

# General and Organic Chemistry Review Primer

## OUTLINE

### GENERAL CHEMISTRY 2

#### Atomic Structure: The Basics 2

- Atomic Number and Mass Number 2
- Radioactivity 3
- Atomic Theory 3
- Electron Configuration in Atoms 4
- The Periodic Table 5

#### Chemical Bonding 8

- Lewis Dot Notation 9
- Molecular Structure 10
- Valence Bond Theory and Orbital Hybridization 12

#### Chemical Reactions 14

- Reaction Kinetics 15
- Chemical Reactions and Equilibrium Constants 16
- Acid-Base Equilibria and pH 17
- Reaction Types 18
- Measuring Chemical Reactions 21

### ORGANIC CHEMISTRY 21

#### Hydrocarbons 22

- Cyclic Hydrocarbons 25
- Aromatic Hydrocarbons 25

#### Substituted Hydrocarbons 26

- Alcohols 26
- Aldehydes 27
- Ketones 27
- Carboxylic Acids 28
- Esters 28
- Ethers 28
- Amines 28
- Amides 30
- Thiols 30

#### Organic Reactions: Substitutions and Eliminations 31

- Substitution Reactions:  $S_N1$  and  $S_N2$  31
- Elimination Reactions: E1, E2, and E1cb 33

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## BIOCHEMISTRY COURSES ARE ALWAYS FAST-PACED AND CHALLENGING.

**I**t is for this reason that success is highly dependent on a student's background in general and organic chemistry. Although courses in these subjects are prerequisites, students often have trouble recalling the detailed chemical information that will help them understand the chemical processes in living organisms. This review is divided into two sections: general and organic chemistry. General chemistry topics include atomic structure, chemical bonding, acids and bases, and the chemical properties of the principal elements found in living organisms. Topics in the organic chemistry section include the structure and chemical properties of carbon-containing compounds, nucleophiles and electrophiles, functional group structure and chemical behavior, and organic reaction classes. Topics that are directly relevant to biochemistry (e.g., biomolecule classes, pH, buffers, kinetics, and thermodynamics) are described within the textbook.

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## GENERAL CHEMISTRY

Chemistry is the investigation of matter and the changes it can undergo. Matter, which can be described as physical substances that occupy space and have mass, is composed of various combinations of the chemical elements. Each chemical element is a pure substance that is composed of one type of atom. About 98 of the 118 known elements occur on earth and an even smaller number occur naturally in living organisms. These elements fall into three categories: *metals* (substances such as sodium and magnesium with high electrical and heat conductivity, metallic luster, and malleability), *nonmetals* (elements such as nitrogen, oxygen, and sulfur, which are defined as a group because of their lack of metallic properties), and *metalloids* (elements such as silicon and boron, which have properties intermediate between metals and nonmetals).

The review of general chemistry includes an overview of atomic structure, atomic electron configurations, the periodic table, chemical bonds, valence bond theory, chemical reaction types, reaction kinetics, and equilibrium constants.

### Atomic Structure: The Basics

Atoms are the smallest units of an element that retain the property of that element. Atomic structure consists of a positively charged central nucleus surrounded by one or more negatively charged electrons. With the exception of the element hydrogen (H), the dense, positively charged nucleus contains positively charged protons and neutrons, which have no charge. (The hydrogen nucleus consists of a single proton.) Atoms are electrically neutral so the number of protons is equal to the number of electrons. When atoms gain or lose one or more electrons, they become charged particles called ions. Ions formed when atoms lose electrons, called *cations*, are positively charged because they have fewer electrons than protons. For example, when a sodium atom (Na) loses an electron, it becomes the positively charged ion  $\text{Na}^+$ . Ions formed by the gain of electrons, called *anions*, are negatively charged. Chlorine (Cl) gains an electron to form the chlorine ion  $\text{Cl}^-$ .

**ATOMIC NUMBER AND MASS NUMBER** Elements are identified by their atomic number and mass number. The *atomic number* of an element is the number of protons in its nucleus. The atomic number uniquely identifies an

element. Carbon (C) has 6 protons in its nucleus, so its atomic number is 6. Any atom with 16 protons in its nucleus is an atom of sulfur (S).

The *mass number* of an element, measured in atomic mass units, is equal to the number of protons and neutrons. Calculating an element's mass number is complicated by the existence of *isotopes*, atoms of an element with the same number of protons but different numbers of neutrons.

Many naturally occurring elements exist as a mixture of isotopes. For example, carbon has three naturally occurring isotopes containing six, seven, and eight neutrons, called carbon-12, carbon-13, and carbon-14, respectively. Carbon-12, the most abundant carbon isotope, is used as a reference standard in the measurement of atomic mass. An atomic mass unit ( $\mu$ ) or dalton (Da), named after the chemist John Dalton, is defined as one twelfth of the mass of an atom of carbon-12. Because the isotopes of an element do not occur with equal frequency, the *average atomic mass unit* (the weighted average of the atomic masses of the naturally occurring isotopes) is used. For example, hydrogen has three isotopes: hydrogen-1, hydrogen-2 (deuterium), and hydrogen-3 (tritium), which contain zero, one, and two neutrons, respectively. The average atomic mass for hydrogen is 1.0078  $\mu$ . This number is very close to 1.0 because hydrogen-1 has an abundance of more than 99.98%.

**RADIOACTIVITY** Some isotopes are radioactive (i.e., they undergo *radioactive decay*, a spontaneous process in which an atomic nucleus undergoes a change that is accompanied by an energy emission). For example, relatively unstable carbon-14 undergoes a form of radioactive decay, referred to as  $\beta$ -decay. In  $\beta$ -decay one neutron in the atom's nucleus is converted into a proton and an electron. The new proton converts the carbon-14 atom to a stable nitrogen-14 atom. The newly created electron is emitted as a  $\beta$ -particle. Hydrogen-3 (tritium) also decays to form the more stable helium-3 (a rare isotope of helium with one neutron instead of two) by the emission of a  $\beta$ -particle. Essentially, the unstable tritium nucleus, which contains one proton and two neutrons, decays to form the helium-3 isotope (two protons and one neutron).

**ATOMIC THEORY** According to the Bohr model of atoms, electrons are in circular orbits with fixed energy levels that occur at specific distances from the nucleus. When an atom absorbs energy, an electron moves from its "ground state" to a higher energy level. The electron returns to its ground state when the atom releases the absorbed energy. As quantum theory revolutionized physics in the early twentieth century, it became apparent that the theory explained many properties of atoms that the Bohr model did not.

*Quantum theory* is based on the principle that both matter and energy have the properties of particles and waves. Using quantum theory, physicists and chemists eventually described an atomic model in which electrons are predicted to occur in complex orbitals that are essentially probability clouds. An orbital is a probability distribution (i.e., variations in an orbital's cloud density correlate with the probability of finding an electron). The different shapes and sizes of orbital clouds depend on the energy level of the electrons within them. Together, four quantum numbers describe the configuration of the electrons and the orbitals in an atom.

The *principal quantum number*  $n$  defines the average distance of an orbital from the nucleus where  $n = 1, 2, 3$ , etc. In other words, the quantum number  $n$  designates the principal energy shell. The higher its  $n$  value, the farther an electron is from the nucleus.

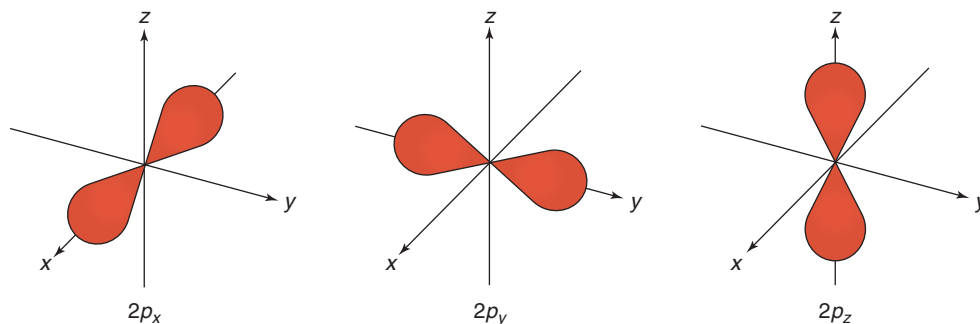
The *angular momentum quantum number*  $l$  (lower case L) determines the shape of an orbital. The  $l$  values of 0, 1, 2, 3, and 4 correspond to the s, p, d, and f subshells. Note that the value of  $n$  indicates the total number of subshells within the principal energy shell. So if  $n = 3$ , the atom's principal shell has three

subshells with  $l$  values of 0, 1, and 2. In such an atom the principal energy shell would contain s, p, and d orbitals. Each subshell also has a specific shape. The s orbital is spherical with the nucleus at its center. Each p orbital is dumbbell-shaped and each d orbital is double dumbbell-shaped. The shape of f orbitals is extremely complex and is not discussed further.

The *magnetic quantum number*  $m$  describes an orbital's orientation in space. Values of  $m$  range from  $-l$  to  $+l$ . With an s orbital,  $l = 0$  so the value of  $m$  is 0. For p orbitals, the value of  $l$  is 1, so  $m$  is equal to  $-1$ , 0, or  $+1$  (i.e., there are three orbitals designated  $p_x$ ,  $p_y$ , and  $p_z$  (Figure 1). For d orbitals  $l = 2$ , so there are five possible orientations:  $-2$ ,  $-1$ , 0,  $+1$ , or  $+2$ .

**FIGURE 1**  
The 2p Orbitals

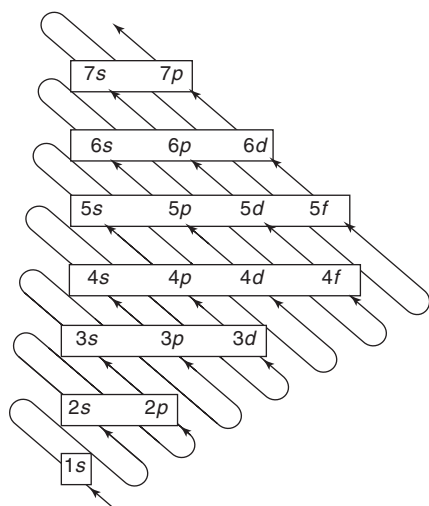
Three 2p orbitals are oriented at right angles to each other.



The fourth quantum number is the *spin quantum number*  $m_s$ , which describes the direction in which an electron is rotating: clockwise or counterclockwise. The values for  $m_s$  can be either  $+1/2$  or  $-1/2$ . Because the *Pauli exclusion principle* states that each electron in an atom has a unique set of the four quantum numbers, it follows that when two electrons are in the same orbital, they must have opposite spins. Such spins are described as “paired.” The spinning of an electron creates a magnetic field. *Diamagnetic* atoms such as nitrogen are not attracted to magnets because they have paired electrons (i.e., the magnetic fields of the paired electrons cancel out). Atoms that contain unpaired electrons (e.g., oxygen) are referred to as *paramagnetic* because they are attracted to magnets.

**FIGURE 2**  
Subshell-Filling Sequence

All of the subshells of a given value of  $n$  are on the same horizontal line. The filling sequence is determined by following the arrows starting at the lower left.

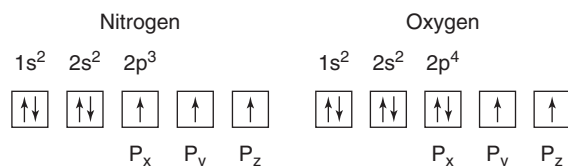


**ELECTRON CONFIGURATION IN ATOMS** Knowing how electrons are distributed in atoms is essential to any understanding of how chemical bonds are formed. There are several rules concerning electron distribution. The most basic rule is the *Aufbau principle*, which stipulates that electrons are put into orbitals, two at a time, in the order of increasing orbital energy (i.e., the inner orbitals are filled before the outer, higher-energy orbitals). Chemists use a shorthand method to illustrate how electrons are arranged around the nucleus of a ground-state atom (an atom at its lowest possible energy state). The electron configuration pattern useful for the elements relevant to living organisms is as follows:  $1s^2 2s^2 2p^6 3s^2 3p^6 4s^2 3d^{10} 4p^6 5s^2 4d^{10} 5p^6 6s^2$ .

The superscripts in the electron configuration pattern indicate the maximum number of electrons in each subshell. Note that because of orbital overlaps, the order of the orbitals being filled becomes more complicated as the filling pattern progresses. Figure 2 is a diagram that will aid in recalling the order in which the subshells are filled.

Determining an element's electron configuration requires knowing its atomic number (the number of protons), which is also equal to the number of electrons. Using the electron configuration pattern, the element's electrons are then used to fill in the orbitals beginning with the lowest energy level. For example, the electron configurations of hydrogen (1 electron) and helium (2 electrons) are  $1s^1$  and  $1s^2$ , respectively. Similarly, the electron configurations of carbon (6 electrons) and chlorine (17 electrons) are  $1s^2 2s^2 2p^2$  and  $1s^2 2s^2 2p^6 3s^2 3p^5$ , respectively. According to *Hund's rule*, when an energy subshell has more than one orbital (e.g., p and d orbitals) there is only 1 electron allowed in each orbital until all the

orbitals have 1 electron. Such electrons have parallel spins. As additional electrons enter the orbitals, they will spin pair with the previously unpaired electrons. The orbital diagrams of nitrogen and oxygen illustrate this rule.



