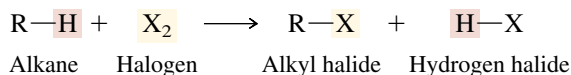# CHAPTER 4

ALCOHOLS AND ALKYL HALIDES

O ur first three chapters established some fundamental principles concerning the *structure* of organic molecules. In this chapter we begin our discussion of organic chemical *reactions* by directing attention to *alcohols* and *alkyl halides*. These two rank among the most useful classes of organic compounds because they often serve as starting materials for the preparation of numerous other families.

Two reactions that lead to alkyl halides will be described in this chapter. Both illustrate functional group transformations. In the first, the hydroxyl group of an alcohol is replaced by halogen on treatment with a hydrogen halide.

$$\text{R—OH} + \text{H—X} \longrightarrow \text{R—X} + \text{H—OH}$$

Alcohol   Hydrogen halide   Alkyl halide   Water
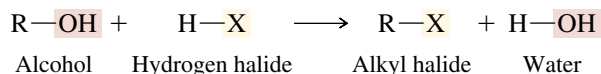
In the second, reaction with chlorine or bromine causes one of the hydrogen substituents of an alkane to be replaced by halogen.

$$\text{R—H} + \text{X}_2 \longrightarrow \text{R—X} + \text{H—X}$$

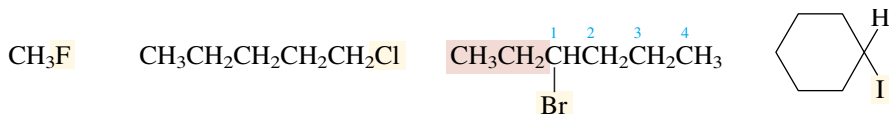Alkane   Halogen   Alkyl halide   Hydrogen halide

Both reactions are classified as *substitutions,* a term that describes the relationship between reactants and products—one functional group replaces another. In this chapter we go beyond the relationship of reactants and products and consider the *mechanism* of each reaction. A **mechanism** attempts to show *how* starting materials are converted into products during a chemical reaction.

While developing these themes of reaction and mechanism, we will also use alcohols and alkyl halides as vehicles to extend the principles of IUPAC nomenclature, con-

tinue to develop concepts of structure and bonding, and see how structure affects properties. A review of *acids and bases* constitutes an important part of this chapter in which a qualitative approach to proton-transfer equilibria will be developed that will be used throughout the remainder of the text.

4.1   IUPAC NOMENCLATURE OF ALKYL HALIDES

The IUPAC rules permit alkyl halides to be named in two different ways, called *functional class* nomenclature and *substitutive* nomenclature. In **functional class nomenclature** the alkyl group and the halide (*fluoride, chloride, bromide,* or *iodide*) are designated as separate words. The alkyl group is named on the basis of its longest continuous chain beginning at the carbon to which the halogen is attached.
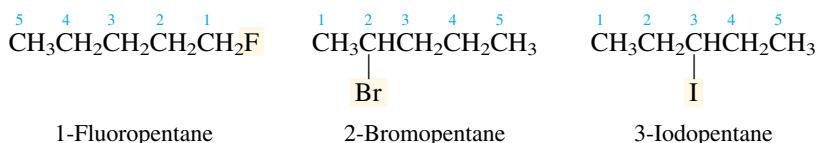
> The IUPAC rules permit certain common alkyl group names to be used. These include *n*-propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *tert*-butyl, and neopentyl (Section 2.10).

CH_3F $CH_3CH_2CH_2CH_2CH_2Cl$ $\overset{1}{C}H_3\overset{2}{C}H_2\overset{3}{C}HCH_2CH_2CH_3$ with Br on C3

Methyl fluoride   Pentyl chloride   1-Ethylbutyl bromide   Cyclohexyl iodide

Substitutive nomenclature of alkyl halides treats the halogen as a *halo-* (*fluoro-, chloro-, bromo-,* or *iodo-*) *substituent* on an alkane chain. The carbon chain is numbered in the direction that gives the substituted carbon the lower locant.

$\overset{5}{C}H_3\overset{4}{C}H_2\overset{3}{C}H_2\overset{2}{C}H_2\overset{1}{C}H_2F$ $\overset{1}{C}H_3\overset{2}{C}H\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H_3$ (Br on C2) $\overset{1}{C}H_3\overset{2}{C}H_2\overset{3}{C}H\overset{4}{C}H_2\overset{5}{C}H_3$ (I on C3)
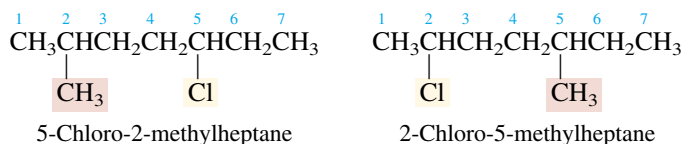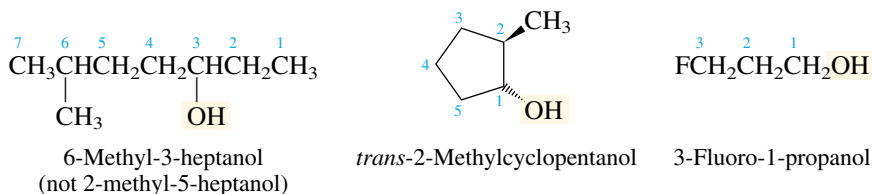
1-Fluoropentane   2-Bromopentane   3-Iodopentane

When the carbon chain bears both a halogen and an alkyl substituent, the two substituents are considered of equal rank, and the chain is numbered so as to give the lower number to the substituent nearer the end of the chain.

$\overset{1}{C}H_3\overset{2}{C}H\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H\overset{6}{C}H_2\overset{7}{C}H_3$ (CH₃ on C2, Cl on C5) $\overset{1}{C}H_3\overset{2}{C}H\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H\overset{6}{C}H_2\overset{7}{C}H_3$ (Cl on C2, CH₃ on C5)

5-Chloro-2-methylheptane   2-Chloro-5-methylheptane

> **PROBLEM 4.1**   Write structural formulas, and give the functional class and substitutive names of all the isomeric alkyl chlorides that have the molecular formula C_4H_9Cl.

Substitutive names are preferred, but functional class names are sometimes more convenient or more familiar and are frequently encountered in organic chemistry.

> Prior to the 1993 version of the IUPAC rules, the term "radicofunctional" was used instead of "functional class."

4.2   IUPAC NOMENCLATURE OF ALCOHOLS

Functional class names of alcohols are derived by naming the alkyl group that bears the hydroxyl substituent (—OH) and then adding *alcohol* as a separate word. The chain is always numbered beginning at the carbon to which the hydroxyl group is attached.

Substitutive names of alcohols are developed by identifying the longest continuous chain that bears the hydroxyl group and replacing the *-e* ending of the

corresponding alkane by the suffix *-ol*. The position of the hydroxyl group is indicated by number, choosing the sequence that assigns the lower locant to the carbon that bears the hydroxyl group.

<div style="float:left; width:30%;">
Several alcohols are commonplace substances, well known by common names that reflect their origin (wood alcohol, grain alcohol) or use (rubbing alcohol). Wood alcohol is *methanol* (methyl alcohol, CH_3OH), grain alcohol is *ethanol* (ethyl alcohol, CH_3CH_2OH), and rubbing alcohol is *2-propanol* [isopropyl alcohol, $(CH_3)_2CHOH$].
</div>

$$CH_3CH_2OH \qquad CH_3\underset{\underset{OH}{|}}{C}HCH_2CH_2CH_2CH_3 \qquad CH_3\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}CH_2CH_2CH_3$$

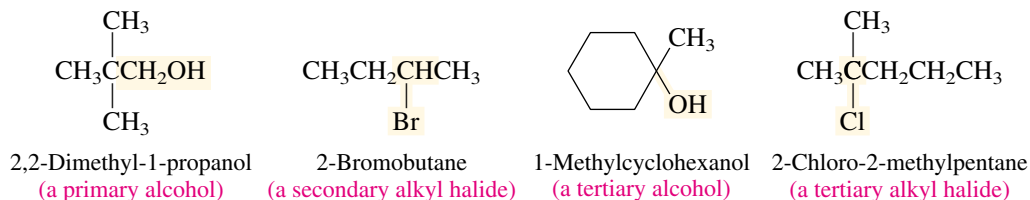|			
Functional class name:	Ethyl alcohol	1-Methylpentyl alcohol	1,1-Dimethylbutyl alcohol
Substitutive name:	Ethanol	2-Hexanol	2-Methyl-2-pentanol

Hydroxyl groups take precedence over ("outrank") alkyl groups and halogen substituents in determining the direction in which a carbon chain is numbered.

$$\overset{7}{C}H_3\overset{6}{C}H\overset{5}{C}H_2\overset{4}{C}H_2\overset{3}{C}H\overset{2}{C}H_2\overset{1}{C}H_3$$

6-Methyl-3-heptanol
(not 2-methyl-5-heptanol)

trans-2-Methylcyclopentanol

$$FCH_2CH_2CH_2OH$$

3-Fluoro-1-propanol

> **PROBLEM 4.2** Write structural formulas, and give the functional class and substitutive names of all the isomeric alcohols that have the molecular formula $C_4H_{10}O$.

4.3 CLASSES OF ALCOHOLS AND ALKYL HALIDES

Alcohols and alkyl halides are classified as primary, secondary, or tertiary according to the classification of the carbon that bears the functional group (Section 2.10). Thus, *primary alcohols* and *primary alkyl halides* are compounds of the type RCH_2G (where G is the functional group), *secondary alcohols* and *secondary alkyl halides* are compounds of the type R_2CHG, and *tertiary alcohols* and *tertiary alkyl halides* are compounds of the type R_3CG.

$$CH_3\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}CH_2OH \qquad CH_3CH_2\underset{\underset{Br}{|}}{C}HCH_3 \qquad \qquad CH_3\underset{\underset{Cl}{|}}{\overset{\overset{CH_3}{|}}{C}}CH_2CH_2CH_3$$

2,2-Dimethyl-1-propanol
(a primary alcohol)

2-Bromobutane
(a secondary alkyl halide)

1-Methylcyclohexanol
(a tertiary alcohol)

2-Chloro-2-methylpentane
(a tertiary alkyl halide)

> **PROBLEM 4.3** Classify the isomeric $C_4H_{10}O$ alcohols as being primary, secondary, or tertiary.

Many of the properties of alcohols and alkyl halides are affected by whether their functional groups are attached to primary, secondary, or tertiary carbons. We will see a number of cases in which a functional group attached to a primary carbon is more reactive than one attached to a secondary or tertiary carbon, as well as other cases in which the reverse is true.
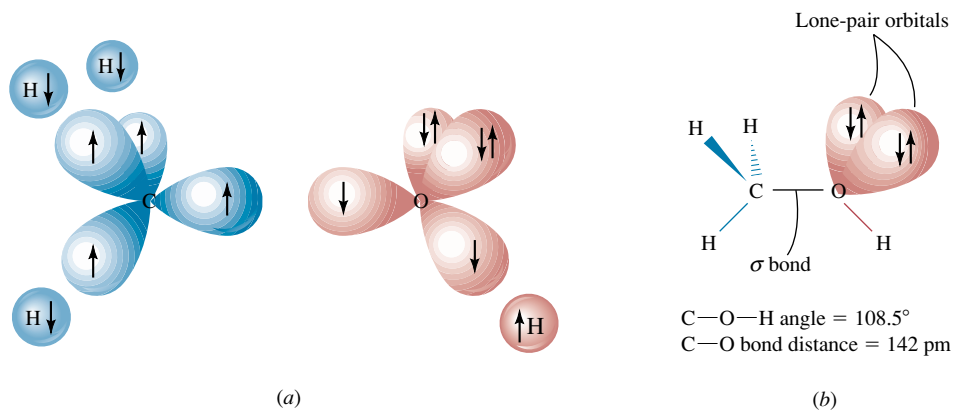
FIGURE 4.1 Orbital hybridization model of bonding in methanol. (*a*) The orbitals used in bonding are the 1*s* orbitals of hydrogen and *sp*^{3}-hybridized orbitals of carbon and oxygen. (*b*) The bond angles at carbon and oxygen are close to tetrahedral, and the carbon–oxygen σ bond is about 10 pm shorter than a carbon–carbon single bond.

Lone-pair orbitals

σ bond

C—O—H angle = 108.5°
C—O bond distance = 142 pm

(*a*)

(*b*)

4.4 BONDING IN ALCOHOLS AND ALKYL HALIDES

The carbon that bears the functional group is *sp*^{3}-hybridized in alcohols and alkyl halides. Figure 4.1 illustrates bonding in methanol. The bond angles at carbon are approximately tetrahedral, as is the C—O—H angle. A similar orbital hybridization model applies to alkyl halides, with the halogen substituent connected to *sp*^{3}-hybridized carbon by a σ bond. Carbon–halogen bond distances in alkyl halides increase in the order C—F (140 pm) < C—Cl (179 pm) < C—Br (197 pm) < C—I (216 pm).

Carbon–oxygen and carbon–halogen bonds are polar covalent bonds, and carbon bears a partial positive charge in alcohols ($^{\delta+}$C—O$^{\delta-}$) and in alkyl halides ($^{\delta+}$C—X$^{\delta-}$). The presence of these polar bonds makes alcohols and alkyl halides polar molecules. The dipole moments of methanol and chloromethane are very similar to each other and to water.

Water
(μ = 1.8 D)

Methanol
(μ = 1.7 D)

Chloromethane
(μ = 1.9 D)
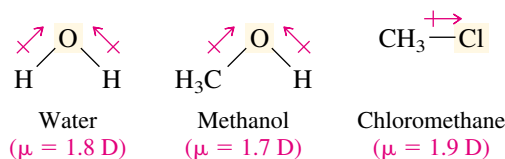
PROBLEM 4.4 Bromine is less electronegative than chlorine, yet methyl bromide and methyl chloride have very similar dipole moments. Why?

Figure 4.2 shows the distribution of electron density in methanol and chloromethane. Both are similar in that the sites of highest electrostatic potential (red) are near the electronegative atoms—oxygen and chlorine. The polarization of the bonds
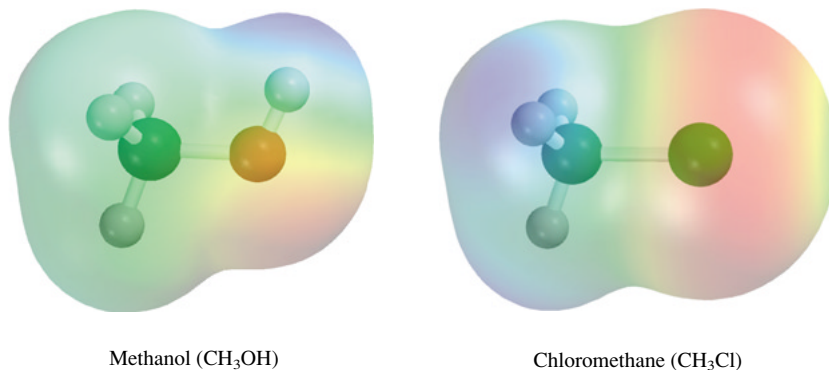

Methanol (CH$_3$OH)

Chloromethane (CH$_3$Cl)

FIGURE 4.2 Electrostatic potential maps of methanol and chloromethane. The most positively charged regions are blue, the most negatively charged ones red. The electrostatic potential is most negative near oxygen in methanol and near chlorine in chloromethane.

to oxygen and chlorine, as well as their unshared electron pairs, contribute to the concentration of negative charge on these atoms.

