonded atoms that approach too closely (Section 3.7) are the most important factors. Thus, three kinds of strain contribute to the overall energy of a cycloalkane.

- **Angle strain**—the strain due to expansion or compression of bond angles
- **Torsional strain**—the strain due to eclipsing of bonds on neighboring atoms
- **Steric strain**—the strain due to repulsive interactions when atoms approach each other too closely

Problem 4.8   Each H   H eclipsing interaction in ethane costs about 4.0 kJ/mol. How many such interactions are present in cyclopropane? What fraction of the overall 115 kJ/mol (27.5 kcal/mol) strain energy of cyclopropane is due to torsional strain?

Problem 4.9   *cis*-1,2-Dimethylcyclopropane has more strain than *trans*-1,2-dimethylcyclopropane. How can you account for this difference? Which of the two compounds is more stable?

4.4 | Conformations of Cycloalkanes

Cyclopropane

Cyclopropane is the most strained of all rings, primarily because of the angle strain caused by its 60° C$-$C$-$C bond angles. In addition, cyclopropane also has considerable torsional strain because the C$-$H bonds on neighboring carbon atoms are eclipsed (Figure 4.4).

Figure 4.4 The structure of cyclopropane, showing the eclipsing of neighboring C$-$H bonds that gives rise to torsional strain. Part **(b)** is a Newman projection along a C$-$C bond.
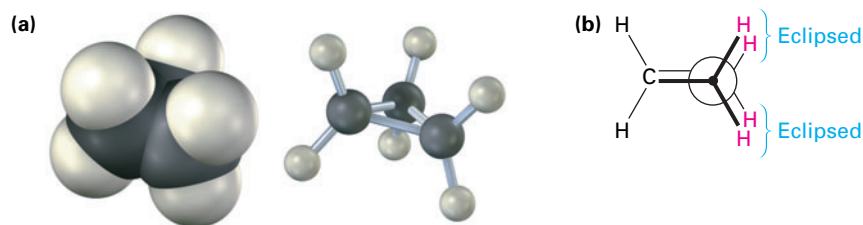
How can the hybrid-orbital model of bonding account for the large distortion of bond angles from the normal 109° tetrahedral value to 60° in cyclopropane? The answer is that cyclopropane has *bent bonds*. In an unstrained alkane, maximum bonding is achieved when two atoms have their overlapping orbitals pointing directly toward each other. In cyclopropane, though, the orbitals can't point directly toward each other; rather, they overlap at an angle. The result is that cyclopropane bonds are weaker and more reactive than typical alkane bonds—255 kJ/mol (61 kcal/mol) for a C$-$C bond in cyclopropane versus 355 kJ/mol (85 kcal/mol) for a C$-$C bond in open-chain propane.

Typical alkane C–C bonds   **Typical bent cyclopropane C–C bonds**
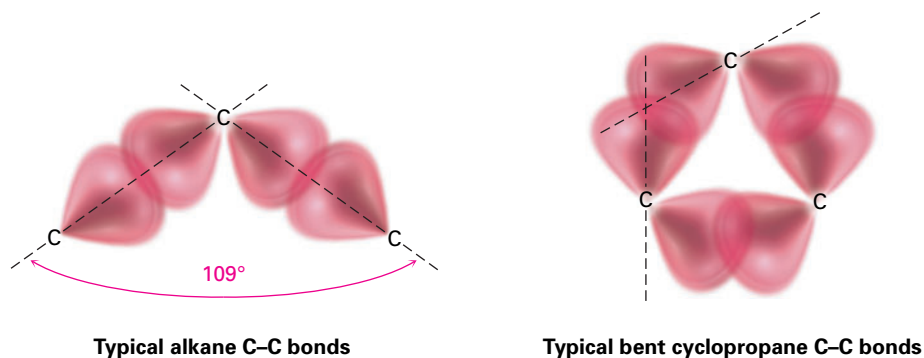
Cyclobutane

Cyclobutane has less angle strain than cyclopropane but has more torsional strain because of its larger number of ring hydrogens. As a result, the total strain for the two compounds is nearly the same—110 kJ/mol (26.4 kcal/mol) for cyclobutane versus 115 kJ/mol (27.5 kcal/mol) for cyclopropane. Experiments show that cyclobutane is not quite flat but is slightly bent so that one carbon atom lies about 25° above the plane of the other three (Figure 4.5). The effect of

this slight bend is to *increase* angle strain but to *decrease* torsional strain, until a minimum-energy balance between the two opposing effects is achieved.
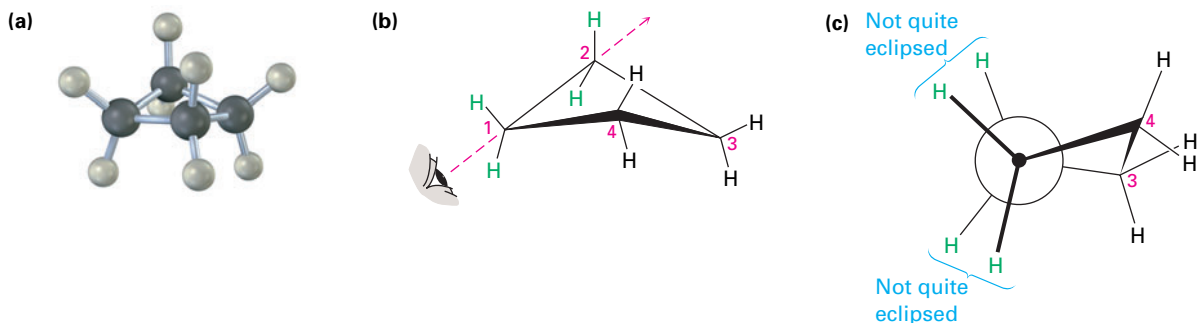

(a)   **(b)**   **(c)** Not quite eclipsed

Not quite eclipsed

Figure 4.5 The conformation of cyclobutane. Part **(c)** is a Newman projection along the C1–C2 bond, showing that neighboring C−H bonds are not quite eclipsed.

Cyclopentane

Cyclopentane was predicted by Baeyer to be nearly strain-free but in fact has a total strain energy of 26 kJ/mol (6.2 kcal/mol). Although planar cyclopentane has practically no angle strain, it has a large amount of torsional strain. Cyclopentane therefore twists to adopt a puckered, nonplanar conformation that strikes a balance between increased angle strain and decreased torsional strain. Four of the cyclopentane carbon atoms are in approximately the same plane, with the fifth carbon atom bent out of the plane. Most of the hydrogens are nearly staggered with respect to their neighbors (Figure 4.6).
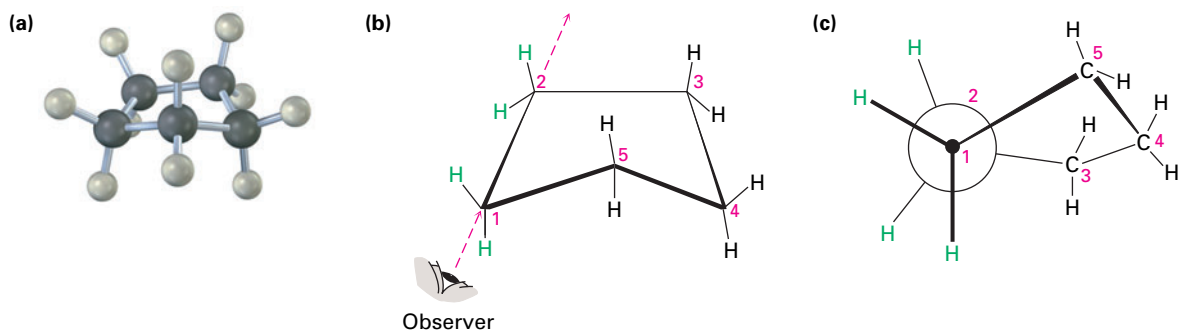

(a)   **(b)**   **(c)**

Observer

Figure 4.6 The conformation of cyclopentane. Carbons 1, 2, 3, and 4 are nearly planar, but carbon 5 is out of the plane. Part **(c)** is a Newman projection along the C1–C2 bond, showing that neighboring C−H bonds are nearly staggered.

Problem 4.10   How many H   H eclipsing interactions would be present if cyclopentane were planar? Assuming an energy cost of 4.0 kJ/mol for each eclipsing interaction, how much torsional strain would planar cyclopentane have? Since the measured total strain of cyclopentane is 26 kJ/mol, how much of the torsional strain is relieved by puckering?

Problem 4.11 Two conformations of *cis*-1,3-dimethylcyclobutane are shown. What is the difference between them, and which do you think is likely to be more stable?

(a)

(b)
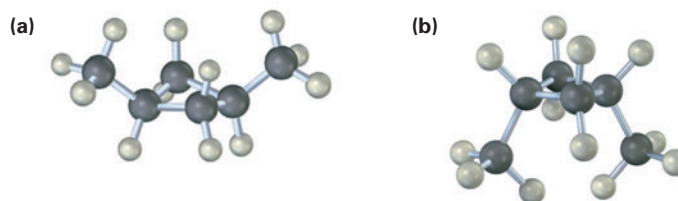
4.5 | Conformations of Cyclohexane

Substituted cyclohexanes are the most common cycloalkanes and occur widely in nature. A large number of compounds, including steroids and many pharmaceutical agents, have cyclohexane rings. The flavoring agent menthol, for instance, has three substituents on a six-membered ring.

Menthol
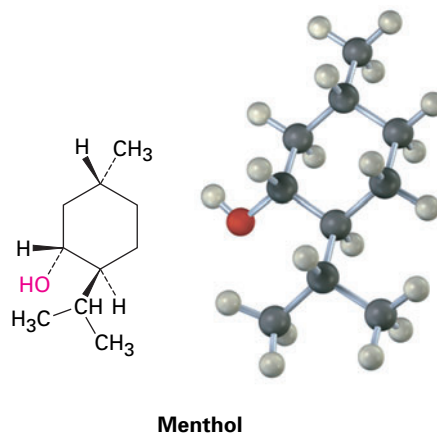
Cyclohexane adopts a strain-free, three-dimensional shape, called a **chair conformation** because of its similarity to a lounge chair, with a back, a seat, and a footrest (Figure 4.7). Chair cyclohexane has neither angle strain nor torsional strain—all C−C−C bond angles are near 109°, and all neighboring C−H bonds are staggered.
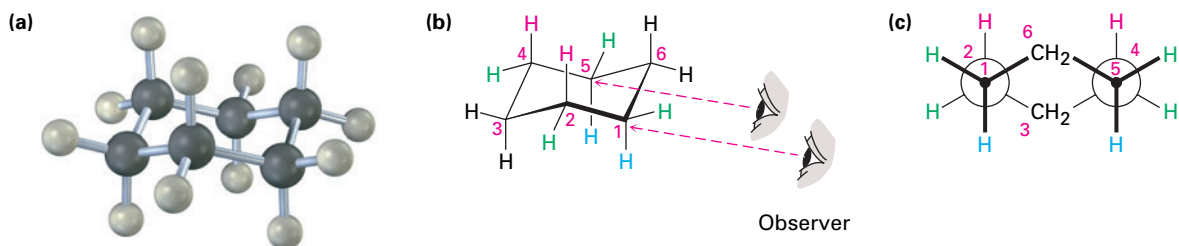
(a)

(b)

(c)

Observer

Figure 4.7 The strain-free chair conformation of cyclohexane. All C−C−C bond angles are 111.5°, close to the ideal 109.5° tetrahedral angle, and all neighboring C−H bonds are staggered.

The easiest way to visualize chair cyclohexane is to build a molecular model. (In fact, do it now.) Two-dimensional drawings like that in Figure 4.7 are useful, but there's no substitute for holding, twisting, and turning a three-dimensional model in your own hands. The chair conformation of cyclohexane can be drawn in three steps.

Step 1 Draw two parallel lines, slanted downward and slightly off-set from each other. This means that four of the cyclohexane carbons lie in a plane.

Step 2 Place the topmost carbon atom above and to the right of the plane of the other four, and connect the bonds.

Step 3 Place the bottommost carbon atom below and to the left of the plane of the middle four, and connect the bonds. Note that the bonds to the bottommost carbon atom are parallel to the bonds to the topmost carbon.
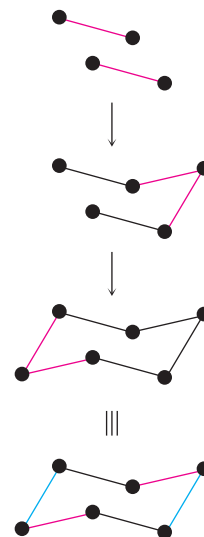
When viewing cyclohexane, it's helpful to remember that the lower bond is in front and the upper bond is in back. If this convention is not defined, an optical illusion can make it appear that the reverse is true. For clarity, all cyclohexane rings drawn in this book will have the front (lower) bond heavily shaded to indicate nearness to the viewer.

This bond is in back.
This bond is in front.
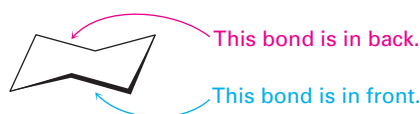
In addition to the chair conformation of cyclohexane, a second arrangement called the **twist-boat conformation** is also nearly free of angle strain. It does, however, have both steric strain and torsional strain and is about 23 kJ/mol (5.5 kcal/mol) higher in energy than the chair conformation. As a result, molecules adopt the twist-boat geometry only under special circumstances.

Steric strain

H ⟷ H
H ⟷ H } **Torsional strain**
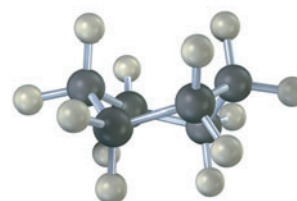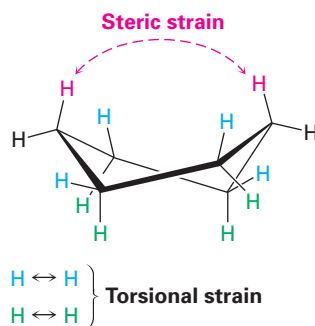
**Twist-boat cyclohexane
(23 kJ/mol strain)**

4.6 | Axial and Equatorial Bonds in Cyclohexane

The chair conformation of cyclohexane has many consequences. We'll see in Section 11.9, for instance, that the chemical behavior of many substituted cyclohexanes is influenced by their conformation. In addition, we'll see in Section 25.5 that simple carbohydrates such as glucose adopt a conformation based on the cyclohexane chair and that their chemistry is directly affected as a result.

Cyclohexane
(chair conformation)

Glucose
(chair conformation)
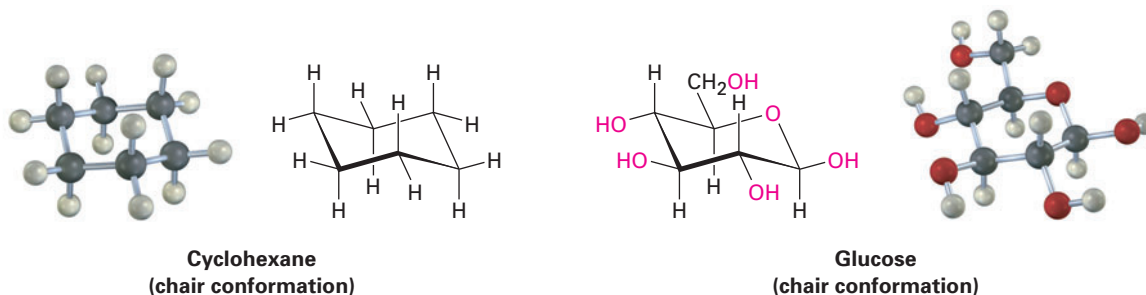
Another consequence of the chair conformation is that there are two kinds of positions for substituents on the cyclohexane ring: *axial* positions and *equatorial* positions (Figure 4.8). The six **axial** positions are perpendicular to the ring, parallel to the ring axis, and the six **equatorial** positions are in the rough plane of the ring, around the ring equator.

Figure 4.8 Axial (red) and equatorial (blue) positions in chair cyclohexane. The six axial hydrogens are parallel to the ring axis, and the six equatorial hydrogens are in a band around the ring equator.
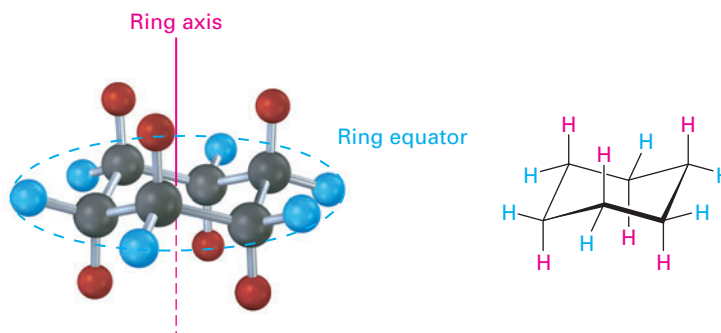
As shown in Figure 4.8, each carbon atom in cyclohexane has one axial and one equatorial hydrogen. Furthermore, each face of the ring has three axial and three equatorial hydrogens in an alternating arrangement. For example, if the top face of the ring has axial hydrogens on carbons 1, 3, and 5, then it has equatorial hydrogens on carbons 2, 4, and 6. Exactly the reverse is true for the bottom face: carbons 1, 3, and 5 have equatorial hydrogens, but carbons 2, 4, and 6 have axial hydrogens (Figure 4.9).

Note that we haven't used the words *cis* and *trans* in this discussion of cyclohexane conformation. Two hydrogens on the same face of the ring are always cis, regardless of whether they're axial or equatorial and regardless of whether they're adjacent. Similarly, two hydrogens on opposite faces of the ring are always trans.

Figure 4.9 Alternating axial and equatorial positions in chair cyclohexane, as shown in a view looking directly down the ring axis. Each carbon atom has one axial and one equatorial position, and each face has alternating axial and equatorial positions.
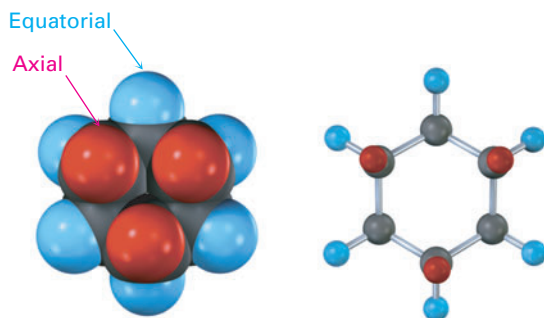
Axial and equatorial bonds can be drawn following the procedure in Figure 4.10. Look at a molecular model as you practice.

Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up–down.
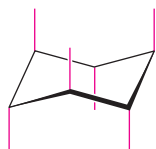
Equatorial bonds: The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alternate between sides around the ring.
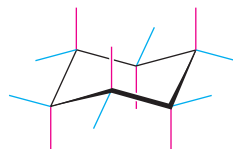
Completed cyclohexane

Figure 4.10 A procedure for drawing axial and equatorial bonds in chair cyclohexane.

Because chair cyclohexane has two kinds of positions, axial and equatorial, we might expect to find two isomeric forms of a monosubstituted cyclohexane. In fact, we don't. There is only *one* methylcyclohexane, *one* bromocyclohexane, *one* cyclohexanol (hydroxycyclohexane), and so on, because cyclohexane rings are *conformationally mobile* at room temperature. Different chair conformations readily interconvert, exchanging axial and equatorial positions. This interconversion, usually called a **ring-flip**, is shown in Figure 4.11.

As shown in Figure 4.11, a chair cyclohexane can be ring-flipped by keeping the middle four carbon atoms in place while folding the two end carbons in opposite directions. In so doing, an axial substituent in one chair form becomes an equatorial substituent in the ring-flipped chair form and vice versa. For example, axial bromocyclohexane becomes equatorial bromocyclohexane after ring-flip. Since the energy barrier to chair–chair interconversion is only

Figure 4.11 A ring-flip in chair cyclohexane interconverts axial and equatorial positions. What is axial (red) in the starting structure becomes equatorial in the ring-flipped structure, and what is equatorial (blue) in the starting structure is axial after ring-flip.
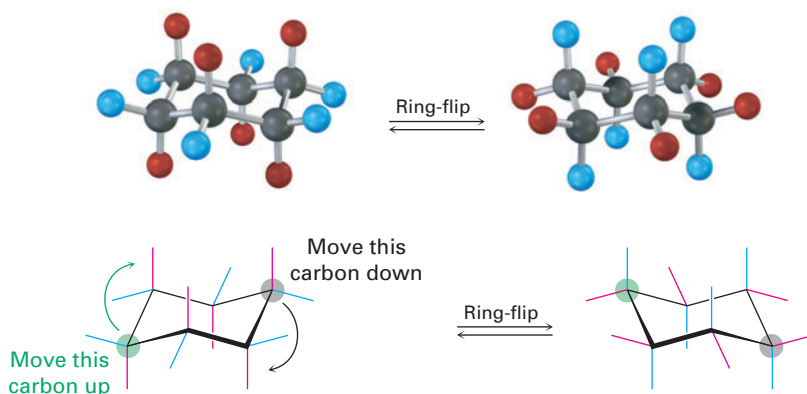
about 45 kJ/mol (10.8 kcal/mol), the process is rapid at room temperature and we see what appears to be a single structure rather than distinct axial and equatorial isomers.


Axial bromocyclohexane   **Equatorial bromocyclohexane**
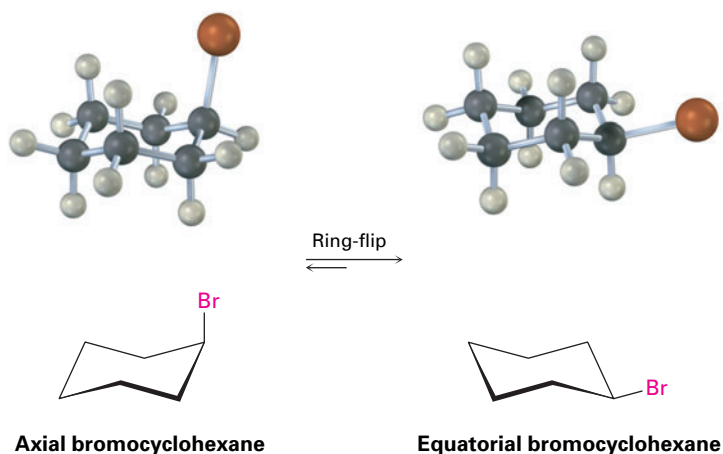
WORKED EXAMPLE 4.2

*Drawing the Chair Conformation of a Substituted Cyclohexane*

Draw 1,1-dimethylcyclohexane in a chair conformation, indicating which methyl group in your drawing is axial and which is equatorial.