For many elements, an electron configuration also reveals how many valence electrons there are. *Valence electrons*, the electrons in the s and p orbitals of the outermost energy level, determine the element's chemistry (i.e., how it will react with other elements). For example, oxygen atoms with an electron configuration of  $1s^2 2s^2 2p^4$  have six valence electrons (i.e., there are a total of six electrons in its 2s and 2p orbitals). Chlorine has seven valence electrons because there are seven electrons in its 3s and 3p orbitals. For many elements, atoms will react so that their outermost energy level or *valence shell* is filled, which is the most stable configuration they can have. The term *octet rule* is used to describe this phenomenon because the atoms of most elements react so that their valence shells contain eight electrons. Hydrogen and lithium are two obvious exceptions. Because a hydrogen atom only has one electron in its 1s orbital, it can gain one electron when it reacts to form a  $1s^2$  orbital or it can give up an electron to form a proton ( $H^+$ ). With three electrons, lithium (Li) has a  $1s^2 2s^1$  configuration. By losing its one valence electron, lithium atoms gain stability by having a filled 1s shell (two electrons). In the reaction of lithium with chlorine forming lithium chloride (LiCl), lithium gives up one electron to become a lithium ion ( $Li^+$ ). The lithium valence electron is donated to chlorine to form the chloride ion ( $Cl^-$ ). Chlorine has thereby increased its valence shell from seven to eight electrons. Understanding the significance of electron configurations, valence, and other properties of the elements is enhanced by familiarity with the periodic table of the elements, which is discussed next. It should be noted that the term *oxidation state* is often used in reference to atoms that have gained or lost electrons. The lithium ion, for example, has a +1 oxidation state and the chloride ion has a -1 oxidation state.

**THE PERIODIC TABLE** The modern periodic table (**Figure 3**) is a chart based on the *periodic law*, which states that the electron configurations of the elements vary periodically with their atomic number. The properties of the elements that depend on their electronic configuration, therefore, also change with increasing atomic number in a periodic pattern. The periodic table is arranged in vertical rows called *groups* or *families* and horizontal rows called *periods*. Certain characteristics of the elements increase or decrease along the vertical or horizontal rows. These characteristics, which affect chemical reactivity, are atomic radius, ionization energy, electron affinity, and electronegativity. The *atomic radius* of a neutral atom is the distance from the nucleus to the outermost electron orbital. *Ionization energy* is defined as the amount of energy required to remove the highest energy electron from each atom in 1 mol of the atoms in the gaseous state (i.e., how strongly an atom holds on to its electrons). *Electron affinity* is the energy that is released when an electron is added to an atom. *Electronegativity* is the tendency of an atom to attract electrons to itself.

Each of the seven horizontal rows of the periodic table, called *periods*, begins with an element with a new shell with its first electron. For example, there is one electron in the 2s, 3s, and 4s subshells of lithium, sodium, and potassium (K), respectively. The atomic radii of the elements in groups 1, 2, and 13 to 18 decrease from left to right. As the number of positively charged protons at the center of the atom increases, the negatively charged electrons are attracted more strongly (i.e., the electrons are drawn closer to the nucleus). The same trend is not seen in

**THE PERIODIC TABLE OF THE ELEMENTS**

IUPAC groups		1	2											13	14	15	16	17	18
Traditional groups (USA)		IA	IIA											IIIA	IVA	VA	VIA	VIIA	0
Periods	1																	1	
	2																	2	
	3																	3	
	4																	4	
	5																	5	
	6																	6	
	7																	7	

1																	2										
3	4											5	6	7	8	9	10										
11	12											13	14	15	16	17	18										
19	20											21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
37	38											39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
55	56											57	58	59	60	61	62	63	64	65	66	67	68	69	70		
87	88											89	90	91	92	93	94	95	96	97	98	99	100	101	102		

57	58	59	60	61	62	63	64	65	66	67	68	69	70
La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb
138.9	140.1	140.9	144.2	[144.9]	150.4	152.0	157.2	158.9	162.5	164.9	167.3	168.9	173.0
89	90	91	92	93	94	95	96	97	98	99	100	101	102
Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No
227.0	232.0	231.0	238.0	[237.0]	[244.1]	[243.1]	[247.1]	[247.1]	[251.1]	[252.1]	[257.1]	[258.1]	[259.1]

Atomic number	27
Symbol	Co
Atomic mass	58.98

Values in brackets are masses of most stable isotopes.

**FIGURE 3****The Periodic Table**

In the modern periodic table elements are organized on the basis of their atomic numbers, electron configurations and recurring chemical properties. Note that the Lanthanides (elements 57–70) and the Actinides (elements 89–102) are not relevant to biochemistry and are not discussed.

the atomic radii of the elements in groups 3 to 12. There is little reduction in atomic size in these elements because of the repulsion between the 4s and 3d electrons.

The ionization energies of the elements in a period typically increase with increasing atomic number. As the atomic radii decrease across a period (i.e., the distance between the outer electron and the nucleus of the atoms decreases), more energy is required to remove the outer electron. For example, it is easier to remove an electron from lithium (atomic number = 3) than from nitrogen (N) (atomic number = 7).

Electron affinity, which can be thought of as the likelihood that a neutral atom will gain an electron, increases from left to right across periods. Metals such as sodium ( $1s^22s^22p^63s^1$ ) have low electron affinities because they become more stable when they lose valence electrons. Elements on the right side of the periodic table have high electron affinities because of vacancies in their valence shells. Chlorine ( $1s^22s^22p^63s^23p^5$ ) has a very high electron affinity because it releases a large amount of energy to become more stable as the chloride ion when it fills its valence shell by gaining one electron. The noble gases [e.g., helium (He), neon (Ne), and argon (Ar)] in group 18 do not conform to this trend because their valence shells are filled; hence, they are chemically unreactive.

Electronegativity, a measure of an atom's affinity for electrons in a chemical bond, increases across a period as atomic radii are decreasing. In the water molecule ( $H_2O$ ), for example, oxygen is more electronegative than the hydrogen atoms because oxygen's larger nucleus strongly attracts its electrons. Hence, in water molecules the electrons in the bonds between each of the two hydrogen atoms and the oxygen atom are shared unequally.

The 18 vertical rows of the periodic table consist of elements with similar chemical and physical properties. The group 1 elements all have one electron in



their outermost shell. With the exception of hydrogen, all of the group 1 elements [lithium (Li), sodium (Na), potassium (K), rubidium (Rb), cesium (Cs), and the rare radioactive francium (Fr)] are referred to as the *alkali metals* because they react vigorously with water to form hydroxides (e.g., NaOH). The alkali metals do so because they readily lose their single valence electron to form cations with a +1 charge. For example, sodium ( $1s^2 2s^2 2p^6 3s^1$ ) reacts with water to form sodium hydroxide (NaOH) and hydrogen gas ( $H_2$ ). NaOH then dissociates to form  $Na^+$  and  $OH^-$ . Because the alkali metals donate their valence electron so readily, they are considered especially strong reducing agents. (*Reducing agents* are elements or compounds that donate electrons in chemical reactions.) Of all the alkali metals, only sodium and potassium have normal functions in living organisms. For example, the balance of sodium ions and potassium ions across the plasma membrane of neurons is critical to the transmission of nerve impulses.

The group 2 alkaline earth metals [beryllium (Be), magnesium (Mg), calcium (Ca), strontium (Sr), barium (Ba), and radium (Ra)] have two electrons in their outermost shell. The electron configurations for the biologically important group 2 elements magnesium (DNA structure and enzyme function) and calcium (bone structure and muscle contraction) are  $1s^2 2s^2 2p^6 3s^2$  and  $1s^2 2s^2 2p^6 3s^2 3p^6 4s^2$ , respectively. With the exception of beryllium, the alkaline earth metals lose their two valence electrons to form cations with a +2 charge [e.g., they react with water to form metal hydroxides such as  $Ca(OH)_2$ ]. Like the group 1 metals, the alkaline earth metals are strong reducing agents, although each element is somewhat less reactive than the alkali metal that precedes it.

Groups 3 to 12 are referred to as the d-block elements because electrons progressively fill the d orbitals. The majority of the d-block elements are the *transition elements*, which have incompletely filled d orbitals. Zinc (Zn, atomic number = 30) is not considered a transition metal because its 3d subshell has 10 electrons. Because electron configurations of elements with high atomic numbers are unwieldy, chemists use a simplification for an element's electron configuration that is an abbreviation for the electron configuration of the noble gas immediately preceding the element. For example, zinc's electron configuration can be described as  $[Ar]3d^{10}4s^2$ .

The transition elements are metals with special properties. Among these are the capacities to have more than one oxidation state and to form colored compounds. Iron is a transition metal found in a large number of proteins in all living organisms. It most notably occurs in hemoglobin, the oxygen-transport protein that gives blood its red color. Iron atoms ( $[Ar]3d^6 4s^2$ ) can form a wide range of oxidation states from -2 to +6, but its most common oxidation states are +2 and +3. Neutral iron atoms can form the +2 ion because the 4s orbital and the 3d orbitals have very similar energies, so that the removal of two electrons to form  $Fe^{+2}$  ( $[Ar]3d^6$ ) requires little energy. The loss of an additional electron to form  $Fe^{+3}$  ( $[Ar]3d^5$ ) requires more energy.

In addition to iron, several other d-block elements are important in living organisms. Manganese (Mn) is found in numerous enzymes in all living organisms. Cobalt (Co) is an important component of vitamin  $B_{12}$  structure. Nickel (Ni) occurs in several enzymes in microorganisms and plants. Copper (Cu) is found in several energy generation proteins. Zinc (Zn) occurs in over 100 enzymes and has structural roles in numerous proteins. Molybdenum (Mo) has a vital role in nitrogen fixation.

The remaining elements in the standard periodic table, groups 13 to 18, are in the *p block*, so named because electrons progressively fill p orbitals. The p-block elements found in living organisms (carbon, nitrogen, phosphorus, sulfur, chlorine, and iodine) are nonmetals. Carbon ( $1s^2 2s^2 2p^2$ ) in group 14 has four electrons available to form stable bonds both with other carbon atoms and with a variety of other elements (most notably hydrogen, oxygen, nitrogen, and sulfur). As a result, carbon can form an almost infinite number of compounds. Carbon is the crucial

**WORKED PROBLEM 1**

Consider the element potassium (atomic number = 19). What is its electronic configuration? How many electrons are in its valence shell? Is elemental potassium paramagnetic or diamagnetic?

**SOLUTION**

The number of electrons in the potassium atom is equal to its atomic number, 19. Using the Aufbau and Pauli exclusion principles and Hund's rule, the electronic configuration is  $1s^2 2s^2 2p^6 3s^2 3p^6 4s^1$ . Potassium has one valence electron because its outermost energy level (4s) has one electron. Elemental potassium is paramagnetic because it has one unpaired electron in its valence shell.

element in most biomolecules, with the exceptions of molecules such as water and ammonia and the electrolytes (e.g.,  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{+2}$ ). (An *electrolyte* is an ionic species that influences the distribution of electric charge and the flow of water across membranes.) Because nitrogen ( $1s^2 2s^2 2p^3$ ) has five electrons in its outer shell, its valence is  $-3$ . In biomolecules nitrogen is found in amines ( $\text{R-NH}_2$ , where R is a carbon-containing group) and amides (e.g., bonds between amino acids in proteins). Phosphorus ( $1s^2 2s^2 2p^6 3s^2 3p^3$ ), in the nitrogen family, most commonly occurs in living organisms as phosphate ( $\text{PO}_4^{-3}$ ); (e.g., in the nucleic acids DNA and RNA and as a structural component of bones and teeth). In living organisms, oxygen ( $1s^2 2s^2 2p^4$ ) is found most abundantly in water molecules, where it has an oxidation state of  $-2$ . Oxygen atoms are also found in all the major classes of biomolecules (e.g., proteins, carbohydrates, fats, and nucleic acids). Sulfur ( $[\text{Ne}]3s^2 3p^6$ ), the second member of the oxygen family, is found in proteins and small molecules such as the vitamin thiamine. It often occurs in biomolecules in the form of thiols ( $\text{R-SH}$ ) and disulfides ( $\text{R-S-S-R}$ ). Of all the members of the halogen family (group 17), only chlorine ( $[\text{Ne}]3s^2 3p^5$ ) and iodine ( $[\text{Kr}]5s^2 4d^{10} 5p^5$ ) routinely occur in living organisms. The functions of chlorine in the form of the chloride ion include the digestion of protein in the animal stomach [hydrochloric acid ( $\text{HCl}$ )] and its function as an electrolyte. Iodine is a component of the thyroid hormones, which regulate diverse metabolic processes in the animal body. It should be noted that phosphorus, sulfur, and chlorine are usually assigned valences of  $-3$ ,  $-2$ , and  $-1$ , respectively. However, because they have vacant d orbitals, they can expand their valence shell and form different oxidation states. For example, phosphorus has a  $+5$  valence in phosphoric acid ( $\text{H}_3\text{PO}_4$ ), sulfur has a valence of  $+6$  in the sulfate ion ( $\text{SO}_4^{2-}$ ), and chlorine has a  $+1$  valence in the hypochlorite ion ( $\text{ClO}^-$ ).

**Chemical Bonding**

A chemical bond is a strong attractive force between the atoms in a chemical compound. Chemical bonds form because of interactions between atoms that involve the rearrangement of their outer shell electrons. According to the octet rule, atoms react so as to achieve the outer electron configuration of the noble gases. They do so because complete outer valence shells are stable because of a reduction in stored potential energy.