Relatively simple notions of attractive forces between opposite charges are sufficient to account for many of the properties of chemical substances. You will find it helpful to keep the polarity of carbon–oxygen and carbon–halogen bonds in mind as we develop the properties of alcohols and alkyl halides in later sections.

4.5   PHYSICAL PROPERTIES OF ALCOHOLS AND ALKYL HALIDES: INTERMOLECULAR FORCES

Boiling Point.   When describing the effect of alkane structure on boiling point in Section 2.14, we pointed out that the forces of attraction between neutral molecules are of three types listed here. The first two of these involve induced dipoles and are often referred to as *dispersion forces,* or *London forces.*

1. Induced-dipole/induced-dipole forces
2. Dipole/induced-dipole forces
3. Dipole–dipole forces

Induced-dipole/induced-dipole forces are the only intermolecular attractive forces available to nonpolar molecules such as alkanes. In addition to these forces, polar molecules engage in dipole–dipole and dipole/induced-dipole attractions. The **dipole–dipole attractive force** is easiest to visualize and is illustrated in Figure 4.3. Two molecules of a polar substance experience a mutual attraction between the positively polarized region of one molecule and the negatively polarized region of the other. As its name implies, the **dipole/induced-dipole force** combines features of both the induced-dipole/induced-dipole and dipole–dipole attractive forces. A polar region of one molecule alters the electron distribution in a nonpolar region of another in a direction that produces an attractive force between them.

Because so many factors contribute to the net intermolecular attractive force, it is not always possible to predict which of two compounds will have the higher boiling point. We can, however, use the boiling point behavior of selected molecules to inform us of the relative importance of various intermolecular forces and the structural features that influence them.

Consider three compounds similar in size and shape: the alkane propane, the alcohol ethanol, and the alkyl halide fluoroethane.

$$CH_3CH_2CH_3 \qquad CH_3CH_2OH \qquad CH_3CH_2F$$

Propane ($\mu = 0$ D)   Ethanol ($\mu = 1.7$ D)   Fluoroethane ($\mu = 1.9$ D)
bp: $-42°C$ bp: $78°C$ bp: $-32°C$

Both polar compounds, ethanol and fluoroethane, have higher boiling points than the nonpolar propane. We attribute this to a combination of dipole/induced-dipole and dipole–dipole attractive forces that stabilize the liquid states of ethanol and fluoroethane, but that are absent in propane.

The most striking aspect of the data, however, is the much higher boiling point of ethanol compared with both propane and fluoroethane. This suggests that the attractive forces in ethanol must be unusually strong. Figure 4.4 shows that this force results from a dipole–dipole attraction between the positively polarized proton of the ⎯OH group of one ethanol molecule and the negatively polarized oxygen of another. The term **hydrogen bonding** is used to describe dipole–dipole attractive forces of this type. The
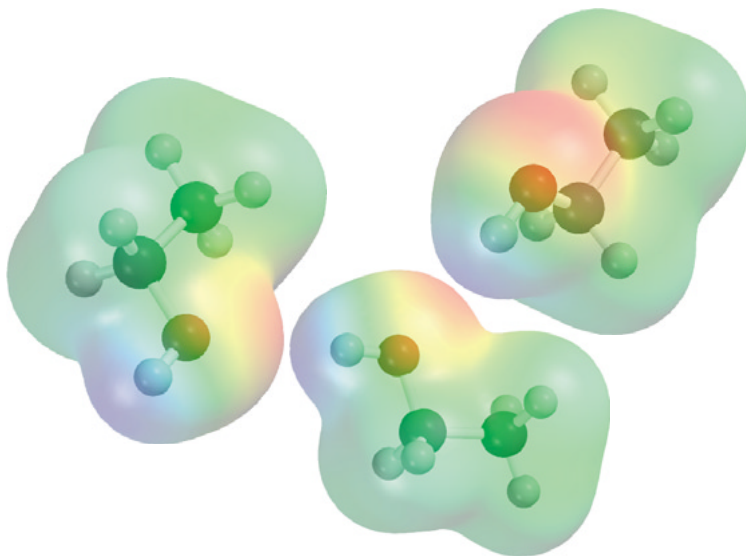
FIGURE 4.3 A dipole–dipole attractive force. Two molecules of a polar substance are oriented so that the positively polarized region of one and the negatively polarized region of the other attract each other.

FIGURE 4.4 Hydrogen bonding in ethanol involves the oxygen of one molecule and the proton of an —OH group of another. Hydrogen bonding is much stronger than most other types of dipole–dipole attractive forces.

proton involved must be bonded to an electronegative element, usually oxygen or nitrogen. Protons in C—H bonds do not participate in hydrogen bonding. Thus fluoroethane, even though it is a polar molecule and engages in dipole–dipole attractions, does not form hydrogen bonds and, therefore, has a lower boiling point than ethanol.

Hydrogen bonding can be expected in molecules that have —OH or —NH groups. Individual hydrogen bonds are about 10–50 times weaker than typical covalent bonds, but their effects can be significant. More than other dipole–dipole attractive forces, intermolecular hydrogen bonds are strong enough to impose a relatively high degree of structural order on systems in which they are possible. As will be seen in Chapter 27, the three-dimensional structures adopted by proteins and nucleic acids, the organic molecules of life, are dictated by patterns of hydrogen bonds.

Hydrogen bonds between —OH groups are stronger than those between —NH groups, as a comparison of the boiling points of water (H_2O, 100°C) and ammonia (NH_3, −33°C) demonstrates.

PROBLEM 4.5 The constitutional isomer of ethanol, dimethyl ether (CH_3OCH_3), is a gas at room temperature. Suggest an explanation for this observation.

Table 4.1 lists the boiling points of some representative alkyl halides and alcohols. When comparing the boiling points of related compounds as a function of the *alkyl group,* we find that the boiling point increases with the number of carbon atoms, as it does with alkanes.

For a discussion concerning the boiling point behavior of alkyl halides, see the January 1988 issue of the *Journal of Chemical Education,* pp. 62–64.

TABLE 4.1	Boiling Points of Some Alkyl Halides and Alcohols				
Name of alkyl group	**Formula**	**Functional group X and boiling point, °C (1 atm)**				
		X = F	**X = Cl**	**X = Br**	**X = I**	**X = OH**
Methyl	CH_3X	−78	−24	3	42	65
Ethyl	CH_3CH_2X	−32	12	38	72	78
Propyl	$CH_3CH_2CH_2X$	−3	47	71	103	97
Pentyl	$CH_3(CH_2)_3CH_2X$	65	108	129	157	138
Hexyl	$CH_3(CH_2)_4CH_2X$	92	134	155	180	157

With respect to the *halogen* in a group of alkyl halides, the boiling point increases as one descends the periodic table; alkyl fluorides have the lowest boiling points, alkyl iodides the highest. This trend matches the order of increasing *polarizability* of the halogens. **Polarizability** is the ease with which the electron distribution around an atom is distorted by a nearby electric field and is a significant factor in determining the strength of induced-dipole/induced-dipole and dipole/induced-dipole attractions. Forces that depend on induced dipoles are strongest when the halogen is a highly polarizable iodine, and weakest when the halogen is a nonpolarizable fluorine.

The boiling points of the chlorinated derivatives of methane increase with the number of chlorine atoms because of an increase in the induced-dipole/induced-dipole attractive forces.

	CH_3Cl	CH_2Cl_2	$CHCl_3$	CCl_4
	Chloromethane (methyl chloride)	Dichloromethane (methylene dichloride)	Trichloromethane (chloroform)	Tetrachloromethane (carbon tetrachloride)
Boiling point:	−24°C	40°C	61°C	77°C

Fluorine is unique among the halogens in that increasing the number of fluorines does not produce higher and higher boiling points.

	CH_3CH_2F	CH_3CHF_2	CH_3CF_3	CF_3CF_3
	Fluoroethane	1,1-Difluoroethane	1,1,1-Trifluoroethane	Hexafluoroethane
Boiling point:	−32°C	−25°C	−47°C	−78°C

These boiling points illustrate why we should do away with the notion that boiling points always increase with increasing molecular weight.

Thus, although the difluoride CH_3CHF_2 boils at a higher temperature than CH_3CH_2F, the trifluoride CH_3CF_3 boils at a lower temperature than either of them. Even more striking is the observation that the hexafluoride CF_3CF_3 is the lowest boiling of any of the fluorinated derivatives of ethane. The boiling point of CF_3CF_3 is, in fact, only 11° higher than that of ethane itself. The reason for this behavior has to do with the very low polarizability of fluorine and a decrease in induced-dipole/induced-dipole forces that accompanies the incorporation of fluorine substituents into a molecule. Their weak intermolecular attractive forces give fluorinated hydrocarbons (**fluorocarbons**) certain desirable physical properties such as that found in the "no stick" *Teflon* coating of frying pans. Teflon is a *polymer* (Section 6.21) made up of long chains of —CF_2CF_2—units.

Solubility in Water. Alkyl halides and alcohols differ markedly from one another in their solubility in water. All alkyl halides are insoluble in water, but low-molecular-weight alcohols (methyl, ethyl, *n*-propyl, and isopropyl) are soluble in water in all proportions. Their ability to participate in intermolecular hydrogen bonding not only affects the boiling points of alcohols, but also enhances their water solubility. Hydrogen-bonded networks of the type shown in Figure 4.5, in which alcohol and water molecules associate with one another, replace the alcohol–alcohol and water–water hydrogen-bonded networks present in the pure substances.

Higher alcohols become more "hydrocarbon-like" and less water-soluble. 1-Octanol, for example, dissolves to the extent of only 1 mL in 2000 mL of water. As the alkyl chain gets longer, the hydrophobic effect (Section 2.14) becomes more important, to the point that it, more than hydrogen bonding, governs the solubility of alcohols.

Density. Alkyl fluorides and chlorides are less dense, and alkyl bromides and iodides more dense, than water.

$CH_3(CH_2)_6CH_2F$	$CH_3(CH_2)_6CH_2Cl$	$CH_3(CH_2)_6CH_2Br$	$CH_3(CH_2)_6CH_2I$
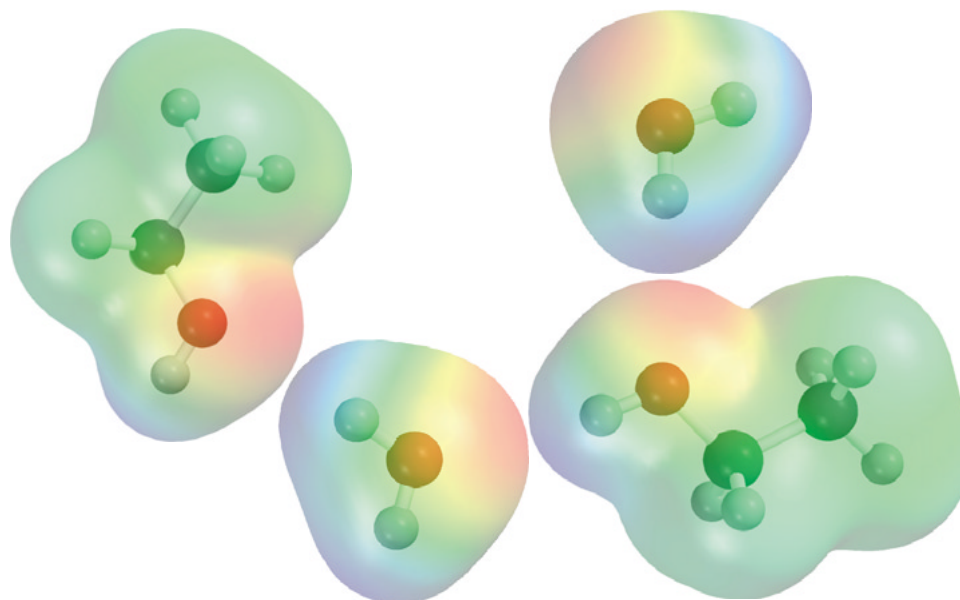
Density
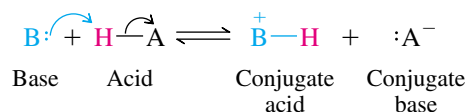(20°C):   0.80 g/mL   0.89 g/mL   1.12 g/mL   1.34 g/mL

Because alkyl halides are insoluble in water, a mixture of an alkyl halide and water separates into two layers. When the alkyl halide is a fluoride or chloride, it is the upper layer and water is the lower. The situation is reversed when the alkyl halide is a bromide or an iodide. In these cases the alkyl halide is the lower layer. Polyhalogenation increases the density. The compounds CH_2Cl_2, $CHCl_3$, and CCl_4, for example, are all more dense than water.

All liquid alcohols have densities of approximately 0.8 g/mL and are, therefore, less dense than water.

4.6 ACIDS AND BASES: GENERAL PRINCIPLES

A solid understanding of acid–base chemistry is a big help in understanding chemical reactivity. This and the next section review some principles and properties of acids and bases and examine how these principles apply to alcohols.

According to the theory proposed by Svante Arrhenius, a Swedish chemist and winner of the 1903 Nobel Prize in chemistry, an acid ionizes in aqueous solution to liberate protons (H^+, hydrogen ions), whereas bases ionize to liberate hydroxide ions (HO^-). A more general theory of acids and bases was devised independently by Johannes Brønsted (Denmark) and Thomas M. Lowry (England) in 1923. In the Brønsted–Lowry approach, an acid is a **proton donor,** and a base is a **proton acceptor.**

$$B: \ + \ H\!-\!A \ \rightleftharpoons \ \overset{+}{B}\!-\!H \ + \ :A^-$$

Base   Acid   Conjugate   Conjugate
   acid   base

Curved arrow notation is used to show the electron pair of the base abstracting a proton from the acid. The pair of electrons in the H—A bond becomes an unshared pair in the anion $^-$:A. Curved arrows track **electron movement,** not atomic movement.

The Brønsted–Lowry definitions of acids and bases are widely used in organic chemistry. As noted in the preceding equation, the **conjugate acid** of a substance is formed when it accepts a proton from a suitable donor. Conversely, the proton donor is converted to its **conjugate base.** A conjugate acid–base pair always differ by a single proton.