Strategy   Draw a chair cyclohexane ring using the procedure in Figure 4.9, and then put two methyl groups on the same carbon. The methyl group in the rough plane of the ring is equatorial, and the other (directly above or below the ring) is axial.

Solution
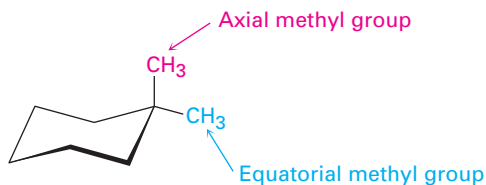
Problem 4.12 Draw two different chair conformations of cyclohexanol (hydroxycyclohexane), showing all hydrogen atoms. Identify each position as axial or equatorial.

Problem 4.13 Draw two different chair conformations of *trans*-1,4-dimethylcyclohexane, and label all positions as axial or equatorial.

Problem 4.14 Identify each of the colored positions—red, blue, and green—as axial or equatorial. Then carry out a ring-flip, and show the new positions occupied by each color.
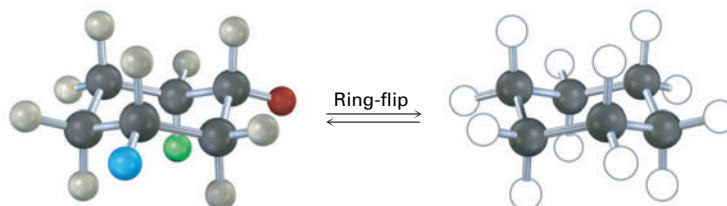
## 4.7 | Conformations of Monosubstituted Cyclohexanes

Even though cyclohexane rings rapidly flip between chair conformations at room temperature, the two conformations of a monosubstituted cyclohexane aren't equally stable. In methylcyclohexane, for instance, the equatorial conformation is more stable than the axial conformation by 7.6 kJ/mol (1.8 kcal/mol). The same is true of other monosubstituted cyclohexanes: a substituent is almost always more stable in an equatorial position than in an axial position.

You might recall from your general chemistry course that it's possible to calculate the percentages of two isomers at equilibrium using the equation $\Delta E = -RT \ln K$, where ΔE is the energy difference between isomers, R is the gas constant [8.315 J/(K · mol)], T is the Kelvin temperature, and K is the equilibrium constant between isomers. For example, an energy difference of 7.6 kJ/mol means that about 95% of methylcyclohexane molecules have the methyl group equatorial at any given instant and only 5% have the methyl group axial. Figure 4.12 plots the relationship between energy and isomer percentages.

Figure 4.12 A plot of the percentages of two isomers at equilibrium versus the energy difference between them. The curves are calculated using the equation $\Delta E = -RT \ln K$.
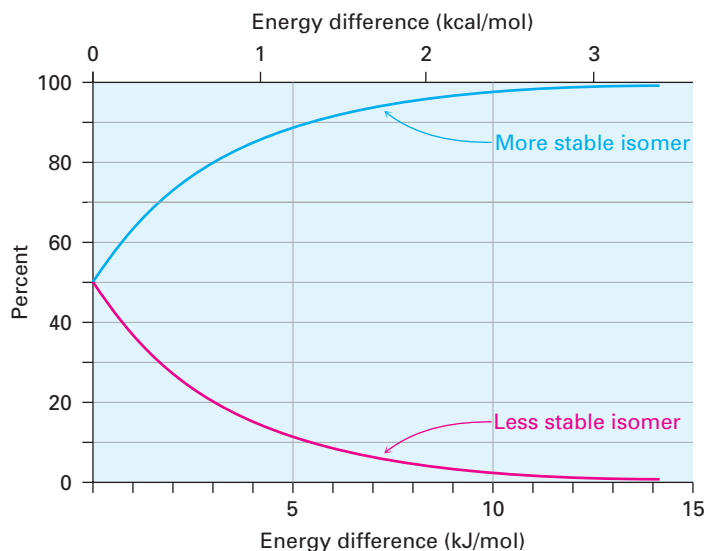
The energy difference between axial and equatorial conformations is due to steric strain caused by **1,3-diaxial interactions**. The axial methyl group on C1 is too close to the axial hydrogens three carbons away on C3 and C5, resulting in 7.6 kJ/mol of steric strain (Figure 4.13).
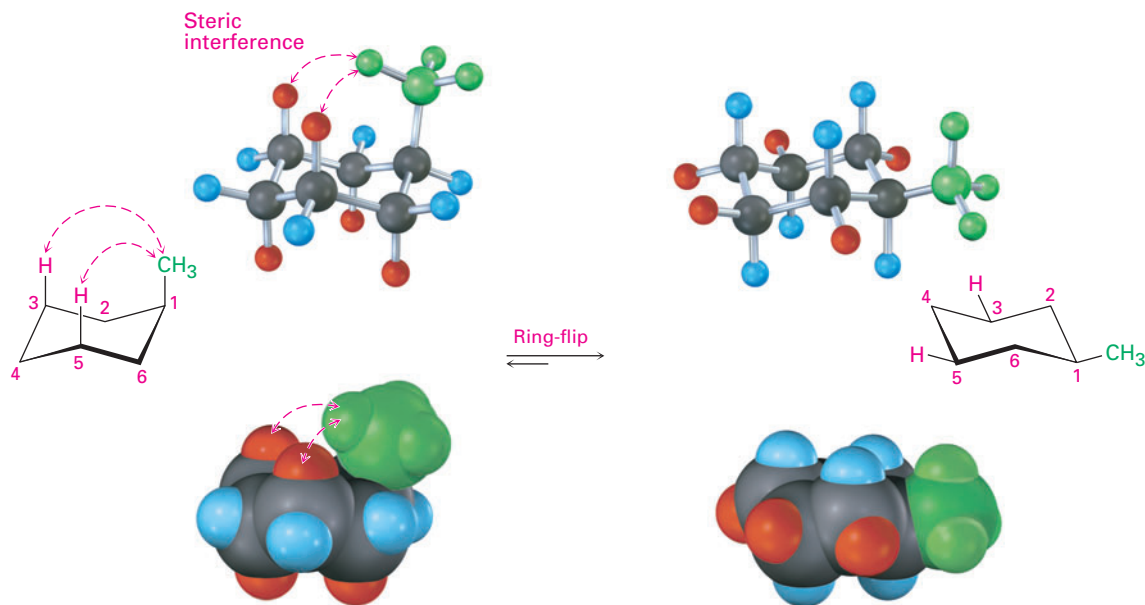

Figure 4.13 Interconversion of axial and equatorial methylcyclohexane, as represented in several formats. The equatorial conformation is more stable than the axial conformation by 7.6 kJ/mol.
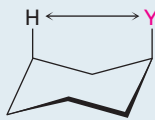
The 1,3-diaxial steric strain in substituted methylcyclohexane is already familiar—we saw it previously as the steric strain between methyl groups in gauche butane. Recall from Section 3.7 that gauche butane is less stable than anti butane by 3.8 kJ/mol (0.9 kcal/mol) because of steric interference between hydrogen atoms on the two methyl groups. Comparing a four-carbon fragment of axial methylcyclohexane with gauche butane shows that the steric interaction is the same in both cases (Figure 4.14). Because axial methylcyclohexane has two such interactions, though, it has $2 \times 3.8 = 7.6$ kJ/mol of steric strain. Equatorial methylcyclohexane, however, has no such interactions and is therefore more stable.

Figure 4.14 The origin of 1,3-diaxial interactions in methylcyclohexane. The steric strain between an axial methyl group and an axial hydrogen atom three carbons away is identical to the steric strain in gauche butane. Note that the —CH$_3$ group in methylcyclohexane moves slightly away from a true axial position to minimize the strain.

**Gauche butane
(3.8 kJ/mol strain)**

**Axial
methylcyclohexane
(7.6 kJ/mol strain)**
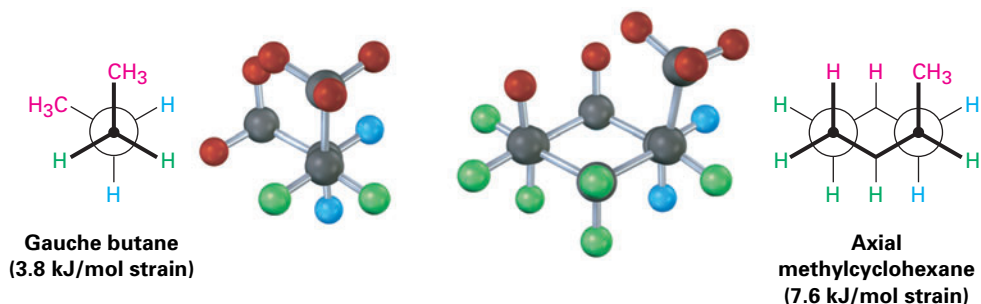
What is true for methylcyclohexane is also true for other monosubstituted cyclohexanes: a substituent is almost always more stable in an equatorial position than in an axial position. The exact amount of 1,3-diaxial steric strain in a given substituted cyclohexane depends on the nature and size of the substituent, as indicated in Table 4.1. Not surprisingly, the amount of steric strain increases through the series $H_3C- < CH_3CH_2- < (CH_3)_2CH- << (CH_3)_3C-$, paralleling the increasing bulk of the alkyl groups. Note that the values in Table 4.1 refer to 1,3-diaxial interactions of the substituent with a *single* hydrogen atom. These values must be doubled to arrive at the amount of strain in a monosubstituted cyclohexane.

Table 4.1   **Steric Strain in Monosubstituted Cyclohexanes**

| | 1,3-Diaxial strain | |
Y	(kJ/mol)	(kcal/mol)
F	0.5	0.12
Cl, Br	1.0	0.25
OH	2.1	0.5
CH_3	3.8	0.9
CH_2CH_3	4.0	0.95
$CH(CH_3)_2$	4.6	1.1
$C(CH_3)_3$	11.4	2.7
C_6H_5	6.3	1.5
CO_2H	2.9	0.7
CN	0.4	0.1

Problem 4.15   What is the energy difference between the axial and equatorial conformations of cyclohexanol (hydroxycyclohexane)?

Problem 4.16   Why do you suppose an axial cyano (−CN) substituent causes practically no 1,3-diaxial steric strain (0.4 kJ/mol)? Use molecular models to help with your answer.

Problem 4.17   Look at Figure 4.12, and estimate the percentages of axial and equatorial conformers present at equilibrium in bromocyclohexane.

4.8 | Conformations of Disubstituted Cyclohexanes

Monosubstituted cyclohexanes are more stable with their substituent in an equatorial position, but the situation in disubstituted cyclohexanes is more complex because the steric effects of both substituents must be taken into account. All steric interactions in both possible chair conformations must be analyzed before deciding which conformation is favored.

Let's look at 1,2-dimethylcyclohexane as an example. There are two isomers, *cis*-1,2-dimethylcyclohexane and *trans*-1,2-dimethylcyclohexane, which

must be considered separately. In the cis isomer, both methyl groups are on the same face of the ring, and the compound can exist in either of the two chair conformations shown in Figure 4.15. (It may be easier for you to see whether a compound is cis- or trans-disubstituted by first drawing the ring as a flat representation and then converting to a chair conformation.) Both chair conformations have one axial methyl group and one equatorial methyl group. The top conformation in Figure 4.15 has an axial methyl group at C2, which has 1,3-diaxial interactions with hydrogens on C4 and C6. The ring-flipped conformation has an axial methyl group at C1, which has 1,3-diaxial interactions with hydrogens on C3 and C5. In addition, both conformations have gauche butane interactions between the two methyl groups. *The two conformations are equal in energy,* with a total steric strain of 3×3.8 kJ/mol = 11.4 kJ/mol (2.7 kcal/mol).

cis-1,2-Dimethylcyclohexane

One gauche interaction (3.8 kJ/mol)
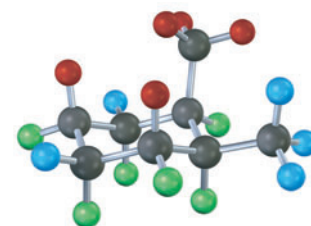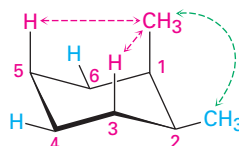Two $CH_3 \leftrightarrow H$ diaxial interactions (7.6 kJ/mol)
Total strain: 3.8 + 7.6 = 11.4 kJ/mol
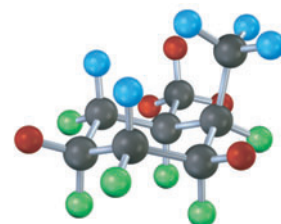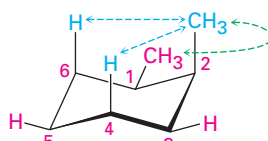
Ring-flip

One gauche interaction (3.8 kJ/mol)
Two $CH_3 \leftrightarrow H$ diaxial interactions (7.6 kJ/mol)
Total strain: 3.8 + 7.6 = 11.4 kJ/mol

Active Figure 4.15 Conformations of *cis*-1,2-dimethylcyclohexane. The two chair conformations are equal in energy because each has one axial methyl group and one equatorial methyl group. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*
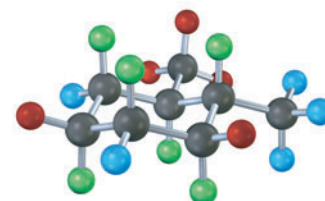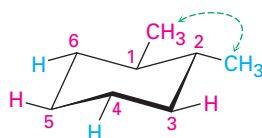
In *trans*-1,2-dimethylcyclohexane, the two methyl groups are on opposite faces of the ring and the compound can exist in either of the two chair conformations shown in Figure 4.16. The situation here is quite different from that of the cis isomer. The top trans conformation in Figure 4.16 has both methyl groups equatorial and therefore has only a gauche butane interaction between methyls (3.8 kJ/mol) but no 1,3-diaxial interactions. The ring-flipped conformation, however, has both methyl groups axial. The axial methyl group at C1 interacts with axial hydrogens at C3 and C5, and the axial methyl group at C2 interacts with axial hydrogens at C4 and C6. These four 1,3-diaxial interactions produce a steric strain of 4×3.8 kJ/mol = 15.2 kJ/mol and make the diaxial conformation $15.2 - 3.8 = 11.4$ kJ/mol less favorable than the diequatorial conformation. We therefore predict that *trans*-1,2-dimethylcyclohexane will exist almost exclusively in the diequatorial conformation.

The same kind of **conformational analysis** just carried out for *cis*- and *trans*-1,2-dimethylcyclohexane can be done for any substituted cyclohexane, such as *cis*-1-*tert*-butyl-4-chlorocyclohexane (see Worked Example 4.3). As you might imagine, though, the situation becomes more complex as the number of

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trans-1,2-Dimethylcyclohexane

One gauche
interaction (3.8 kJ/mol)

Ring-flip
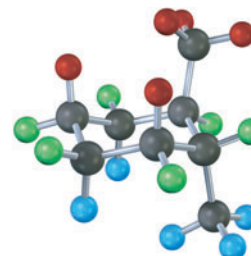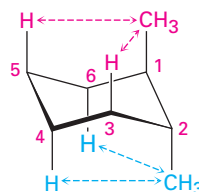
Four CH₃ ↔ H diaxial
interactions (15.2 kJ/mol)

Figure 4.16 Conformations of *trans*-1,2-dimethylcyclohexane. The conformation with both methyl groups equatorial is favored by 11.4 kJ/mol (2.7 kcal/mol) over the conformation with both methyl groups axial.

substituents increases. For instance, compare glucose with mannose, a carbohydrate present in seaweed. Which do you think is more strained? In glucose, all substituents on the six-membered ring are equatorial, while in mannose, one of the −OH groups is axial, making mannose more strained.
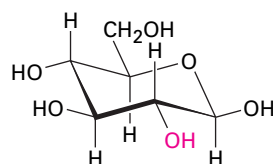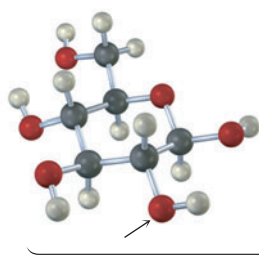
Glucose
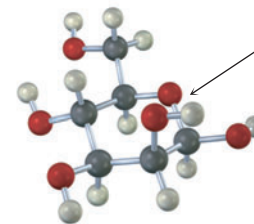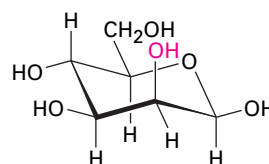
Mannose

A summary of the various axial and equatorial relationships among substituent groups in the different possible cis and trans substitution patterns for disubstituted cyclohexanes is given in Table 4.2.

Table 4.2   Axial and Equatorial Relationships in Cis- and Trans-Disubstituted Cyclohexanes

| Cis/trans substitution pattern	Axial/equatorial relationships		
1,2-Cis disubstituted	a,e	or	e,a
1,2-Trans disubstituted	a,a	or	e,e
1,3-Cis disubstituted	a,a	or	e,e
1,3-Trans disubstituted	a,e	or	e,a
1,4-Cis disubstituted	a,e	or	e,a
1,4-Trans disubstituted	a,a	or	e,e

WORKED EXAMPLE 4.3   *Drawing the Most Stable Conformation of a Substituted Cyclohexane*

Draw the most stable conformation of *cis*-1-*tert*-butyl-4-chlorocyclohexane. By how much is it favored?

Strategy   Draw the possible conformations, and calculate the strain energy in each. Remember that equatorial substituents cause less strain than axial substituents.

Solution   First draw the two chair conformations of the molecule:

2 × 1.0 = 2.0 kJ/mol steric strain   2 × 11.4 = 22.8 kJ/mol steric strain
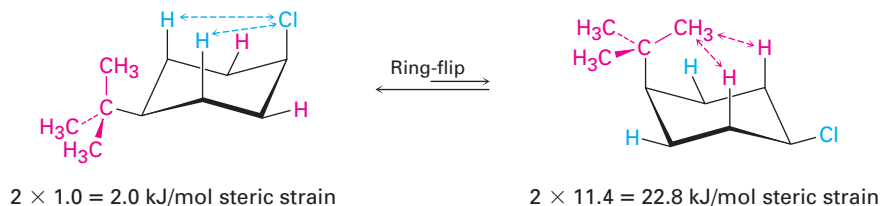
  In the left-hand conformation, the *tert*-butyl group is equatorial and the chlorine is axial. In the right-hand conformation, the *tert*-butyl group is axial and the chlorine is equatorial. These conformations aren't of equal energy because an axial *tert*-butyl substituent and an axial chloro substituent produce different amounts of steric strain. Table 4.1 shows that the 1,3-diaxial interaction between a hydrogen and a *tert*-butyl group costs 11.4 kJ/mol (2.7 kcal/mol), whereas the interaction between a hydrogen and a chlorine costs only 1.0 kJ/mol (0.25 kcal/mol). An axial *tert*-butyl group therefore produces (2 × 11.4 kJ/mol) − (2 × 1.0 kJ/mol) = 20.8 kJ/mol (4.9 kcal/mol) more steric strain than does an axial chlorine, and the compound preferentially adopts the conformation with the chlorine axial and the *tert*-butyl equatorial.

Problem 4.18   Draw the most stable chair conformation of the following molecules, and estimate the amount of strain in each:
(a) *trans*-1-Chloro-3-methylcyclohexane   (b) *cis*-1-Ethyl-2-methylcyclohexane
(c) *cis*-1-Bromo-4-ethylcyclohexane   (d) *cis*-1-*tert*-Butyl-4-ethylcyclohexane

Problem 4.19   Identify each substituent in the following compound as axial or equatorial, and tell whether the conformation shown is the more stable or less stable chair form (yellow-green = Cl):
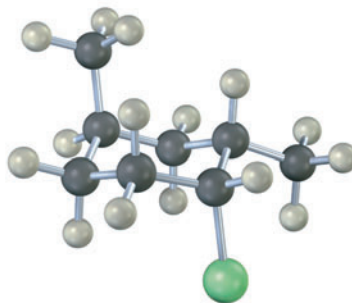
4.9 | Conformations of Polycyclic Molecules

The last point we'll consider about cycloalkane stereochemistry is to see what happens when two or more cycloalkane rings are fused together along a common bond to construct a **polycyclic** molecule—for example, decalin.
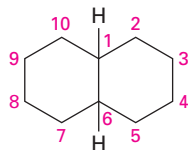

Decalin—two fused cyclohexane rings

Decalin consists of two cyclohexane rings joined to share two carbon atoms (the *bridgehead* carbons, C1 and C6) and a common bond. Decalin can exist in either of two isomeric forms, depending on whether the rings are trans fused or cis fused. In *cis*-decalin, the hydrogen atoms at the bridgehead carbons are on the same face of the rings; in *trans*-decalin, the bridgehead hydrogens are on opposite faces. Figure 4.17 shows how both compounds can be represented using chair cyclohexane conformations. Note that *cis*- and *trans*-decalin are not interconvertible by ring-flips or other rotations. They are cis–trans stereoisomers and have the same relationship to each other that *cis*- and *trans*-1,2-dimethylcyclohexane have.