Two major types of chemical bonds are ionic and covalent. The bonds differ in how valence electrons are shared among the bonded atoms. *Ionic bonds* form when electrons are transferred from atoms with a tendency to release electrons (e.g., alkali or alkaline earth metals) to electronegative atoms that tend to gain electrons. The transfer process results in the formation of oppositely charged atoms called *ions*. The positively charged ion product is called a *cation*, and the negatively charged ion product is called an *anion*. For example, the transfer of

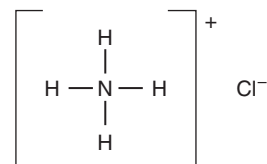


sodium's single electron to chlorine (valence = 7) yields the cation  $\text{Na}^+$  and the anion  $\text{Cl}^-$ . The ionic bond in  $\text{NaCl}$  is the electrostatic attraction between the positive and negative ions.

In *covalent bonds* electrons are shared between atoms with similar electronegativity values. A single covalent bond consists of two shared electrons. For example, there is one covalent bond in molecular hydrogen ( $\text{H}_2$ ). The two hydrogen atoms, with one electron each, complete their valence shell by sharing their electrons. Elements such as carbon, nitrogen, and oxygen can form multiple covalent bonds. Carbon, for example, can form double and triple bonds. In the molecule ethylene a carbon-carbon double bond involves the sharing of two sets of valence electrons. The triple covalent bond in molecular nitrogen ( $\text{N}_2$ ) is an example of the sharing of three sets of valence electrons.

Covalent bonds between atoms with moderate differences in electronegativity are referred to as *polar covalent bonds*. In such bonds the electrons are shared unequally, with the electron density shifted toward the atom with the greater electronegativity. The electrical asymmetry in such bonds causes one end of the molecule to possess a slightly negative charge and the other end a slightly positive charge. These partial charges are indicated by the lowercase Greek letter  $\delta$ :  $\delta^+$  and  $\delta^-$ . For example, in the water molecule  $\text{H}_2\text{O}$  the oxygen atom has a significantly larger electronegativity value than the hydrogen atoms. As a result, the electron pairs between oxygen and each of the hydrogen atoms are drawn closer to the oxygen atom. Each hydrogen atom has a partial positive charge ( $\delta^+$ ) and the oxygen has a partial negative charge ( $\delta^-$ ).

In a *coordinate covalent bond*, a shared pair of electrons in the bond comes from one atom. The reaction between ammonia ( $\text{NH}_3$ ) and  $\text{HCl}$  provides a simple example. The product ammonium chloride ( $\text{NH}_4\text{Cl}$ ) results when a covalent bond is formed between the nitrogen with its lone pair and the proton that has dissociated from  $\text{HCl}$ .

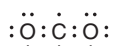


**LEWIS DOT NOTATION** Chemists often describe chemical bonds using Lewis dot structures. Devised by the chemist G. N. Lewis, Lewis dot structures are a shorthand notation for explaining how the valence electrons of the atoms in various compounds combine to form covalent bonds. Molecular hydrogen ( $\text{H}_2$ ) is a simple example. Because each hydrogen atom has one electron, the Lewis dot structure for the hydrogen atom is  $\text{H}\cdot$ . The energy shell of  $\text{H}_2$  has a maximum of two electrons, and the formation of  $\text{H}_2$  is depicted as

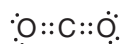


The following rules facilitate the drawing of Lewis structures for more complicated molecules:

- (1) **Determine the number of valence electrons for each atom in the molecule.** For example, carbon dioxide ( $\text{CO}_2$ ) has one carbon atom with four valence electrons and two oxygen atoms each with six valence electrons.
- (2) **Determine the identity of the central atom in the Lewis structure.** This atom will often be the one with the lowest electronegativity. Recall that electronegativity decreases from right to left across and from top to bottom of the periodic table. In the case of  $\text{CO}_2$ , carbon is less electronegative than oxygen, so carbon is the central atom.
- (3) **Arrange the electrons so that each atom donates one electron to a single bond between it and another atom and then count the electrons around each atom.** Are the octets complete? For  $\text{CO}_2$ , a first try would yield



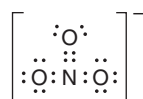
Note, however, that in this structure each carbon only has six electrons and each oxygen atom has seven electrons. Because the octets are incomplete, more electrons must be shared, an indication that there are double or triple bonds in the molecule. In the case of  $\text{CO}_2$ , rearranging the electrons results in the following Lewis dot structure in which there are two double bonds and all three atoms have a full octet of electrons.



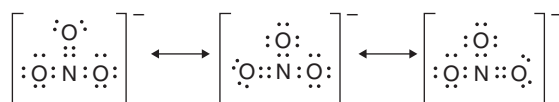
In molecules such as ammonia ( $\text{NH}_3$ ), it is obvious that although the nitrogen atom is more electronegative than the hydrogens, it is the only atom in the molecule that can form multiple bonds. Hence, the nitrogen atom is the central atom in ammonia molecules. Its Lewis dot structure is



For a large number of molecules, there is more than one valid Lewis dot structure. The nitrate ion ( $\text{NO}_3^-$ ) is a typical example. Considering that nitrogen has five valence electrons and each oxygen atom has six valence electrons, the following Lewis dot structure of the nitrate ion satisfies the octet rule:



However, there is no reason why the double bond should appear where it does in this formula. It could easily appear in either of the two other locations around the nitrogen atom. Therefore, there are three valid Lewis dot structures for the nitrate ion.



When this situation occurs, the ion or molecule is said to be a *resonance hybrid*. (The double-headed arrows are used in the representation of resonance structures.) In the case of the nitrate ion, it is considered to have a structure that is the average of these three states.

**MOLECULAR STRUCTURE** Molecules are three-dimensional arrangements of atoms. Understanding molecular structure, also referred to as molecular shape, is important because structure provides insight into the physical and chemical properties of molecules. Physical properties that are affected by molecular shape include boiling point, melting point, and water solubility. The shape of molecules also powerfully affects chemical reactivity.

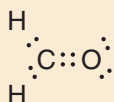
According to the *valence shell electron pair repulsion (VSEPR) theory*, repulsive forces between valence shell bonding and nonbonding electrons (lone pairs) determine molecular geometry (molecular shape). In other words, the valence electron pairs on the central atom in a molecule orient themselves in space so that repulsion is minimized (i.e., their total energy is minimized). Lone pairs of electrons have a greater repulsive effect than bonding pairs. (A *lone pair* is a valence electron pair on a central atom that is not involved in bonding.) The term electron group is used in discussions of VSEPR theory. An *electron group* is defined as a set of valence electrons in a region around a central atom that exerts repulsion on other valence electrons. Electron groups include bonding and nonbonding electron pairs or the pairs of electrons in double or triple bonds.

**WORKED PROBLEM 2**

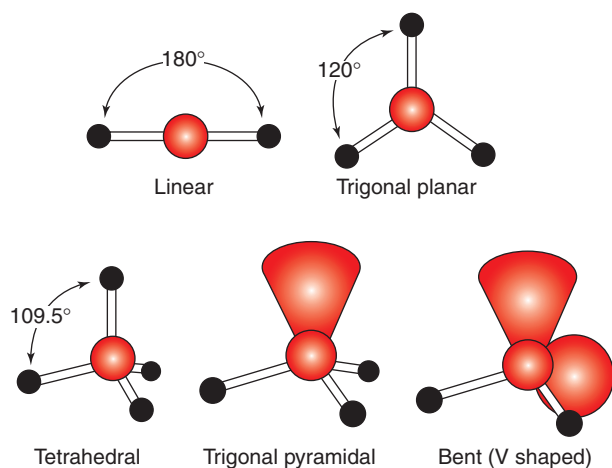
What is the Lewis electron dot formula for formaldehyde ( $\text{H}_2\text{C}=\text{O}$ )?

**SOLUTION**

The valence electrons for hydrogen, carbon, and oxygen are 2 (1 for each atom), 4, and 6, respectively, for a total of 12 electrons. Single bonds between the elements account for 6 electrons, leaving 6 electrons unaccounted for. Group the remaining 6 electrons around the most electronegative atom (oxygen) until a total of 8 electrons (bonding and nonbonding) is reached. Using one pair of these electrons to form a double bond between carbon and oxygen completes the carbon octet. The final Lewis structure is given below.



Ascertaining a molecule's three-dimensional shape begins with a correct Lewis dot structure. The molecule's geometry is then determined based on the number of bonding and nonbonding electrons on the central atom (**Figure 4**). If there are two electron pairs, the molecule has a linear shape. Carbon dioxide ( $\text{CO}_2$ ), for example, is a *linear* molecule with two electron groups. Its bond angle is  $180^\circ$ . Formaldehyde ( $\text{H}_2\text{C}=\text{O}$ ), with three electron groups, has *trigonal planar* geometry with bond angles of  $120^\circ$ . Molecules with a central atom with four pairs of electrons have a tetrahedral shape. Methane ( $\text{CH}_4$ ), with its four carbon-hydrogen bonds, has bond angles of  $109.5^\circ$ . If one of the four electron groups in a tetrahedron is a lone pair, the molecular shape is *trigonal pyramidal*. Because of the strong repulsion of the lone pair, bond angles are less than  $109.5^\circ$ . For example, the lone pair in  $\text{NH}_3$  forces the  $\text{NH}$  bonding electron pairs closer together with bond angles of  $107.3^\circ$ .



**FIGURE 4**  
Common Molecular Geometries

These structures illustrate the spatial orientations of electron groups. Note that unpaired electrons are indicated by an enlarged representation of an orbital.

Three-dimensional shape also affects molecular polarity. In polar covalent bonds there is an unequal sharing of electrons because the atoms have different electronegativities. This separation of charge is called a *dipole*. Although a polar molecule always contains polar bonds, some molecules with polar bonds are nonpolar. Molecular polarity requires an asymmetric distribution of polar bonds. For example,  $\text{CO}_2$  contains two  $\text{C}-\text{O}$  dipole bonds. Carbon dioxide is a nonpolar molecule because of its linear shape (i.e., its bond dipoles are symmetrical and cancel each other out). Water, which also has two polar bonds (two  $\text{O}-\text{H}$

**WORKED PROBLEM 3**

Dimethyl ether has the following formula:  $\text{CH}_3\text{—O—CH}_3$ . What is the shape of dimethyl ether? Does this molecule have a dipole moment?

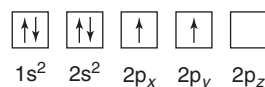
**SOLUTION**

The oxygen in dimethyl ether has four electron pairs including two lone electron pairs. As a result, the oxygen has a tetrahedral shape with an overall bent shape for the dimethyl ether molecule. Because the molecule has a bent shape and the electron distribution is uneven, dimethyl ether has a dipole moment.

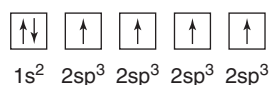
bonds), is a polar molecule because of its geometry. Water is tetrahedral because it contains four electron groups: two bonding pairs and two lone pairs. As a result of the greater repulsions from the lone pairs on the oxygen, however, the bond angle of a water molecule is  $104.5^\circ$ . Water's "bent" geometry (refer to **Figure 4**) makes it an asymmetric molecule and therefore polar.

**VALENCE BOND THEORY AND ORBITAL HYBRIDIZATION** Although the VSEPR theory accounts for molecular shape, it does not explain how the orbitals of the individual atoms interact to form the covalent bonds in molecules. The concept of *orbital hybridization*, the result of quantum mechanical calculations, explains how the mixing of atomic orbitals results in the formation of the more stable hybrid orbitals found in molecules. Each type of hybrid orbital corresponds to a type of electron group arrangement predicted by VSEPR theory. The three most common hybrid orbitals observed in biomolecules are  $sp^3$ ,  $sp^2$ , and  $sp$ .

Carbon has an electron configuration of  $1s^2 2s^2 2p^2$ , which can also be represented as



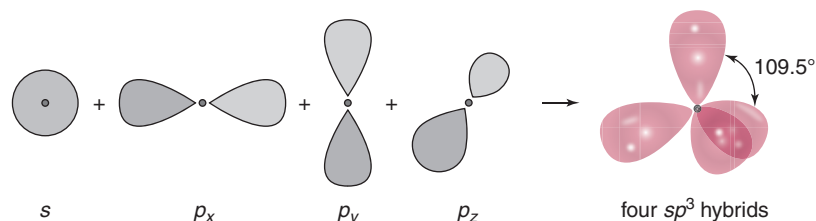
It appears from this diagram that carbon only has two bonding electrons. The carbon atoms in molecules such as methane, however, are bonded to four hydrogen atoms in a tetrahedral arrangement. During methane formation, as a result of the attraction of each of the hydrogen nuclei (i.e., protons) for carbon's lower-energy valence electrons, the two  $2s$  electrons move into  $2p$  orbitals.



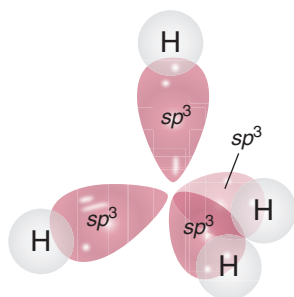
As they do so, they mix, forming four identical  $sp^3$  orbitals (**Figure 5**).

**FIGURE 5** **$sp^3$  Orbitals**

Hybridization of an  $s$  orbital and all three  $p$  orbitals gives four identical  $sp^3$  orbitals.