In aqueous solution, an acid transfers a proton to water. Water acts as a Brønsted base.

$$\text{Water (base)} \quad \text{Acid} \quad \text{Conjugate acid of water} \quad \text{Conjugate base}$$
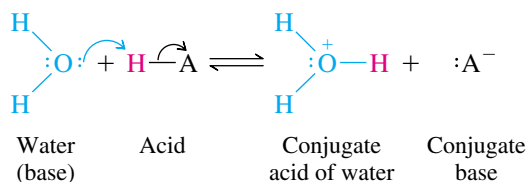
The systematic name for the conjugate acid of water (H_3O^+) is **oxonium ion.** Its common name is **hydronium ion.**

The strength of an acid is measured by its **acid dissociation constant** or **ionization constant K_a.**

$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

Table 4.2 lists a number of Brønsted acids and their acid dissociation constants. Strong acids are characterized by K_a values that are greater than that for hydronium ion (H_3O^+, $K_a = 55$). Essentially every molecule of a strong acid transfers a proton to water in dilute aqueous solution. Weak acids have K_a values less than that of H_3O^+; they are incompletely ionized in dilute aqueous solution.

A convenient way to express acid strength is through the use of pK_a, defined as follows:

$$pK_a = -\log_{10} K_a$$

Thus, water, with $K_a = 1.8 \times 10^{-16}$, has a pK_a of 15.7; ammonia, with $K_a \approx 10^{-36}$, has a pK_a of 36. The stronger the acid, the larger the value of its K_a and the smaller the value of pK_a. Water is a very weak acid, but is a far stronger acid than ammonia. Table 4.2 includes pK_a as well as K_a values for acids. Because both systems are widely used, you should practice converting K_a to pK_a and vice versa.

An important part of the Brønsted–Lowry picture of acids and bases concerns the relative strengths of an acid and its conjugate base. The stronger the acid, the weaker the conjugate base, and vice versa. Ammonia (NH_3) is the second weakest acid in Table 4.2. Its conjugate base, amide ion (H_2N^-), is therefore the second strongest base. Hydroxide (HO^-) is a moderately strong base, much stronger than the halide ions F^-, Cl^-, Br^-, and I^-, which are very weak bases. Fluoride is the strongest base of the halides but is 10^{12} times less basic than hydroxide ion.

TABLE 4.2	Acid Dissociation Constants K_a and pK_a Values for Some Brønsted Acids*			
Acid	**Formula†**	**Dissociation constant, K_a**	**pK_a**	**Conjugate base**
Hydrogen iodide	HI	$\approx 10^{10}$	≈ -10	I^-
Hydrogen bromide	HBr	$\approx 10^9$	≈ -9	Br^-
Hydrogen chloride	HCl	$\approx 10^7$	≈ -7	Cl^-
Sulfuric acid	$HOSO_2OH$	1.6×10^5	-4.8	$HOSO_2O^-$
Hydronium ion	$H{-}\overset{+}{O}H_2$	55	-1.7	H_2O
Hydrogen fluoride	HF	3.5×10^{-4}	3.5	F^-
Acetic acid	$CH_3\overset{\overset{O}{\|}}{C}OH$	1.8×10^{-5}	4.7	$CH_3\overset{\overset{O}{\|}}{C}O^-$
Ammonium ion	$H{-}\overset{+}{N}H_3$	5.6×10^{-10}	9.2	NH_3
Water	HOH	$1.8 \times 10^{-16\ddagger}$	15.7	HO^-
Methanol	CH_3OH	$\approx 10^{-16}$	≈ 16	CH_3O^-
Ethanol	CH_3CH_2OH	$\approx 10^{-16}$	≈ 16	$CH_3CH_2O^-$
Isopropyl alcohol	$(CH_3)_2CHOH$	$\approx 10^{-17}$	≈ 17	$(CH_3)_2CHO^-$
tert-Butyl alcohol	$(CH_3)_3COH$	$\approx 10^{-18}$	≈ 18	$(CH_3)_3CO^-$
Ammonia	H_2NH	$\approx 10^{-36}$	≈ 36	H_2N^-
Dimethylamine	$(CH_3)_2NH$	$\approx 10^{-36}$	≈ 36	$(CH_3)_2N^-$

*Acid strength decreases from top to bottom of the table. Strength of conjugate base increases from top to bottom of the table.
†The most acidic proton—the one that is lost on ionization—is highlighted.
‡The "true" K_a for water is 1×10^{-14}. Dividing this value by 55.5 (the number of moles of water in 1 L of water) gives a K_a of 1.8×10^{-16} and puts water on the same concentration basis as the other substances in the table. A paper in the May 1990 issue of the *Journal of Chemical Education* (p. 386) outlines the justification for this approach. For a dissenting view, see the March 1992 issue of the *Journal of Chemical Education* (p. 255).

PROBLEM 4.8 As noted in Problem 4.7, hydrogen cyanide (HCN) has a pK_a of 9.1. Is cyanide ion (CN^-) a stronger base or a weaker base than hydroxide ion (HO^-)?
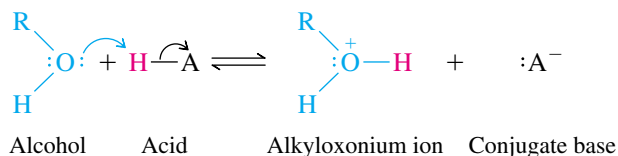
In any proton-transfer process the position of equilibrium favors formation of the weaker acid and the weaker base.

$$\text{Stronger acid + stronger base} \overset{K>1}{\rightleftharpoons} \text{weaker acid + weaker base}$$

This is one of the most important equations in chemistry.

Table 4.2 is set up so that the strongest acid is at the top of the acid column, with the strongest base at the bottom of the conjugate base column. An acid will transfer a proton to the conjugate base of any acid that lies below it in the table, and the equilibrium constant for the reaction will be greater than one.

Table 4.2 contains both inorganic and organic compounds. Organic compounds are similar to inorganic ones when the functional groups responsible for their acid–base properties are the same. Thus, alcohols (ROH) are similar to water (HOH) in both their Brønsted acidity (ability to donate a proton *from oxygen*) and Brønsted basicity (ability to accept a proton *on oxygen*). Just as proton transfer to a water molecule gives oxonium ion (hydronium ion, H_3O^+), proton transfer to an alcohol gives an **alkyloxonium ion** (ROH_2^+).

We shall see that several important reactions of alcohols involve strong acids either as reagents or as catalysts to increase the rate of reaction. In all these reactions the first step is formation of an alkyloxonium ion by proton transfer from the acid to the oxygen of the alcohol.

PROBLEM 4.9 Write an equation for proton transfer from hydrogen chloride to *tert*-butyl alcohol. Use curved arrows to track electron movement, and identify the acid, base, conjugate acid, and conjugate base.

PROBLEM 4.10 Is the equilibrium constant for proton transfer from hydrogen chloride to *tert*-butyl alcohol greater than 1 or less than 1?

Alkyl halides are neither very acidic nor very basic and are absent from Table 4.2. In general, compounds, including alkyl halides, in which all the protons are bonded to carbon are exceedingly weak acids—too weak to be included in the table.
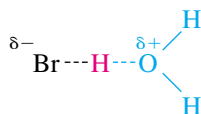
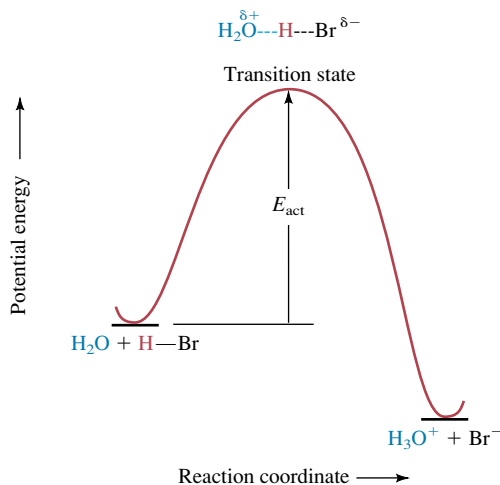## 4.7   ACID–BASE REACTIONS: A MECHANISM FOR PROTON TRANSFER

Potential energy diagrams of the type used in Chapter 3 to describe conformational processes can also help us understand more about chemical reactions. Consider the transfer of a proton from hydrogen bromide to water:
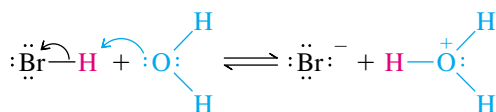
A potential energy diagram for this reaction is shown in Figure 4.6. Because the transfer of a proton from hydrogen bromide to water is exothermic, the products are placed lower in energy than the reactants. The diagram depicts the reaction as occurring in a single **elementary step.** An elementary step is one that involves only one transition state. A reaction can proceed by way of a single elementary step, in which case it is described as a **concerted** reaction, or by a series of elementary steps. In the case of proton transfer from hydrogen bromide to water, breaking of the H—Br bond and making of the H2O—H bond occur "in concert" with each other. The species present at the transition state is not a stable structure and cannot be isolated or examined directly. Its structure is assumed to be one in which the proton being transferred is partially bonded to both bromine and oxygen simultaneously, although not necessarily to the same extent.
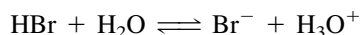
Dashed lines in transition-state structures represent *partial* bonds, that is, bonds in the process of being made or broken.

$$\overset{\delta+}{H_2O}\text{---}H\text{---}\overset{\delta-}{Br}$$

Transition state

Potential energy →

E_{act}

$H_2O + H\text{—}Br$

$H_3O^+ + Br^-$

Reaction coordinate →

The **molecularity** of an elementary step is given by the number of species that undergo a chemical change in that step. The elementary step

$$HBr + H_2O \rightleftharpoons Br^- + H_3O^+$$

is **bimolecular** because it involves one molecule of hydrogen bromide and one molecule of water.

> **PROBLEM 4.11** Represent the structure of the transition state for proton transfer from hydrogen chloride to *tert*-butyl alcohol.

Proton transfer from hydrogen bromide to water and alcohols ranks among the most rapid chemical processes and occurs almost as fast as the molecules collide with one another. Thus the height of the energy barrier separating reactants and products, the *activation energy* for proton transfer, must be quite low.

The concerted nature of proton transfer contributes to its rapid rate. The energy cost of breaking the H—Br bond is partially offset by the energy released in making the $H_2\overset{+}{O}$—H bond. Thus, the activation energy is far less than it would be for a hypothetical stepwise process involving an initial, unassisted ionization of the H—Br bond, followed by a combination of the resulting H^+ with water.

The 1967 Nobel Prize in chemistry was shared by Manfred Eigen, a German chemist who developed novel methods for measuring the rates of very fast reactions such as proton transfers.
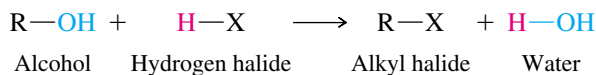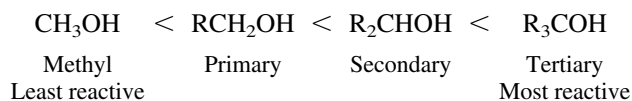
4.8 PREPARATION OF ALKYL HALIDES FROM ALCOHOLS AND HYDROGEN HALIDES

Much of what organic chemists do is directed toward practical goals. Chemists in the pharmaceutical industry synthesize new compounds as potential drugs for the treatment of disease. Agricultural chemicals designed to increase crop yields include organic compounds used for weed control, insecticides, and fungicides. Among the "building block" molecules used as starting materials to prepare new substances, alcohols and alkyl halides are especially valuable.

The procedures to be described in the remainder of this chapter use either an alkane or an alcohol as the starting material for preparing an alkyl halide. By knowing how to
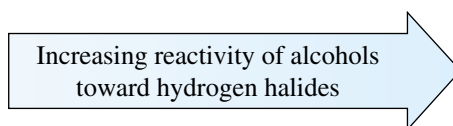
prepare alkyl halides, we can better appreciate the material in later chapters, where alkyl halides figure prominently in key chemical transformations. The preparation of alkyl halides also serves as a focal point to develop the principles of reaction mechanisms. We'll begin with the preparation of alkyl halides from alcohols by reaction with hydrogen halides.
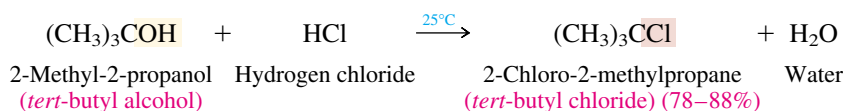
$$R{-}OH + \quad H{-}X \quad \longrightarrow \quad R{-}X \quad + H{-}OH$$

Alcohol   Hydrogen halide   Alkyl halide   Water

The order of reactivity of the hydrogen halides parallels their acidity: HI > HBr > HCl >> HF. Hydrogen iodide is used infrequently, however, and the reaction of alcohols with hydrogen fluoride is not a useful method for the preparation of alkyl fluorides.
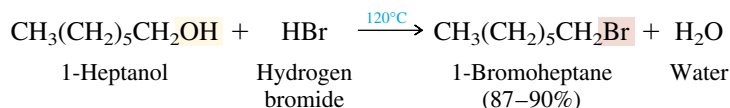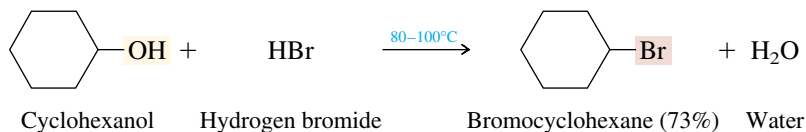
Among the various classes of alcohols, tertiary alcohols are observed to be the most reactive and primary alcohols the least reactive.
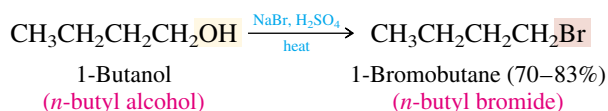
Increasing reactivity of alcohols toward hydrogen halides

$$CH_3OH \quad < \quad RCH_2OH \quad < \quad R_2CHOH \quad < \quad R_3COH$$

Methyl   Primary   Secondary   Tertiary
Least reactive   Most reactive

Tertiary alcohols are converted to alkyl chlorides in high yield within minutes on reaction with hydrogen chloride at room temperature and below.

$$(CH_3)_3COH \quad + \quad HCl \quad \xrightarrow{25°C} \quad (CH_3)_3CCl \quad + H_2O$$

2-Methyl-2-propanol   Hydrogen chloride   2-Chloro-2-methylpropane   Water
(*tert*-butyl alcohol)   (*tert*-butyl chloride) (78–88%)

Secondary and primary alcohols do not react with hydrogen chloride at rates fast enough to make the preparation of the corresponding alkyl chlorides a method of practical value. Therefore, the more reactive hydrogen halide HBr is used; even then, elevated temperatures are required in order to increase the rate of reaction.
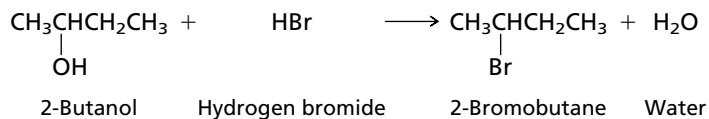
The efficiency of a synthetic transformation is normally expressed as a **percent yield,** or percentage of the *theoretical yield.* **Theoretical yield** is the amount of product that could be formed if the reaction proceeded to completion and did not lead to any products other than those given in the equation.