Figure 4.17 Representations of *cis*- and *trans*-decalin. The red hydrogen atoms at the bridgehead carbons are on the same face of the rings in the cis isomer but on opposite faces in the trans isomer.

cis-Decalin

trans-Decalin
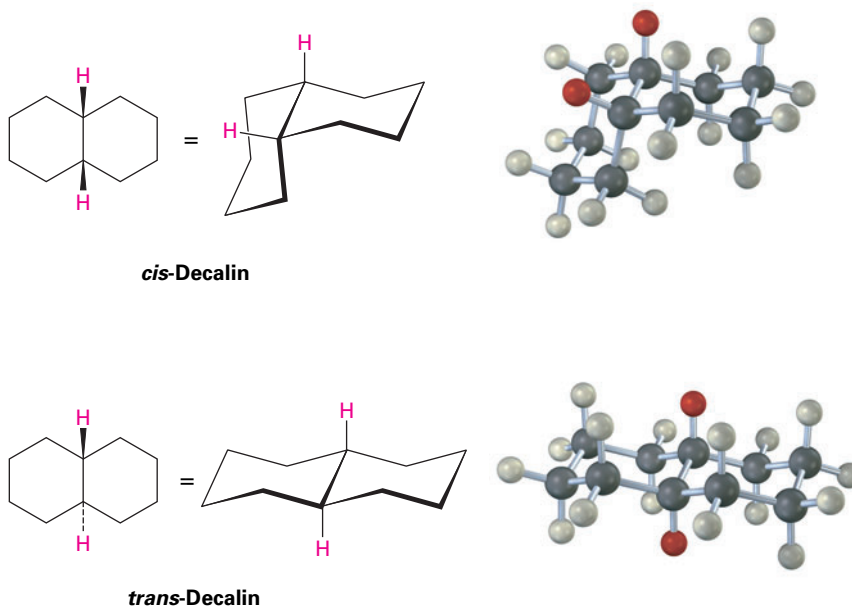
Polycyclic compounds are common in nature, and many valuable substances have fused-ring structures. For example, steroids, such as the male hormone testosterone, have 3 six-membered rings and 1 five-membered ring fused together. Although steroids look complicated compared with cyclohexane or decalin, the same principles that apply to the conformational analysis of simple cyclohexane rings apply equally well (and often better) to steroids.
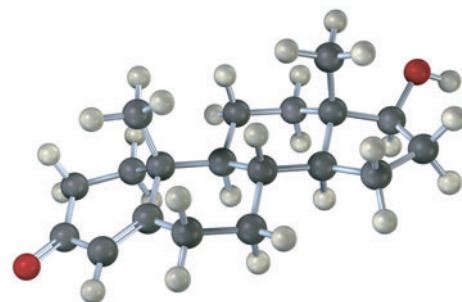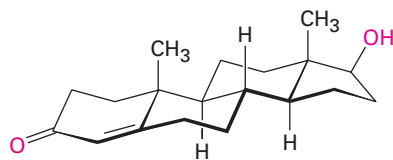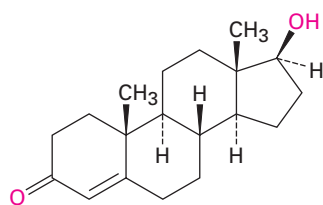
Testosterone (a steroid)

Another common ring system is the norbornane, or bicyclo[2.2.1]heptane, structure. Like decalin, norbornane is a *bicycloalkane,* so called because *two* rings would have to be broken open to generate an acyclic structure. Its systematic name, bicyclo[2.2.1]heptane, reflects the fact that the molecule has seven carbons, is bicyclic, and has three "bridges" of 2, 2, and 1 carbon atoms connecting the two bridgehead carbons.

A 1-carbon bridge

A 2-carbon bridge

Bridgehead carbons
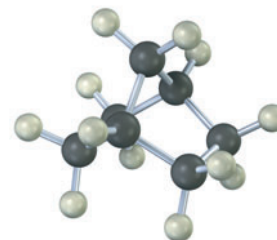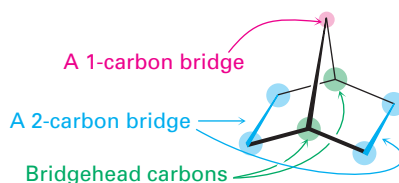
**Norbornane
(bicyclo[2.2.1]heptane)**

Norbornane has a conformationally locked boat cyclohexane ring (Section 4.5) in which carbons 1 and 4 are joined by an additional CH_2 group. Note how, in drawing this structure, a break in the rear bond indicates that the vertical bond crosses in front of it. Making a molecular model is particularly helpful when trying to see the three-dimensionality of norbornane.

Substituted norbornanes, such as camphor, are found widely in nature, and many have been important historically in developing organic structural theories.
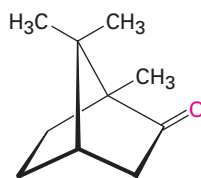
Camphor
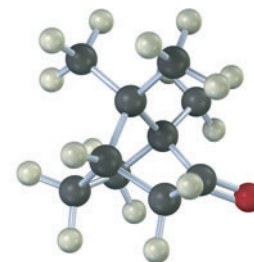
Problem 4.20 | Which isomer is more stable, *cis*-decalin or *trans*-decalin? Explain.

Focus On . . .

Molecular Mechanics

Computer programs make it possible to portray accurate representations of molecular geometry.

All the structural models in this book are computer-drawn. To make sure they accurately portray bond angles, bond lengths, torsional interactions, and steric interactions, the most stable geometry of each molecule has been calculated on a desktop computer using a commercially available *molecular mechanics* program based on work by N. L. Allinger of the University of Georgia.

The idea behind molecular mechanics is to begin with a rough geometry for a molecule and then calculate a total strain energy for that starting geometry, using mathematical equations that assign values to specific kinds of molecular interactions. Bond angles that are too large or too small cause angle strain; bond lengths that are too short or too long cause stretching or compressing strain; unfavorable eclipsing interactions around single bonds cause torsional strain; and nonbonded atoms that approach each other too closely cause steric, or *van der Waals,* strain.

$$E_{\text{total}} = E_{\text{bond stretching}} + E_{\text{angle strain}} + E_{\text{torsional strain}} + E_{\text{van der Waals}}$$

After calculating a total strain energy for the starting geometry, the program automatically changes the geometry slightly in an attempt to lower strain—perhaps by lengthening a bond that is too short or decreasing an angle that is too large. Strain is recalculated for the new geometry, more changes are made, and more calculations are done. After dozens or hundreds of iterations, the calculation ultimately converges on a minimum energy that corresponds to the most favorable, least strained conformation of the molecule.

Molecular mechanics calculations have proved to be enormously useful in pharmaceutical research, where the complementary fit between a drug molecule and a receptor molecule in the body is often a key to designing new pharmaceutical agents (Figure 4.18).

Figure 4.18 The structure of Tamiflu (oseltamivir phosphate), an antiviral agent active against type A influenza, and a molecular model of its minimum-energy conformation, as calculated by molecular mechanics.
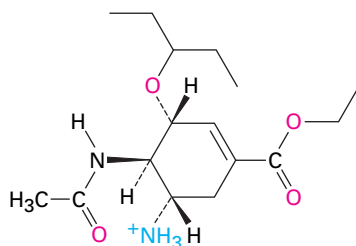
Tamiflu (oseltamivir phosphate)
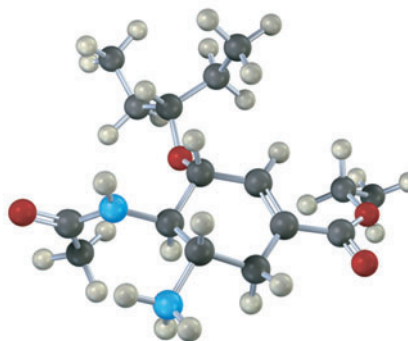
SUMMARY AND KEY WORDS

A **cycloalkane** is a saturated cyclic hydrocarbon with the general formula C_nH_{2n}. In contrast to open-chain alkanes, where nearly free rotation occurs around C−C bonds, rotation is greatly reduced in cycloalkanes. Disubstituted cycloalkanes can therefore exist as **cis–trans isomers**. The cis isomer has both substituents on the same face of the ring; the trans isomer has substituents on opposite faces. Cis–trans isomers are just one kind of **stereoisomers**—isomers that have the same connections between atoms but different three-dimensional arrangements.

Not all cycloalkanes are equally stable. Three kinds of strain contribute to the overall energy of a cycloalkane: (1) **angle strain** is the resistance of a bond angle to compression or expansion from the normal 109° tetrahedral value, (2) *torsional strain* is the energy cost of having neighboring C−H bonds eclipsed rather than staggered, and (3) *steric strain* is the repulsive interaction that arises when two groups attempt to occupy the same space.

Cyclopropane (115 kJ/mol strain) and cyclobutane (110.4 kJ/mol strain) have both angle strain and torsional strain. Cyclopentane is free of angle strain but has a substantial torsional strain due to its large number of eclipsing interactions. Both cyclobutane and cyclopentane pucker slightly away from planarity to relieve torsional strain.

Cyclohexane is strain-free because it adopts a puckered **chair conformation**, in which all bond angles are near 109° and all neighboring C−H bonds are staggered. Chair cyclohexane has two kinds of positions: **axial** and **equatorial**. Axial positions are oriented up and down, parallel to the ring axis, whereas equatorial positions lie in a belt around the equator of the ring. Each carbon atom has one axial and one equatorial position.

Chair cyclohexanes are conformationally mobile and can undergo a **ring-flip**, which interconverts axial and equatorial positions. Substituents on the ring are more stable in the equatorial position because axial substituents cause **1,3-diaxial interactions**. The amount of 1,3-diaxial steric strain caused by an axial substituent depends on its bulk.

EXERCISES

Organic **KNOWLEDGE TOOLS**

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 Online homework for this chapter may be assigned in Organic OWL.

■ indicates problems assignable in Organic OWL.

▲ denotes problems linked to Key Ideas of this chapter and testable in ThomsonNOW.

VISUALIZING CHEMISTRY

(Problems 4.1–4.20 appear within the chapter.)

4.21 ■ Name the following cycloalkanes:

(a)   **(b)**
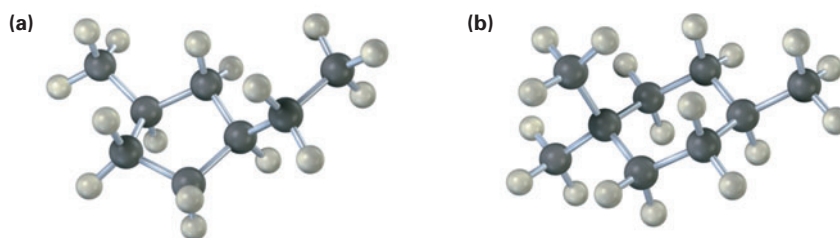
4.22 ■ Name the following compound, identify each substituent as axial or equatorial, and tell whether the conformation shown is the more stable or less stable chair form (yellow-green = Cl):
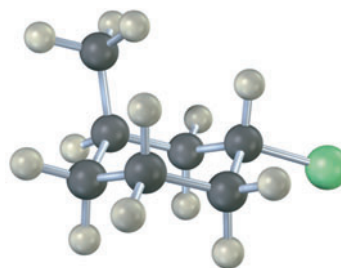
4.23 ▲ A trisubstituted cyclohexane with three substituents—red, yellow, and blue—undergoes a ring-flip to its alternative chair conformation. Identify each substituent as axial or equatorial, and show the positions occupied by the three substituents in the ring-flipped form.

Ring-flip

■ Assignable in OWL   ▲ Key Idea Problems
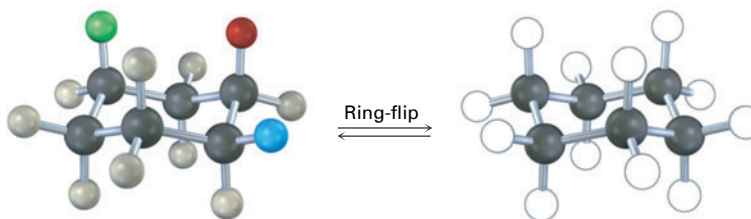
4.24 Glucose exists in two forms having a 36:64 ratio at equilibrium. Draw a skeletal structure of each, describe the difference between them, and tell which of the two you think is more stable (red = O):
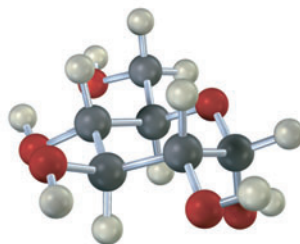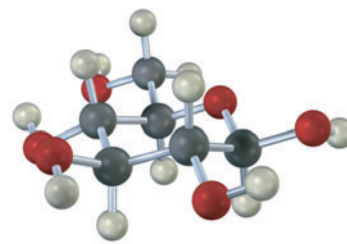
α-Glucose   *β*-Glucose

ADDITIONAL PROBLEMS

4.25 Draw the five cycloalkanes with the formula C_5H_{10}.

4.26 ■ Draw two constitutional isomers of *cis*-1,2-dibromocyclopentane.

4.27 ■ Draw a stereoisomer of *trans*-1,3-dimethylcyclobutane.

4.28 ■ Hydrocortisone, a naturally occurring hormone produced in the adrenal glands, is often used to treat inflammation, severe allergies, and numerous other conditions. Is the indicated −OH group in the molecule axial or equatorial?
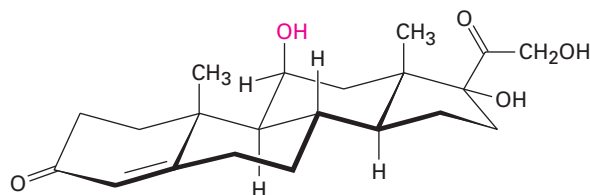
Hydrocortisone

4.29 A 1,2-cis disubstituted cyclohexane, such as *cis*-1,2-dichlorocyclohexane, must have one group axial and one group equatorial. Explain.

4.30 A 1,2-trans disubstituted cyclohexane must have either both groups axial or both groups equatorial. Explain.

4.31 Why is a 1,3-cis disubstituted cyclohexane more stable than its trans isomer?

4.32 ■ Which is more stable, a 1,4-trans disubstituted cyclohexane or its cis isomer?

4.33 *cis*-1,2-Dimethylcyclobutane is less stable than its trans isomer, but *cis*-1,3-dimethylcyclobutane is more stable than its trans isomer. Draw the most stable conformations of both, and explain.

4.34 ■ Draw the two chair conformations of *cis*-1-chloro-2-methylcyclohexane. Which is more stable, and by how much?

4.35 ■ Draw the two chair conformations of *trans*-1-chloro-2-methylcyclohexane. Which is more stable?

■ Assignable in OWL   ▲ Key Idea Problems

4.36 ■ Galactose, a sugar related to glucose, contains a six-membered ring in which all the substituents except the −OH group indicated below in red are equatorial. Draw galactose in its more stable chair conformation.

Galactose
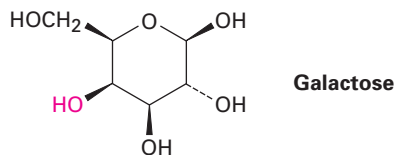
4.37 Draw the two chair conformations of menthol, and tell which is more stable.
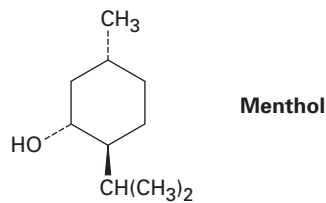
Menthol

4.38 There are four cis–trans isomers of menthol (Problem 4.37), including the one shown. Draw the other three.

4.39 Identify each pair of relationships among the −OH groups in glucose (red–blue, red–green, red–black, blue–green, blue–black, green–black) as cis or trans.

Glucose
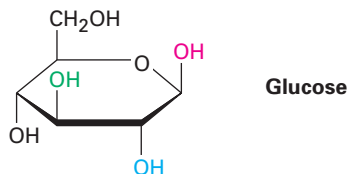
4.40 ▲ Draw 1,3,5-trimethylcyclohexane using a hexagon to represent the ring. How many cis–trans stereoisomers are possible?

4.41 ■ From the data in Figure 4.12 and Table 4.1, estimate the percentages of molecules that have their substituents in an axial orientation for the following compounds:
(a) Isopropylcyclohexane **(b)** Fluorocyclohexane
(c) Cyclohexanecarbonitrile, $C_6H_{11}CN$

4.42 ■ ▲ Assume that you have a variety of cyclohexanes substituted in the positions indicated. Identify the substituents as either axial or equatorial. For example, a 1,2-cis relationship means that one substituent must be axial and one equatorial, whereas a 1,2-trans relationship means that both substituents are axial or both are equatorial.
(a) 1,3-Trans disubstituted **(b)** 1,4-Cis disubstituted
(c) 1,3-Cis disubstituted **(d)** 1,5-Trans disubstituted
(e) 1,5-Cis disubstituted **(f)** 1,6-Trans disubstituted

4.43 ▲ The diaxial conformation of *cis*-1,3-dimethylcyclohexane is approximately 23 kJ/mol (5.4 kcal/mol) less stable than the diequatorial conformation. Draw the two possible chair conformations, and suggest a reason for the large energy difference.

■ Assignable in OWL ▲ Key Idea Problems

4.44 Approximately how much steric strain does the 1,3-diaxial interaction between the two methyl groups introduce into the diaxial conformation of *cis*-1,3-dimethylcyclohexane? (See Problem 4.43.)

4.45 In light of your answer to Problem 4.44, draw the two chair conformations of 1,1,3-trimethylcyclohexane, and estimate the amount of strain energy in each. Which conformation is favored?

4.46 We saw in Problem 4.20 that *cis*-decalin is less stable than *trans*-decalin. Assume that the 1,3-diaxial interactions in *trans*-decalin are similar to those in axial methylcyclohexane [that is, one CH_2 H interaction costs 3.8 kJ/mol (0.9 kcal/mol)], and calculate the magnitude of the energy difference between *cis*- and *trans*-decalin.

4.47 Using molecular models as well as structural drawings, explain why *trans*-decalin is rigid and cannot ring-flip, whereas *cis*-decalin can easily ring-flip.

4.48 *trans*-Decalin is more stable than its cis isomer, but *cis*-bicyclo[4.1.0]heptane is more stable than its trans isomer. Explain.
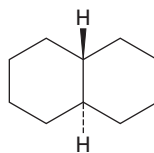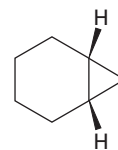
trans-Decalin   **cis-Bicyclo[4.1.0]heptane**

4.49 ▲ *myo*-Inositol, one of the isomers of 1,2,3,4,5,6-hexahydroxycyclohexane, acts as a growth factor in both animals and microorganisms. Draw the most stable chair conformation of *myo*-inositol.
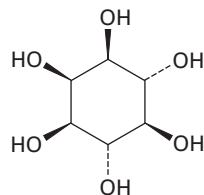
myo-**Inositol**

4.50 How many cis–trans stereoisomers of *myo*-inositol (Problem 4.49) are there? Draw the structure of the most stable isomer.

4.51 ■ One of the two chair structures of *cis*-1-chloro-3-methylcyclohexane is more stable than the other by 15.5 kJ/mol (3.7 kcal/mol). Which is it? What is the energy cost of a 1,3-diaxial interaction between a chlorine and a methyl group?

4.52 The German chemist J. Bredt proposed in 1935 that bicycloalkenes such as 1-norbornene, which have a double bond to the bridgehead carbon, are too strained to exist. Make a molecular model of 1-norbornene, and explain Bredt's proposal.

1-Norbornene

4.53 ■ Tell whether each of the following substituents on a steroid is axial or equatorial. (A substituent that is "up" is on the top face of the molecule as drawn, and a substituent that is "down" is on the bottom face.)
(a) Substituent up at C3
(b) Substituent down at C7
(c) Substituent down at C11
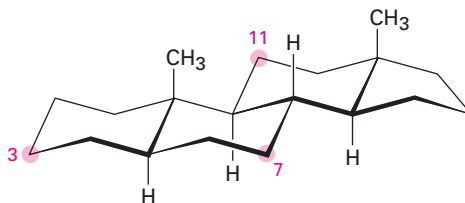
4.54 Amantadine is an antiviral agent that is active against influenza A infection and against some strains of H5N1 avian flu. Draw a three-dimensional representation of amantadine showing the chair cyclohexane rings.

Amantadine
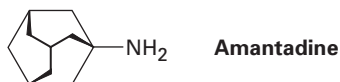
4.55 Ketones react with alcohols to yield products called *acetals.* Why does the all-cis isomer of 4-*tert*-butyl-1,3-cyclohexanediol react readily with acetone and an acid catalyst to form an acetal while other stereoisomers do not react? In formulating your answer, draw the more stable chair conformations of all four stereoisomers and the product acetal. Use molecular models for help.

An acetal
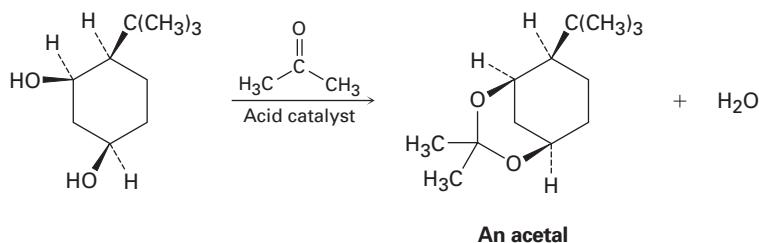
4.56 Alcohols undergo an *oxidation* reaction to yield carbonyl compounds on treatment with CrO_3. For example, 2-*tert*-butylcyclohexanol gives 2-*tert*-butylcyclohexanone. If axial −OH groups are generally more reactive than their equatorial isomers, which do you think would react faster, the cis isomer of 2-*tert*-butylcyclohexanol or the trans isomer? Explain.
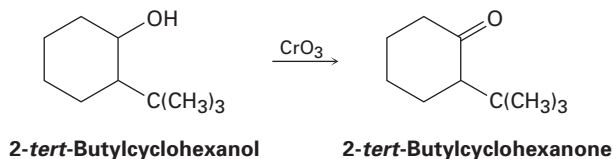
2-*tert*-Butylcyclohexanol   **2-*tert*-Butylcyclohexanone**

■ Assignable in OWL   ▲ Key Idea Problems

5

An Overview of Organic Reactions

When first approached, organic chemistry can seem overwhelming. It's not so much that any one part is difficult to understand, it's that there are so many parts: literally millions of compounds, dozens of functional groups, and an endless number of reactions. With study, though, it becomes evident that there are only a few fundamental ideas that underlie all organic reactions. Far from being a collection of isolated facts, organic chemistry is a beautifully logical subject that is unified by a few broad themes. When these themes are understood, learning organic chemistry becomes much easier and memorization is minimized. The aim of this book is to describe the themes and clarify the patterns that unify organic chemistry.

WHY THIS CHAPTER?

All chemical reactions, whether in the laboratory or in living organisms, follow the same "rules." Reactions in living organisms often look more complex than laboratory reactions because of the size of the biomolecules and the involvement of biological catalysts called *enzymes,* but the principles governing all reactions are the same.

To understand both organic and biological chemistry, it's necessary to know not just *what* occurs, but also *why* and *how* chemical reactions take place. In this chapter, we'll start with an overview of the fundamental kinds of organic reactions, we'll see why reactions occur, and we'll see how reactions can be described. Once this background is out of the way, we'll then be ready to begin studying the details of organic chemistry.