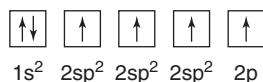
In the methane molecule (**Figure 6**), each of the four  $sp^3$  hybrid orbitals overlaps with the  $1s$  orbital of hydrogen to form a sigma bond. A *sigma bond* ( $\sigma$ ), which is formed by the overlapping by the outermost orbitals of two atoms, is the strongest type of covalent bond.



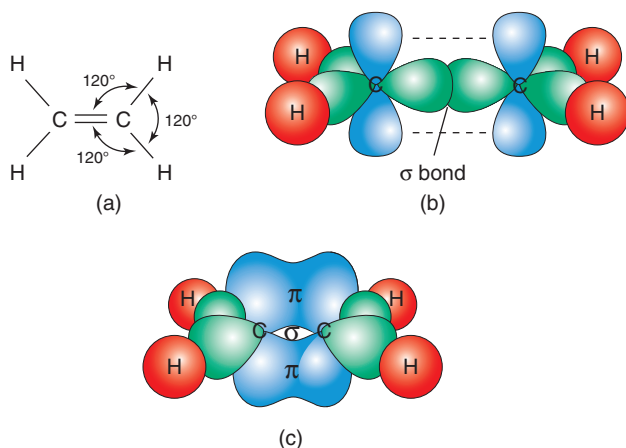
**FIGURE 6**  
**Structure of Methane**

Methane ( $\text{CH}_4$ ) has a tetrahedral geometry with four  $\sigma$  bonds formed by the overlap of four  $sp^3$  orbitals of carbon with four  $1s$  orbitals of hydrogen atoms.

Each of the two carbon atoms in the molecule ethene ( $\text{H}_2\text{C}=\text{CH}_2$ ) is bonded to three atoms in trigonal planar geometry. Carbon's  $2s$  orbital mixes with two of the three available  $2p$  orbitals to form three  $sp^2$  orbitals.



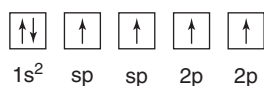
Two of the three  $sp^2$  orbitals of each carbon atom overlap the orbital of a hydrogen atom, forming a total of four  $\sigma$  bonds. The third  $sp^2$  orbital of the two carbon atoms overlap to form a carbon-carbon  $\sigma$  bond. The  $p$  orbitals, one on each carbon, overlap to form a pi ( $\pi$ ) bond (**Figure 7**). A *double bond* in molecules such as ethene consists of a  $\sigma$  bond and a  $\pi$  bond.



**FIGURE 7**  
**Ethene Structure**

(a) Each carbon atom in ethene (also known as ethylene) has three  $sp^2$  orbitals with bond angles of  $120^\circ$ , which have a trigonal planar geometry. (b) Two of the  $sp^2$  orbitals of each carbon (green) overlap with an  $s$  orbital of hydrogen (red) forming a total of 4  $\sigma$  bonds. The remaining two  $sp^2$  orbitals, one from each carbon, overlap to form a carbon-carbon  $\sigma$  bond. (c) Two  $p$  orbitals (blue), one from each carbon atom, overlap to form a  $\pi$  bond.

Acetylene ( $\text{C}_2\text{H}_2$ ) is a molecule with a triple bond with each carbon bonded to two other atoms in a linear geometry. Carbon's  $2s$  orbital



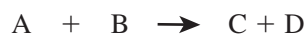
mixes with one  $2p$  orbital to form 2  $sp$  hybrid orbitals. Each carbon also possesses two unhybridized  $2p$  orbitals. Acetylene has a triple bond consisting of one  $\sigma$  bond and two  $\pi$  bonds. The carbon-carbon  $\sigma$  bond is formed by the overlap of an

sp hybrid orbital from each carbon atom. Each  $\pi$  bond is formed by the overlap of two of carbon's 2p orbitals. Each of the two carbon-hydrogen  $\sigma$  bonds is formed by the overlap of carbon's other sp orbital with the 1s orbital of hydrogen.

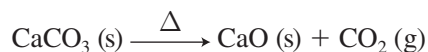
## Chemical Reactions

In chemical reactions the atoms in chemical substances are rearranged to form new substances as chemical bonds are broken and formed. According to the *collision theory*, the reaction rate in bimolecular reactions depends on the frequency of successful collisions between the chemical species. Successful collisions occur when there is sufficient energy at the moment of impact (called the *activation energy*) and the colliding species are oriented during the collision in a manner that favors the rearrangement of the atoms and electrons. *Catalysts* are substances that increase reaction rates without being affected by the reaction. They do so by lowering the activation energy of the reaction by providing an alternative pathway for the reaction. For example, the metal iron is used as a catalyst in the Haber process, the industrial method of converting nitrogen and hydrogen gases into ammonia ( $\text{NH}_3$ ). As the  $\text{N}_2$  and  $\text{H}_2$  molecules become adsorbed onto the surface of the metal, where they are more likely to be in a favorable orientation for successful collisions, the bonds in both molecules are weakened. Once formed, the ammonia molecules desorb from the catalyst.

Chemical reactions are described with chemical equations. The substances undergoing the reaction, called *reactants*, appear on the left-hand side of the equation, and the *products* of the reaction are on the right-hand side. An arrow between the reactants and products symbolizes the chemical change that occurs as a result of the reaction. For example, the chemical equation for the reaction in which molecule A reacts with molecule B to form molecules C and D is



Other symbols that may appear in a chemical equation provide information about the physical state of the reactants and products or a required energy source. The equation for the decomposition of calcium carbonate, for example, is



In this equation the letter s indicates that the reactant  $\text{CaCO}_3$  and the product CaO (calcium oxide) are solids. The letter g indicates that  $\text{CO}_2$  is a gas. The uppercase Greek letter delta ( $\Delta$ ) above the arrow indicates that the reaction requires an input of energy in the form of heat. Reactions that require an input of energy in the form of heat are described as *endothermic*. If light energy is involved in a reaction,  $h\nu$  ( $\nu$  is the lowercase Greek letter nu) is placed above the arrow.

All chemical equations must obey the *law of conservation of matter*, which states that during chemical reactions mass is neither created nor destroyed. In other words, the mass of the reactants must be equal to the mass of the products. For example, in the equation for the reaction in which methane ( $\text{CH}_4$ ) reacts with molecular oxygen ( $\text{O}_2$ ) to form carbon dioxide ( $\text{CO}_2$ ) and water, the number of each type of atom on both sides of the arrow must be equal.



In this balanced equation the same number of carbon, hydrogen, and oxygen atoms is on both sides of the arrow because the number 2 has been placed before the formulas for molecular oxygen and water.



**WORKED PROBLEM 4**

Consider the following reaction equation:



Balance the equation and identify the elements that are oxidized, reduced, or unchanged by the reaction. Use the generalizations that the oxidation state of hydrogen and group 1 metals is +1 and that of oxygen is -2.

**SOLUTION**

Balancing a chemical reaction equation requires that the number and types of atoms be the same. To satisfy this requirement, the number 4 is placed before the reactant KClO and the product KCl. The reaction becomes



Using the oxidation state information given above, oxidation numbers are assigned to each element:



Sulfur is the element that is oxidized (i.e., its oxidation number increases from -2 to +6). Chlorine is reduced because its oxidation number is lowered from +1 to -1. Elements whose oxidation numbers remain unchanged are hydrogen, potassium, and oxygen.

**REACTION KINETICS** As informative as a chemical reaction's equation is, it reveals nothing about several important properties of the reaction: (1) How fast does the reaction occur? (2) When the reaction ends, what will be the ratio of product to reactant molecules? (3) Does the reaction require or release energy? The science of chemical kinetics seeks to answer these and other questions about chemical reaction rates (i.e., the change in the number of product and reactant molecules as the reaction progresses).

Reaction rate is defined as the change in the concentration of reactant or product per unit time. For the general reaction



the rate is equal to  $k[\text{A}]^m[\text{B}]^n$ , where  $k$  is the rate constant, and  $[\text{A}]$  and  $[\text{B}]$  are the concentrations of the reactants A and B, respectively. The exponents  $m$  and  $n$  are used to determine the reaction's order, a number that relates the rate at which a chemical reaction occurs to the concentrations of the reactants. For example, if  $m$  is equal to 1, the reaction rate doubles when the concentration of reactant A doubles. If  $m$  is equal to 2, the rate quadruples when the concentration of reactant A doubles. (Refer to pp. 198–200 in the textbook for a more detailed description of reaction order.) The rate constant and order of a reaction can only be determined by experiment. Experiments performed over the course of the past century have revealed that the following factors influence reaction rate:

- (1) Reactant structure—the nature and the strength of chemical bonds affect reaction rates. For example, salt formation, the exchange of ions, is a fast process compared with the breaking and forming of covalent bonds.

- (2) Reactant concentration—the number of molecules of a substance per unit volume affects the likelihood of collisions. Reaction rates increase as the reactant molecules become more crowded.
- (3) Physical state—whether the reactants are in the same phase (solid, liquid, or gas) affects reaction rates because reactants must come into contact with each other. When reactants are in the aqueous phase, for example, thermal motion brings them into contact. When reactants are in different phases, contact only occurs at the interface between the phases. In such circumstances increasing interface surface area raises a reaction's rate. For example, when reactants are in the solid and liquid phases, grinding the solid into small pieces increases its surface area that is in contact with the liquid phase.
- (4) Temperature—at higher temperatures molecules have more thermal energy and are, therefore, more likely to collide with each other.
- (5) Catalysts—substances that accelerate a reaction's rate, but remain unchanged afterward. A catalyst provides a different pathway for the reaction, thereby lowering the activation energy.

**CHEMICAL REACTIONS AND EQUILIBRIUM CONSTANTS** Many chemical reactions are reversible (i.e., they occur in both forward and reverse directions). Reversible reactions are indicated in reaction equations with double arrows. When a reversible reaction begins (i.e., when the reactants are mixed together), reactants begin to be converted into product. At some point in time, which differs for each reaction, some product molecules are reconverted back into reactant molecules. Eventually, the reaction reaches a dynamic equilibrium state in which both the forward and the reverse reactions occur, but there is no net change in the ratio of reactant and product molecules. The extent to which the reaction proceeds to product is measured by an equilibrium constant ( $K_{\text{eq}}$ ), which reflects the concentrations of reactants and products under specific conditions of temperature and pressure. For a reaction with the equation



$K_{\text{eq}}$  is calculated as the ratio of the molar concentrations of product and reactant, each of which is raised to the power of its coefficient.

$$K_{\text{eq}} = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

Note that  $K_{\text{eq}}$  is also equal to  $k_f/k_r$ , the ratio of the forward and reverse rates of the reaction. A high  $K_{\text{eq}}$  value (significantly greater than 1) indicates that when a reaction reaches equilibrium, the concentration of the reactant is low (i.e., the reaction favors the production of product). If the  $K_{\text{eq}}$  value is lower than 1, then product concentration is lower than reactant concentration when equilibrium has been reached. When  $K_{\text{eq}}$  is greater than 1000, the reaction has gone to completion (i.e., almost all reactants have been converted to product).

In 1885 the French chemist Henri Louis Le Chatelier reported his discovery of a remarkable feature of systems at equilibrium. For a chemical reaction at equilibrium a change in the conditions of the reaction (e.g., temperature, pressure, or the concentrations of its components) triggers a shift in the equilibrium to counteract the change. Chemists and chemical engineers use *Le Chatelier's principle* to manipulate chemical reactions to maximize product synthesis. The Haber-Bosch process for making ammonia ( $\text{NH}_3$ ) from  $\text{N}_2$  and  $\text{H}_2$  is a prominent example.

All living organisms require a source of useable nitrogen-containing molecules. As a result of the extraordinary difficulty in breaking the stable triple bond of  $\text{N}_2$ , *nitrogen fixation* (the conversion of  $\text{N}_2$  to  $\text{NH}_3$ , a molecule that can be assimilated into organic molecules such as amino acids) is largely limited to

a select group of microorganisms. Note that the synthesis of ammonia is an *exothermic reaction* (i.e., it releases heat energy):



where a joule (J) is a unit of energy and a kilojoule (kJ) is 1000 joules.

The Haber-Bosch industrial process for synthesizing ammonia maximizes the reaction's yield in several ways:

- (1) An iron-based catalyst (iron oxide with small amounts of other metal oxides), which increases the rate at which equilibrium is attained, converts a slow reaction to one that is fast enough to be commercially feasible.
- (2) Ammonia, the product of the reaction, is removed from the reaction vessel. As a result, the system produces more  $\text{NH}_3$  to reestablish equilibrium.
- (3) An increase in the pressure within the reaction vessel (to 200 atm), obtained by decreasing volume, causes an increase in ammonia synthesis. Note that in this reaction 4 mol of reactant molecules are converted to 2 mol of product. The equilibrium shifts toward ammonia synthesis because there are fewer molecules of this gas.
- (4) By lowering the temperature of the reaction (i.e., by removing heat from an exothermic reaction), the equilibrium is shifted toward more ammonia synthesis. There is a limit to how much the temperature can be lowered, however, because the catalyst requires heat to be efficient. As a result, the reaction vessel operates at  $400^\circ\text{C}$ , a temperature that is hot enough for the catalyst yet relatively cool for an industrial process.