Cyclohexanol   Hydrogen bromide   Bromocyclohexane (73%)   Water

$$CH_3(CH_2)_5CH_2OH + \quad HBr \quad \xrightarrow{120°C} CH_3(CH_2)_5CH_2Br + H_2O$$

1-Heptanol   Hydrogen   1-Bromoheptane   Water
                  bromide   (87–90%)

The same kind of transformation may be carried out by heating an alcohol with sodium bromide and sulfuric acid.

$$CH_3CH_2CH_2CH_2OH \xrightarrow[\text{heat}]{NaBr, H_2SO_4} CH_3CH_2CH_2CH_2Br$$

1-Butanol   1-Bromobutane (70–83%)
(*n*-butyl alcohol)   (*n*-butyl bromide)

We'll often find it convenient to write chemical equations in the abbreviated form shown here, in which reagents, especially inorganic ones, are not included in the body of the equation but instead are indicated over the arrow. Inorganic products—in this case, water—are usually omitted. These simplifications focus our attention on the organic reactant and its functional group transformation.

PROBLEM 4.12   Write chemical equations for the reaction that takes place between each of the following pairs of reactants:

(a) 2-Butanol and hydrogen bromide

(b) 3-Ethyl-3-pentanol and hydrogen chloride

(c) 1-Tetradecanol and hydrogen bromide

SAMPLE SOLUTION   (a) An alcohol and a hydrogen halide react to form an alkyl halide and water. In this case 2-bromobutane was isolated in 73% yield.

$$CH_3CHCH_2CH_3 \ + \quad HBr \quad \longrightarrow \ CH_3CHCH_2CH_3 \ + \ H_2O$$
$$\qquad | \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad | $$
$$\quad OH \qquad\qquad\qquad\qquad\qquad\qquad\qquad Br$$

| 2-Butanol | Hydrogen bromide | 2-Bromobutane | Water |

4.9   MECHANISM OF THE REACTION OF ALCOHOLS WITH HYDROGEN HALIDES

The reaction of an alcohol with a hydrogen halide is a **substitution.** A halogen, usually chlorine or bromine, replaces a hydroxyl group as a substituent on carbon. Calling the reaction a substitution tells us the relationship between the organic reactant and its product but does not reveal the mechanism. In developing a mechanistic picture for a particular reaction, we combine some basic principles of chemical reactivity with experimental observations to deduce the most likely sequence of elementary steps.

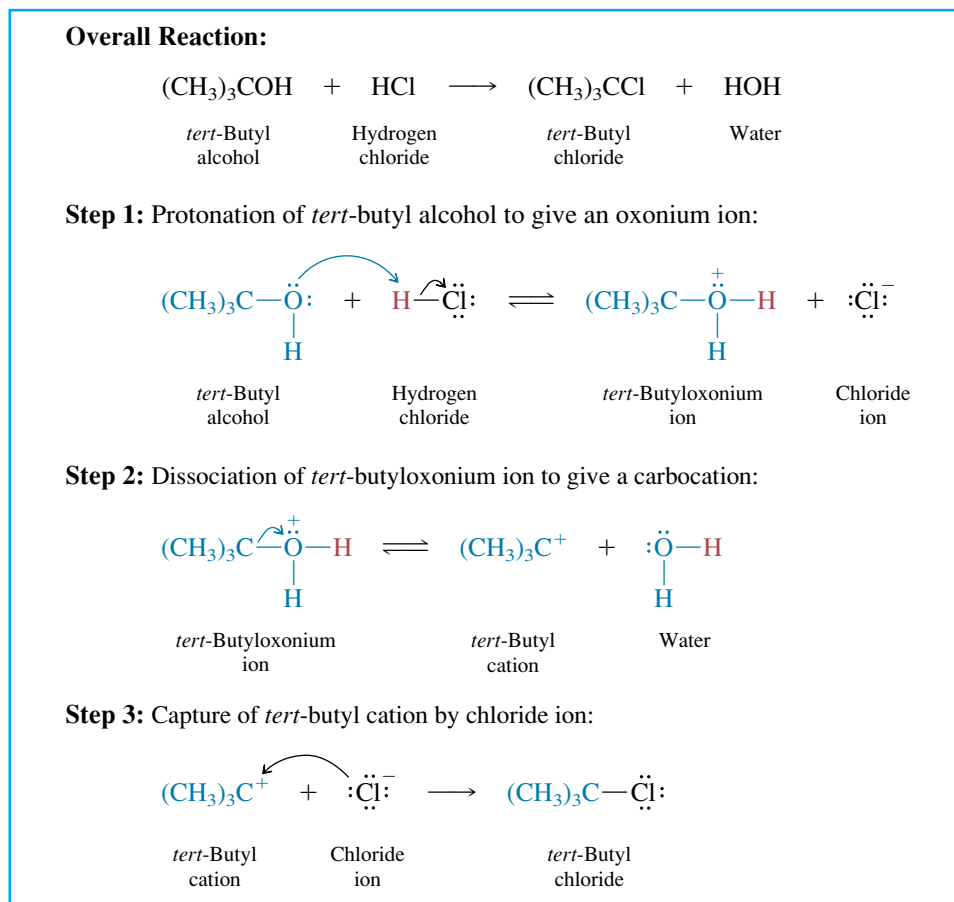Consider the reaction of *tert*-butyl alcohol with hydrogen chloride:

$$(CH_3)_3COH \ + \quad HCl \quad \longrightarrow \ (CH_3)_3CCl \ + \ H_2O$$

| *tert*-Butyl alcohol | Hydrogen chloride | *tert*-Butyl chloride | Water |

The generally accepted mechanism for this reaction is presented as a series of three elementary steps in Figure 4.7. We say "generally accepted" because a reaction mechanism can never be proved to be correct. A mechanism is our best present assessment of how a reaction proceeds and must account for all experimental observations. If new experimental data appear that conflict with the mechanism, the mechanism must be modified to accommodate them. If the new data are consistent with the proposed mechanism, our confidence grows that it is likely to be correct.

We already know about step 1 of the mechanism outlined in Figure 4.7; it is an example of a Brønsted acid–base reaction of the type discussed in Section 4.6 and formed the basis of Problems 4.9 through 4.11.

Steps 2 and 3, however, are new to us. Step 2 involves dissociation of an alkyloxonium ion to a molecule of water and a **carbocation,** a species that contains a positively charged carbon. In step 3, this carbocation reacts with chloride ion to yield *tert*-butyl chloride. Both the alkyloxonium ion and the carbocation are **intermediates** in the reaction. They are not isolated, but are formed in one step and consumed in another during the passage of reactants to products. If we add the equations for steps 1 through 3 together, the equation for the overall process results. A valid reaction mechanism must

If you have not already written out the solutions to Problems 4.9 to 4.11, you should do so now.
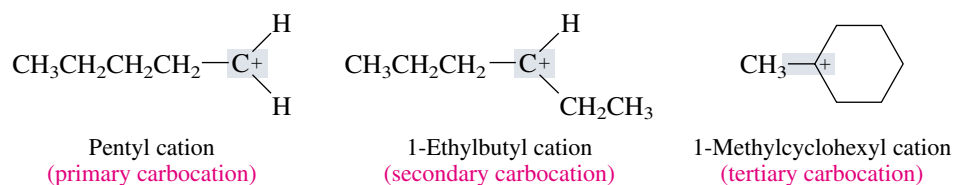
Overall Reaction:

$$(CH_3)_3COH \quad + \quad HCl \quad \longrightarrow \quad (CH_3)_3CCl \quad + \quad HOH$$

| *tert*-Butyl alcohol | Hydrogen chloride | *tert*-Butyl chloride | Water |

Step 1: Protonation of *tert*-butyl alcohol to give an oxonium ion:

| *tert*-Butyl alcohol | Hydrogen chloride | *tert*-Butyloxonium ion | Chloride ion |

Step 2: Dissociation of *tert*-butyloxonium ion to give a carbocation:

| *tert*-Butyloxonium ion | *tert*-Butyl cation | Water |

Step 3: Capture of *tert*-butyl cation by chloride ion:

| *tert*-Butyl cation | Chloride ion | *tert*-Butyl chloride |

account for the consumption of all reactants and the formation of all products, be they organic or inorganic. So that we may better understand the chemistry expressed in steps 2 and 3, we need to examine carbocations in more detail.

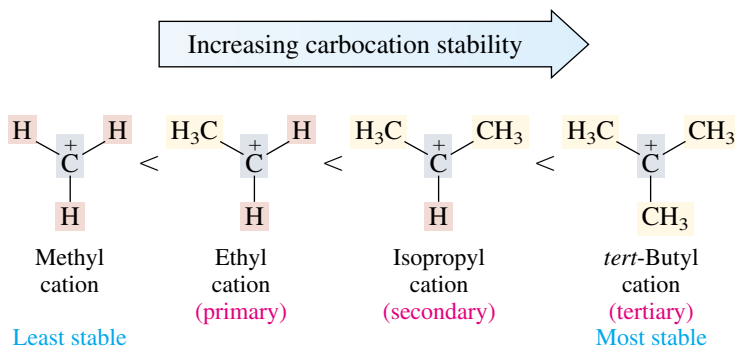## 4.10   STRUCTURE, BONDING, AND STABILITY OF CARBOCATIONS

Carbocations are sometimes called *carbonium ions* or *carbenium ions.* An article in the November 1986 issue of the *Journal of Chemical Education,* pp. 930–933, traces the historical development of these and related terms.

Carbocations are classified as primary, secondary, or tertiary according to the number of carbons that are directly attached to the positively charged carbon. They are named by appending "cation" as a separate word after the IUPAC name of the appropriate alkyl group. The chain is numbered beginning with the positively charged carbon (the positive charge is always at C-1).

| Pentyl cation (primary carbocation) | 1-Ethylbutyl cation (secondary carbocation) | 1-Methylcyclohexyl cation (tertiary carbocation) |

An electrostatic potential map of *tert*-butyl cation appears on the first page of this chapter.

Common names that have been incorporated into IUPAC nomenclature such as isopropyl, *sec*-butyl, and so on, are permitted. Thus 1,1-dimethylethyl cation $(CH_3)_3C^+$ may be called *tert*-butyl cation.

The properties of carbocations are intimately related to their structure, and so let's think about the bonding in methyl cation, CH_3^+. The positively charged carbon contributes three valence electrons, and each hydrogen contributes one for a total of six electrons, which are used to form three C—H σ bonds. As we saw in Section 1.17, carbon is sp^2-hybridized when it is bonded to three atoms or groups. We therefore choose the sp^2 hybridization model for bonding shown in Figure 4.8. Carbon forms σ bonds to three hydrogens by overlap of its sp^2 orbitals with hydrogen 1s orbitals. The three σ bonds are coplanar. Remaining on carbon is an unhybridized 2p orbital that contains no electrons. The axis of this empty p orbital is perpendicular to the plane defined by the three σ bonds.

Evidence from a variety of sources convinces us that carbocations can exist, but are relatively unstable. When carbocations are involved in chemical reactions, it is as reactive intermediates, formed in one step and consumed rapidly thereafter.

Numerous studies have shown that the more stable a carbocation is, the faster it is formed. These studies also demonstrate that *alkyl groups directly attached to the positively charged carbon stabilize a carbocation.* Thus, the observed order of carbocation stability is

FIGURE 4.8 Structure of methyl cation CH_3^+. Carbon is sp^2-hybridized. Each hydrogen is attached to carbon by a σ bond formed by overlap of a hydrogen 1s orbital with an sp^2 hybrid orbital of carbon. All four atoms lie in the same plane. The unhybridized 2p orbital of carbon is unoccupied, and its axis is perpendicular to the plane of the atoms.

Increasing carbocation stability

Methyl cation	Ethyl cation	Isopropyl cation	*tert*-Butyl cation
	(primary)	(secondary)	(tertiary)
Least stable			Most stable

As carbocations go, CH_3^+ is particularly unstable, and its existence as an intermediate in chemical reactions has never been demonstrated. Primary carbocations, although more stable than CH_3^+, are still too unstable to be involved as intermediates in chemical reactions. The threshold of stability is reached with secondary carbocations. Many reactions, including the reaction of secondary alcohols with hydrogen halides, are believed to involve secondary carbocations. The evidence in support of tertiary carbocation intermediates is stronger yet.

> **PROBLEM 4.13**   Of the isomeric $C_5H_{11}^+$ carbocations, which one is the most stable?

Because alkyl groups stabilize carbocations, we conclude that they release electrons to the positively charged carbon, dispersing the positive charge. They do this through a combination of effects. One involves polarization of the σ bonds to the positively charged carbon. As illustrated for ethyl cation in Figure 4.9, the positively charged carbon draws the electrons in its σ bonds toward itself and away from the atoms attached to it. Electrons in a C—C σ bond are more polarizable than those in a C—H bond, so replacing hydrogens by alkyl groups reduces the net charge on the sp^2-hybridized carbon. The electron-donating or electron-withdrawing effect of a group that is transmitted through σ bonds is called an **inductive effect.**
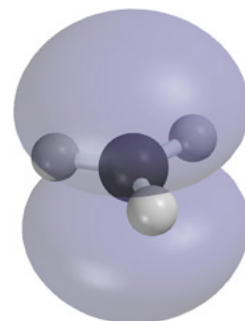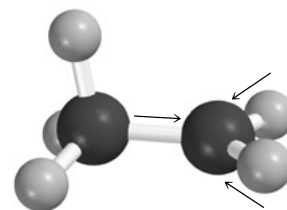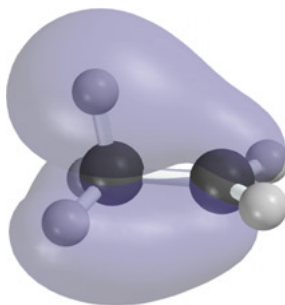
FIGURE 4.9 The charge in ethyl cation is stabilized by polarization of the electron distribution in the σ bonds to the positively charged carbon atom. Alkyl groups release electrons better than hydrogen.