5.1 | Kinds of Organic Reactions

Organic chemical reactions can be organized broadly in two ways—by *what kinds* of reactions occur and by *how* those reactions occur. Let's look first at the kinds of reactions that take place. There are four general types of organic reactions: *additions, eliminations, substitutions,* and *rearrangements.*

▍ **Addition reactions** occur when two reactants add together to form a single product with no atoms "left over." An example that we'll be studying soon

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is the reaction of an alkene, such as ethylene, with HBr to yield an alkyl bromide.

These two reactants . . .   [Ethylene structure]   +   H—Br   ⟶   [Bromoethane structure]   . . . add to give this product.

Ethylene
(an alkene)

Bromoethane
(an alkyl halide)
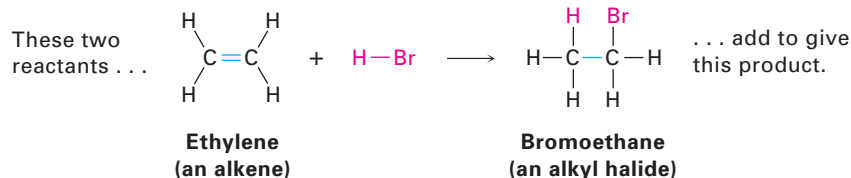
▎ **Elimination reactions** are, in a sense, the opposite of addition reactions. They occur when a single reactant splits into two products, often with formation of a small molecule such as water or HBr. An example is the acid-catalyzed reaction of an alcohol to yield water and an alkene.

This one reactant . . .   [Ethanol structure]   ⇌ *Acid catalyst*   [Ethylene structure]   + H_2O . . . gives these two products.

Ethanol
(an alcohol)

Ethylene
(an alkene)
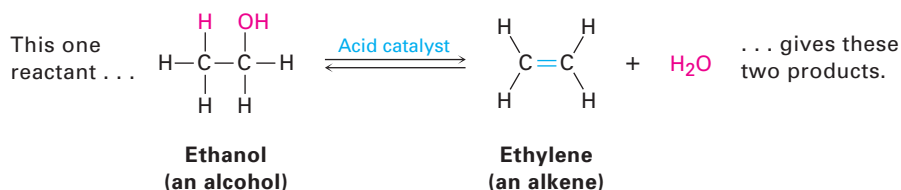
▎ **Substitution reactions** occur when two reactants exchange parts to give two new products. An example is the reaction of an alkane with Cl_2 in the presence of ultraviolet light to yield an alkyl chloride. A Cl atom from Cl_2 substitutes for an H atom of the alkane, and two new products result.

These two reactants . . .   [Methane structure]   +   Cl—Cl   → *Light*   [Chloromethane structure]   +   H—Cl   . . . give these two products.

Methane
(an alkane)

Chloromethane
(an alkyl halide)
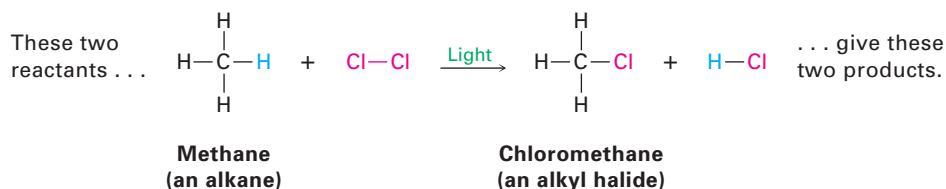
▎ **Rearrangement reactions** occur when a single reactant undergoes a reorganization of bonds and atoms to yield an isomeric product. An example is the conversion of the alkene 1-butene into its constitutional isomer 2-butene by treatment with an acid catalyst.

This reactant . . .   [1-Butene structure]   ⇌ *Acid catalyst*   [2-Butene structure]   . . . gives this isomeric product.

1-Butene

2-Butene
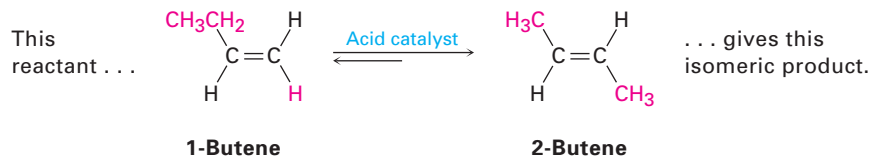
Problem 5.1 │ Classify each of the following reactions as an addition, elimination, substitution, or rearrangement:

(a) $CH_3Br + KOH \rightarrow CH_3OH + KBr$
(b) $CH_3CH_2Br \rightarrow H_2C{=}CH_2 + HBr$
(c) $H_2C{=}CH_2 + H_2 \rightarrow CH_3CH_3$

5.2 | How Organic Reactions Occur: Mechanisms

Having looked at the kinds of reactions that take place, let's now see how reactions occur. An overall description of how a reaction occurs is called a **reaction mechanism**. A mechanism describes in detail exactly what takes place at each stage of a chemical transformation—which bonds are broken and in what order, which bonds are formed and in what order, and what the relative rates of the steps are. A complete mechanism must also account for all reactants used and all products formed.

All chemical reactions involve bond-breaking and bond-making. When two molecules come together, react, and yield products, specific bonds in the reactant molecules are broken and specific bonds in the product molecules are formed. Fundamentally, there are two ways in which a covalent two-electron bond can break. A bond can break in an electronically *symmetrical* way so that one electron remains with each product fragment, or a bond can break in an electronically *unsymmetrical* way so that both bonding electrons remain with one product fragment, leaving 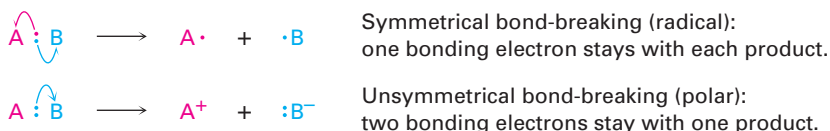the other with a vacant orbital. The symmetrical cleavage is said to be *homolytic,* and the unsymmetrical cleavage is said to be *heterolytic.* We'll develop the point in more detail later, but you might note for now that the movement of *one* electron in the symmetrical process is indicated using a half-headed, or "fishhook," arrow ($\curvearrowright$), whereas the movement of *two* electrons in the unsymmetrical process is indicated using a full-headed curved arrow ($\curvearrowright$).

A : B $\longrightarrow$ A· + ·B   **Symmetrical bond-breaking (radical):**
one bonding electron stays with each product.

A : B $\longrightarrow$ A⁺ + :B⁻   **Unsymmetrical bond-breaking (polar):**
two bonding electrons stay with one product.

Just as there are two ways in which a bond can break, there are two ways in which a covalent two-electron bond can form. A bond can form in an electronically symmetrical way if one electron is donated to the new bond by each reactant or in an unsymmetrical way if both bonding electrons are donated by one reactant.

A· + ·B $\longrightarrow$ A : B   **Symmetrical bond-making (radical):**
one bonding electron is donated by each reactant.

A⁺ + :B⁻ $\longrightarrow$ A : B   **Unsymmetrical bond-making (polar):**
two bonding electrons are donated by one reactant.
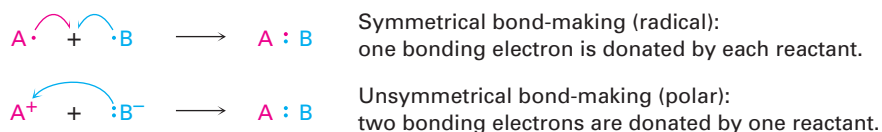
Processes that involve symmetrical bond-breaking and bond-making are called **radical reactions**. A **radical**, often called a *free radical,* is a neutral chemical species that contains an odd number of electrons and thus has a single, unpaired electron in one of its orbitals. Processes that involve unsymmetrical bond-breaking and bond-making are called **polar reactions**. Polar reactions involve species that have an even number of electrons and thus have only electron pairs in their orbitals. Polar processes are by far the more common reaction type in both organic and biological chemistry, and a large part of this book is devoted to their description.

In addition to polar and radical reactions, there is a third, less commonly encountered process called a *pericyclic reaction.* Rather than explain pericyclic reactions now, though, we'll look at them more carefully in Chapter 30.

5.3 | Radical Reactions

Radical reactions are not as common as polar reactions but are nevertheless important in some industrial processes and in numerous biological pathways. Let's see briefly how they occur.

A radical is highly reactive because it contains an atom with an odd number of electrons (usually seven) in its valence shell, rather than a stable, noble-gas octet. A radical can achieve a valence-shell octet in several ways. For example, the radical might abstract an atom and one bonding electron from another reactant, leaving behind a new radical. The net result is a radical substitution reaction:
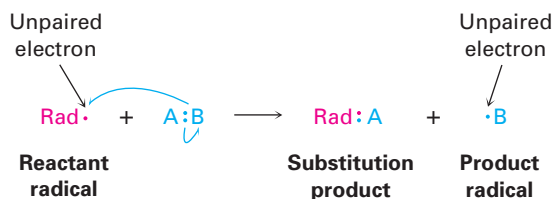
Alternatively, a reactant radical might add to a double bond, taking one electron from the double bond and yielding a new radical. The net result is a radical addition reaction:
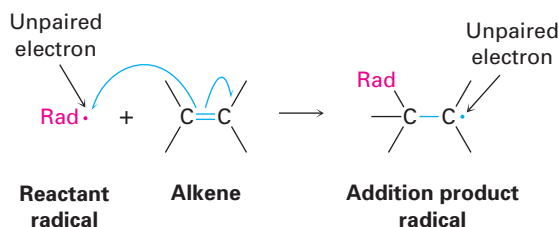
As an example of an industrially useful radical reaction, look at the chlorination of methane to yield chloromethane. This substitution reaction is the first step in the preparation of the solvents dichloromethane (CH_2Cl_2) and chloroform ($CHCl_3$).
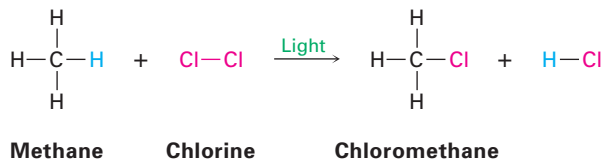
Like many radical reactions in the laboratory, methane chlorination requires three kinds of steps: *initiation*, *propagation*, and *termination*.

Initiation Irradiation with ultraviolet light begins the reaction by breaking the relatively weak Cl–Cl bond of a small number of Cl_2 molecules to give a few reactive chlorine radicals.

Propagation   Once produced, a reactive chlorine radical collides with a methane molecule in a propagation step, abstracting a hydrogen atom to give HCl and a methyl radical ($\cdot$ CH$_3$). This methyl radical reacts further with Cl$_2$ in a second propagation step to give the product chloromethane plus a new chlorine radical, which cycles back and repeats the first propagation step. Thus, once the sequence has been initiated, it becomes a self-sustaining cycle of repeating steps (a) and (b), making the overall process a *chain reaction.*

(a) $:\!\overset{..}{\underset{..}{Cl}}\!\cdot$ +   H$:$CH$_3$ $\longrightarrow$ H$:\!\overset{..}{\underset{..}{Cl}}\!:$ + $\cdot$CH$_3$

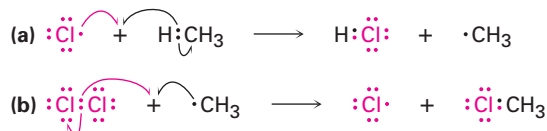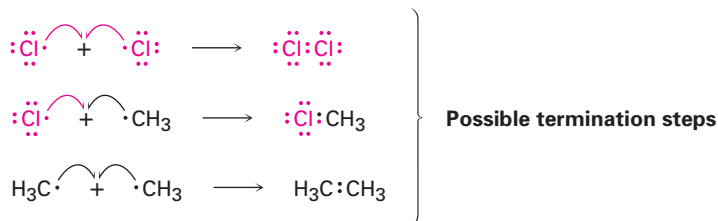**(b)** $:\!\overset{..}{\underset{..}{Cl}}\!:\!\overset{..}{\underset{..}{Cl}}\!:$ + $\cdot$CH$_3$ $\longrightarrow$ $:\!\overset{..}{\underset{..}{Cl}}\!\cdot$ + $:\!\overset{..}{\underset{..}{Cl}}\!:CH_3$

Termination   Occasionally, two radicals might collide and combine to form a stable product. When that happens, the reaction cycle is broken and the chain is ended. Such termination steps occur infrequently, however, because the concentration of radicals in the reaction at any given moment is very small. Thus, the likelihood that two radicals will collide is also small.

$:\!\overset{..}{\underset{..}{Cl}}\!\cdot$ + $\cdot\overset{..}{\underset{..}{Cl}}\!:$ $\longrightarrow$ $:\!\overset{..}{\underset{..}{Cl}}\!:\!\overset{..}{\underset{..}{Cl}}\!:$

$:\!\overset{..}{\underset{..}{Cl}}\!\cdot$ + $\cdot$CH$_3$ $\longrightarrow$ $:\!\overset{..}{\underset{..}{Cl}}\!:CH_3$ **Possible termination steps**

H$_3$C$\cdot$ + $\cdot$CH$_3$ $\longrightarrow$ H$_3$C$:$CH$_3$

As a biological example of a radical reaction, let's look at the biosynthesis of *prostaglandins,* a large class of molecules found in virtually all body tissues and fluids. A number of pharmaceuticals are based on or derived from prostaglandins, including medicines that induce labor during childbirth, reduce intraocular pressure in glaucoma, control bronchial asthma, and help treat congenital heart defects.

Prostaglandin biosynthesis is initiated by abstraction of a hydrogen atom from arachidonic acid by an iron–oxygen radical, thereby generating a new, carbon radical in a substitution reaction. Don't be intimidated by the size of the molecules; focus only on the changes occurring in each step. (To help you do that, the unchanged part of the molecule is "ghosted," with only the reactive part clearly visible.)

Arachidonic acid

Oxygen radical

Radical substitution
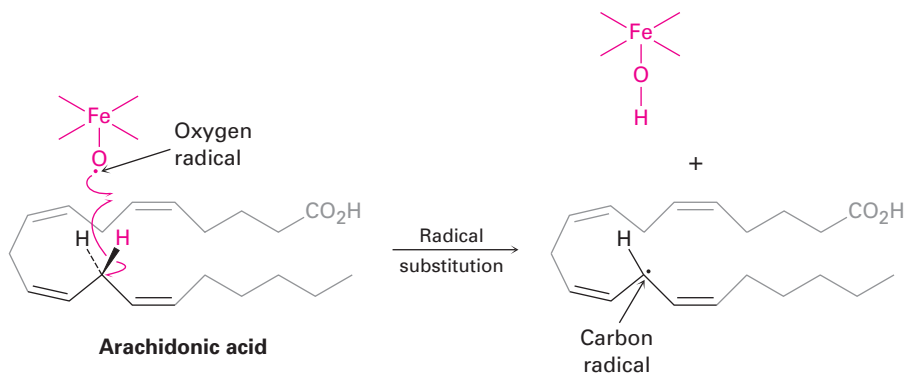
Carbon radical

Following the initial abstraction of a hydrogen atom, the carbon radical then reacts with O_2 to give an oxygen radical, which reacts with a C=C bond within the same molecule in an addition reaction. Several further transformations ultimately yield prostaglandin H_2.

Prostaglandin H₂ (PGH₂)
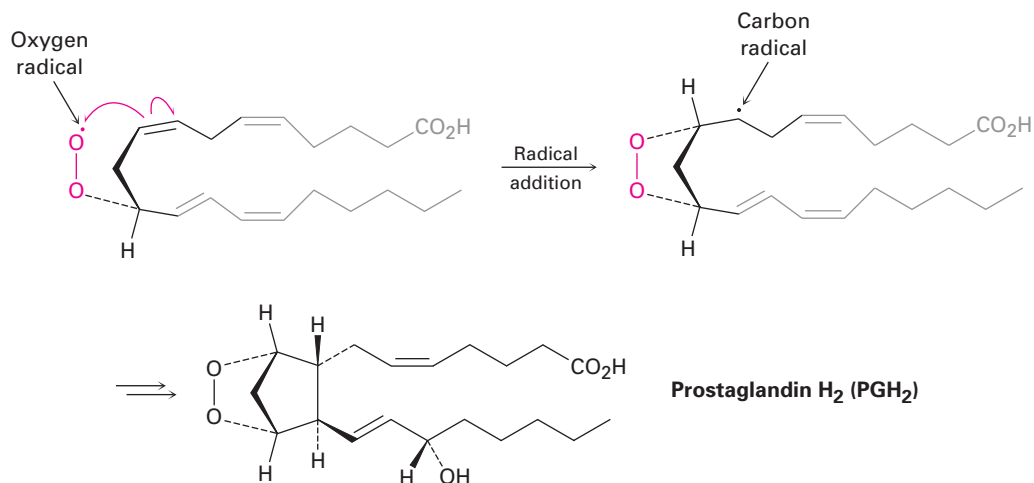
Problem 5.2   Radical chlorination of alkanes is not generally useful because mixtures of products often result when more than one kind of C−H bond is present in the substrate. Draw and name all monochloro substitution products $C_6H_{13}Cl$ you might obtain by reaction of 2-methylpentane with Cl_2.
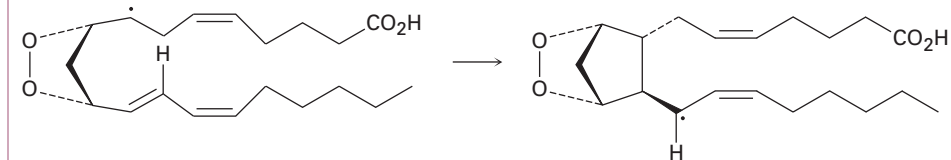
Problem 5.3   Using a curved fishhook arrow, propose a mechanism for formation of the cyclopentane ring of prostaglandin H_2. What kind of reaction is occurring?

5.4   Polar Reactions

Polar reactions occur because of the electrical attraction between positive and negative centers on functional groups in molecules. To see how these reactions take place, let's first recall the discussion of polar covalent bonds in Section 2.1 and then look more deeply into the effects of bond polarity on organic molecules.

Most organic compounds are electrically neutral; they have no net charge, either positive or negative. We saw in Section 2.1, however, that certain bonds within a molecule, particularly the bonds in functional groups, are polar. Bond polarity is a consequence of an unsymmetrical electron distribution in a bond and is due to the difference in electronegativity of the bonded atoms.

Elements such as oxygen, nitrogen, fluorine, and chlorine are more electronegative than carbon, so a carbon atom bonded to one of these atoms has a partial positive charge ($\delta+$). Conversely, metals are less electronegative than

carbon, so a carbon atom bonded to a metal has a partial negative charge ($\delta-$). Electrostatic potential maps of chloromethane and methyllithium illustrate these charge distributions, showing that the carbon atom in chloromethane is electron-poor (blue) while the carbon in methyllithium is electron-rich (red).

Chloromethane   **Methyllithium**
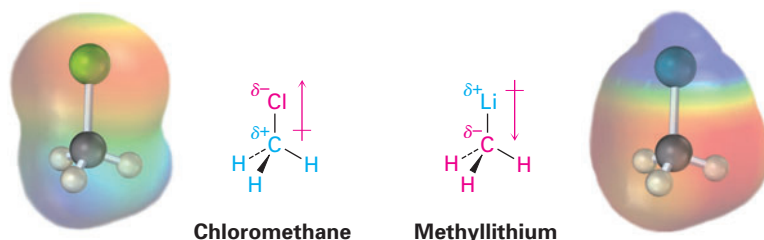
The polarity patterns of some common functional groups are shown in Table 5.1. Carbon is always positively polarized except when bonded to a metal.

Table 5.1 | Polarity Patterns in Some Common Functional Groups

Alcohol	$\overset{\delta+\ \delta-}{-C-OH}$	Carbonyl $\quad \overset{\delta+\ \delta-}{C=O}$
Alkene	$C=C$ (Symmetrical, nonpolar)	Carboxylic acid
Alkyl halide	$\overset{\delta+\ \delta-}{-C-X}$	Carboxylic acid chloride
Amine	$\overset{\delta+\ \delta-}{-C-NH_2}$	Aldehyde
Ether	$\overset{\delta+\ \delta-\ \delta+}{-C-O-C-}$	Ester
Thiol	$\overset{\delta+\ \delta-}{-C-SH}$	Ketone
Nitrile	$\overset{\delta+\ \delta-}{-C\equiv N}$	
Grignard reagent	$\overset{\delta-\ \delta+}{-C-MgBr}$	
Alkyllithium	$\overset{\delta-\ \delta+}{-C-Li}$	

This discussion of bond polarity is oversimplified in that we've considered only bonds that are inherently polar due to differences in electronegativity. Polar bonds can also result from the interaction of functional groups with acids or bases. Take an alcohol such as methanol, for example. In neutral methanol, the carbon atom is somewhat electron-poor because the electronegative oxygen attracts the electrons in the C−O bond. On protonation of the methanol oxygen by an acid, however, a full positive charge on oxygen attracts the electrons in the C−O bond much more strongly and makes the carbon much more electron-poor. We'll see numerous examples throughout this book of reactions that are catalyzed by acids because of the resultant increase in bond polarity.