**ACID-BASE EQUILIBRIA AND pH** When acids and bases dissolve in water, they dissociate, forming ions. Hydrochloric acid and acetic acid ( $\text{CH}_3\text{COOH}$ ) are two well-known acids. HCl dissociates in water to yield chloride and hydrogen ions, and acetic acid dissociates to yield acetate ( $\text{CH}_3\text{COO}^-$ ) and hydrogen ions. Sodium hydroxide (NaOH) and methylamine ( $\text{CH}_3\text{NH}_2$ ) are examples of bases. In water NaOH dissociates to yield sodium and hydroxide ions and methylamine forms methylammonium ( $\text{CH}_3\text{NH}_3^+$ ) and hydroxide ( $-\text{OH}$ ) ions. The strength of an acid or a base is determined by the degree to which it dissociates. HCl is a strong acid because its dissociation in water is complete (i.e., 100% of HCl molecules dissociate into chloride and hydrogen ions). *Weak acids* and weak bases are so named because they dissociate only to a limited extent and establish a dynamic equilibrium with their ions. The general equation for the dissociation of a weak acid is



where HA is the undissociated acid and  $\text{A}^-$  is the conjugate base of the acid. The degree to which a weak acid dissociates is expressed as an acid dissociation constant  $K_a$ , the quotient of the equilibrium concentrations of the ions  $\text{A}^-$  and  $\text{H}^+$  and the undissociated acid (HA).

$$K_a = \frac{[\text{A}^-][\text{H}^+]}{[\text{HA}]}$$

The dissociation constants of weak acids and bases are usually expressed as the negative log of the equilibrium constant ( $-\log K_a$  or  $-\log K_b$ ), where the term  $-\log$  is replaced by the letter p. The extent to which a weak acid dissociates is referred to as its  $\text{p}K_a$  value. The dissociation constant and  $\text{p}K_a$  for acetic acid at  $25^\circ\text{C}$ , for example, are  $1.8 \times 10^{-5}$  and 4.76, respectively. The behavior of weak acids and bases is especially important in biochemistry because many biomolecules possess carboxylate, amino, and other functional groups that can accept or donate hydrogen

ions. For example, refer to pp. 138–140 for a description of the effect of hydrogen ion concentration on amino acids, the molecules used to construct proteins.

Water also has a slight capacity to dissociate into ions.

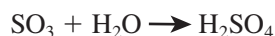


The hydrogen ion concentration of pure water at 25°C is  $1.0 \times 10^{-7}$  M. Because one hydroxide ion is produced for each hydrogen ion, the hydroxide ion concentration is also  $1.0 \times 10^{-7}$  M. The product of these two values (i.e.,  $[\text{H}^+][\text{OH}^-]$ ), referred to as the ion product for water, is  $1 \times 10^{-14}$ . The concentrations of hydrogen and hydroxide ions change depending on the substances that are dissolved in water, but their product is always  $1 \times 10^{-14}$ .

For weak acids and bases, hydrogen ion concentrations in aqueous solution can vary from 1 M to  $1 \times 10^{-14}$  M. For the sake of convenience, hydrogen ion concentrations are usually converted to pH values. The term pH simply means that the concentration of hydrogen ions in a solution has been converted to its negative log value (i.e.,  $\text{pH} = -\log [\text{H}^+]$ ). Refer to pp. 92–101 for a more detailed description of pH and the pH scale, a convenient means of expressing the acidity or alkalinity of substances.

**REACTION TYPES** There are several basic types of chemical reaction: synthesis reactions, decomposition reactions, displacement reactions, double displacement reactions, acid-base reactions, and redox reactions. Each is discussed briefly.

*Synthetic reactions* (also referred to as combination reactions) involve two or more substances that combine together to form a single new substance. The reaction of sulfur trioxide ( $\text{SO}_3$ ) with water, for example, yields sulfuric acid ( $\text{H}_2\text{SO}_4$ ).



### WORKED PROBLEM 5

The  $K_a$  for acetic acid is  $1.8 \times 10^{-5}$ . Determine the hydrogen ion concentration of a 0.1 M solution of acetic acid in water. What is the pH of this solution?

#### SOLUTION

The equation for the dissociation of acetic acid is

$$K_a = [\text{acetate}][\text{H}^+]/[\text{acetic acid}]$$

Because acetic acid is a weak acid, it is assumed that the dissociation of acetic acid has no substantive effect on acetic acid concentration. The values of the concentrations of acetate and hydrogen ions are equal to each other and are set at  $x$ . The equation for determining the hydrogen ion concentration in a 0.1 M solution is

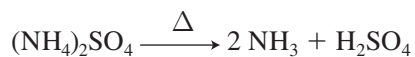
$$\begin{aligned} 1.8 \times 10^{-5} &= x^2/0.1, \text{ which becomes} \\ 1.8 \times 10^{-6} &= x^2 \end{aligned}$$

Solving for  $x$  yields  $1.35 \times 10^{-3}$ , the hydrogen ion concentration in the acetic acid solution.

The pH of the 0.1 M solution of acetic acid is calculated as follows:

$$\begin{aligned} \text{pH} &= -\log[\text{H}^+] \\ &= -\log(1.35 \times 10^{-3}) \\ &= 3 - 0.13 = 2.87 \end{aligned}$$

In *decomposition reactions*, a compound breaks down to form simpler products when the reactant absorbs enough energy so that one or more of its bonds breaks. For example, ammonium sulfate,  $(\text{NH}_4)_2\text{SO}_4$ , decomposes upon heating to yield ammonia ( $\text{NH}_3$ ) and  $\text{H}_2\text{SO}_4$ .



In *displacement* or substitution reactions a more reactive element replaces a less active element. For example, if an iron nail is placed in an aqueous solution of copper (II) sulfate (i.e., copper with a +2 oxidation state), the color of the solution turns from blue to green because the iron displaces the copper from copper sulfate to yield iron sulfate.



The surface of the iron nail turns to reddish brown because of the deposition of metallic copper. Predicting whether a specific metal will displace another is accomplished by referring to the *activity series of metals*, a list of metals (found in general chemistry textbooks) that is arranged in order of strength of metal reactivity from highest to lowest.

In *double displacement reactions* two compounds exchange their ions to form two new compounds. For example, silver nitrate reacts with potassium bromide in aqueous solution to yield silver bromide and potassium nitrate.



The silver bromide product is insoluble in water and precipitates out of solution.

*Acid-base reactions* are a type of double displacement reaction. The *Bronsted-Lowry theory* defines acids and bases as proton donors and proton acceptors, respectively. For example, hydrogen chloride reacts with water to yield the hydronium ion  $\text{H}_3\text{O}^+$  and chloride ion.

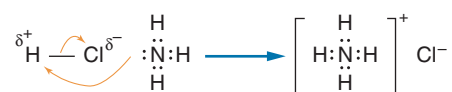


In this reaction the hydrogen chloride donates a proton ( $\text{H}^+$ ) to  $\text{H}_2\text{O}$  (acting as a base because it accepts the proton) to form the  $\text{H}_3\text{O}^+$  and chloride ion. In this reaction  $\text{Cl}^-$  is the *conjugate base* of the acid HCl. Together these two species constitute a *conjugate acid-base pair*. Similarly,  $\text{H}_3\text{O}^+$  is the conjugate acid of  $\text{H}_2\text{O}$ . They also form a conjugate acid-base pair.

In another way of explaining acid-base reactions, referred to as the *Lewis acid and base theory*, acids and bases are defined in terms of atomic structure and bonding. A *Lewis acid* is a chemical species that accepts an electron pair and has a vacant low energy orbital. Examples of Lewis acids include cations such as  $\text{Cu}^{+2}$  and  $\text{Fe}^{+2}$  and molecules such as carbon monoxide (CO) with multiple bonds and atoms with different electronegativities. A Lewis base is defined as a chemical species that donates an electron pair and possesses lone pair electrons. Examples include  $\text{NH}_3$ ,  $\text{OH}^-$ , and cyanide ions ( $\text{CN}^-$ ). The product of a Lewis acid-base reaction contains a new covalent bond.

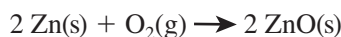


In the reaction of HCl with ammonia, HCl is polarized with the slightly positive hydrogen and the chloride slightly negative.

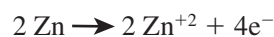


Ammonia ( $\text{:NH}_3$ ) acting as a Lewis base is attracted to the hydrogen atom. As the lone pair on the nitrogen approaches the HCl, the latter becomes more polarized (i.e., the hydrogen becomes more positive), eventually causing the formation of a coordinate covalent bond between the nitrogen and the hydrogen as the hydrogen-chloride bond breaks.

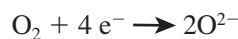
*Redox reactions*, also referred to as oxidation-reduction reactions, involve the exchange of electrons between chemical species. In the reaction of metallic zinc with molecular oxygen to form zinc oxide, for example, the zinc atoms are oxidized (i.e., they lose electrons) and oxygen atoms are reduced (i.e., they gain electrons).



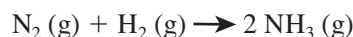
Although oxidation and reduction occur simultaneously, for convenience they may be considered two separate half-reactions, one involving oxidation and the other reduction. The oxidation half-reaction is



where the two zinc atoms lose two electrons each. In the reduction half-reaction



the two atoms of oxygen gain a total of four electrons. In redox reactions, the species that gives up or “donates” electrons is referred to as the *reducing agent*. The species that accepts the electrons is referred to as the *oxidizing agent*. In the reaction of zinc with molecular oxygen, zinc is the reducing agent and molecular oxygen serves as the oxidizing agent. It should be noted that any type of reaction in which the oxidation state of the reactants changes could also be classified as a redox reaction. For example, in the Haber reaction



in which molecular nitrogen reacts with molecular hydrogen to form ammonia, the oxidation number of nitrogen atoms changes from 0 to  $-3$ , and hydrogen atoms change from 0 to  $+1$ . The displacement reaction described on p. 19 in which iron displaces the copper ion in copper (II) sulfate, is also a redox reaction because the oxidation state of iron changes from 0 to  $+2$  and that of copper changes from  $+2$  to 0.

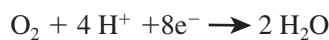
*Combustion reactions* are a type of redox reaction in which fuel molecules react with an oxidizing agent to release large amounts of energy, usually in the form of heat and light. Reactions that release energy are described as *exothermic*. The burning of the hydrocarbon methane (natural gas) is a typical combustion reaction.



The oxidation half-reaction is



The reduction half reaction is

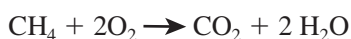




Molecular oxygen is the oxidizing agent in the combustion of methane. The eight electrons removed from methane, the reducing agent, are used in combination with four protons to reduce the oxygen atoms to form two water molecules. It should be noted that cellular respiration, the biochemical mechanism whereby aerobic (oxygen-utilizing) living cells extract energy from fuel molecules such as the sugar glucose, is a slower kind of combustion reaction.

**MEASURING CHEMICAL REACTIONS** Chemists use the mole concept as a means of determining the amounts of the reactants and products in chemical reactions. A *mole* is defined as the amount of a substance that contains as many particles (e.g., atoms, molecules, or ions) as there are atoms in 12 g of carbon-12. This number, which is  $6.022 \times 10^{23}$  particles, is referred to as *Avogadro's number*. So there are  $6.022 \times 10^{23}$  molecules in 1 mol of H<sub>2</sub>O and  $6.022 \times 10^{23}$  sodium ions in 1 mol of NaCl.

The molar mass of substances (mass per mole of particles) is used to determine the amounts of reactants and products in a reaction. For example, in the reaction of methane (CH<sub>4</sub>) with O<sub>2</sub> to yield carbon dioxide and water, how much water is produced from the combustion of 8 g of methane? Solving this problem begins with a balanced equation:



According to this reaction equation, the combustion of every mole of methane yields 2 mol of water. The number of moles of methane is calculated by dividing the mass of methane (8 g) by the molecular mass of methane, which is 16 g (the carbon atom has a mass of 12 g and each of the four hydrogens is 1 g). (Refer to the periodic table for atomic mass numbers.) By this calculation there are 0.5 mol of methane in the reaction. Because the ratio of methane to water is 1 to 2, the 0.5 mol of methane are multiplied by 2 to yield 1 mol of water. Because the molecular mass of water is 18 g, the combustion of 8 g of CH<sub>4</sub> produces 18 g of H<sub>2</sub>O.

Moles are also used to express concentrations of substances in solution. *Molarity* is defined as the number of moles in 1 liter (l) of solution. For example, what is the molarity of a solution of 5 g of NaCl in 2 l of water? First, the number of moles of NaCl must be determined by dividing the mass of NaCl (5 g) by the formula weight of NaCl (58.5 g; i.e., 23 g for sodium and 35.5 g for chlorine). By this calculation (i.e.,  $5/58.5$ ) there are 0.085 mol of NaCl in the 2 l of solution. Molarity of the solution is determined by dividing the number of moles by the number of liters. The molarity of the solution in this problem is 0.085 mol/2 l, which is equal to 0.0425 M (moles per liter, or molar). This number is rounded off to 0.043 M because of the rule of significant figures. Refer to a general chemistry textbook for a discussion of significant figures.

### WORKED PROBLEM 6

The empirical formula of the sugar glucose is C<sub>6</sub>H<sub>12</sub>O<sub>6</sub>. (a) How many moles are there in 270 g of glucose? (b) Calculate the molarity of a solution of 324 g of glucose dissolved in 2.0 l of water.