A second effect, called **hyperconjugation,** is also important. We'll again consider
ethyl cation, but this time direct our attention to the electrons in the C—H bonds of the
methyl group. Figure 4.10 illustrates how an orbital associated with the methyl group
can overlap with the vacant *p* orbital of the positively charged carbon to give an extended
orbital that encompasses both CH_3 and C^+. This allows the electrons of the methyl group
to be shared by both carbons (thereby increasing their delocalization) and to stabilize the
carbocation. Notice that according to hyperconjugation, electrons in the C—H bond of
a $^+$C—C—H unit are more stabilizing than $^+$C—H electrons. Thus, successive replace-
ment of the hydrogens attached to CH_3^+ by alkyl groups increases the opportunities for
hyperconjugation, which is consistent with the observed order of increasing carbocation
stability: methyl $<$ primary $<$ secondary $<$ tertiary. Finally, although we have devel-
oped this picture for hyperconjugation of a $^+$C—C—H unit, it also applies to
$^+$C—C—C as well as many others.

The positive charge on carbon and the vacant *p* orbital combine to make carboca-
tions strongly **electrophilic** ("electron-loving," or "electron-seeking"). **Nucleophiles** are
just the opposite. A nucleophile is "nucleus-seeking"; it has an unshared pair of elec-
trons that it can use to form a covalent bond. Step 3 of the mechanism of the reaction
of *tert*-butyl alcohol with hydrogen chloride is an example of a reaction between an elec-
trophile and a nucleophile and is depicted from a structural perspective in Figure 4.11.

Carbocation
(electrophile)

Halide anion
(nucleophile)

Alkyl halide
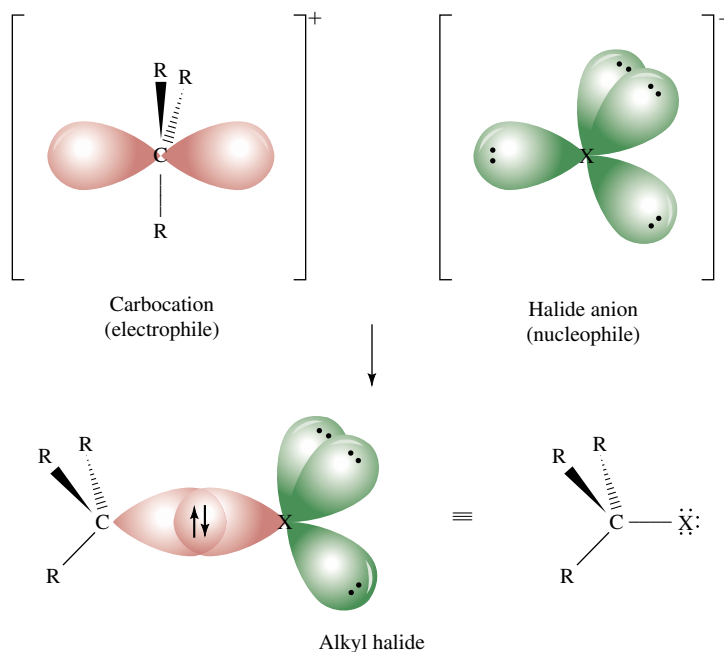
The crucial electronic interaction is between an unshared electron pair of the nucleophilic chloride anion and the vacant 2p orbital of the electrophilic carbocation.

Figure 4.12 maps the electrostatic potential in methyl cation and shows that the region of positive charge coincides with where we expect the vacant 2p orbital to be—centered on carbon and above and below the plane of the atoms.

A number of years ago G. N. Lewis extended our understanding of acid–base behavior to include reactions other than proton transfers. According to Lewis, *an acid is an electron-pair acceptor* and *a base is an electron-pair donor.* Thus, carbocations are electron-pair acceptors and are **Lewis acids.** Halide anions are electron-pair donors and are **Lewis bases.** It is generally true that electrophiles are Lewis acids, and nucleophiles are Lewis bases.
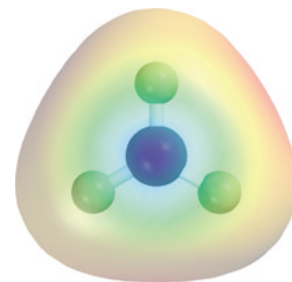
FIGURE 4.12 Electrostatic potential map of methyl cation (CH$_3^+$). The regions of lowest electron density are blue, are centered on carbon, and are located above and below the plane defined by the four atoms.

4.11   POTENTIAL ENERGY DIAGRAMS FOR MULTISTEP REACTIONS: THE S$_N$1 MECHANISM

The mechanism for the reaction of *tert*-butyl alcohol with hydrogen chloride presented in Figure 4.7 involves a sequence of three elementary steps. Each step has its own transition state, and the potential energy diagram in Figure 4.13 for the overall process is a composite of the energy diagrams for the three steps.

Reading from left to right in Figure 4.13, the first maximum corresponds to the transition state for proton transfer from hydrogen chloride to *tert*-butyl alcohol. This step is **bimolecular.** The proton that is transferred is partially bonded both to chlorine and to the oxygen of the alcohol at the transition state.

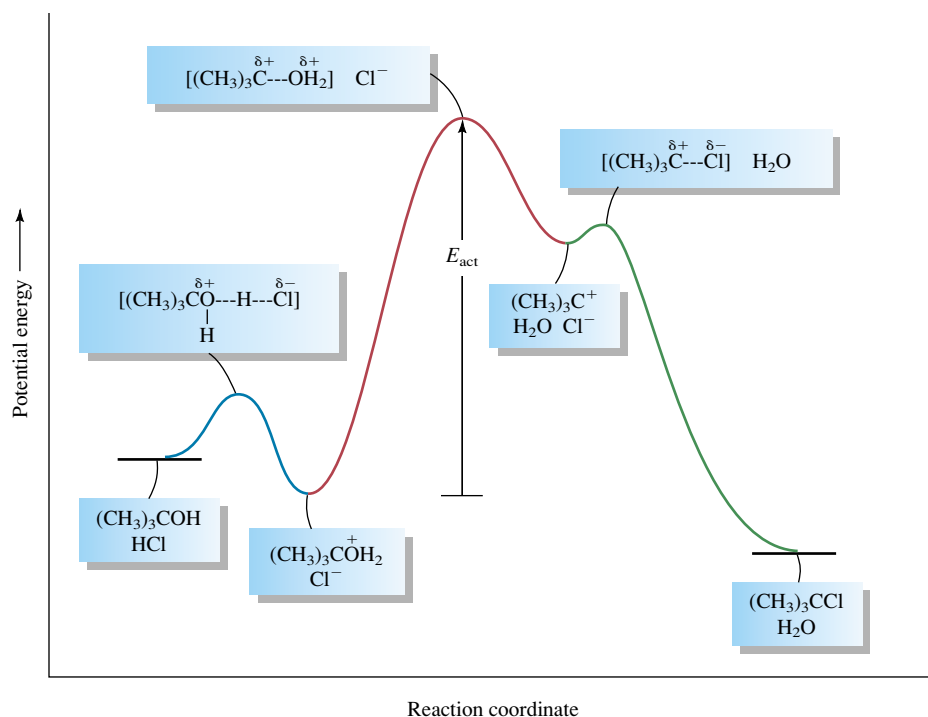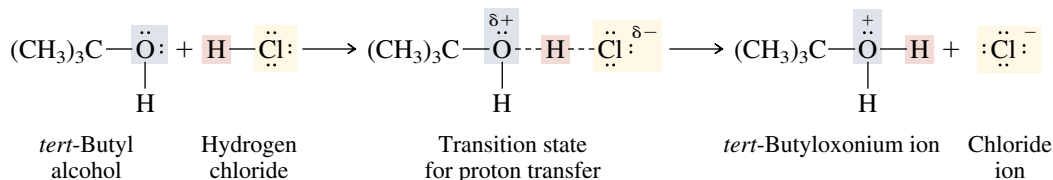| *tert*-Butyl alcohol | Hydrogen chloride | Transition state for proton transfer | *tert*-Butyloxonium ion | Chloride ion |

FIGURE 4.13 Energy diagram depicting the intermediates and transition states involved in the reaction of *tert*-butyl alcohol with hydrogen chloride.

This is a rapid process, and therefore the activation energy for the first step is relatively low.

Once formed, the alkyloxonium ion dissociates by cleavage of its carbon–oxygen bond, giving a carbocation.

| *tert*-Butyloxonium ion | Transition state for dissociation of alkyloxonium ion | *tert*-Butyl cation | Water |
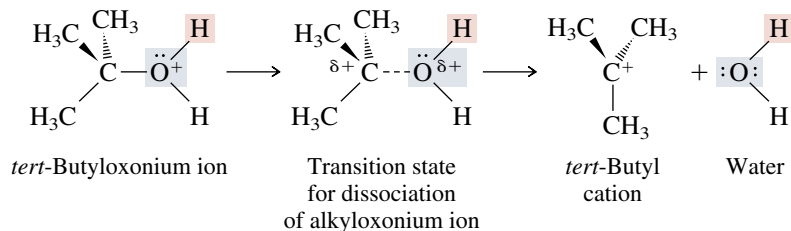
Only one species, the alkyloxonium ion, undergoes a chemical change in this step, making it **unimolecular.** Unlike the bimolecular proton transfer step that precedes it, in which formation of a new bond accompanies the cleavage of an old one, unimolecular dissociation of the alkyloxonium ion gives a carbocation without simultaneous formation of a new bond. Thus, the activation energy for carbocation formation is relatively high.

In the third step, the carbocation intermediate is captured by a chloride ion, and the energy barrier for this cation–anion combination is relatively low. The transition state is characterized by partial bond formation between the nucleophile (chloride anion) and the electrophile (*tert*-butyl cation).

| *tert*-Butyl cation | Chloride anion | Transition state for cation–anion combination | *tert*-Butyl chloride |
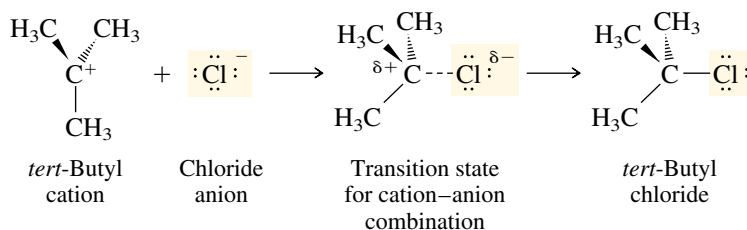
Two species, the carbocation and the anion, react in this step, making it **bimolecular.** Note that molecularity refers only to individual elementary steps in a multistep mechanism, not to the overall reaction itself. Step 1 of the mechanism (proton transfer) is bimolecular, step 2 (dissociation of the alkyloxonium ion) is unimolecular, and step 3 (cation–anion combination) is bimolecular.

Of the three steps in the mechanism, step 2 has the highest activation energy and is the slowest step. A reaction can proceed no faster than its slowest step, which is referred to as the **rate-determining step.** In the reaction of *tert*-butyl alcohol with hydrogen chloride, formation of the carbocation by dissociation of the alkyloxonium ion is the rate-determining step.

Substitution reactions, of which the reaction of alcohols with hydrogen halides is but one example, will be discussed in more detail in Chapter 8. There, we will make extensive use of a shorthand notation for a mechanism originally introduced by Sir Christopher Ingold in the 1930s. Ingold proposed the symbol, S_N, to stand for *substitution nucleophilic,* to be followed by the number *1* or *2* according to whether the rate-determining step is unimolecular or bimolecular. The reaction of *tert*-butyl alcohol with hydrogen chloride, for example, is said to follow an **S_N1 mechanism** because its slow step (dissociation of *tert*-butyloxonium ion) is unimolecular.

## 4.12   EFFECT OF ALCOHOL STRUCTURE ON REACTION RATE

We saw in Section 4.8 that the reactivity of alcohols with hydrogen halides increases in the order primary < secondary < tertiary. To be valid, the mechanism proposed in Figure 4.7 and represented by the energy diagram in Figure 4.13 must account for this order of relative reactivity. When considering rate effects, we focus on the slow step of a reaction mechanism and analyze how that step is influenced by changes in reactants or reaction conditions.

As mentioned, the slow step in the S_N1 mechanism is the dissociation of the alkyloxonium ion to the carbocation. The rate of this step is proportional to the concentration of the alkyloxonium ion:

$$\text{Rate} = k[\text{alkyloxonium ion}]$$

where k is a constant of proportionality called the *rate constant.* The value of k is related to the activation energy for alkyloxonium ion dissociation and is different for different alkyloxonium ions. A low activation energy implies a large value of k and a rapid rate of alkyloxonium ion dissociation. Conversely, a large activation energy is characterized by a small k for dissociation and a slow rate.

> The rate of any chemical reaction increases with increasing temperature. Thus the value of k for a reaction is not constant, but increases as the temperature increases.

Consider what happens when the alkyloxonium ion dissociates to a carbocation and water. The positive charge resides mainly on oxygen in the alkyloxonium ion but is shared between oxygen and carbon at the transition state.

Alkyloxonium ion	Transition state	Carbocation	Water
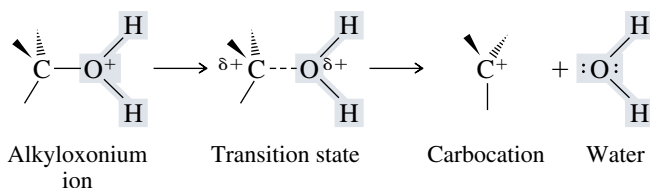
The transition state for carbocation formation begins to resemble the carbocation. If we assume that structural features that stabilize carbocations also stabilize transition states that have carbocation character, it follows that alkyloxonium ions derived from tertiary alcohols have a lower energy of activation for dissociation and are converted to their corresponding carbocations faster than those derived from secondary and primary alcohols. Figure 4.14 depicts the effect of alkyloxonium ion structure on the activation energy for, and thus the rate of, carbocation formation. Once the carbocation is formed, it is rapidly captured by halide ion, so that the rate of alkyl halide formation is governed by the rate of carbocation formation.