Methanol—weakly electron-poor carbon

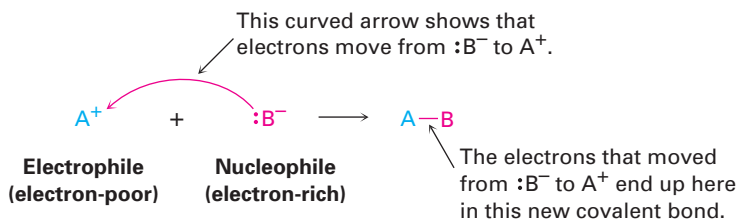**Protonated methanol— strongly electron-poor carbon**
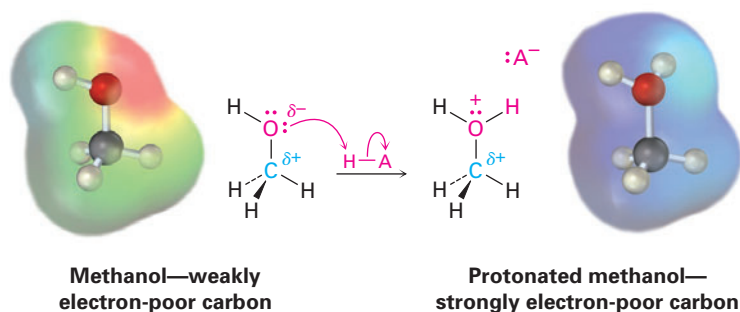
Yet a further consideration is the *polarizability* (as opposed to polarity) of atoms in a molecule. As the electric field around a given atom changes because of changing interactions with solvent or other polar molecules nearby, the electron distribution around that atom also changes. The measure of this response to an external electrical influence is called the polarizability of the atom. Larger atoms with more, loosely held electrons are more polarizable, and smaller atoms with fewer, tightly held electrons are less polarizable. Thus, sulfur is more polarizable than oxygen, and iodine is more polarizable than chlorine. The effect of this higher polarizability for sulfur and iodine is that carbon–sulfur and carbon–iodine bonds, although nonpolar according to electronegativity values (Figure 2.2), nevertheless usually react as if they were polar.
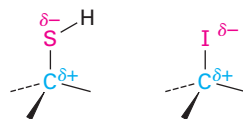
What does functional-group polarity mean with respect to chemical reactivity? Because unlike charges attract, the fundamental characteristic of all polar organic reactions is that electron-rich sites react with electron-poor sites. Bonds are made when an electron-rich atom shares a pair of electrons with an electron-poor atom, and bonds are broken when one atom leaves with both electrons from the former bond.

As we saw in Section 2.11, chemists indicate the movement of an electron pair during a polar reaction by using a curved, full-headed arrow. A curved arrow shows where electrons move when reactant bonds are broken and product bonds are formed. It means that an electron pair moves *from* the atom

(or bond) at the tail of the arrow *to* the atom at the head of the arrow during the reaction.

This curved arrow shows that electrons move from :B⁻ to A⁺.

$$A^+ \quad + \quad :B^- \quad \longrightarrow \quad A-B$$

Electrophile   **Nucleophile**
(electron-poor)   **(electron-rich)**

The electrons that moved from :B⁻ to A⁺ end up here in this new covalent bond.

In referring to the electron-rich and electron-poor species involved in polar reactions, chemists use the words *nucleophile* and *electrophile*. A **nucleophile** is a substance that is "nucleus-loving." (Remember that a nucleus is positively charged.) A nucleophile has a negatively polarized, electron-rich atom and can form a bond by donating a pair of electrons to a positively polarized, electron-poor atom. Nucleophiles may be either neutral or negatively charged; ammonia, water, hydroxide ion, and chloride ion are examples. An **electrophile**, by contrast, is "electron-loving." An electrophile has a positively polarized, electron-poor atom and can form a bond by accepting a pair of electrons from a nucleophile. Electrophiles can be either neutral or positively charged. Acids (H⁺ donors), alkyl halides, and carbonyl compounds are examples (Figure 5.1).
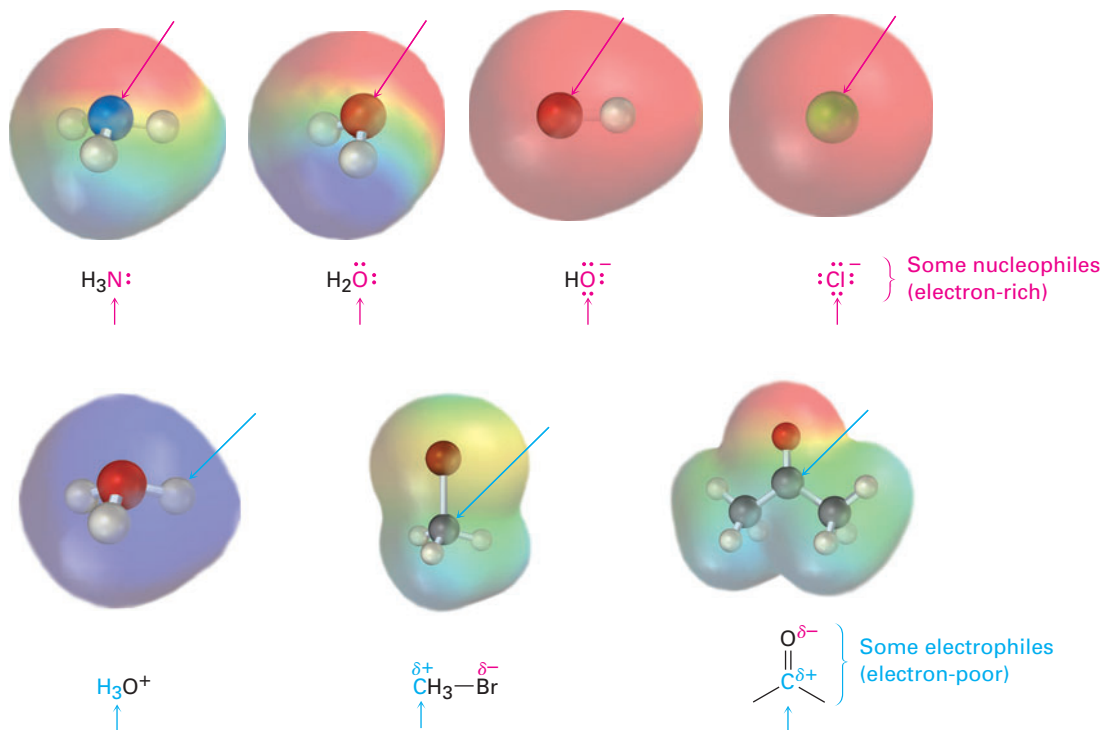

$H_3N:$

$H_2\ddot{O}:$

$H\ddot{O}:^-$

$:\ddot{C}l:^-$ } Some nucleophiles (electron-rich)

H_3O^+

$\overset{\delta+}{C}H_3 - \overset{\delta-}{Br}$

$\overset{O^{\delta-}}{\underset{C^{\delta+}}{\|}}$ } Some electrophiles (electron-poor)

Figure 5.1 Some nucleophiles and electrophiles. Electrostatic potential maps identify the nucleophilic (red; negative) and electrophilic (blue; positive) atoms.

If the definitions of nucleophiles and electrophiles sound similar to those given in Section 2.11 for Lewis acids and Lewis bases, that's because there is

indeed a correlation. Lewis bases are electron donors and behave as nucleophiles, whereas Lewis acids are electron acceptors and behave as electrophiles. Thus, much of organic chemistry is explainable in terms of acid–base reactions. The main difference is that the words *acid* and *base* are used broadly, while *nucleophile* and *electrophile* are used primarily when bonds to carbon are involved.

WORKED EXAMPLE 5.1	***Identifying Electrophiles and Nucleophiles***

ThomsonNOW™ Click *Organic Interactive* to **identify and characterize nucleophiles and electrophiles in organic reactions**.

Which of the following species is likely to behave as a nucleophile and which as an electrophile?

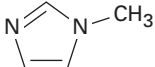(a) NO_2^+ (b) CN^- (c) CH_3NH_2 (d) $(CH_3)_3S^+$

Strategy Nucleophiles have an electron-rich site, either because they are negatively charged or because they have a functional group containing an atom that has a lone pair of electrons. Electrophiles have an electron-poor site, either because they are positively charged or because they have a functional group containing an atom that is positively polarized.

Solution (a) NO_2^+ (nitronium ion) is likely to be an electrophile because it is positively charged.

(b) $:C{\equiv}N^-$ (cyanide ion) is likely to be a nucleophile because it is negatively charged.

(c) CH_3NH_2 (methylamine) is likely to be a nucleophile because it has a lone pair of electrons on the nitrogen atom.

(d) $(CH_3)_3S^+$ (trimethylsulfonium ion) is likely to be an electrophile because it is positively charged.

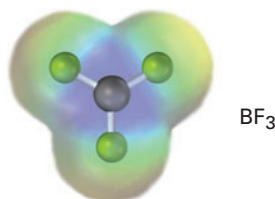**Problem 5.4** Which of the following species is likely to be a nucleophile and which an electrophile?

(a) CH_3Cl (b) CH_3S^- (c)   (d)

$$\underset{CH_3CH}{\overset{\overset{\textstyle O}{\|}}{}}$$

Problem 5.5 An electrostatic potential map of boron trifluoride is shown. Is BF_3 likely to be a nucleophile or an electrophile? Draw a Lewis structure for BF_3, and explain your answer.

BF_3

5.5 | An Example of a Polar Reaction: Addition of HBr to Ethylene

Let's look at a typical polar process—the addition reaction of an alkene, such as ethylene, with hydrogen bromide. When ethylene is treated with HBr at room temperature, bromoethane is produced. Overall, the reaction can be formulated as

| **Ethylene (nucleophile)** | | **Hydrogen bromide (electrophile)** | | **Bromoethane** |
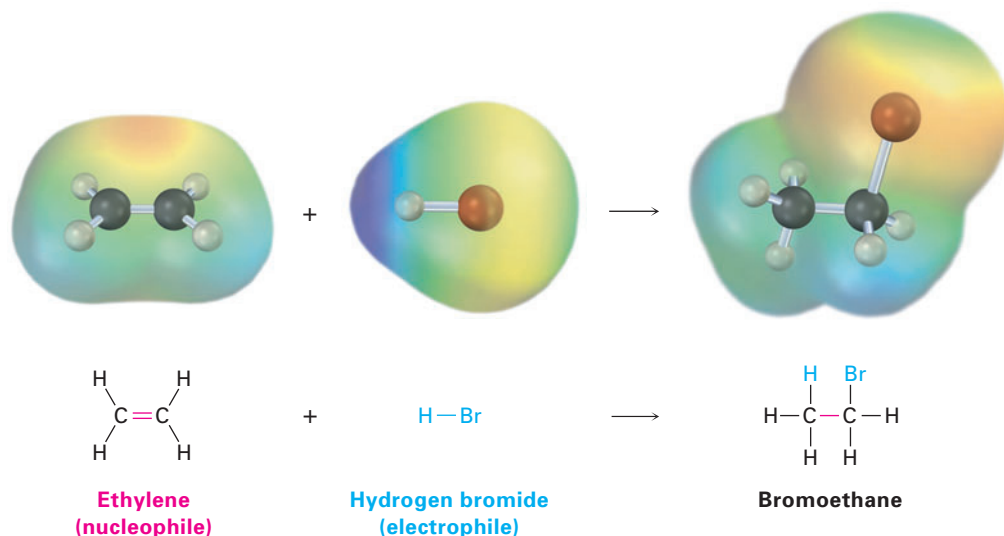
The reaction is an example of a polar reaction type known as an *electrophilic addition reaction* and can be understood using the general ideas discussed in the previous section. Let's begin by looking at the two reactants.

What do we know about ethylene? We know from Section 1.8 that a carbon–carbon double bond results from orbital overlap of two sp^2-hybridized carbon atoms. The σ part of the double bond results from sp^2–sp^2 overlap, and the π part results from p–p overlap.

What kind of chemical reactivity might we expect of a C=C bond? We know that *alkanes,* such as ethane, are relatively inert because all valence electrons are tied up in strong, nonpolar C−C and C−H bonds. Furthermore, the bonding electrons in alkanes are relatively inaccessible to approaching reactants because they are sheltered in σ bonds between nuclei. The electronic situation in *alkenes* is quite different, however. For one thing, double bonds have a greater electron density than single bonds—four electrons in a double bond versus only two in a single bond. Furthermore, the electrons in the π bond are accessible to approaching reactants because they are located above and below the plane of the double bond rather than being sheltered between the nuclei (Figure 5.2). As a result, the double bond is nucleophilic and the chemistry of alkenes is dominated by reactions with electrophiles.

What about the second reactant, HBr? As a strong acid, HBr is a powerful proton (H^+) donor and electrophile. Thus, the reaction between HBr and ethylene is a typical electrophile–nucleophile combination, characteristic of all polar reactions.

Figure 5.2 A comparison of carbon–carbon single and double bonds. A double bond is both more accessible to approaching reactants than a single bond and more electron-rich (more nucleophilic). An electrostatic potential map of ethylene indicates that the double bond is the region of highest negative charge (red).

Carbon–carbon σ bond:
stronger; less accessible
bonding electrons

Carbon–carbon π bond:
weaker; more accessible electrons
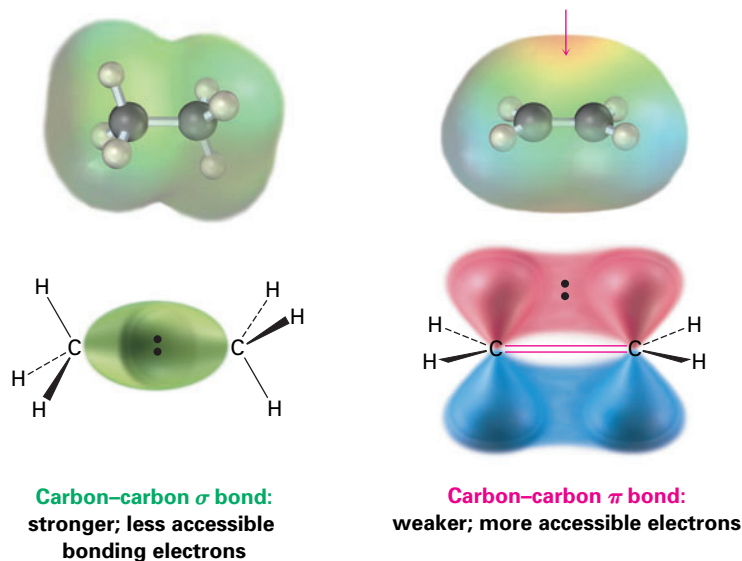
We'll see more details about alkene electrophilic addition reactions shortly, but for the present we can imagine the reaction as taking place in two steps by the pathway shown in Figure 5.3. The reaction begins when the alkene donates a pair of electrons from its C=C bond to HBr to form a new C−H bond plus Br⁻, as indicated by the path of the curved arrows in the first step of Figure 5.3. One curved arrow begins at the middle of the double bond (the source of the electron pair) and points to the hydrogen atom in HBr (the atom to which a bond will form). This arrow indicates that a new C−H bond forms using electrons from the former C=C bond. A second curved arrow begins in the middle of the H−Br bond and points to the Br, indicating that the H−Br bond breaks and the electrons remain with the Br atom, giving Br⁻.

When one of the alkene carbon atoms bonds to the incoming hydrogen, the other carbon atom, having lost its share of the double-bond electrons, now has only six valence electrons and is left with a positive charge. This positively charged species—a carbon-cation, or **carbocation**—is itself an electrophile that can accept an electron pair from nucleophilic Br⁻ anion in a second step, forming a C−Br bond and yielding the observed addition product. Once again, a curved arrow in Figure 5.3 shows the electron-pair movement from Br⁻ to the positively charged carbon.

The electrophilic addition of HBr to ethylene is only one example of a polar process; there are many others that we'll study in detail in later chapters. But regardless of the details of individual reactions, all polar reactions take place between an electron-poor site and an electron-rich site and involve the donation of an electron pair from a nucleophile to an electrophile.

Problem 5.6 | What product would you expect from reaction of cyclohexene with HBr? With HCl?
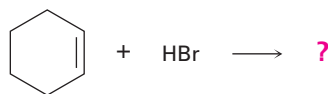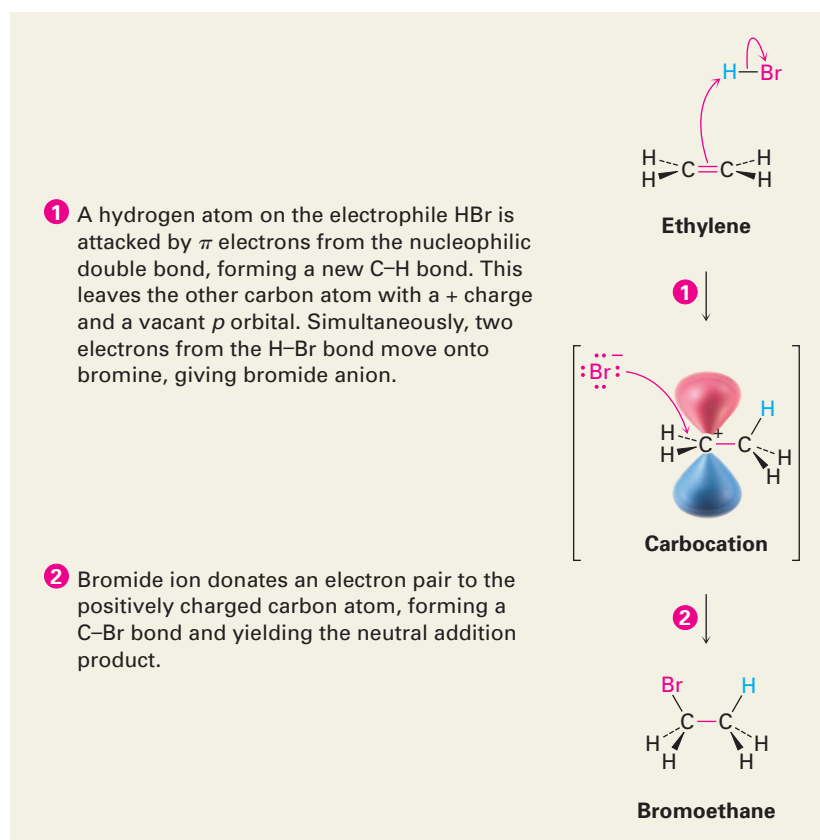

$+$ HBr $\longrightarrow$ **?**

Figure 5.3 **MECHANISM:** The electrophilic addition reaction of ethylene and HBr. The reaction takes place in two steps, both of which involve electrophile–nucleophile interactions.

1 A hydrogen atom on the electrophile HBr is attacked by π electrons from the nucleophilic double bond, forming a new C–H bond. This leaves the other carbon atom with a + charge and a vacant *p* orbital. Simultaneously, two electrons from the H–Br bond move onto bromine, giving bromide anion.

2 Bromide ion donates an electron pair to the positively charged carbon atom, forming a C–Br bond and yielding the neutral addition product.

Ethylene

Carbocation

Bromoethane

© John McMurry

Problem 5.7 | Reaction of HBr with 2-methylpropene yields 2-bromo-2-methylpropane. What is the structure of the carbocation formed during the reaction? Show the mechanism of the reaction.

2-Methylpropene   **2-Bromo-2-methylpropane**
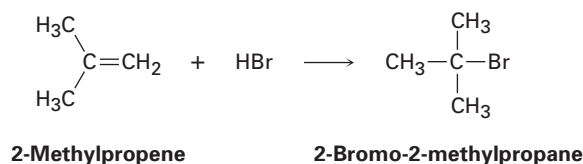
## 5.6 | **Using Curved Arrows in Polar Reaction Mechanisms**

It takes practice to use curved arrows properly in reaction mechanisms, but there are a few rules and a few common patterns you should look for that will help you become more proficient.

Rule 1 **Electrons move *from* a nucleophilic source (Nu: or Nu:⁻) *to* an electrophilic sink (E or E⁺).** The nucleophilic source must have an electron pair available, usually either in a lone pair or in a multiple bond. For example:

Key IDEAS

Test your knowledge of Key Ideas by using resources in ThomsonNOW or by answering end-of-chapter problems marked with ▲.
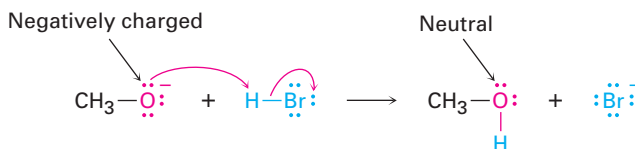
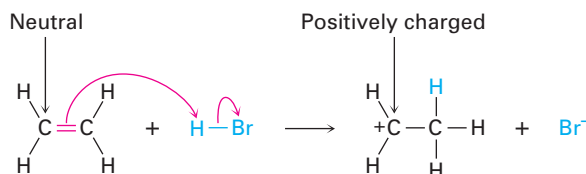Electrons usually flow *from* one of these nucleophiles.
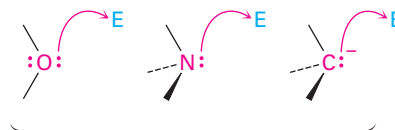
The electrophilic sink must be able to accept an electron pair, usually because it has either a positively charged atom or a positively polarized atom in a functional group. For example:

Electrons usually flow *to* one of these electrophiles.
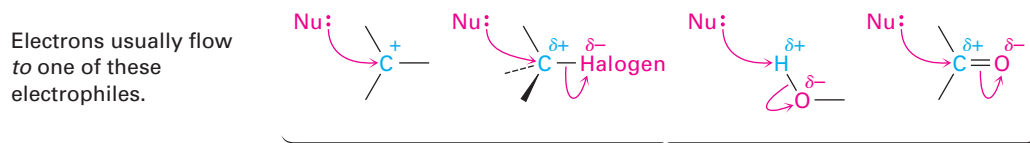
Rule 2 **The nucleophile can be either negatively charged or neutral.** If the nucleophile is negatively charged, the atom that gives away an electron pair becomes neutral. For example:

Negatively charged | Neutral

$$CH_3-\overset{..}{\underset{..}{O}}{:}^{-} \ + \ H-\overset{..}{\underset{..}{Br}}{:} \ \longrightarrow \ CH_3-\overset{..}{\underset{..}{O}}{:} \ + \ {:}\overset{..}{\underset{..}{Br}}{:}^{-}$$

If the nucleophile is neutral, the atom that gives away an electron pair acquires a positive charge. For example:

Neutral | Positively charged

If the electrophile is neutral, the atom that ultimately accepts the electron pair acquires a negative charge. For this to happen, however, the negative charge must be stabilized by being on an electronegative atom such as oxygen, nitrogen, or a halogen. For example:

Rule 3 **The electrophile can be either positively charged or neutral.** If the electrophile is positively charged, the atom bearing that charge becomes neutral after accepting an electron pair. For example:
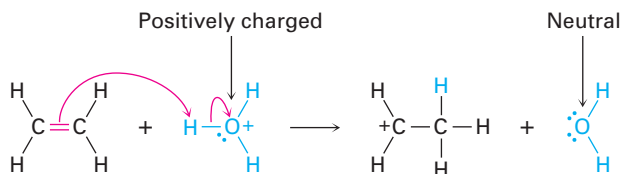
Positively charged | Neutral

If the electrophile is neutral, the atom that ultimately accepts the electron pair acquires a negative charge. For this to happen, however, the negative charge must be stabilized by being on an electronegative atom such as oxygen, nitrogen, or a halogen. For example:

Neutral | Negatively charged
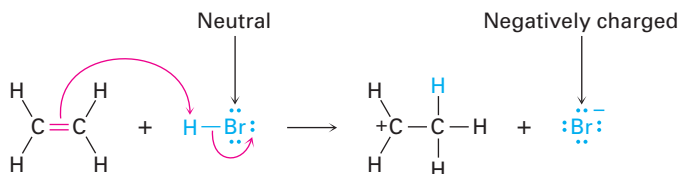
The result of Rules 2 and 3 together is that charge is conserved during the reaction. A negative charge in one of the reactants gives a negative charge in one of the products, and a positive charge in one of the reactants gives a positive charge in one of the products.