#### SOLUTION

(a) The number of moles of glucose is calculated by dividing the molecular mass of glucose by its mass. First, the molecular mass of glucose must be determined by adding the sums of the masses of each atom in glucose.

$$\begin{array}{l} \text{Carbon: } 12 \text{ g} \times 6 \text{ atoms} = 72 \text{ g} \\ \text{Hydrogen: } 1 \text{ g} \times 12 \text{ atoms} = 12 \text{ g} \\ \text{Oxygen: } 16 \text{ g} \times 6 \text{ atoms} = 96 \text{ g} \end{array}$$

**WORKED PROBLEM 6 CONT.**

Adding these numbers, the molecular mass (m) of glucose is determined to be 180 g. The number of moles of glucose in 270 g is calculated by dividing the mass of glucose (270 g) by the molecular mass (180 g).

$$\text{Moles} = 270 \text{ g} / 180 \text{ g} = 1.5$$

There are 1.5 mol of glucose in 270 g of the substance.

(b) The molarity of the glucose solution is calculated by first determining the number of moles of glucose in 300 g.

$$\text{Moles} = 324 / 180 = 1.8 \text{ mol}$$

The molarity of the glucose solution is then calculated by dividing the number of moles by the number of liters.

$$\text{Mol/l} = 1.8 / 2 = 0.9 \text{ M.}$$

The molarity of the glucose solution is 0.9 M.

## ORGANIC CHEMISTRY

Organic chemistry is the investigation of carbon-containing compounds. An entire field is devoted to molecules composed of carbon because of its astonishing versatility. In addition to its capacity to form stable covalent bonds with other carbon atoms to form long chains, branch chains, and rings, carbon also forms stable covalent bonds with a variety of other elements (e.g., hydrogen, oxygen, nitrogen, and sulfur). Carbon can also form carbon-carbon double and triple bonds. As a result of these properties, the possibilities for molecules with different arrangements of carbon and the other elements are virtually limitless. For students embarking on the study of biochemistry, a thorough understanding of the principles of organic chemistry is essential because, as stated previously, with the exceptions of inorganic molecules such as  $\text{H}_2\text{O}$ ,  $\text{O}_2$ ,  $\text{NH}_3$ , and  $\text{CO}_2$  and several minerals (e.g.,  $\text{Na}^+$ ,  $\text{Ca}^{2+}$ , and  $\text{Fe}^{2+}$ ), biomolecules are organic molecules. The structural and functional properties of proteins, nucleic acids (DNA and RNA), fats, and sugars can only be appreciated when students know how carbon-based molecules behave. This review will focus on the structures and the chemical properties of the major classes of organic molecules: the *hydrocarbons* (molecules only containing carbon and hydrogen) and *substituted hydrocarbons* (hydrocarbon molecules in which one or more hydrogens has been replaced with another atom or group of atoms).

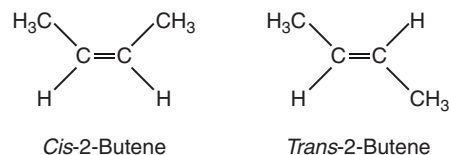
### Hydrocarbons

Because hydrocarbon molecules contain only carbon and hydrogen, they are nonpolar. They dissolve in nonpolar solvents such as hexane and chloroform, but not in water. Such molecules are described as *hydrophobic* (“water-hating”). The hydrocarbons are classified into four groups: (1) saturated hydrocarbons (molecules containing only single bonds), (2) unsaturated hydrocarbons (molecules with one or more carbon-carbon double or triple bonds), (3) cyclic hydrocarbons (molecules containing one or more carbon rings), and (4) aromatic hydrocarbons (molecules that contain one or more aromatic rings, which can be described as cyclic molecules with alternating double and single bonds).

The *saturated hydrocarbons*, referred to as the *alkanes*, are either normal (straight chains) or branched chains. These molecules are “saturated” because they will not react with hydrogen. The straight-chain alkanes belong to a

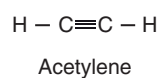


isomers. The rigidity of the carbon-carbon double bond prevents rotation, thereby producing another class of isomers: geometric isomers. *Geometric isomers* occur when each of the carbons in the double bond has two different groups on it. For example, there are two geometric isomers of 2-butene: *cis*-2-butene, in which the methyl groups are on the same side of the double bond, and *trans*-2-butene, in which the methyl groups are on opposite sides of the double bond.



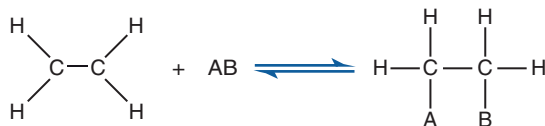
Note that 1-butene does not form geometric isomers because one of the double-bonded carbons does not have two different groups.

The alkynes such as ethyne (or acetylene)



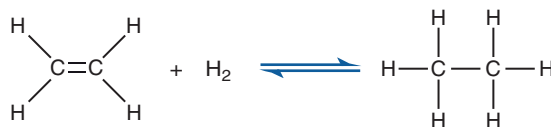
contain triple bonds composed of 1  $\sigma$  bond and 2  $\pi$  bonds. The carbon-carbon triple bond is rare in biomolecules and is not discussed further.

The principal reaction of alkenes is the *electrophilic addition reaction* in which an *electrophile* (an electron-deficient species) forms a bond by accepting an electron pair from a *nucleophile* (an electron-rich species).

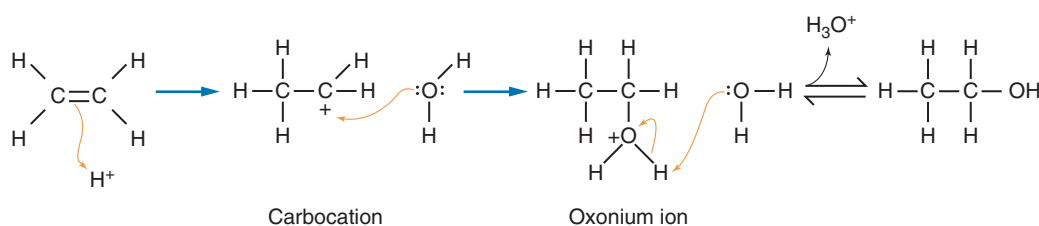


Electrophiles have positive charges or they may have an incomplete octet. Examples include  $\text{H}^+$ ,  $\text{CH}_3^+$ , and polarized neutral molecules such as HCl. Nucleophiles have negative charges (e.g.,  $\text{OH}^-$ ), contain atoms with lone pairs (e.g.,  $\text{H}_2\text{O}$  and  $\text{NH}_3$ ), or have  $\pi$  bonds.

Hydrogenation and hydration are two addition reactions that occur frequently in living organisms. In a laboratory or industrial hydrogenation reaction a metal catalyst (e.g., nickel or platinum) is required to promote the addition of  $\text{H}_2$  to an alkene to yield an alkane.



Hydration reactions of alkenes are electrophilic addition reactions that yield alcohols. The reaction (**Figure 8**) requires a small amount of a strong acid catalyst such as sulfuric acid ( $\text{H}_2\text{SO}_4$ ) because water is too weak an acid to initiate protonation of the alkene. In the presence of the sulfuric acid, the electron pair in the  $\pi$  cloud polarizes toward the hydronium ion ( $\text{H}_3\text{O}^+$ ) and forms a new carbon-hydrogen ion. The newly formed *carbocation* (a molecule containing a positively charged carbon atom) is then attacked by the nucleophilic water molecule to yield an *oxonium ion* (a molecule containing an oxygen cation with three bonds). The alcohol product is formed as the oxonium ion transfers a proton to a water molecule. It is important to note that in hydration reactions of propene and larger alkenes, the most highly substituted carbocation will form (Markovnikov's rule). For example, the principal product of propene hydration is 2-propanol and not 1-propanol.



**FIGURE 8**  
**Acid Catalyzed Hydration**  
**of an Alkene**

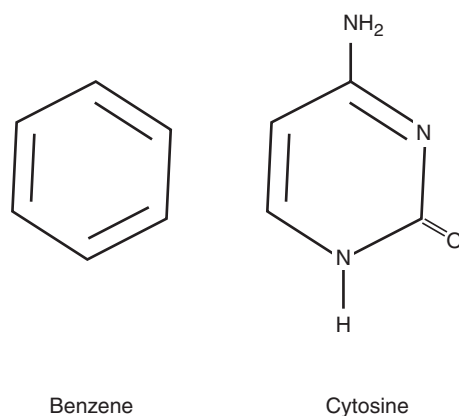
In the first step protonation of the double bond forms a carbocation. Nucleophilic attack by water gives a protonated alcohol. Deprotonation by a water molecule yields the alcohol. Note that the arrows in this and other reaction mechanisms indicate the movement of electrons.

**CYCLIC HYDROCARBONS** As their name suggests, the cyclic hydrocarbons are the cyclic counterparts of the alkanes and alkenes. The general formula of the cyclic alkanes,  $C_nH_{2n}$ , has two fewer hydrogens than the alkane formula  $C_nH_{2n+2}$ . As with the alkanes, the cycloalkanes undergo combustion and halogenation reactions.

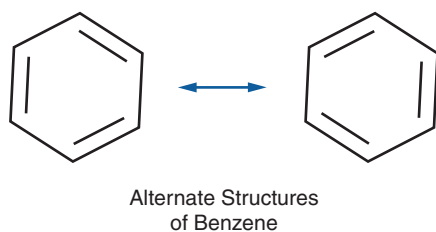
Ring strain, observed in cycloalkane rings with three or four carbons, is caused by unfavorable bond angles that are the result of distortion of tetrahedral carbons. As a result, the carbon-carbon bonds in these molecules are weak and reactive. There is minimal or no ring strain in cycloalkane rings with five to seven carbons. Cyclohexane has no ring strain because it is puckered so that its bond angles are near the tetrahedral angles. The most stable puckered conformation is the chair form.

Because of greater ring strain, cyclopropene and cyclobutene are even less stable than cyclopropane and cyclobutane.

**AROMATIC HYDROCARBONS** Aromatic hydrocarbons are planar (flat) hydrocarbon rings with alternating single and double bonds. Heterocyclic aromatic compounds have two or more different elements in their rings. The simplest aromatic hydrocarbon is benzene. Cytosine, a pyrimidine base found in DNA and RNA, is an example of a heterocyclic aromatic molecule.



Despite the presence of double bonds, benzene and the other aromatic molecules do not undergo reactions typical of the alkenes. In fact, aromatic compounds are remarkably stable. This stability is the result of the unique bonding arrangement of aromatic rings. Each carbon has three  $sp^2$  orbitals that form three  $\sigma$  bonds with two other carbon atoms and with one hydrogen atom. The 2p orbital of each of the six carbon atoms overlaps side to side above and below the plane of the ring to form a continuous circular  $\pi$  bonding system. Instead of two alternate structures of benzene,



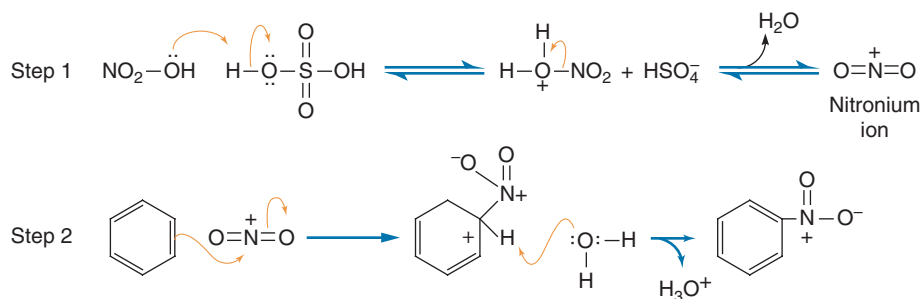
benzene is instead a resonance hybrid, which is indicated by the fact that all of the carbon-carbon bonds in benzene are the same length. (In alkenes carbon-carbon double bonds are shorter than carbon-carbon single bonds.) Each carbon atom is joined to its neighbors by the equivalent of one and a half bonds. Resonance explains why aromatics do not undergo the addition reactions observed with alkenes: the delocalizing of the  $\pi$  electrons around an aromatic ring confers considerable stability to the molecule.

Not all cyclic compounds that contain double bonds are aromatic molecules. According to *Huckel's rule*, to be aromatic a ring molecule must be planar and have  $4n + 2$  electrons in the  $\pi$  cloud, where  $n$  is a positive integer. For benzene, which has six  $\pi$  electrons,  $n$  is equal to 1 [ $4(1) + 2 = 6$ ]. In addition, every atom in an aromatic ring has either a p orbital or an unshared pair of electrons. For example, cytosine is aromatic because the NH adjacent to the carbonyl group donates its lone pair of electrons to the ring's  $\pi$  electron cloud.

Despite their resistance to addition reactions, aromatic compounds are not inert. They can undergo substitution reactions. In *electrophilic aromatic substitution reactions*, an electrophile reacts with an aromatic ring and substitutes for one of the hydrogens. For example, benzene reacts with  $\text{HNO}_3$  in the presence of  $\text{H}_2\text{SO}_4$  to yield nitrobenzene and water (**Figure 9**). In the first step in the reaction a strong electrophile is generated. In this case the nitronium ion ( $^+\text{NO}_2$ ) is created when the sulfuric acid protonates the nitric acid on the OH group and the resulting water molecule leaves. In the second step a pair of  $\pi$  electrons in the benzene attack the electrophile, resulting in the formation of a resonance-stabilized carbocation intermediate. In the final step the aromatic ring is regenerated when a water molecule abstracts a proton from the carbon atom bonded to the electrophile.

**FIGURE 9****Nitration of Benzene**

The nitronium ion, a powerful electrophile, is created by the protonation of  $\text{HNO}_3$  by  $\text{H}_2\text{SO}_4$ . The product loses a water molecule to leave  $\text{O}=\text{N}^+=\text{O}$ . In the second step, the nitronium ion reacts with the nucleophilic benzene. The aromaticity of nitrobenzene is restored with the loss of a proton to a water molecule.