Inferring the structure of the transition state on the basis of what is known about the species that lead to it or may be formed by way of it is a practice with a long history in organic chemistry. A justification of this practice was advanced in 1955 by George S. Hammond, who reasoned that *if two states, such as a transition state and an intermediate derived from it, are similar in energy, then they are similar in structure.* This rationale is known as **Hammond's postulate.** In the formation of a carbocation from an alkyloxonium ion, the transition state is closer in energy to the carbocation than it is to the alkyloxonium ion, and so its structure more closely resembles the carbocation and it responds in a similar way to the stabilizing effects of alkyl substituents.

$$\overset{\delta+}{CH_3}\text{---}\overset{\delta+}{OH_2}$$

$CH_3{}^+$, H_2O

E_{act}

$CH_3\overset{+}{OH}_2$

Methyloxonium
ion

$$\overset{\delta+}{RCH_2}\text{---}\overset{\delta+}{OH_2}$$

$RCH_2{}^+$, H_2O

E_{act}

$RCH_2\overset{+}{OH}_2$

A primary
alkyloxonium ion

$$\overset{\delta+}{R_2CH}\text{---}\overset{\delta+}{OH_2}$$

R_2CH^+, H_2O

E_{act}

$R_2CH\overset{+}{OH}_2$

A secondary
alkyloxonium ion

$$\overset{\delta+}{R_3C}\text{---}\overset{\delta+}{OH_2}$$

R_3C^+, H_2O

E_{act}

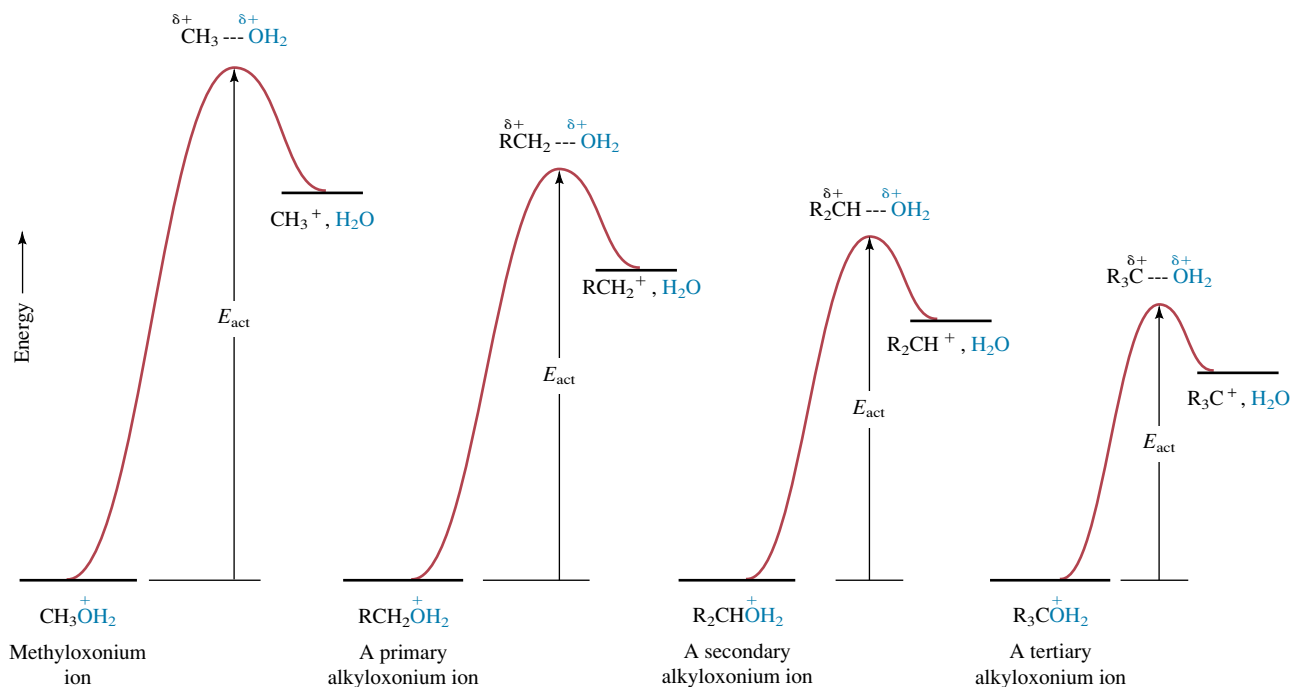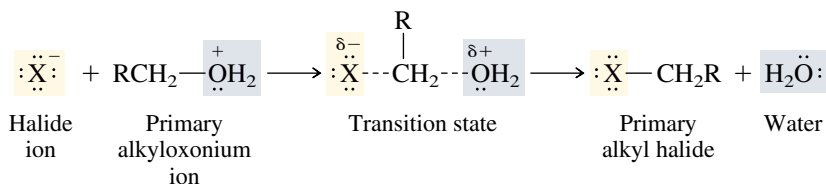$R_3C\overset{+}{OH}_2$

A tertiary
alkyloxonium ion

Energy →

FIGURE 4.14 Diagrams comparing energies of activation for formation of carbocations from alkyloxonium ions of methyl, primary, secondary, and tertiary alcohols.

4.13 REACTION OF PRIMARY ALCOHOLS WITH HYDROGEN HALIDES. THE S_N2 MECHANISM

Unlike tertiary and secondary carbocations, primary carbocations are too high in energy to be intermediates in chemical reactions. Since primary alcohols are converted, albeit rather slowly, to alkyl halides on treatment with hydrogen halides, they must follow some other mechanism that avoids carbocation intermediates. This alternative mechanism is believed to be one in which the carbon–halogen bond begins to form before the carbon–oxygen bond of the alkyloxonium ion is completely broken.

$$:\ddot{X}:^- + RCH_2\text{---}\overset{+}{OH}_2 \longrightarrow \overset{\delta-}{:\ddot{X}}\text{---}CH_2\text{---}\overset{\delta+}{OH}_2 \longrightarrow :\ddot{X}\text{---}CH_2R + H_2\ddot{O}:$$

Halide ion / Primary alkyloxonium ion / Transition state (R above) / Primary alkyl halide / Water

The halide nucleophile helps to "push off" a water molecule from the alkyloxonium ion. According to this mechanism, both the halide ion and the alkyloxonium ion are involved in the same bimolecular elementary step. In Ingold's terminology, introduced in Section 4.11 and to be described in detail in Chapter 8, nucleophilic substitutions characterized by a bimolecular rate-determining step are given the mechanistic symbol S_N2.

PROBLEM 4.14 1-Butanol and 2-butanol are converted to their corresponding bromides on being heated with hydrogen bromide. Write a suitable mechanism for each reaction, and assign each the appropriate symbol (S_N1 or S_N2).
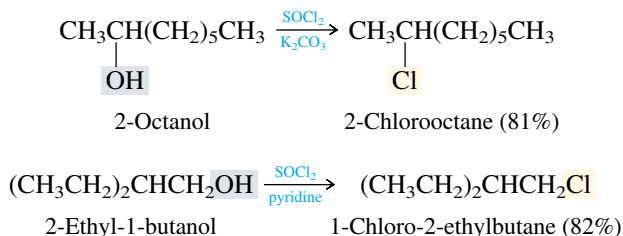
4.14   OTHER METHODS FOR CONVERTING ALCOHOLS TO ALKYL HALIDES

Alkyl halides are such useful starting materials for preparing other functional group types that chemists have developed several different methods for converting alcohols to alkyl halides. Two methods, based on the inorganic reagents *thionyl chloride* and *phosphorus tribromide,* bear special mention.

Thionyl chloride reacts with alcohols to give alkyl chlorides. The inorganic byproducts in the reaction, sulfur dioxide and hydrogen chloride, are both gases at room temperature and are easily removed, making it an easy matter to isolate the alkyl chloride.

$$ROH \ + \ SOCl_2 \longrightarrow \ RCl \ + \ SO_2 \ + \ HCl$$

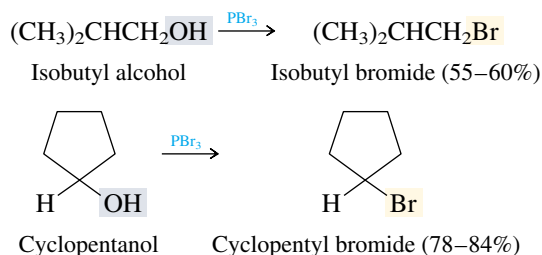| Alcohol | Thionyl chloride | Alkyl chloride | Sulfur dioxide | Hydrogen chloride |
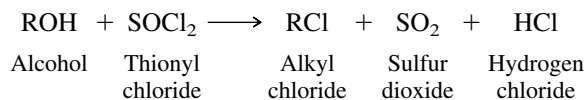
Because tertiary alcohols are so readily converted to chlorides with hydrogen chloride, thionyl chloride is used mainly to prepare primary and secondary alkyl chlorides. Reactions with thionyl chloride are normally carried out in the presence of potassium carbonate or the weak organic base pyridine.

$$CH_3CH(CH_2)_5CH_3 \xrightarrow[K_2CO_3]{SOCl_2} CH_3CH(CH_2)_5CH_3$$

OH (2-Octanol)   Cl (2-Chlorooctane (81%))

$$(CH_3CH_2)_2CHCH_2OH \xrightarrow[pyridine]{SOCl_2} (CH_3CH_2)_2CHCH_2Cl$$

2-Ethyl-1-butanol   1-Chloro-2-ethylbutane (82%)

Phosphorus tribromide reacts with alcohols to give alkyl bromides and phosphorous acid.

$$3ROH \ + \ PBr_3 \longrightarrow \ 3RBr \ + \ H_3PO_3$$

| Alcohol | Phosphorus tribromide | Alkyl bromide | Phosphorous acid |
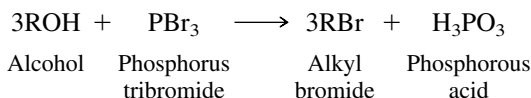
Phosphorous acid is water-soluble and may be removed by washing the alkyl halide with water or with dilute aqueous base.

$$(CH_3)_2CHCH_2OH \xrightarrow{PBr_3} (CH_3)_2CHCH_2Br$$

Isobutyl alcohol   Isobutyl bromide (55–60%)

Cyclopentanol   Cyclopentyl bromide (78–84%)

Thionyl chloride and phosphorus tribromide are specialized reagents used to bring about particular functional group transformations. For this reason, we won't present the mechanisms by which they convert alcohols to alkyl halides, but instead will limit ourselves to those mechanisms that have broad applicability and enhance our knowledge of fundamental principles. In those instances you will find that a mechanistic understanding is of great help in organizing the reaction types of organic chemistry.

## 4.15	HALOGENATION OF ALKANES

The rest of this chapter describes a second method for preparing alkyl halides, one that uses alkanes as reactants. It involves substitution of a halogen atom for one of the alkane's hydrogens.
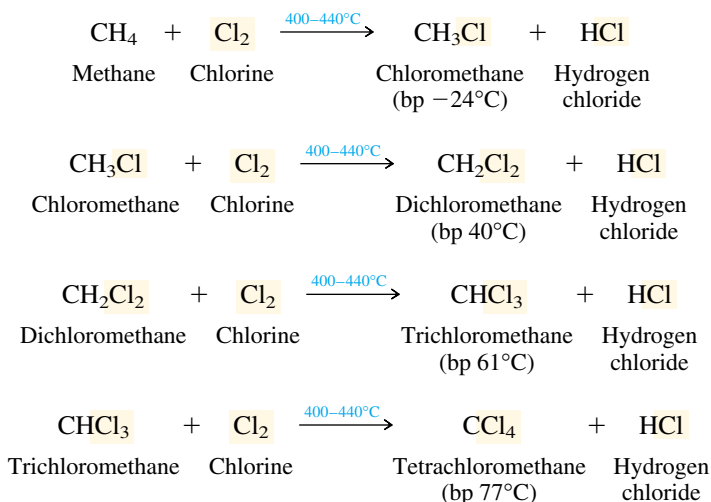
$$R{-}H + X_2 \longrightarrow R{-}X + H{-}X$$

Alkane	Halogen	Alkyl halide	Hydrogen halide
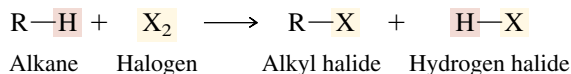
The alkane is said to undergo *fluorination, chlorination, bromination,* or *iodination* according to whether X_2 is F_2, Cl_2, Br_2, or I_2, respectively. The general term is **halogenation. Chlorination** and **bromination** are the most widely used.

The reactivity of the halogens decreases in the order $F_2 > Cl_2 > Br_2 > I_2$. Fluorine is an extremely aggressive oxidizing agent, and its reaction with alkanes is strongly exothermic and difficult to control. Direct fluorination of alkanes requires special equipment and techniques, is not a reaction of general applicability, and will not be discussed further.

Chlorination of alkanes is less exothermic than fluorination, and bromination less exothermic than chlorination. Iodine is unique among the halogens in that its reaction with alkanes is endothermic and alkyl iodides are never prepared by iodination of alkanes.

Volume II of *Organic Reactions,* an annual series that reviews reactions of interest to organic chemists, contains the statement "Most organic compounds burn or explode when brought in contact with fluorine."

## 4.16	CHLORINATION OF METHANE

The gas-phase chlorination of methane is a reaction of industrial importance and leads to a mixture of chloromethane (CH_3Cl), dichloromethane (CH_2Cl_2), trichloromethane ($CHCl_3$), and tetrachloromethane (CCl_4) by sequential substitution of hydrogens.

$$CH_4 + Cl_2 \xrightarrow{400-440°C} CH_3Cl + HCl$$

Methane	Chlorine	Chloromethane (bp −24°C)	Hydrogen chloride

$$CH_3Cl + Cl_2 \xrightarrow{400-440°C} CH_2Cl_2 + HCl$$

Chloromethane	Chlorine	Dichloromethane (bp 40°C)	Hydrogen chloride

$$CH_2Cl_2 + Cl_2 \xrightarrow{400-440°C} CHCl_3 + HCl$$

Dichloromethane	Chlorine	Trichloromethane (bp 61°C)	Hydrogen chloride

$$CHCl_3 + Cl_2 \xrightarrow{400-440°C} CCl_4 + HCl$$

Trichloromethane	Chlorine	Tetrachloromethane (bp 77°C)	Hydrogen chloride

Chlorination of methane provides approximately one-third of the annual U.S. production of chloromethane. The reaction of methanol with hydrogen chloride is the major synthetic method for the preparation of chloromethane.

One of the chief uses of chloromethane is as a starting material from which silicone polymers are made. Dichloromethane is widely used as a paint stripper. Trichloromethane was once used as an inhalation anesthetic, but its toxicity caused it to be replaced by safer materials many years ago. Tetrachloromethane is the starting material for the preparation of several chlorofluorocarbons (CFCs), at one time widely used as refrigerant gases. In 1987, most of the world's industrialized nations agreed to phase out all uses of CFCs by the year 2000 because these compounds have been implicated in atmospheric processes that degrade the earth's ozone layer.