Rule 4   **The octet rule must be followed.** That is, no second-row atom can be left with ten electrons (or four for hydrogen). If an electron pair moves *to* an atom that already has an octet (or two for hydrogen), another electron pair must simultaneously move *from* that atom to maintain the octet. When two electrons move from the C=C bond of ethylene to the hydrogen atom of H_3O^+, for instance, two electrons must leave that hydrogen. This means that the H−O bond must break and the electrons must stay with the oxygen, giving neutral water.

This hydrogen already has two electrons. When another electron pair moves to the hydrogen from the double bond, the electron pair in the H–O bond must leave.
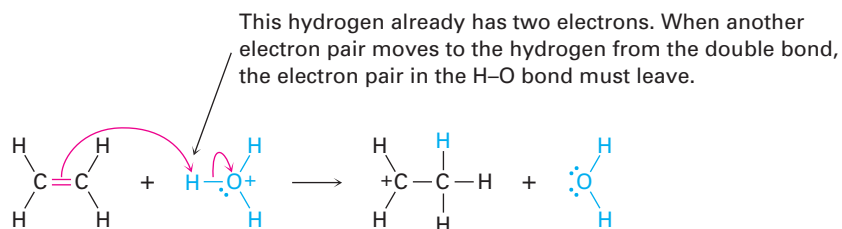
ThomsonNOW Click *Organic Interactive* to **practice writing organic mechanisms using curved arrows**.

Worked Example 5.2 gives another example of drawing curved arrows.


WORKED EXAMPLE 5.2   *Using Curved Arrows in Reaction Mechanisms*

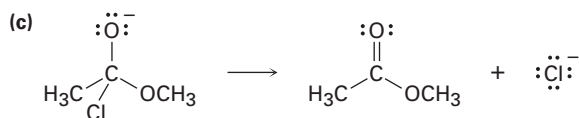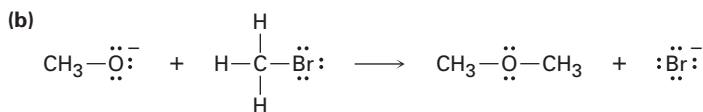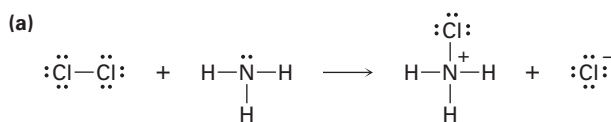Add curved arrows to the following polar reaction to show the flow of electrons:
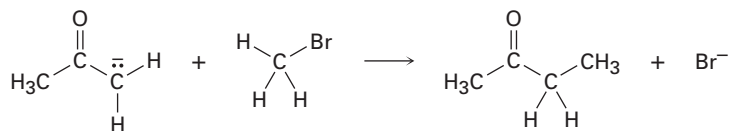
Strategy   First, look at the reaction and identify the bonding changes that have occurred. In this case, a C−Br bond has broken and a C−C bond has formed. The formation of the C−C bond involves donation of an electron pair from the nucleophilic carbon atom of the reactant on the left to the electrophilic carbon atom of CH_3Br, so we draw a curved arrow originating from the lone pair on the negatively charged C atom and pointing to the C atom of CH_3Br. At the same time the C−C bond forms, the C−Br bond must break so that the octet rule is not violated. We therefore draw a second curved arrow from the C−Br bond to Br. The bromine is now a stable Br^- ion.
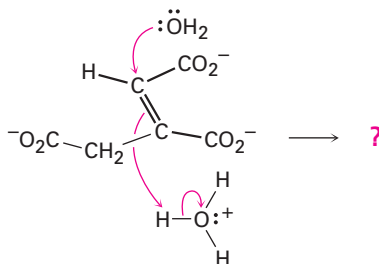
Solution
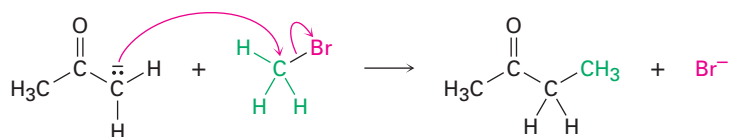
Problem 5.8 | Add curved arrows to the following polar reactions to indicate the flow of electrons in each:

(a)

$$:\ddot{Cl}-\ddot{Cl}: \quad + \quad H-\overset{\displaystyle H}{\underset{\displaystyle H}{N}}-H \quad \longrightarrow \quad H-\overset{\overset{\displaystyle :\ddot{Cl}:}{\displaystyle |}}{\underset{\displaystyle H}{\overset{+}{N}}}-H \quad + \quad :\ddot{\underset{..}{Cl}}:^-$$

(b)

$$CH_3-\ddot{\underset{..}{O}}:^- \quad + \quad H-\overset{\displaystyle H}{\underset{\displaystyle H}{C}}-\ddot{Br}: \quad \longrightarrow \quad CH_3-\ddot{\underset{..}{O}}-CH_3 \quad + \quad :\ddot{\underset{..}{Br}}:^-$$

(c)

$$\longrightarrow$$

$$+ \quad :\ddot{\underset{..}{Cl}}:^-$$

Problem 5.9 | Predict the products of the following polar reaction, a step in the citric acid cycle for food metabolism, by interpreting the flow of electrons indicated by the curved arrows:

5.7 | Describing a Reaction: Equilibria, Rates, and Energy Changes

Every chemical reaction can go in either forward or reverse direction. Reactants can go forward to products, and products can revert to reactants. As you may remember from your general chemistry course, the position of the resulting chemical equilibrium is expressed by an equation in which K_{eq}, the equilibrium constant, is equal to the product concentrations multiplied together, divided by the reactant concentrations multiplied together, with each concentration raised to the power of its coefficient in the balanced equation. For the generalized reaction
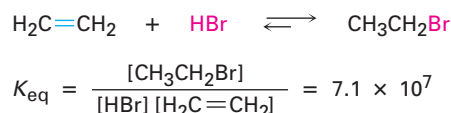
$$a A + b B \quad \rightleftharpoons \quad c C + d D$$

we have

$$K_{eq} = \frac{[C]^c \, [D]^d}{[A]^a \, [B]^b}$$

The value of the equilibrium constant tells which side of the reaction arrow is energetically favored. If K_{eq} is much larger than 1, then the product concentration term $[C]^c [D]^d$ is much larger than the reactant concentration term $[A]^a [B]^b$, and the reaction proceeds as written from left to right. If K_{eq} is near 1, appreciable amounts of both reactant and product are present at equilibrium. And if K_{eq} is much smaller than 1, the reaction does not take place as written but instead goes in the reverse direction, from right to left.

In the reaction of ethylene with HBr, for example, we can write the following equilibrium expression, and we can determine experimentally that the equilibrium constant at room temperature is approximately 7.1×10^7:

$$H_2C=CH_2 \ + \ HBr \ \rightleftharpoons \ CH_3CH_2Br$$

$$K_{eq} \ = \ \frac{[CH_3CH_2Br]}{[HBr] \, [H_2C=CH_2]} \ = \ 7.1 \times 10^7$$

Because K_{eq} is relatively large, the reaction proceeds as written and greater than 99.999 99% of the ethylene is converted into bromoethane. For practical purposes, an equilibrium constant greater than about 10^3 means that the amount of reactant left over will be barely detectable (less than 0.1%).

What determines the magnitude of the equilibrium constant? For a reaction to have a favorable equilibrium constant and proceed as written, the energy of the products must be lower than the energy of the reactants. In other words, energy must be *released.* The situation is analogous to that of a rock poised precariously in a high-energy position near the top of a hill. When it rolls downhill, the rock releases energy until it reaches a more stable low-energy position at the bottom.

The energy change that occurs during a chemical reaction is called the **Gibbs free-energy change (ΔG).** For a favorable reaction, ΔG has a negative value, meaning that energy is lost by the chemical system and released to the surroundings. Such reactions are said to be **exergonic.** For an unfavorable reaction, ΔG has a positive value, meaning that energy is absorbed by the chemical system *from* the surroundings. Such reactions are said to be **endergonic.** You might also recall from general chemistry that the *standard* free-energy change for a reaction is denoted $\Delta G°$, where the superscript ° means that the reaction is carried out under standard conditions, with pure substances in their most stable form at 1 atm pressure and a specified temperature, usually 298 K.

$K_{eq} > 1$; energy out: $\Delta G°$ negative

$K_{eq} < 1$; energy in: $\Delta G°$ positive
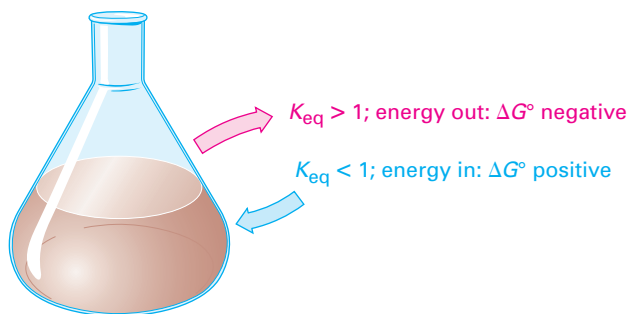
Because the equilibrium constant, K_{eq}, and the standard free-energy change, $\Delta G°$, both measure whether a reaction is favored, they are mathematically related by the equation

$$\Delta G° = -RT \ln K_{eq} \quad \text{or} \quad K_{eq} = e^{-\Delta G°/RT}$$

where $R = 8.314 \text{ J/(K} \cdot \text{mol)} = 1.987 \text{ cal/(K} \cdot \text{mol)}$
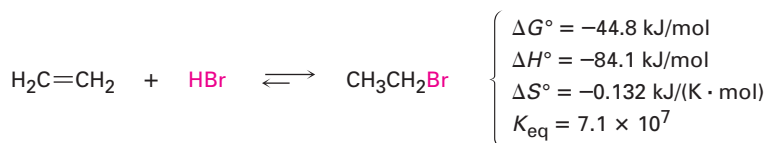
$T = $ Kelvin temperature

$e = 2.718$

$\ln K_{eq} = $ natural logarithm of K_{eq}

The free-energy change ΔG is made up of two terms, an *enthalpy* term, ΔH, and a temperature-dependent *entropy* term, $T\Delta S$. Of the two terms, the enthalpy term is often larger and more dominant.

$$\Delta G° = \Delta H° - T\Delta S°$$

For the reaction of ethylene with HBr at room temperature (298 K), the approximate values are

$$H_2C{=}CH_2 \ + \ HBr \ \rightleftarrows \ CH_3CH_2Br \quad \begin{cases} \Delta G° = -44.8 \text{ kJ/mol} \\ \Delta H° = -84.1 \text{ kJ/mol} \\ \Delta S° = -0.132 \text{ kJ/(K} \cdot \text{mol)} \\ K_{eq} = 7.1 \times 10^7 \end{cases}$$

The **enthalpy change, ΔH,** also called the **heat of reaction**, is a measure of the change in total bonding energy during a reaction. If ΔH is negative, as in the reaction of HBr with ethylene, the bonds in the products are stronger (more stable) than the bonds in the reactants, heat is released, and the reaction is said to be **exothermic**. If ΔH is positive, the bonds in the products are weaker (less stable) than the bonds in the reactants, heat is absorbed, and the reaction is said to be **endothermic**. For example, if a reaction breaks reactant bonds with a total strength of 380 kJ/mol and forms product bonds with a total strength of 400 kJ/mol, then ΔH for the reaction is −20 kJ/mol and the reaction is exothermic.

The **entropy change, ΔS,** is a measure of the change in the amount of molecular randomness, or freedom of motion, that accompanies a reaction. For example, in an elimination reaction of the type

$$A \qquad B + C$$

there is more freedom of movement and molecular randomness in the products than in the reactant because one molecule has split into two. Thus, there is a net increase in entropy during the reaction and ΔS has a positive value.

On the other hand, for an addition reaction of the type

$$A + B \qquad C$$

the opposite is true. Because such reactions restrict the freedom of movement of two molecules by joining them together, the product has less randomness than the reactants and ΔS has a negative value. The reaction of ethylene and

HBr to yield bromoethane, which has $\Delta S° = -0.132$ kJ/(K · mol), is an example. Table 5.2 describes the thermodynamic terms more fully.

Table 5.2 | **Explanation of Thermodynamic Quantities: $\Delta G° = \Delta H° - T\Delta S°$**

Term	Name	Explanation
$\Delta G°$	Gibbs free-energy change	The energy difference between reactants and products. When $\Delta G°$ is negative, the reaction is **exergonic**, has a favorable equilibrium constant, and can occur spontaneously. When $\Delta G°$ is positive, the reaction is **endergonic**, has an unfavorable equilibrium constant, and cannot occur spontaneously.
$\Delta H°$	Enthalpy change	The heat of reaction, or difference in strength between the bonds broken in a reaction and the bonds formed. When $\Delta H°$ is negative, the reaction releases heat and is **exothermic**. When $\Delta H°$ is positive, the reaction absorbs heat and is **endothermic**.
$\Delta S°$	Entropy change	The change in molecular randomness during a reaction. When $\Delta S°$ is negative, randomness decreases; when $\Delta S°$ is positive, randomness increases.

Knowing the value of K_{eq} for a reaction is useful, but it's important to realize the limitations. An equilibrium constant tells only the *position* of the equilibrium, or how much product is theoretically possible. It doesn't tell the *rate* of reaction, or how fast the equilibrium is established. Some reactions are extremely slow even though they have favorable equilibrium constants. Gasoline is stable at room temperature, for instance, because the rate of its reaction with oxygen is slow at 298 K. At higher temperatures, however, such as contact with a lighted match, gasoline reacts rapidly with oxygen and undergoes complete conversion to the equilibrium products water and carbon dioxide. Rates (*how fast* a reaction occurs) and equilibria (*how much* a reaction occurs) are entirely different.

| **Rate**	**Is the reaction fast or slow?**
Equilibrium	**In what direction does the reaction proceed?**

Problem 5.10 | Which reaction is more energetically favored, one with $\Delta G° = -44$ kJ/mol or one with $\Delta G° = +44$ kJ/mol?

Problem 5.11 | Which reaction is likely to be more exergonic, one with $K_{eq} = 1000$ or one with $K_{eq} = 0.001$?

## 5.8 | Describing a Reaction: Bond Dissociation Energies

We've just seen that heat is released (negative ΔH) when a bond is formed and absorbed (positive ΔH) when a bond is broken. The measure of the heat change that occurs on breaking a bond is called the *bond strength,* or **bond dissociation energy (D)**, defined as the amount of energy required to break a given bond to produce two radical fragments when the molecule is in the gas phase at 25 °C.

$$A : B \xrightarrow{\text{Bond dissociation energy}} A· \ + \ ·B$$
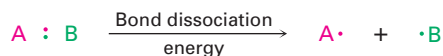
Each specific bond has its own characteristic strength, and extensive tables of data are available. For example, a C−H bond in methane has a bond dissociation energy D = 438.4 kJ/mol (104.8 kcal/mol), meaning that 438.4 kJ/mol must be added to break a C−H bond of methane to give the two radical fragments ·CH$_3$ and ·H. Conversely, 438.4 kJ/mol of energy is released when a methyl radical and a hydrogen atom combine to form methane. Table 5.3 lists some other bond strengths.

Table 5.3   Some Bond Dissociation Energies, D

Bond	D (kJ/mol)	Bond	D (kJ/mol)	Bond	D (kJ/mol)
H—H	436	(CH$_3$)$_3$C—I	209	C$_2$H$_5$—CH$_3$	355
H—F	570	H$_2$C=CH—H	444	(CH$_3$)$_2$CH—CH$_3$	351
H—Cl	432	H$_2$C=CH—Cl	368	(CH$_3$)$_3$C—CH$_3$	339
H—Br	366	H$_2$C=CHCH$_2$—H	361	H$_2$C=CH—CH$_3$	406
H—I	298	H$_2$C=CHCH$_2$—Cl	289	H$_2$C=CHCH$_2$—CH$_3$	310
Cl—Cl	243	C$_6$H$_5$—H (phenyl)	464	H$_2$C=CH$_2$	611
Br—Br	193			C$_6$H$_5$—CH$_3$ (phenyl)	427
I—I	151	C$_6$H$_5$—Cl (phenyl)	405		
CH$_3$—H	438			C$_6$H$_5$—CH$_2$—CH$_3$ (phenyl)	332
CH$_3$—Cl	351	C$_6$H$_5$—CH$_2$—H (phenyl)	368		
CH$_3$—Br	293			CH$_3$C(=O)—H	368
CH$_3$—I	234	C$_6$H$_5$—CH$_2$—Cl (phenyl)	293		
CH$_3$—OH	380			HO—H	498
CH$_3$—NH$_2$	335	C$_6$H$_5$—Br (phenyl)	337	HO—OH	213
C$_2$H$_5$—H	420			CH$_3$O—H	437
C$_2$H$_5$—Cl	338			CH$_3$S—H	371
C$_2$H$_5$—Br	285	C$_6$H$_5$—OH (phenyl)	469	C$_2$H$_5$O—H	436
C$_2$H$_5$—I	222				
C$_2$H$_5$—OH	380			CH$_3$C(=O)—CH$_3$	322
(CH$_3$)$_2$CH—H	401				
(CH$_3$)$_2$CH—Cl	339			CH$_3$CH$_2$O—CH$_3$	339
(CH$_3$)$_2$CH—Br	274	HC≡C—H	552	NH$_2$—H	449
(CH$_3$)$_3$C—H	390	CH$_3$—CH$_3$	376	H—CN	518
(CH$_3$)$_3$C—Cl	330				
(CH$_3$)$_3$C—Br	263				

Think for a moment about the connection between bond strengths and chemical reactivity. In an exothermic reaction, more heat is released than is absorbed. But since making product bonds releases heat and breaking reactant bonds absorbs heat, the bonds in the products must be stronger than the bonds in the reactants. In other words, exothermic reactions are favored by stable products with strong bonds and by reactants with weak, easily broken bonds.

Sometimes, particularly in biochemistry, reactive substances that undergo highly exothermic reactions, such as ATP (adenosine triphosphate), are referred to as "energy-rich" or "high-energy" compounds. Such labels don't mean that ATP is special or different from other compounds; they mean only that ATP has relatively weak bonds that require a smaller amount of heat to break, thus leading to a larger release of heat on reaction. When a typical organic phosphate such as glycerol 3-phosphate reacts with water, for instance, only 9 kJ/mol of heat is released ($\Delta H° = -9$ kJ/mol), but when ATP reacts with water, 30 kJ/mol of heat is released ($\Delta H° = -30$ kJ/mol). The difference between the two reactions is due to the fact that the bond broken in ATP is substantially weaker than the bond broken in glycerol 3-phosphate.
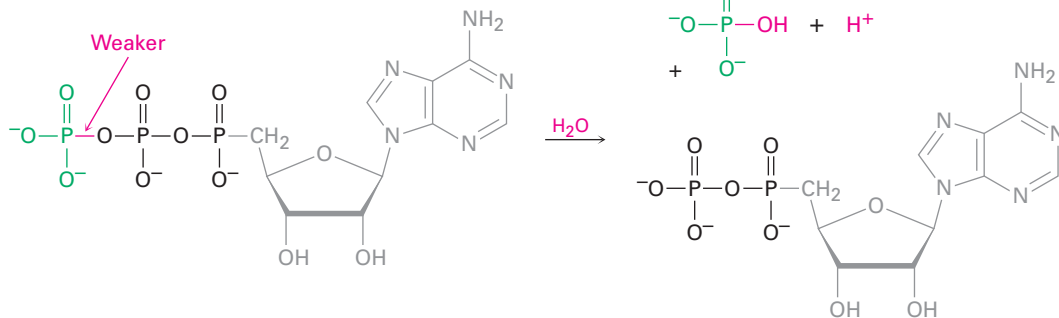
$\Delta H°' = -9$ kJ/mol

Stronger
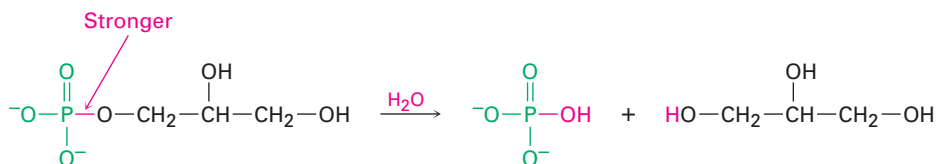
Glycerol 3-phosphate   **Glycerol**

$\Delta H°' = -30$ kJ/mol

Weaker

Adenosine triphosphate (ATP)   **Adenosine diphosphate (ADP)**

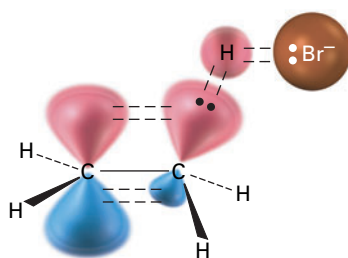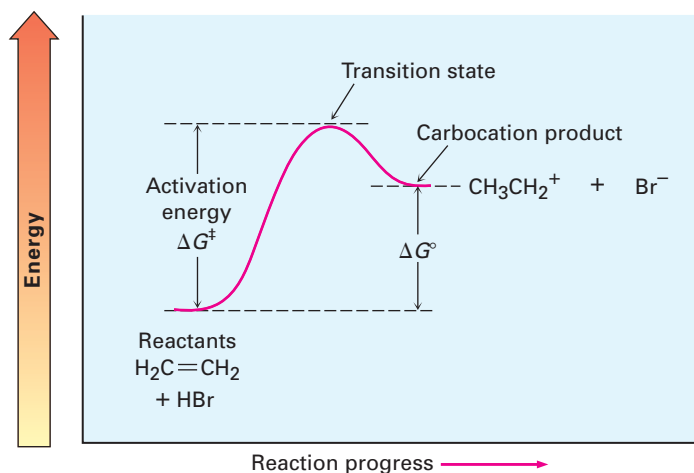## 5.9 Describing a Reaction: Energy Diagrams and Transition States

For a reaction to take place, reactant molecules must collide and reorganization of atoms and bonds must occur. Let's again look at the addition reaction of HBr and ethylene, which takes place in two steps.