**Substituted Hydrocarbons**

Substituted hydrocarbons are produced by replacing one or more hydrogens on hydrocarbon molecules with functional groups. A *functional group* is a specific group of atoms within a molecule that is responsible for the molecule's chemical reactivity. Functional groups also separate the substituted hydrocarbons into families. For example, methanol ( $\text{CH}_3-\text{OH}$ ), a member of the alcohol family of organic molecules, is the product when the functional group  $-\text{OH}$  is substituted for a hydrogen atom on methane ( $\text{CH}_4$ ). There are three general classes of functional groups that are important in biomolecules: oxygen-containing, nitrogen-containing, and sulfur-containing molecules. The structural and chemical properties of each class are briefly discussed. Also refer to **Table 1.1** on p. 6 of the textbook for a brief overview of the functional groups. There are six major families of organic molecules that contain oxygen: alcohols, aldehydes, ketones, carboxylic acids, esters, and ethers. Amines and amides possess nitrogen-containing functional groups. The major type of sulfur-containing functional group is the sulfhydryl group, which occurs in thiols.

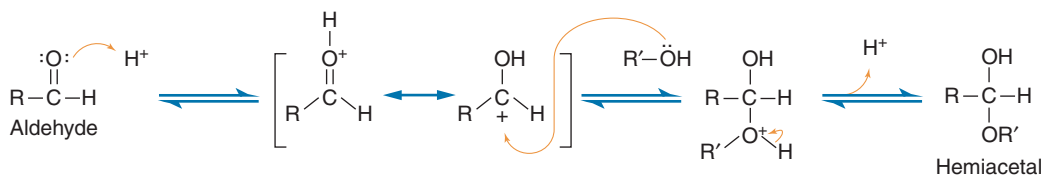
**ALCOHOLS** In alcohols the hydroxyl group ( $-\text{OH}$ ) is bonded to an  $\text{sp}^3$  hybridized carbon. The presence of the polar  $-\text{OH}$  group makes alcohol molecules polar,



allowing them to form hydrogen bonds with each other and with other polar molecules. A *hydrogen bond* is an attractive force between a hydrogen atom attached to an electronegative atom (e.g., oxygen or nitrogen) of one molecule and an electronegative atom of a different molecule. For alcohols with up to four carbons (methanol, ethanol, propanol, and butanol), the polar OH group allows them to dissolve in water because hydrogen bonds form between the hydrogen of the OH group of the alcohol and the oxygen of a water molecule. Such molecules are described as *hydrophilic* (“water-loving”). Alcohols with five or more carbons are not water-soluble because the hydrophobic properties of hydrocarbon components of these molecules are dominant. Alcohols can be classified by the number of alkyl groups (designated as R groups) attached to the carbon adjacent to the -OH group. Ethanol ( $\text{CH}_3\text{CH}_2\text{—OH}$ ) is a primary alcohol. In a secondary alcohol ( $\text{RR}'\text{CH—OH}$ ) such as 2-propanol, the carbon atom bonded to the OH group is also attached to two alkyl groups. Tertiary alcohols ( $\text{RR}'\text{R}''\text{C—OH}$ ) such as 2-methyl-2-propanol have three alkyl groups bonded to the carbon bearing the OH group. Alcohols are weak acids (i.e., a strong base can remove the proton from an alcohol’s hydroxyl group to form the alkoxide ion  $\text{R—O}^-$ ). Tertiary alcohols are less acidic than primary alcohols because the alkyl groups inhibit the solvation of the alkoxide ion. The increased electron density on the oxygen atom in these molecules also decreases proton removal.

Alcohols react with carboxylic acids to form esters. They can also be oxidized to give the carbonyl group-containing aldehydes, ketones, or carboxylic acids. The *carbonyl group* ( $\text{C=O}$ ) in which a carbon is double-bonded to an oxygen atom is a structural feature of the aldehydes, ketones, carboxylic acids, and esters. (Amides, which contain both nitrogen atoms and carbonyl groups, are described on p. 30.) The carbonyl group is polar because of the difference in electronegativity between oxygen and carbon. The slightly positive carbon is electrophilic and therefore able to react with nucleophiles.

**ALDEHYDES** The functional group of the aldehydes is a carbonyl group bonded to a hydrogen atom [ $\text{—(C=O)—H}$ ]. The simplest aldehyde is formaldehyde (also referred to as methanal) in which the aldehyde group is bonded to a hydrogen atom. In all other aldehydes the aldehyde group is bonded to an alkyl group. The general formula for aldehydes is abbreviated as  $\text{R—CHO}$ . Acetaldehyde ( $\text{CH}_3\text{CHO}$ ) is the oxidation product of ethanol. The reaction of an aldehyde with an alcohol yields a hemiacetal (**Figure 10**).

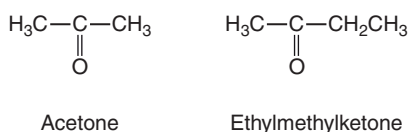


**FIGURE 10**  
**Hemiacetal Formation**

The reaction begins with the acid catalyst protonating the carbonyl group. The alcohol, acting as a nucleophile, attacks the resonance stabilized carbocation. The hemiacetal product forms with the release of a proton from the positively charged intermediate.

Note that hemiacetals are unstable and their formation is readily reversible. The reaction of the aldehyde group of aldose sugars with an intramolecular OH group to form the more stable cyclic hemiacetals (see p. 243 in the textbook) is an important feature of the chemistry of carbohydrates (Chapter 7).

**KETONES** Ketones are molecules in which a carbonyl group is flanked by two R groups [ $\text{R—(C=O)—R}'$ ]. The names of members of the ketone family end in -one. For example, dimethyl ketone is usually referred to by its original name, acetone. Ethylmethyl ketone is also referred to as 2-butanone.





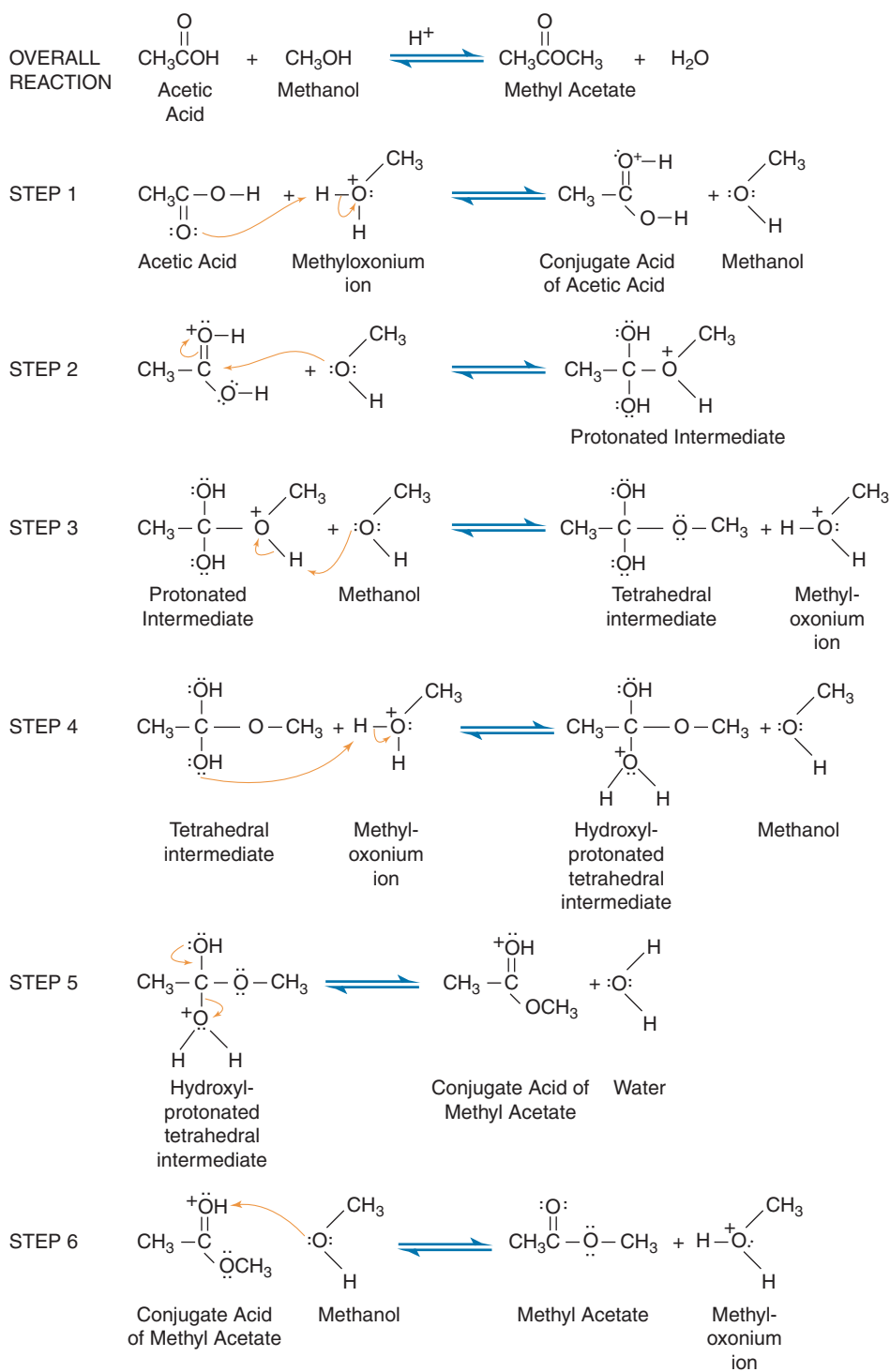


FIGURE 11

**Formation of Methyl Acetate**

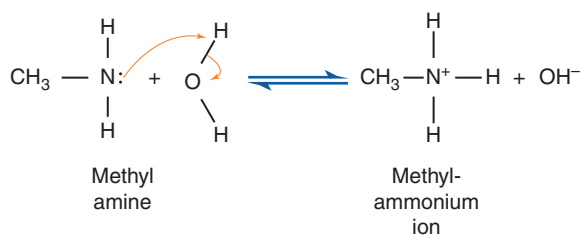
**Step 1** Acetic acid is protonated on its carbonyl oxygen to form the conjugate acid of acetic acid.

**Step 2** A molecule of methanol, acting as a nucleophile, attacks the electrophilic carbon of the protonated acetic acid. **Step 3** The oxonium ion (the protonated intermediate formed in step 2)

loses a proton to form a neutral tetrahedral intermediate. **Step 4** The tetrahedral intermediate is protonated on one of its hydroxyl oxygens. **Step 5** The hydroxyl-protonated intermediate formed in step 4 loses a molecule of water to yield the protonated form of the ester. **Step 6** The loss of a proton from the protonated product of step 5 (the conjugate acid of methyl acetate) yields methyl acetate.

the hydrogen atoms of ammonia has been replaced by an organic group (e.g., alkyl or aromatic groups). Methylamine ( $\text{CH}_3\text{NH}_2$ ) is an example of a primary amine. In secondary amines, such as dimethylamine ( $\text{CH}_3\text{—NH—CH}_3$ ), two hydrogens have been replaced by organic groups. Tertiary amines such as triethylamine [ $(\text{CH}_3\text{CH}_2)_3\text{N}$ ] are molecules in which all three hydrogens have been replaced with organic groups. Amines with small organic groups are water soluble, although the solubility of tertiary amines is limited because they do not have any hydrogen atoms bonded to the electronegative nitrogen atom. Like ammonia, amines are weak bases because of the lone pair of electrons on the

nitrogen atom, which can accept a proton. Protonation of the nitrogen converts the amine into a cation.



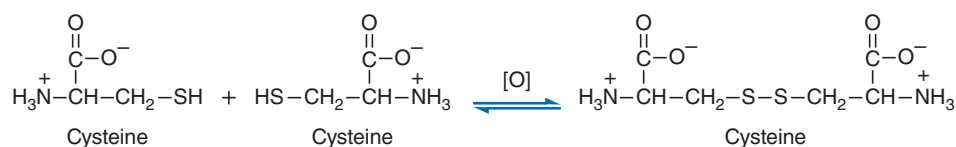
There are an enormous number of biomolecules that contain amine nitrogens. Examples include the amino acids (components of proteins), the nitrogenous bases of the nucleic acids, and the alkaloids (complex molecules produced by plants such as caffeine, morphine, and nicotine that have significant physiological effects on humans).

**AMIDES** Amides are amine derivatives of carboxylic acids with the general formula  $[\text{R}(\text{C}=\text{O})-\text{NR}_2]$  where the R groups bonded to the nitrogen can be hydrogens or hydrocarbon groups. In contrast to the amines, amides are neutral molecules. The C—N bond is a resonance hybrid because of the attraction of the carbonyl group for the nitrogen's lone pair. As a result, amides are not weak bases (i.e., they have little capacity to accept protons).