The chlorination of methane is carried out at rather high temperatures (400–440°C), even though each substitution in the series is exothermic. The high temperature provides the energy to initiate the reaction. The term "initiation step" has a specific meaning in organic chemistry, one that is related to the mechanism of the reaction. This mechanism, to be presented in Section 4.18, is fundamentally different from the mechanism by which alcohols react with hydrogen halides. Alcohols are converted to alkyl halides in reactions involving ionic (or "polar") intermediates—alkyloxonium ions and carbocations. The intermediates in the chlorination of methane and other alkanes are quite different; they are neutral ("nonpolar") species called **free radicals.**
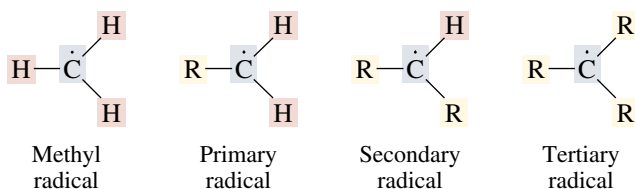
4.17   STRUCTURE AND STABILITY OF FREE RADICALS

Free radicals are species that contain unpaired electrons. The octet rule notwithstanding, not all compounds have all of their electrons paired. Oxygen (O_2) is the most familiar example of a compound with unpaired electrons; it has two of them. Compounds that have an odd number of electrons, such as nitrogen dioxide (NO_2), must have at least one unpaired electron.

$$:\ddot{O}\!-\!\ddot{O}: \qquad :\ddot{O}\!=\!\dot{N}\!-\!\ddot{O}: \qquad \cdot\dot{N}\!=\!\ddot{O}:$$

Oxygen   Nitrogen dioxide   Nitrogen monoxide
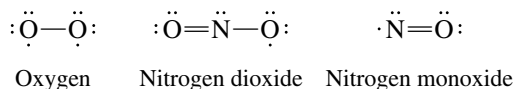
Nitrogen monoxide ("nitric oxide") is another stable free radical. Although known for hundreds of years, NO has only recently been discovered to be an extremely important biochemical messenger and moderator of so many biological processes that it might be better to ask "Which ones is it not involved in?"

The free radicals that we usually see in carbon chemistry are much less stable than these. Simple alkyl radicals, for example, require special procedures for their isolation and study. We will encounter them here only as reactive intermediates, formed in one step of a reaction mechanism and consumed in the next. Alkyl radicals are classified as primary, secondary, or tertiary according to the number of carbon atoms directly attached to the carbon that bears the unpaired electron.

> The journal *Science* selected nitric oxide as its "Molecule of the Year" for 1992.

Methyl   Primary   Secondary   Tertiary
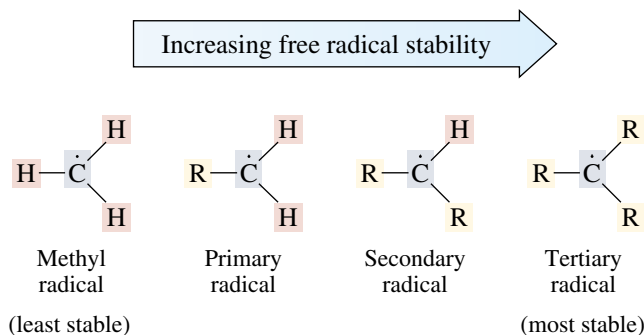radical   radical   radical   radical

An alkyl radical is neutral and has one more electron than the corresponding carbocation. Thus, bonding in methyl radical may be approximated by simply adding an electron to the vacant $2p$ orbital of sp^2-hybridized carbon in methyl cation (Figure 4.15a). Alternatively, we could assume that carbon is sp^3-hybridized and place the unpaired electron in an sp^3 orbital (Figure 4.15b).

Of the two extremes, experimental studies indicate that the planar sp^2 model describes the bonding in alkyl radicals better than the pyramidal sp^3 model. Methyl radical is planar, and more highly substituted radicals such as *tert*-butyl radical are flattened pyramids closer in shape to that expected for sp^2-hybridized carbon than for sp^3.

Free radicals, like carbocations, have an unfilled $2p$ orbital and are stabilized by substituents, such as alkyl groups, that release electrons. Consequently, the order of free-radical stability parallels that of carbocations.

Increasing free radical stability

H—C with H (top) and H (bottom)   R—C with H (top) and H (bottom)   R—C with H (top) and R (bottom)   R—C with R (top) and R (bottom)

Methyl radical   Primary radical   Secondary radical   Tertiary radical

(least stable)   (most stable)

> **PROBLEM 4.15** Write a structural formula for the most stable of the free radicals that have the formula C_5H_{11}.

Some of the evidence indicating that alkyl substituents stabilize free radicals comes from bond energies. The strength of a bond is measured by the energy required to break it. A covalent bond can be broken in two ways. In a **homolytic cleavage** a bond between two atoms is broken so that each of them retains one of the electrons in the bond.

$$X{:}Y \longrightarrow X{\cdot} + {\cdot}Y$$

Homolytic bond cleavage

> A curved arrow shown as a single-barbed fishhook signifies the movement of *one* electron. "Normal" curved arrows track the movement of a *pair* of electrons.
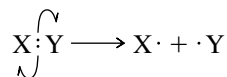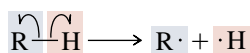
In contrast, in a **heterolytic cleavage** one fragment retains both electrons.

$$X{:}Y \longrightarrow X^+ + {:}Y^-$$
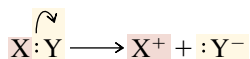
Heterolytic bond cleavage

We assess the relative stability of alkyl radicals by measuring the enthalpy change (ΔH°) for the homolytic cleavage of a C—H bond in an alkane:

$$R{-}H \longrightarrow R{\cdot} + {\cdot}H$$

The more stable the radical, the lower the energy required to generate it by C—H bond homolysis.

FIGURE 4.15 Orbital hybridization models of bonding in methyl radical. (*a*) If the structure of the CH$_3$ radical is planar, then carbon is sp^2-hybridized with an unpaired electron in a 2p orbital. (*b*) If CH$_3$ is pyramidal, carbon is sp^3-hybridized with an electron in an sp^3 orbital. Model (*a*) is more consistent with experimental observations.
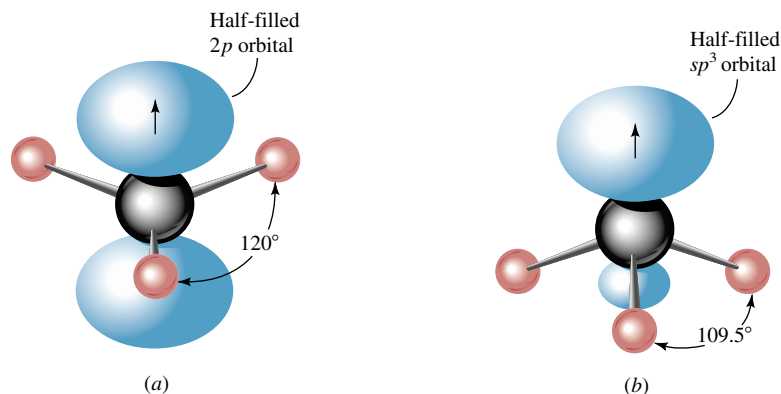

Half-filled 2p orbital

120°

(*a*)

Half-filled sp^3 orbital

109.5°

(*b*)

TABLE 4.3	Bond Dissociation Energies of Some Representative Compounds*				
	Bond dissociation energy			**Bond dissociation energy**	
Bond	**kJ/mol**	**(kcal/mol)**	**Bond**	**kJ/mol**	**(kcal/mol)**
Diatomic molecules					
H—H	435	(104)			
F—F	159	(38)	H—F	568	(136)
Cl—Cl	242	(58)	H—Cl	431	(103)
Br—Br	192	(46)	H—Br	366	(87.5)
I—I	150	(36)	H—I	297	(71)
Alkanes					
CH_3—H	435	(104)	CH_3—CH_3	368	(88)
CH_3CH_2—H	410	(98)	CH_3CH_2—CH_3	355	(85)
$CH_3CH_2CH_2$—H	410	(98)			
$(CH_3)_2CH$—H	397	(95)			
$(CH_3)_2CHCH_2$—H	410	(98)	$(CH_3)_2CH$—CH_3	351	(84)
$(CH_3)_3C$—H	380	(91)	$(CH_3)_3C$—CH_3	334	(80)
Alkyl halides					
CH_3—F	451	(108)	$(CH_3)_2CH$—F	439	(105)
CH_3—Cl	349	(83.5)	$(CH_3)_2CH$—Cl	339	(81)
CH_3—Br	293	(70)	$(CH_3)_2CH$—Br	284	(68)
CH_3—I	234	(56)	$(CH_3)_3C$—Cl	330	(79)
CH_3CH_2—Cl	338	(81)	$(CH_3)_3C$—Br	263	(63)
$CH_3CH_2CH_2$—Cl	343	(82)			
Water and alcohols					
HO—H	497	(119)	CH_3CH_2—OH	380	(91)
CH_3O—H	426	(102)	$(CH_3)_2CH$—OH	385	(92)
CH_3—OH	380	(91)	$(CH_3)_3C$—OH	380	(91)

*Bond dissociation energies refer to bond indicated in structural formula for each substance.
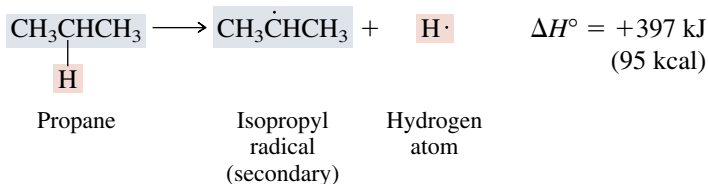
The energy required for homolytic bond cleavage is called the **bond dissociation energy (BDE).** A list of some bond dissociation energies is given in Table 4.3.

As the table indicates, C—H bond dissociation energies in alkanes are approximately 375 to 435 kJ/mol (90–105 kcal/mol). Homolysis of the H—CH_3 bond in methane gives methyl radical and requires 435 kJ/mol (104 kcal/mol). The dissociation energy of the H—CH_2CH_3 bond in ethane, which gives a primary radical, is somewhat less (410 kJ/mol, or 98 kcal/mol) and is consistent with the notion that ethyl radical (primary) is more stable than methyl.

The dissociation energy of the terminal C—H bond in propane is exactly the same as that of ethane. The resulting free radical is primary ($R\dot{C}H_2$) in both cases.

$$CH_3CH_2CH_2\text{—}H \longrightarrow CH_3CH_2\dot{C}H_2 + H\cdot \qquad \Delta H° = +410 \text{ kJ}$$
$$(98 \text{ kcal})$$

Propane   *n*-Propyl   Hydrogen
                 radical   atom
                 (primary)
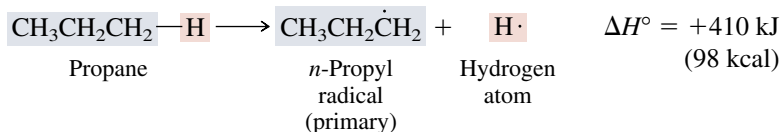
Note, however, that Table 4.3 includes two entries for propane. The second entry corresponds to the cleavage of a bond to one of the hydrogens of the methylene (CH_2) group. It requires slightly less energy to break a C—H bond in the methylene group than in the methyl group.

$$CH_3CHCH_3 \longrightarrow CH_3\dot{C}HCH_3 + H\cdot \qquad \Delta H° = +397 \text{ kJ}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad (95 \text{ kcal})$$

H

Propane   Isopropyl   Hydrogen
                 radical   atom
                 (secondary)

Since the starting material (propane) and one of the products (H·) are the same in both processes, the difference in bond dissociation energies is equal to the energy difference between an *n*-propyl radical (primary) and an isopropyl radical (secondary). As depicted in Figure 4.16, the secondary radical is 13 kJ/mol (3 kcal/mol) more stable than the primary radical.

Similarly, by comparing the bond dissociation energies of the two different types of C—H bonds in 2-methylpropane, we see that a tertiary radical is 30 kJ/mol (7 kcal/mol) more stable than a primary radical.

$$CH_3CHCH_2\text{—}H \longrightarrow CH_3CH\dot{C}H_2 + H\cdot \qquad \Delta H° = +410 \text{ kJ}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad (98 \text{ kcal})$$

$$\quad | \qquad\qquad\qquad\qquad\qquad | $$
$$\quad CH_3 \qquad\qquad\qquad\quad CH_3$$

2-Methylpropane   Isobutyl   Hydrogen
                         radical   atom
                         (primary)

$$\qquad H$$

$$CH_3\overset{|}{\underset{|}{C}}CH_3 \longrightarrow CH_3\dot{C}CH_3 + H\cdot \qquad \Delta H° = +380 \text{ kJ}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad (91 \text{ kcal})$$

$$\quad CH_3 \qquad\qquad\qquad CH_3$$

2-Methylpropane   *tert*-Butyl   Hydrogen
                         radical   atom
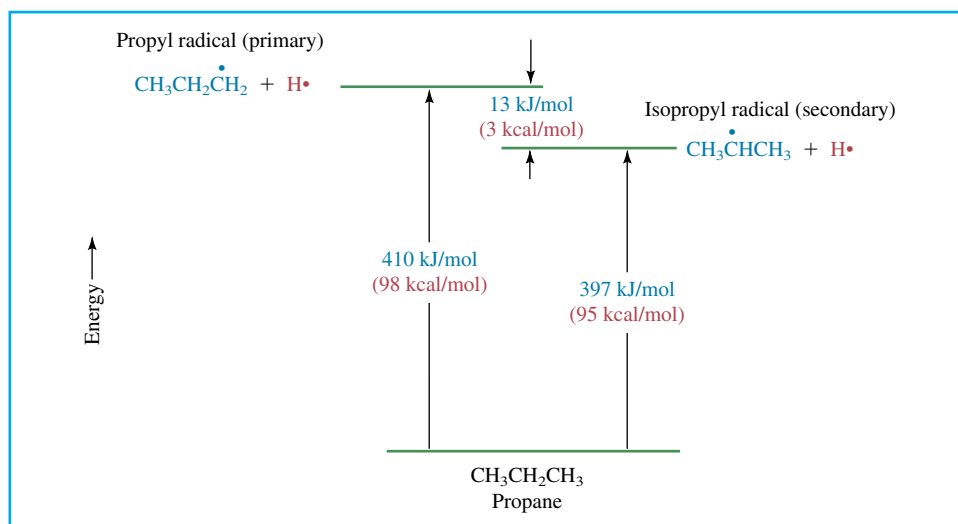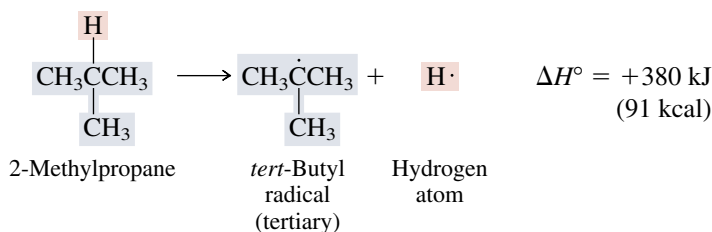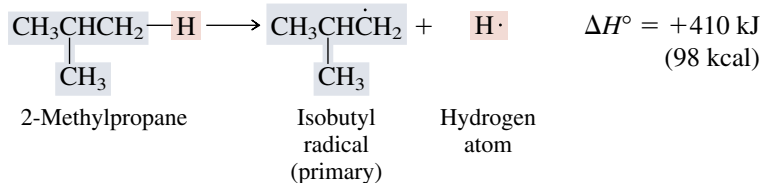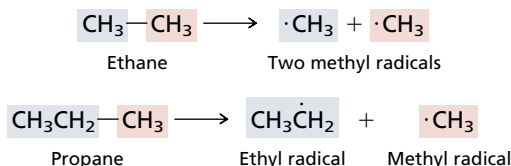   (tertiary)

FIGURE 4.16 Diagram showing how bond dissociation energies of methylene and methyl C—H bonds in propane reveal a difference in stabilities between two isomeric free radicals. The secondary radical is more stable than the primary.