158 CHAPTER 5 An Overview of Organic Reactions

Carbocation
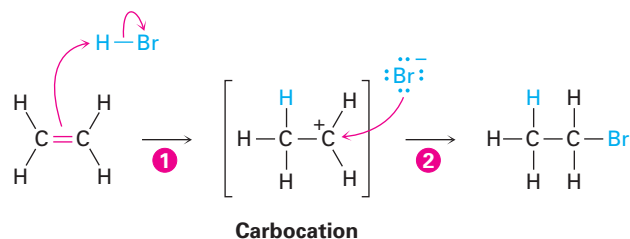
As the reaction proceeds, ethylene and HBr must approach each other, the ethylene π bond and the H−Br bond must break, a new C−H bond must form in the first step, and a new C−Br bond must form in the second step.

To depict graphically the energy changes that occur during a reaction, chemists use reaction energy diagrams, such as that shown in Figure 5.4. The vertical axis of the diagram represents the total energy of all reactants, and the horizontal axis, called the *reaction coordinate,* represents the progress of the reaction from beginning to end. Let's see how the addition of HBr to ethylene can be described in an energy diagram.

Figure 5.4 An energy diagram for the first step in the reaction of ethylene with HBr. The energy difference between reactants and transition state, $\Delta G^{\ddagger}$, defines the reaction rate. The energy difference between reactants and carbocation product, $\Delta G°$, defines the position of the equilibrium.

At the beginning of the reaction, ethylene and HBr have the total amount of energy indicated by the reactant level on the left side of the diagram in Figure 5.4. As the two reactants collide and reaction commences, their electron clouds repel each other, causing the energy level to rise. If the collision has occurred with enough force and proper orientation, the reactants continue to approach each other despite the rising repulsion until the new C−H bond starts to form. At some point, a structure of maximum energy is reached, a structure called the *transition state.*

The **transition state** represents the highest-energy structure involved in this step of the reaction. It is unstable and can't be isolated, but we can nevertheless imagine it to be an activated complex of the two reactants in which both the C=C π bond and H−Br bond are partially broken and the new C−H bond is partially formed (Figure 5.5).

The energy difference between reactants and transition state is called the **activation energy**, $\Delta G^{\ddagger}$, and determines how rapidly the reaction occurs at a given temperature. (The double-dagger superscript, $\ddagger$, always refers to the transition state.) A large activation energy results in a slow reaction because few collisions occur with enough energy for the reactants to reach the transition state.

Active Figure 5.5 A hypothetical transition-state structure for the first step of the reaction of ethylene with HBr. The C=C π bond and H−Br bond are just beginning to break, and the C−H bond is just beginning to form. *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*

A small activation energy results in a rapid reaction because almost all collisions occur with enough energy for the reactants to reach the transition state.

As an analogy, you might think of reactants that need enough energy to climb the activation barrier to the transition state as similar to hikers who need enough energy to climb to the top of a mountain pass. If the pass is a high one, the hikers need a lot of energy and surmount the barrier with difficulty. If the pass is low, however, the hikers need less energy and reach the top easily.

As a rough generalization, many organic reactions have activation energies in the range 40 to 150 kJ/mol (10–35 kcal/mol). The reaction of ethylene with HBr, for example, has an activation energy of approximately 140 kJ/mol (34 kcal/mol). Reactions with activation energies less than 80 kJ/mol take place at or below room temperature, whereas reactions with higher activation energies normally require a higher temperature to give the reactants enough energy to climb the activation barrier.

Once the transition state is reached, the reaction can either continue on to give the carbocation product or revert back to reactant. When reversion to reactant occurs, the transition-state structure comes apart and an amount of free energy corresponding to $-\Delta G^{\ddagger}$ is released. When the reaction continues on to give the carbocation, the new C−H bond forms fully and an amount of energy corresponding to the difference between transition state and carbocation product is released. The net change in energy for the step, $\Delta G°$, is represented in the diagram as the difference in level between reactant and product. Since the carbocation is higher in energy than the starting alkene, the step is endergonic, has a positive value of $\Delta G°$, and absorbs energy.

Not all energy diagrams are like that shown for the reaction of ethylene and HBr. Each reaction has its own energy profile. Some reactions are fast (small $\Delta G^{\ddagger}$) and some are slow (large $\Delta G^{\ddagger}$); some have a negative $\Delta G°$, and some have a positive $\Delta G°$. Figure 5.6 illustrates some different possibilities.

Active Figure 5.6 Some hypothetical energy diagrams: **(a)** a fast exergonic reaction (small $\Delta G^{\ddagger}$, negative $\Delta G°$); **(b)** a slow exergonic reaction (large $\Delta G^{\ddagger}$, negative $\Delta G°$); **(c)** a fast endergonic reaction (small $\Delta G^{\ddagger}$, small positive $\Delta G°$); **(d)** a slow endergonic reaction (large $\Delta G^{\ddagger}$, positive $\Delta G°$). *Sign in at* **www.thomsonedu.com** *to see a simulation based on this figure and to take a short quiz.*
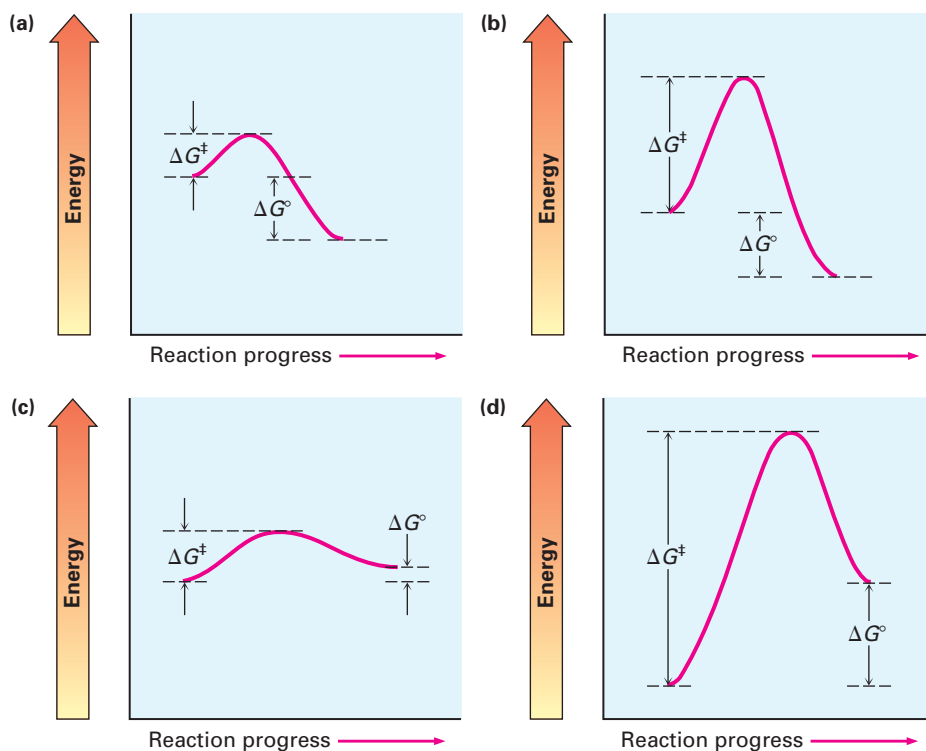
Problem 5.12 | Which reaction is faster, one with $\Delta G^{\ddagger} = +45$ kJ/mol or one with $\Delta G^{\ddagger} = +70$ kJ/mol?

## 5.10 | Describing a Reaction: Intermediates

How can we describe the carbocation formed in the first step of the reaction of ethylene with HBr? The carbocation is clearly different from the reactants, yet it isn't a transition state and it isn't a final product.

Reaction intermediate
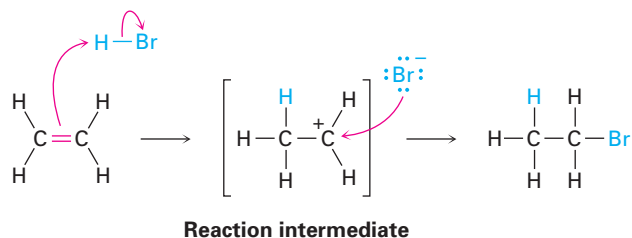
We call the carbocation, which exists only transiently during the course of the multistep reaction, a **reaction intermediate**. As soon as the intermediate is formed in the first step by reaction of ethylene with H^{+}, it reacts further with Br^{-} in a second step to give the final product, bromoethane. This second step has its own activation energy ($\Delta G^{\ddagger}$), its own transition state, and its own energy change ($\Delta G°$). We can picture the second transition state as an activated complex between the electrophilic carbocation intermediate and the nucleophilic bromide anion, in which Br^{-} donates a pair of electrons to the positively charged carbon atom as the new C−Br bond starts to form.

A complete energy diagram for the overall reaction of ethylene with HBr is shown in Figure 5.7. In essence, we draw a diagram for each of the individual steps and then join them so that the carbocation *product* of step 1 is the *reactant* for step 2. As indicated in Figure 5.7, the reaction intermediate lies at an energy

Figure 5.7 An energy diagram for the overall reaction of ethylene with HBr. Two separate steps are involved, each with its own transition state. The energy minimum between the two steps represents the carbocation reaction intermediate.
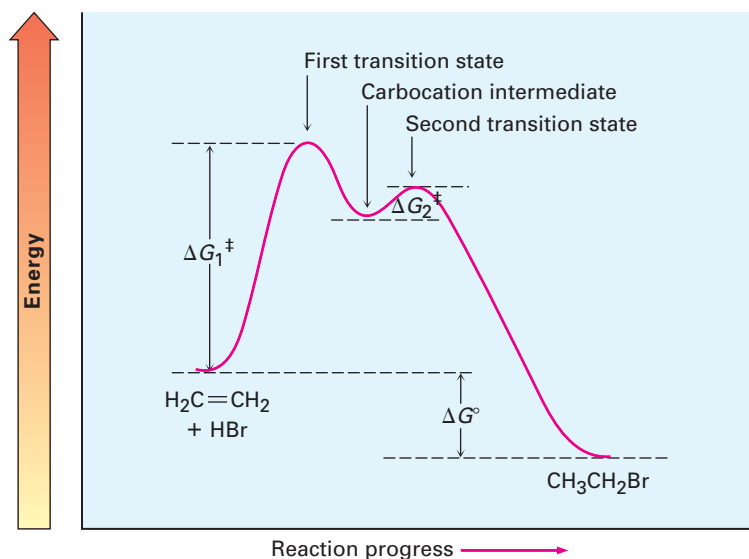
minimum between steps. Since the energy level of the intermediate is higher than the level of either the reactant that formed it or the product it yields, the intermediate can't normally be isolated. It is, however, more stable than the two transition states that neighbor it.

Each step in a multistep process can always be considered separately. Each step has its own $\Delta G^{\ddagger}$ and its own $\Delta G°$. The *overall* $\Delta G°$ of the reaction, however, is the energy difference between initial reactants and final products.

The biological reactions that take place in living organisms have the same energy requirements as reactions that take place in the laboratory and can be described in similar ways. They are, however, constrained by the fact that they must have low enough activation energies to occur at moderate temperatures, and they must release energy in relatively small amounts to avoid overheating the organism. These constraints are generally met through the use of large, structurally complex, enzyme catalysts that change the mechanism of a reaction to an alternative pathway that proceeds through a series of small steps rather than one or two large steps. Thus, a typical energy diagram for a biological reaction might look like that in Figure 5.8.

Figure 5.8 An energy diagram for a typical, enzyme-catalyzed biological reaction (blue curve) versus an uncatalyzed laboratory reaction (red curve). The biological reaction involves many steps, each of which has a relatively small activation energy and small energy change. The end result is the same, however.
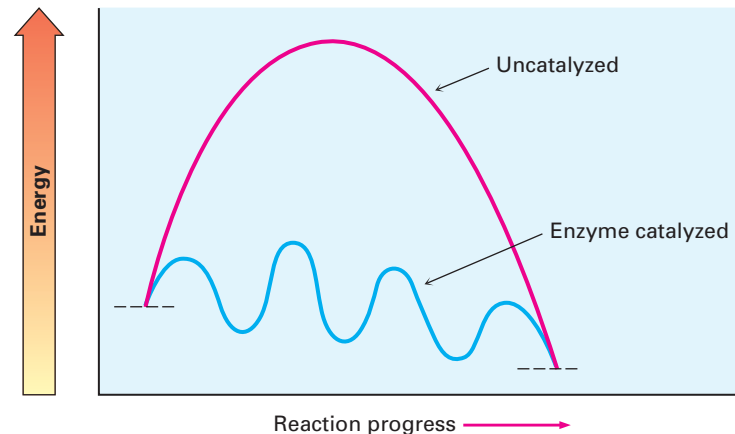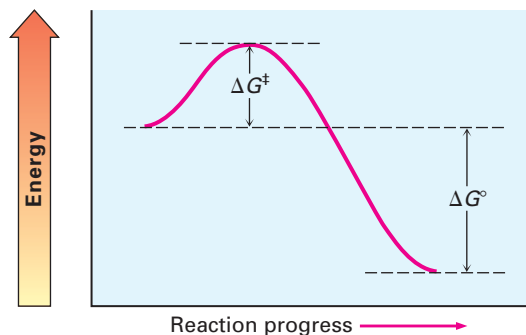

WORKED EXAMPLE 5.3   *Drawing Energy Diagrams for Reactions*

Sketch an energy diagram for a one-step reaction that is fast and highly exergonic.

Strategy   A fast reaction has a small $\Delta G^{\ddagger}$, and a highly exergonic reaction has a large negative $\Delta G°$.

Solution

Problem 5.13 | Sketch an energy diagram for a two-step reaction with an endergonic first step and an exergonic second step. Label the parts of the diagram corresponding to reactant, product, and intermediate.

5.11 A Comparison between Biological Reactions and Laboratory Reactions

In comparing laboratory reactions with biological reactions, several differences are apparent. For one thing, laboratory reactions are usually carried out in an organic solvent such as diethyl ether or dichloromethane to dissolve the reactants and bring them into contact, whereas biological reactions occur in the aqueous medium inside cells. For another thing, laboratory reactions often take place over a wide range of temperatures without catalysts, while biological reactions take place at the temperature of the organism and are catalyzed by *enzymes*.

We'll look at enzymes in more detail in Section 26.10, but you may already be aware that an enzyme is a large, globular protein molecule that contains in its structure a protected pocket called its *active site*. The active site is lined by acidic or basic groups as needed for catalysis and has precisely the right shape to bind and hold a substrate molecule in the orientation necessary for reaction. Figure 5.9 shows a molecular model of hexokinase, along with an X-ray crystal structure of the glucose substrate and adenosine diphosphate (ADP) bound in the active site. Hexokinase is an enzyme that catalyzes the initial step of glucose metabolism—the transfer of a phosphate group from ATP to glucose, giving glucose 6-phosphate and ADP. The structures of ATP and ADP were shown at the end of Section 5.8.

**Glucose**   **Glucose 6-phosphate**
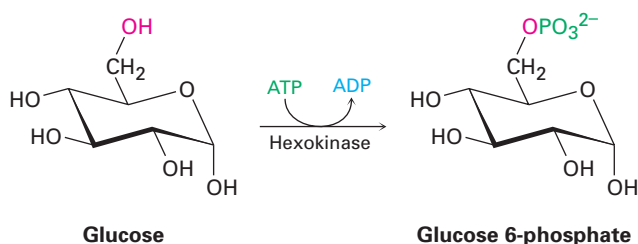
Note how the hexokinase-catalyzed phosphorylation reaction of glucose is written. It's common when writing biological equations to show only the structure of the primary reactant and product, while abbreviating the structures of various biological "reagents" and by-products such as ATP and ADP. A curved arrow intersecting the straight reaction arrow indicates that ATP is also a reactant and ADP also a product.

Yet another difference is that laboratory reactions are often done using relatively small, simple reagents such as Br_2, HCl, $NaBH_4$, CrO_3, and so forth, while biological reactions usually involve relatively complex "reagents" called *coenzymes.* In the hexokinase-catalyzed phosphorylation of glucose just shown,

Figure 5.9 Models of hexo-kinase in space-filling and wire-frame formats, showing the cleft that contains the active site where substrate binding and reaction catalysis occur. At the bottom is an X-ray crystal struc-ture of the enzyme active site, showing the positions of both glucose and ADP as well as a lysine amino acid that acts as a base to deprotonate glucose.

Active site

Adenosine diphosphate (ADP)

Lysine
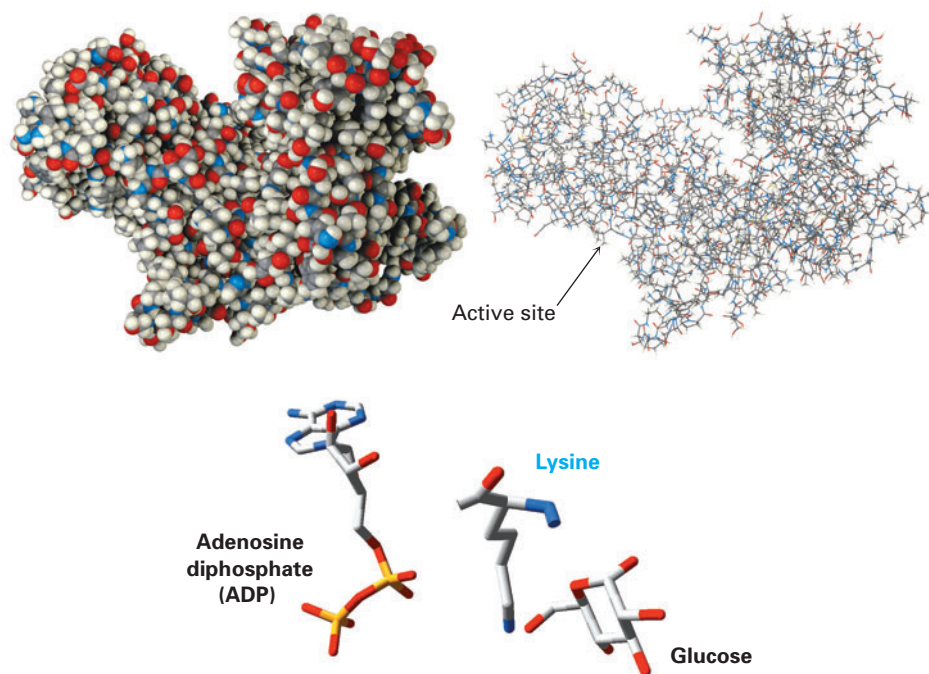
Glucose

for instance, ATP is the coenzyme. Of all the atoms in the entire coenzyme, only the one phosphate group shown in red is transferred to the glucose substrate.
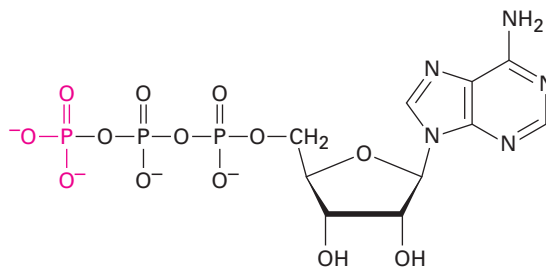
Adenosine triphosphate, ATP
(a coenzyme)

Don't be intimidated by the size of the molecule; most of the structure is there to provide an overall shape for binding to the enzyme and to provide appropriate solubility behavior. When looking at biological molecules, focus on the small part of the molecule where the chemical change takes place.

One final difference between laboratory and biological reactions is in their specificity. A catalyst might be used in the laboratory to catalyze the reaction of thousands of different substances, but an enzyme, because it can bind only a specific substrate molecule having a specific shape, will catalyze only a specific reaction. It's this exquisite specificity that makes biological chemistry so remark-able and that makes life possible. Table 5.4 summarizes some of the differences between laboratory and biological reactions.

Table 5.4 | **A Comparison of Typical Laboratory and Biological Reactions**

	Laboratory reaction	Biological reaction
Solvent	Organic liquid, such as ether	Aqueous environment in cells
Temperature	Wide range; −80 to 150 °C`	Temperature of organism
Catalyst	Either none or very simple	Large, complex enzymes needed
Reagent size	Usually small and simple	Large, complex coenzymes
Specificity	Little specificity for substrate	Very high specificity for substrate

Focus On . . .

Where Do Drugs Come From?

It has been estimated that major pharmaceutical companies in the United States spend some $33 billion per year on drug research and development, while government agencies and private foundations spend another $28 billion. What does this money buy? For the period 1981–2004, the money resulted in a total of 912 new molecular entities (NMEs)—new biologically active chemical substances approved for sale as drugs by the U.S. Food and Drug Administration (FDA). That's an average of only 38 new drugs each year spread over all diseases and conditions, and the number has been steadily falling. In 2004, only 23 NMEs were approved.

Where do the new drugs come from? According to a study carried out at the U.S. National Cancer Institute, only 33% of new drugs are entirely synthetic and completely unrelated to any naturally occurring substance. The remaining 67% take their lead, to a greater or lesser extent, from nature. Vaccines and genetically engineered proteins of biological origin account for 15% of NMEs, but most new drugs come from *natural products,* a catchall term generally taken to mean small molecules found in bacteria, plants, and other living organisms. Unmodified natural products isolated directly from the producing organism account for 28% of NMEs, while natural products that have been chemically modified in the laboratory account for the remaining 24%.

Approved for sale in March, 1998, Viagra has been used by more than 16 million men. It is currently undergoing study as a treatment for preeclampsia, a complication of pregnancy that is responsible for as many as 70,000 deaths each year. Where do new drugs like this come from?