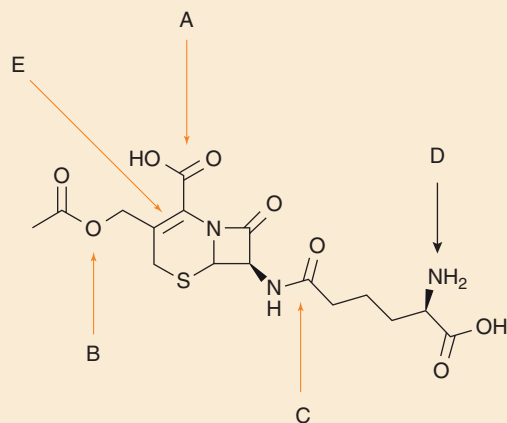
Resonance hybridization explains why the amide functional group is planar with the nitrogen's  $sp^2$  orbital forming a  $\pi$  bond with the carbonyl carbon atom. In living organisms, the amide functional group is the linkage, referred to as the peptide bond, that connects amino acids in polypeptides. Amides are classified according to how many carbon atoms are bonded to the nitrogen atom. Molecules with the molecular formula  $\text{R}(\text{C}=\text{O})-\text{NH}_2$  are primary amides. The substitution of one of the nitrogen's hydrogens with an alkyl group yields a secondary amide  $[\text{R}(\text{C}=\text{O})-\text{NHR}']$ . Amides with two alkyl groups attached to the nitrogen are tertiary amides  $[\text{R}(\text{C}=\text{O})-\text{NR}_2]$ .

**THIOLS** A thiol is a molecule in which an  $sp^3$  carbon is bonded to a sulfhydryl group (-SH). Although thiols are considered the sulfur analogs of alcohols, the low polarity of the SH bonds limits their capacity to form hydrogen bonds. As a result, thiols are not as soluble in water as their alcohol counterparts. Thiols are stronger acids than their alcohol equivalents, however, in part because of the weakness of the S—H bond. For the same reason, thiolates ( $\text{R}-\text{S}^-$ ), the conjugate bases of the thiols, are weaker bases than the alkoxides ( $\text{R}-\text{O}^-$ ). Thiolates are excellent nucleophiles because sulfur's 3p electrons are easily polarized. The sulfhydryl group of thiols is easily oxidized to form disulfides ( $\text{RS}-\text{SR}$ ). For example, two molecules of the amino acid cysteine react to form cystine, which contains a disulfide bond.



**WORKED PROBLEM 7**

Cephalosporin c is one of a class of antibiotics, known as the cephalosporins, that kill bacteria by preventing the cross-linking of peptidoglycan, a key structural element in the cell wall. Its structure is shown below. Identify the indicated functional groups.

**SOLUTION**

A = carboxylic acid   B = ester   C = amide   D = amine   E = alkene

This reaction is especially important in numerous proteins that contain cysteine. The disulfide bond that forms when cysteine residues are linked is an important stabilizing feature of protein structure.

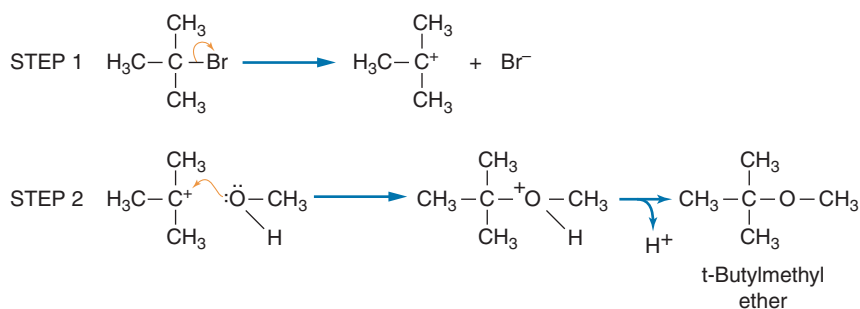
## Organic Reactions: Substitutions and Eliminations

There are a very large number of organic reaction types. Electrophilic addition reactions (p. P-24), electrophilic aromatic substitution reactions (p. P-26), and nucleophilic acyl substitution (p. P-28) have already been described. There are two additional reaction classes, aliphatic substitution and elimination reactions, which students should be familiar with. (The term *aliphatic* refers to non-aromatic hydrocarbon compounds.)

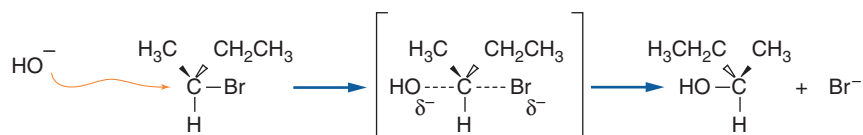
**SUBSTITUTION REACTIONS** Aliphatic substitution reactions, which involve tetrahedral carbons, are designated as either  $S_N1$  or  $S_N2$ .  $S_N1$  (substitution nucleophilic *unimolecular*) reactions, which often involve secondary or tertiary alkyl halides (molecules in which a halogen atom such as chloride has been substituted for a hydrogen in an alkane) or alcohols, proceed in two steps. In the first step of an  $S_N1$  reaction, a planar carbocation forms as the leaving group (a stable ion or a neutral molecule) is displaced.  $S_N1$  reactions are considered unimolecular because the rate of the reaction depends only on the rate of carbocation formation. In the second step the nucleophile attacks the electrophilic carbocation to form the product. Good reactants for  $S_N1$  reactions are molecules with tertiary carbons that can form a stable carbocation when the leaving group is released. Examples of nucleophiles in  $S_N1$  reactions include alcohols and water. Because carbocations are  $sp^2$  hybridized and have an empty p orbital, the nucleophile can attack on either side of the ion. As a result, two isomeric products may be produced. A typical example of an  $S_N1$  reaction is the reaction of *t*-butyl bromide with methanol (**Figure 12**).

**FIGURE 12****Example of S<sub>N</sub>1 Reaction**

In the first and slowest step the alkyl halide *t*-butyl bromide forms the *t*-butyl carbocation as the leaving group bromide is released. In step 2, the nucleophilic oxygen of methanol attacks the carbocation. The product methyl *t*-butyl ether is formed as a proton is released from the oxonium ion into the solvent.



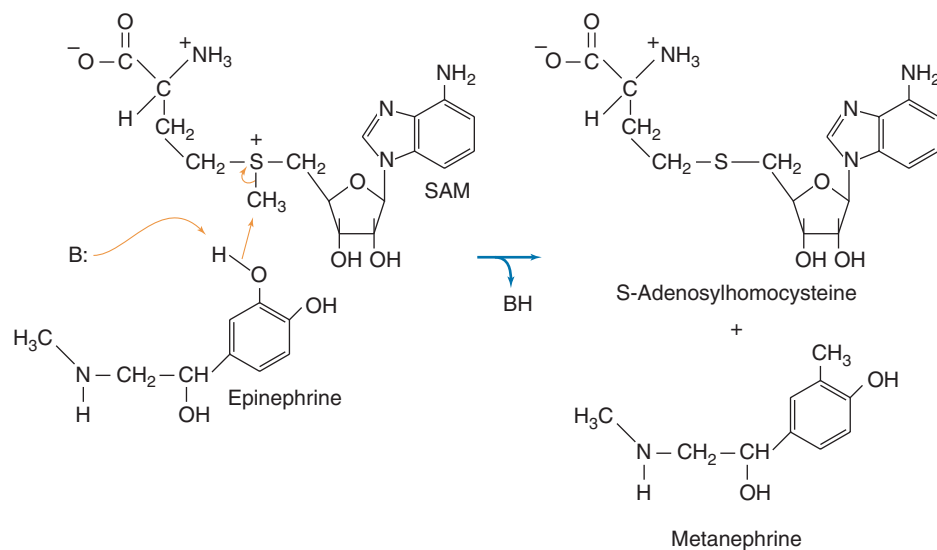
S<sub>N</sub>2 (substitution nucleophilic bimolecular) reactions differ from S<sub>N</sub>1 reactions in that there are no carbocation-like intermediates and reaction rates are determined by the concentrations of both the nucleophilic and the electrophilic reactants. S<sub>N</sub>2 reactions proceed in one step: as the nucleophile, functioning as a Lewis base (an electron pair donor), donates its electron pair to an electrophilic carbon that has been polarized by an electronegative atom. As a result, the leaving group leaves. If the electrophilic carbon is asymmetric (i.e., four different groups are attached), an inverted configuration around this carbon will be observed in the product. Because the nucleophile attacks the back of the electrophilic reactant, S<sub>N</sub>2 reactions occur most rapidly with primary carbons, followed by secondary carbons. Molecules with tertiary carbons do not undergo S<sub>N</sub>2 reactions because of *steric hindrance* (the reactive site on a molecule is blocked by adjacent groups).



A class of enzymes referred to as the *S*-adenosylmethionine-dependent methyltransferases catalyzes some of the best known examples of S<sub>N</sub>2 reactions in biochemistry. *S*-Adenosylmethionine (SAM) is widely used in methylation reactions as a methyl group donor. SAM's methyl group is readily donated because it is attached to an electron-withdrawing sulfur atom. The inactivation of the neurotransmitter epinephrine (adrenalin) catalyzed by catechol-*O*-methyltransferase (COMT) is illustrated in **Figure 13**.

**FIGURE 13****COMT-Catalyzed Methylation of Epinephrine: An S<sub>N</sub>2 Mechanism**

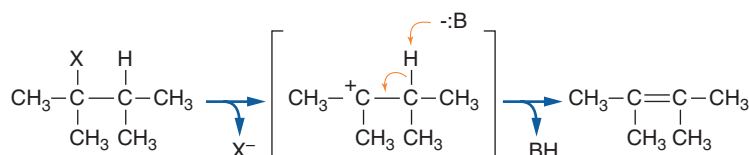
When epinephrine enters the active site of the enzyme, a basic amino acid R group deprotonates one of the hydroxyl groups of epinephrine, forming a nucleophilic alkoxide group. The alkoxide then attacks the methyl carbon atom of SAM. This carbon is electrophilic because it is bonded to an electron-withdrawing positively charged sulfur atom. As the alkoxide attacks, the sulfur-carbon bond begins to break to form the more stable sulfide leaving group. The products of the reactions are *S*-adenosylhomocysteine and epinephrine's inactive methylated derivative metanephrine.





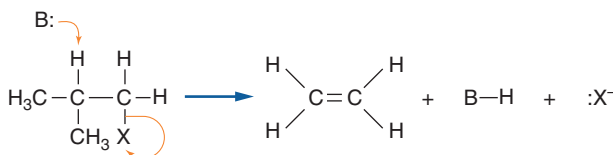
**ELIMINATION REACTIONS** As their name suggests, elimination reactions involve the loss of two atoms or groups from a molecule. This loss is usually accompanied by the formation of a  $\pi$  bond. There are three types of elimination reactions: E1, E2, and E1cb.

In E1 (elimination *unimolecular*) reactions, the first and slowest step is carbocation formation. For this reason E1 reactions are similar to  $S_N1$  reactions because the reaction rates of both depend on one molecule, the precursor of the carbocation. In the second and faster step a weak base (often a solvent molecule) abstracts a proton from a carbon atom next to the carbocation to yield a carbon-carbon double bond.



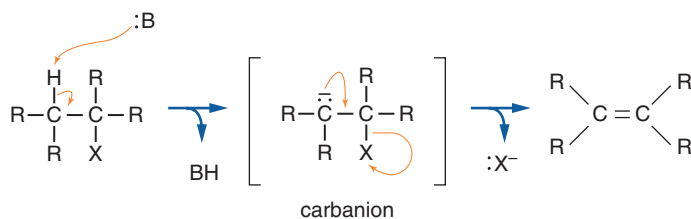
Note that the carbon bonded to “X” in the reactant molecule is  $sp^3$  hybridized, whereas the same carbon in the product is  $sp^2$  hybridized. Molecules with tertiary carbons groups are good substrates for E1 reactions because reaction rates depend on the stability of the carbocation.

E2 (elimination *bimolecular*) reactions involve the simultaneous removal of a  $\beta$ -proton by a strong base and release of the leaving group. (A  $\beta$ -proton is bonded to the carbon adjacent to the carbon bearing the leaving group.) Molecules with tertiary carbons typically undergo E2 reactions.



For an E2 reaction mechanism to be possible, the  $\beta$ -hydrogen and the leaving group must be anticoplanar (i.e., in a geometric arrangement in which they are  $180^\circ$  from each other on neighboring carbons).

Although all three forms of elimination reactions occur in living organisms, the E1cb is more commonly observed. E1cb (elimination *unimolecular conjugate base*) reactions involve the formation of a *carbanion* (an organic ion bearing a negatively charged carbon). Carbanions are nucleophiles that are stabilized by adjacent electronegative atoms and resonance effects. The E1cb mechanism involves the removal of a proton from the reactant to form the carbanion, followed by the slower loss of the leaving group.



The second phase, the loss of the leaving group, is the rate-limiting step in E1cb reactions. The presence of an electron-withdrawing atom or group (X in this illustration) makes the C—H acidic. Note that the carbanion form of the

**FIGURE 14****Enolase-Catalyzed Dehydration of Glycerate-2-Phosphate: An E1cb Mechanism**

Within the active site of the enzyme enolase, the amino nitrogen of a precisely oriented side chain of an amino acid, acting as a base, abstracts the acidic hydrogen at carbon-2 to produce a carbanion. The carbanion electrons displace the hydroxyl (-OH) group from carbon-3, forming a carbon-carbon  $\pi$  bond. The actual leaving group is  $\text{H}_2\text{O}$ , the hydroxyl group having been protonated by a nearby carboxyl (-COOH) group.

reactant is the conjugate base referred to in the term E1cb. The conversion of glycerate-2-phosphate, an intermediate in glucose degradation, to phosphoenolpyruvate provides an example of an E1cb mechanism (**Figure 14**). This reaction is catalyzed by the enzyme enolase.