© BSIP/Phototake

Origin of New Drugs 1981–2002

Natural products (28%)
Natural product related (24%)
Synthetic (33%)
Biological (15%)
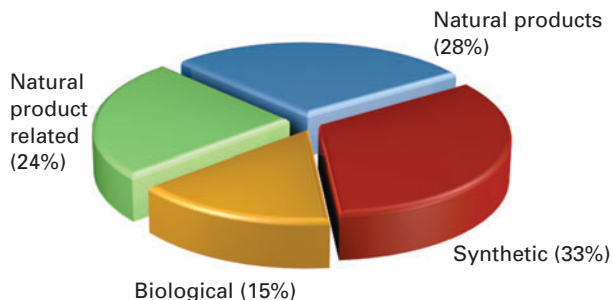
Many years of work go into screening many thousands of substances to identify a single compound that might ultimately gain approval as an NME. But after that single compound has been identified, the work has just begun because it takes an average of 9 to 10 years for a drug to make it through the approval process. First, the safety of the drug in animals must be demonstrated and an economical method of manufacture must be devised. With these preliminaries out of the way, an Investigational New Drug (IND) application is submitted to the FDA for permission to begin testing in humans.

Human testing takes 5 to 7 years and is divided into three phases. Phase I clinical trials are carried out on a small group of healthy volunteers to establish safety and look for side effects. Several months to a year are needed, and only about 70% of drugs pass at this point. Phase II clinical trials next test the drug for 1 to 2 years in several hundred patients with the target disease, looking both for safety and for efficacy, and only about 33% of the original group pass. Finally, phase III trials are undertaken on a large sample of patients to document definitively the drug's safety, dosage, and efficacy. If the drug is one of the 25% of the original group that have made it this far, all the data are then gathered into a New Drug Application (NDA) and sent to the FDA for review and approval, which can take another 2 years. Ten years and at least $500 million has now been spent, and only 20% of the drugs that began testing have succeeded. Finally, though, the drug will begin to appear in medicine cabinets. The following timeline shows the process.
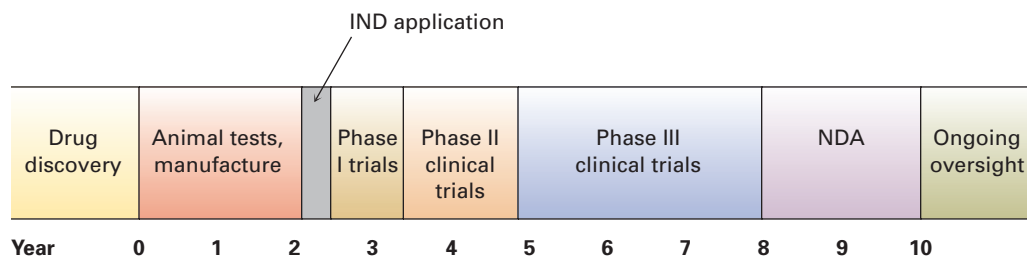
SUMMARY AND KEY WORDS

activation energy ($\Delta G^{\ddagger}$), 158

addition reaction, 137

bond dissociation energy (*D*), 155

carbocation, 148

electrophile, 145

elimination reaction, 138

endergonic, 153

endothermic, 154

enthalpy change (ΔH), 154

entropy change (ΔS), 154

exergonic, 153

There are four common kinds of reactions: **addition reactions** take place when two reactants add together to give a single product; **elimination reactions** take place when one reactant splits apart to give two products; **substitution reactions** take place when two reactants exchange parts to give two new products; and **rearrangement reactions** take place when one reactant undergoes a reorganization of bonds and atoms to give an isomeric product.

A full description of how a reaction occurs is called its **mechanism**. There are two general kinds of mechanisms by which reactions take place: **radical** mechanisms and **polar** mechanisms. Polar reactions, the more common type, occur because of an attractive interaction between a **nucleophilic** (electron-rich) site in one molecule and an **electrophilic** (electron-poor) site in another molecule. A bond is formed in a polar reaction when the nucleophile donates an electron pair to the electrophile. This movement of electrons is indicated by a curved arrow showing the direction of electron travel from the nucleophile to

the electrophile. Radical reactions involve species that have an odd number of electrons. A bond is formed when each reactant donates one electron.

Polar $B:^-$ + A^+ $\longrightarrow$ $A:B$

Nucleophile   **Electrophile**

Radical $B\cdot$ + $\cdot A$ $\longrightarrow$ $A:B$
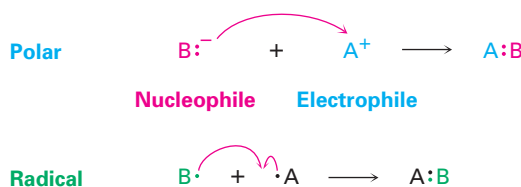
The energy changes that take place during reactions can be described by considering both rates (how fast the reactions occur) and equilibria (how much the reactions occur). The position of a chemical equilibrium is determined by the value of the **free-energy change (ΔG)** for the reaction, where $\Delta G = \Delta H - T\Delta S$. The **enthalpy** term (ΔH) corresponds to the net change in strength of chemical bonds broken and formed during reaction; the **entropy** term (ΔS) corresponds to the change in the amount of randomness during the reaction. Reactions that have negative values of ΔG release energy, are said to be **exergonic**, and have favorable equilibria. Reactions that have positive values of ΔG absorb energy, are said to be **endergonic**, and have unfavorable equilibria.

A reaction can be described pictorially using an energy diagram that follows the reaction course from reactant through transition state to product. The **transition state** is an activated complex occurring at the highest-energy point of a reaction. The amount of energy needed by reactants to reach this high point is the **activation energy, $\Delta G^{\ddagger}$**. The higher the activation energy, the slower the reaction.

Many reactions take place in more than one step and involve the formation of a **reaction intermediate**. An intermediate is a species that lies at an energy minimum between steps on the reaction curve and is formed briefly during the course of a reaction.

EXERCISES

Organic KNOWLEDGE TOOLS

Online homework for this chapter may be assigned in Organic OWL.

■ indicates problems assignable in Organic OWL.

▲ denotes problems linked to Key Ideas of this chapter and testable in ThomsonNOW.

VISUALIZING CHEMISTRY

(Problems 5.1–5.13 appear within the chapter.)

5.14 ■ The following alkyl halide can be prepared by addition of HBr to two different alkenes. Draw the structures of both (reddish brown = Br).

■ Assignable in OWL   ▲ Key Idea Problems
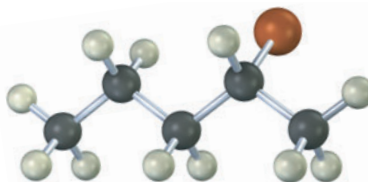
5.15 ■ The following structure represents the carbocation intermediate formed in the addition reaction of HBr to two different alkenes. Draw the structures of both.

5.16 Electrostatic potential maps of **(a)** formaldehyde (CH_2O) and **(b)** methanethiol (CH_3SH) are shown. Is the formaldehyde carbon atom likely to be electrophilic or nucleophilic? What about the methanethiol sulfur atom? Explain.

(a)   **(b)**

Formaldehyde   **Methanethiol**
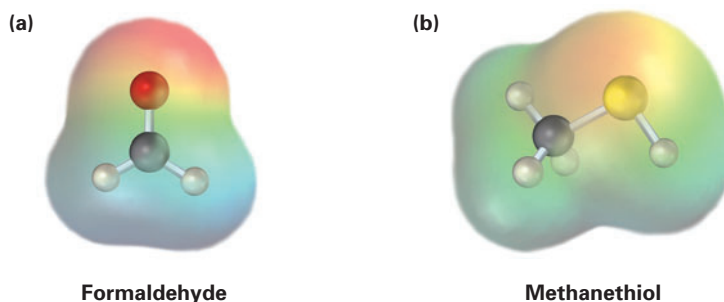
5.17 ■ Look at the following energy diagram:
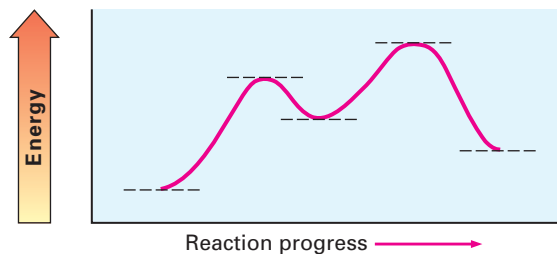
(a) Is $\Delta G°$ for the reaction positive or negative? Label it on the diagram.
(b) How many steps are involved in the reaction?
(c) How many transition states are there? Label them on the diagram.

5.18 Look at the following energy diagram for an enzyme-catalyzed reaction:
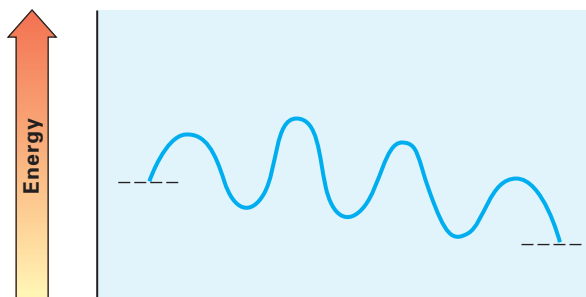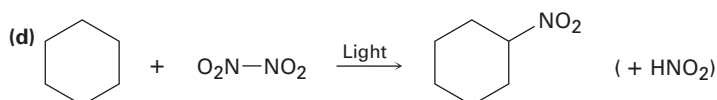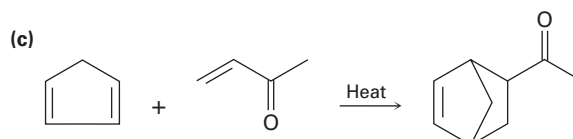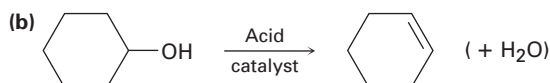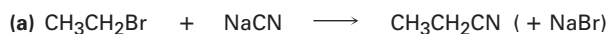
(a) How many steps are involved?
(b) Which step is most exergonic?
(c) Which step is the slowest?

■ Assignable in OWL   ▲ Key Idea Problems

ADDITIONAL PROBLEMS

5.19 ■ Identify the functional groups in the following molecules, and show the polarity of each:

(a) $CH_3CH_2C\equiv N$

(b) —OCH₃

(c)
CH₃CCH₂COCH₃

(d)

(e)
NH₂

(f)
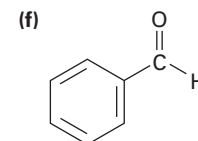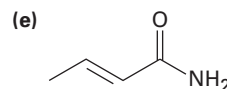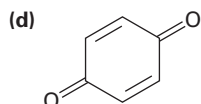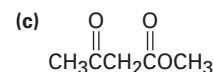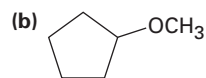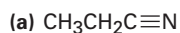
5.20 ■ Identify the following reactions as additions, eliminations, substitutions, or rearrangements:

(a) CH_3CH_2Br + $NaCN$ $\longrightarrow$ CH_3CH_2CN (+ NaBr)

(b) —OH $\xrightarrow[\text{catalyst}]{\text{Acid}}$ (+ H_2O)

(c) + $\xrightarrow{\text{Heat}}$

(d) + O_2N-NO_2 $\xrightarrow{\text{Light}}$ (+ HNO_2)

5.21 What is the difference between a transition state and an intermediate?

5.22 Draw an energy diagram for a one-step reaction with $K_{eq} < 1$. Label the parts of the diagram corresponding to reactants, products, transition state, $\Delta G°$, and $\Delta G^{\ddagger}$. Is $\Delta G°$ positive or negative?

5.23 Draw an energy diagram for a two-step reaction with $K_{eq} > 1$. Label the overall $\Delta G°$, transition states, and intermediate. Is $\Delta G°$ positive or negative?

5.24 Draw an energy diagram for a two-step exergonic reaction whose second step is faster than its first step.

5.25 Draw an energy diagram for a reaction with $K_{eq} = 1$. What is the value of $\Delta G°$ in this reaction?
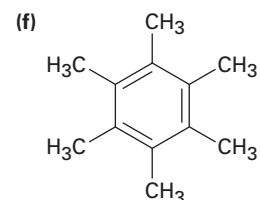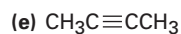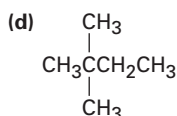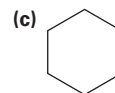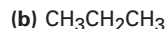
5.26 ■ The addition of water to ethylene to yield ethanol has the following thermodynamic parameters:

$$H_2C=CH_2 + H_2O \rightleftharpoons CH_3CH_2OH \quad \begin{cases} \Delta H° = -44 \text{ kJ/mol} \\ \Delta S° = -0.12 \text{ kJ/(K·mol)} \\ K_{eq} = 24 \end{cases}$$
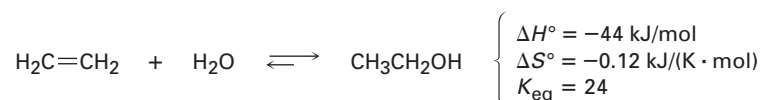
(a) Is the reaction exothermic or endothermic?

(b) Is the reaction favorable (spontaneous) or unfavorable (nonspontaneous) at room temperature (298 K)?


■ Assignable in OWL   ▲ Key Idea Problems

5.27 When a mixture of methane and chlorine is irradiated, reaction commences immediately. When irradiation is stopped, the reaction gradually slows down but does not stop immediately. Explain.

5.28 Radical chlorination of pentane is a poor way to prepare 1-chloropentane, but radical chlorination of neopentane, $(CH_3)_4C$, is a good way to prepare neopentyl chloride, $(CH_3)_3CCH_2Cl$. Explain.

5.29 ■ Despite the limitations of radical chlorination of alkanes, the reaction is still useful for synthesizing certain halogenated compounds. For which of the following compounds does radical chlorination give a single monochloro product?

(a) CH_3CH_3

(b) $CH_3CH_2CH_3$

(c)

(d)
$$CH_3CCH_2CH_3$$
with CH_3 groups above and below the central carbon

(e) $CH_3C{\equiv}CCH_3$

(f)
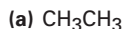
5.30 ■ ▲ Add curved arrows to the following reactions to indicate the flow of electrons in each:

(a)

(b)
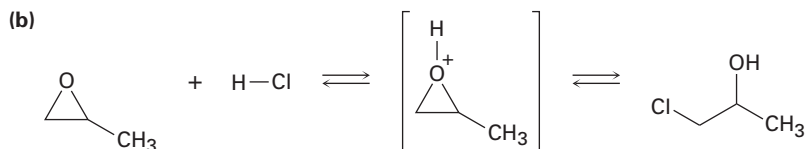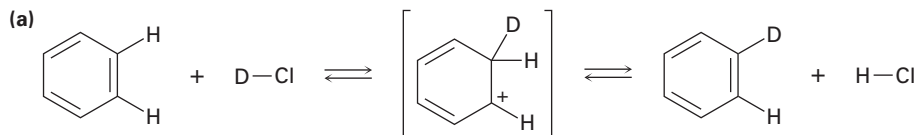
5.31 ■ ▲ Follow the flow of electrons indicated by the curved arrows in each of the following reactions, and predict the products that result:

(a)

(b)
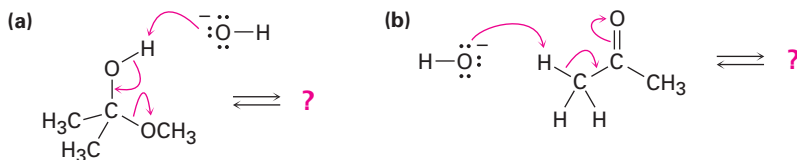
5.32 ■ When isopropylidenecyclohexane is treated with strong acid at room temperature, isomerization occurs by the mechanism shown below to yield 1-isopropylcyclohexene:

Isopropylidenecyclohexane   **1-Isopropylcyclohexene**
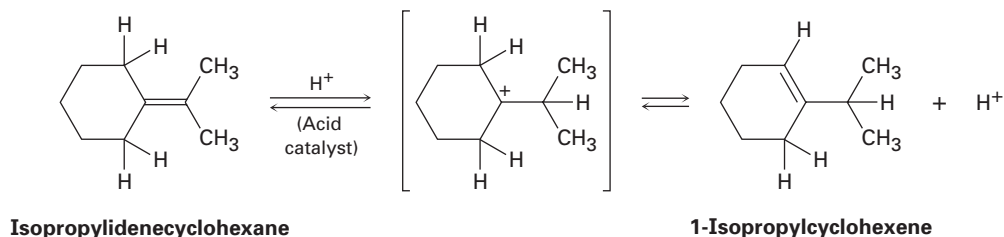
At equilibrium, the product mixture contains about 30% isopropylidenecyclohexane and about 70% 1-isopropylcyclohexene.
(a) What is an approximate value of K_{eq} for the reaction?
(b) Since the reaction occurs slowly at room temperature, what is its approximate $\Delta G^{\ddagger}$?
(c) Draw an energy diagram for the reaction.

5.33 ▲ Add curved arrows to the mechanism shown in Problem 5.32 to indicate the electron movement in each step.

5.34 ■ 2-Chloro-2-methylpropane reacts with water in three steps to yield 2-methyl-2-propanol. The first step is slower than the second, which in turn is much slower than the third. The reaction takes place slowly at room temperature, and the equilibrium constant is near 1.


2-Chloro-2-   **2-Methyl-2-propanol**
methylpropane
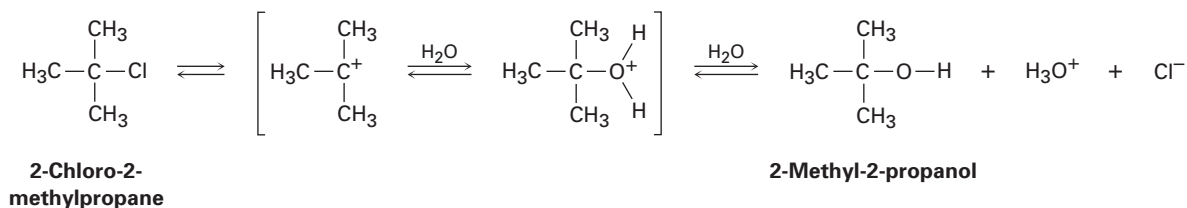
(a) Give approximate values for $\Delta G^{\ddagger}$ and ΔG° that are consistent with the above information.
(b) Draw an energy diagram for the reaction, labeling all points of interest and making sure that the relative energy levels on the diagram are consistent with the information given.

5.35 ▲ Add curved arrows to the mechanism shown in Problem 5.34 to indicate the electron movement in each step.

5.36 ■ The reaction of hydroxide ion with chloromethane to yield methanol and chloride ion is an example of a general reaction type called a *nucleophilic substitution reaction*:

$$HO^- + CH_3Cl \rightleftharpoons CH_3OH + Cl^-$$

The value of ΔH° for the reaction is -75 kJ/mol, and the value of ΔS° is $+54$ J/(K · mol). What is the value of ΔG° (in kJ/mol) at 298 K? Is the reaction exothermic or endothermic? Is it exergonic or endergonic?

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■ Assignable in OWL   ▲ Key Idea Problems

5.37 ■ ▲ Ammonia reacts with acetyl chloride (CH_3COCl) to give acetamide (CH_3CONH_2). Identify the bonds broken and formed in each step of the reaction, and draw curved arrows to represent the flow of electrons in each step.
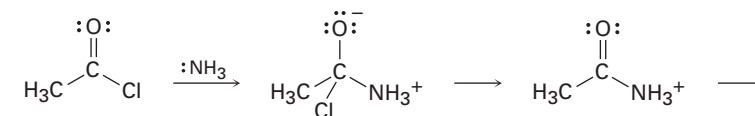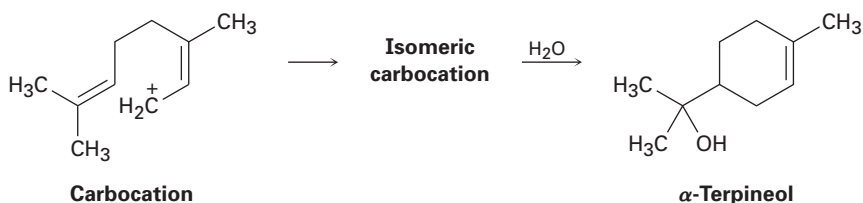

Acetyl chloride
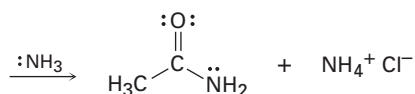
Acetamide

5.38 The naturally occurring molecule α-terpineol is biosynthesized by a route that includes the following step:

Carbocation   **α-Terpineol**

   (a) Propose a likely structure for the isomeric carbocation intermediate.
   (b) Show the mechanism of each step in the biosynthetic pathway, using curved arrows to indicate electron flow.

5.39 Predict the product(s) of each of the following biological reactions by interpreting the flow of electrons as indicated by the curved arrows:
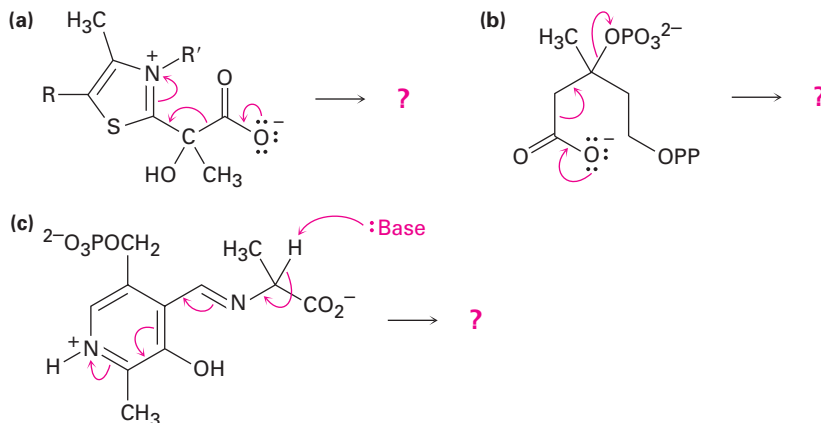
5.40 ■ Reaction of 2-methylpropene with HBr might, in principle, lead to a mixture of two alkyl bromide addition products. Name them, and draw their structures.

5.41 ■ Draw the structures of the two carbocation intermediates that might form during the reaction of 2-methylpropene with HBr (Problem 5.40). We'll see in the next chapter that the stability of carbocations depends on the number of alkyl substituents attached to the positively charged carbon—the more alkyl substituents there are, the more stable the cation. Which of the two carbocation intermediates you drew is more stable?

■ Assignable in OWL   ▲ Key Idea Problems