Propyl radical (primary)
$CH_3CH_2\dot{C}H_2 + H\bullet$

13 kJ/mol
(3 kcal/mol)

Isopropyl radical (secondary)
$CH_3\dot{C}HCH_3 + H\bullet$

Energy →

410 kJ/mol
(98 kcal/mol)

397 kJ/mol
(95 kcal/mol)

$CH_3CH_2CH_3$
Propane

PROBLEM 4.16   Carbon–carbon bond dissociation energies have been measured for alkanes. Without referring to Table 4.3, identify the alkane in each of the following pairs that has the lower carbon–carbon bond dissociation energy, and explain the reason for your choice.

(a) Ethane or propane

(b) Propane or 2-methylpropane

(c) 2-Methylpropane or 2,2-dimethylpropane

SAMPLE SOLUTION   (a) First write the equations that describe homolytic carbon–carbon bond cleavage in each alkane.

$$CH_3\text{—}CH_3 \longrightarrow \cdot CH_3 + \cdot CH_3$$

Ethane   Two methyl radicals

$$CH_3CH_2\text{—}CH_3 \longrightarrow CH_3\dot{C}H_2 + \cdot CH_3$$

Propane   Ethyl radical   Methyl radical

Cleavage of the carbon–carbon bond in ethane yields two methyl radicals, whereas propane yields an ethyl radical and one methyl radical. Ethyl radical is more stable than methyl, and so less energy is required to break the carbon–carbon bond in propane than in ethane. The measured carbon–carbon bond dissociation energy in ethane is 368 kJ/mol (88 kcal/mol), and that in propane is 355 kJ/mol (85 kcal/mol).

Like carbocations, most free radicals are exceedingly reactive species—too reactive to be isolated but capable of being formed as transient intermediates in chemical reactions. Methyl radical, as we shall see in the following section, is an intermediate in the chlorination of methane.

4.18   MECHANISM OF METHANE CHLORINATION

The generally accepted mechanism for the chlorination of methane is presented in Figure 4.17. As we noted earlier (section 4.16), the reaction is normally carried out in the gas phase at high temperature. The reaction itself is strongly exothermic, but energy must be put into the system in order to get it going. This energy goes into breaking the weakest bond in the system, which, as we see from the bond dissociation energy data in Table 4.3, is the Cl—Cl bond with a bond dissociation energy of 242 kJ/mol (58 kcal/mol). The step in which Cl—Cl bond homolysis occurs is called the **initiation step.**

Each chlorine atom formed in the initiation step has seven valence electrons and is very reactive. Once formed, a chlorine atom abstracts a hydrogen atom from methane as shown in step 2 in Figure 4.17. Hydrogen chloride, one of the isolated products from the overall reaction, is formed in this step. A methyl radical is also formed, which then attacks a molecule of Cl_2 in step 3. Attack of methyl radical on Cl_2 gives chloromethane, the other product of the overall reaction, along with a chlorine atom which then cycles back to step 2, repeating the process. Steps 2 and 3 are called the **propagation steps** of the reaction and, when added together, give the overall equation for the reaction. Since one initiation step can result in a great many propagation cycles, the overall process is called a **free-radical chain reaction.**

> The bond dissociation energy of the other reactant, methane, is much higher. It is 435 kJ/mol (104 kcal/mol).

PROBLEM 4.17   Write equations for the initiation and propagation steps for the formation of dichloromethane by free-radical chlorination of chloromethane.

FIGURE 4.17 Equations describing the initiation and propagation steps in the free-radical mechanism for the chlorination of methane. Together the two propagation steps give the overall equation for the reaction.


(a) Initiation

Step 1: Dissociation of a chlorine molecule into two chlorine atoms:

Chlorine molecule → Two chlorine atoms

(b) Chain propagation

Step 2: Hydrogen atom abstraction from methane by a chlorine atom:

Chlorine atom + Methane → Hydrogen chloride + Methyl radical

Step 3: Reaction of methyl radical with molecular chlorine:

Chlorine molecule + Methyl radical → Chlorine atom + Chloromethane

(c) Sum of steps 2 and 3

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$

Methane Chlorine Chloromethane Hydrogen chloride

In practice, side reactions intervene to reduce the efficiency of the propagation steps. The chain sequence is interrupted whenever two odd-electron species combine to give an even-electron product. Reactions of this type are called **chain-terminating steps.** Some commonly observed chain-terminating steps in the chlorination of methane are shown in the following equations.

Combination of a methyl radical with a chlorine atom:

Methyl radical Chlorine atom → Chloromethane
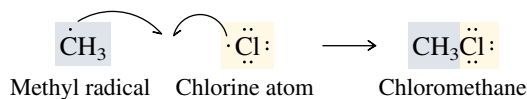
Combination of two methyl radicals:

Two methyl radicals → Ethane
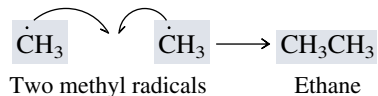
FROM BOND ENERGIES TO HEATS OF REACTION

You have seen that measurements of heats of reaction, such as heats of combustion, can provide quantitative information concerning the relative stability of constitutional isomers (Section 2.15) and stereoisomers (Section 3.12). The box in Section 2.15 described how heats of reaction can be manipulated arithmetically to generate heats of formation (ΔH_f°) for many molecules. The following material shows how two different sources of thermochemical information, heats of formation and bond dissociation energies (Table 4.3), can reveal whether a particular reaction is exothermic or endothermic and by how much.

Consider the chlorination of methane to chloromethane. The heats of formation of the reactants and products appear beneath the equation. These heats of formation for the chemical compounds are taken from published tabulations; the heat of formation of chlorine, as it is for all elements, is zero.

$$CH_4 \ + \ Cl_2 \ \longrightarrow \ CH_3Cl \ + \ HCl$$

$$\begin{array}{lcccc} \Delta H_f^\circ\text{:} & -74.8 & 0 & -81.9 & -92.3 \\ \text{(kJ/mol)} \end{array}$$
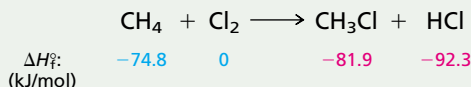
The overall heat of reaction is given by

$$\Delta H^\circ = \sum \text{(heats of formation of products)} - \sum \text{(heats of formation of reactants)}$$

$$\Delta H^\circ = (-81.9 \text{ kJ} - 92.3 \text{ kJ}) - (-74.8 \text{ kJ}) \ = -99.4 \text{ kJ}$$

Thus, the chlorination of methane is calculated to be an exothermic reaction on the basis of heat of formation data.

The same conclusion is reached using bond dissociation energies. The following equation shows the bond dissociation energies of the reactants and products taken from Table 4.3:
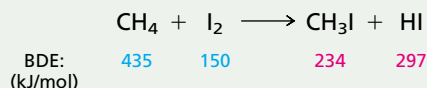
$$CH_4 \ + \ Cl_2 \ \longrightarrow \ CH_3Cl \ + \ HCl$$

$$\begin{array}{lcccc} \text{BDE:} & 435 & 242 & 349 & 431 \\ \text{(kJ/mol)} \end{array}$$
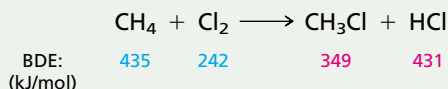
Because stronger bonds are formed at the expense of weaker ones, the reaction is exothermic and

$$\Delta H^\circ = \sum \text{(BDE of bonds broken)} - \sum \text{(BDE of bonds formed)}$$

$$\Delta H^\circ = (435 \text{ kJ} + 242 \text{ kJ}) - (349 \text{ kJ} + 431 \text{ kJ}) \ = -103 \text{ kJ}$$

This value is in good agreement with that obtained from heat of formation data.

Compare chlorination of methane with iodination. The relevant bond dissociation energies are given in the equation.

$$CH_4 \ + \ I_2 \ \longrightarrow \ CH_3I \ + \ HI$$

$$\begin{array}{lcccc} \text{BDE:} & 435 & 150 & 234 & 297 \\ \text{(kJ/mol)} \end{array}$$

$$\Delta H^\circ = \sum \text{(BDE of bonds broken)} - \sum \text{(BDE of bonds formed)}$$

$$\Delta H^\circ = (435 \text{ kJ} + 150 \text{ kJ}) - (234 \text{ kJ} + 297 \text{ kJ}) \ = +54 \text{ kJ}$$

A positive value for ΔH° signifies an **endothermic** reaction. The reactants are more stable than the products, and so iodination of alkanes is not a feasible reaction. You would not want to attempt the preparation of iodomethane by iodination of methane.

A similar analysis for fluorination of methane gives $\Delta H^\circ = -426$ kJ for its heat of reaction. Fluorination of methane is four times as exothermic as chlorination. A reaction this exothermic, if it also occurs at a rapid rate, can proceed with explosive violence.

Bromination of methane is exothermic, but less exothermic than chlorination. The value calculated from bond dissociation energies is $\Delta H^\circ = -30$ kJ. Although bromination of methane is energetically favorable, economic considerations cause most of the methyl bromide prepared commercially to be made from methanol by reaction with hydrogen bromide.
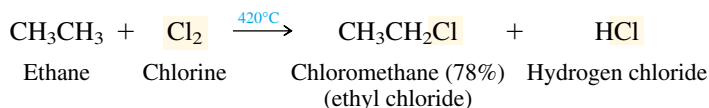
Combination of two chlorine atoms:

$$:\ddot{\overset{..}{Cl}}\cdot \quad \cdot\ddot{\overset{..}{Cl}}: \longrightarrow \quad Cl_2$$

Two chlorine atoms   Chlorine molecule
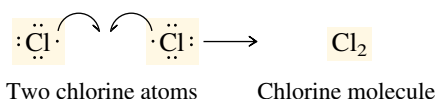
Termination steps are, in general, less likely to occur than the propagation steps. Each of the termination steps requires two free radicals to encounter each other in a medium that contains far greater quantities of other materials (methane and chlorine molecules) with which they can react. Although some chloromethane undoubtedly arises via direct combination of methyl radicals with chlorine atoms, most of it is formed by the propagation sequence shown in Figure 4.17.

4.19   HALOGENATION OF HIGHER ALKANES

Like the chlorination of methane, chlorination of ethane is carried out on an industrial scale as a high-temperature gas-phase reaction.

$$CH_3CH_3 + Cl_2 \xrightarrow{420°C} CH_3CH_2Cl + HCl$$

Ethane   Chlorine   Chloromethane (78%)   Hydrogen chloride
                                (ethyl chloride)

As in the chlorination of methane, it is often difficult to limit the reaction to monochlorination, and derivatives having more than one chlorine atom are also formed.

> **PROBLEM 4.18** Chlorination of ethane yields, in addition to ethyl chloride, a mixture of two isomeric dichlorides. What are the structures of these two dichlorides?

In the laboratory it is more convenient to use light, either visible or ultraviolet, as the source of energy to initiate the reaction. Reactions that occur when light energy is absorbed by a molecule are called **photochemical reactions.** Photochemical techniques permit the reaction of alkanes with chlorine to be performed at room temperature.

Photochemical energy is indicated by writing "light" or "hv" above the arrow. The symbol hv is equal to the energy of a light photon and will be discussed in more detail in Section 13.1.

$$\diamondsuit + Cl_2 \xrightarrow{hv} \diamondsuit-Cl + HCl$$

Cyclobutane   Chlorine   Chlorocyclobutane (73%)   Hydrogen
                                (cyclobutyl chloride)   chloride
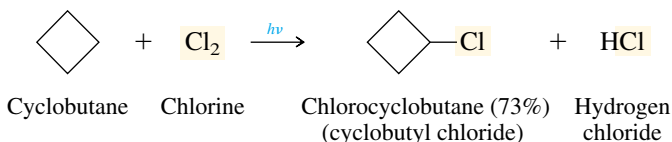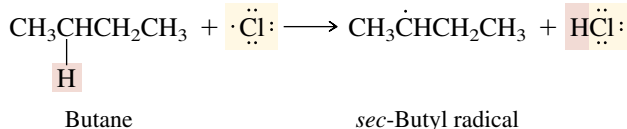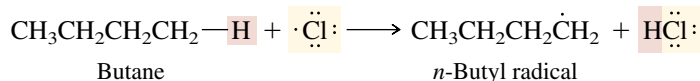
Methane, ethane, and cyclobutane share the common feature that each one can give only a *single* monochloro derivative. All the hydrogens of cyclobutane, for example, are equivalent, and substitution of any one gives the same product as substitution of any other. Chlorination of alkanes in which all the hydrogens are not equivalent is more complicated in that a mixture of every possible monochloro derivative is formed, as the chlorination of butane illustrates:
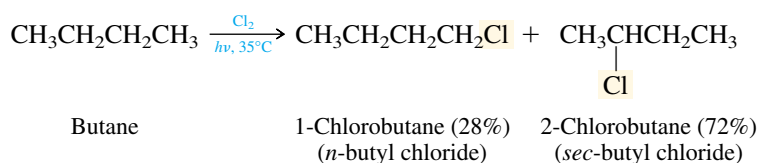
The percentages cited in this equation reflect the composition of the monochloride fraction of the product mixture rather than the isolated yield of each component.

$$CH_3CH_2CH_2CH_3 \xrightarrow[hv,\ 35°C]{Cl_2} CH_3CH_2CH_2CH_2Cl + CH_3\underset{\underset{Cl}{|}}{CH}CH_2CH_3$$

Butane   1-Chlorobutane (28%)   2-Chlorobutane (72%)
                        (*n*-butyl chloride)   (*sec*-butyl chloride)

These two products arise because in one of the propagation steps a chlorine atom may abstract a hydrogen atom from either a methyl or a methylene group of butane.
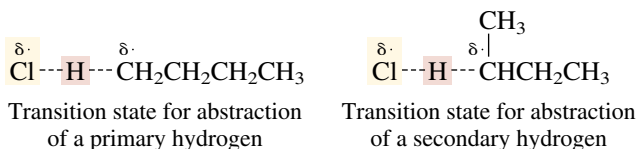
$$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{—H} + \cdot\ddot{\text{Cl}}: \longrightarrow \text{CH}_3\text{CH}_2\text{CH}_2\dot{\text{C}}\text{H}_2 + \text{H}\ddot{\text{Cl}}:$$

<div align="center">Butane   n-Butyl radical</div>

$$\text{CH}_3\text{CHCH}_2\text{CH}_3 + \cdot\ddot{\text{Cl}}: \longrightarrow \text{CH}_3\dot{\text{C}}\text{HCH}_2\text{CH}_3 + \text{H}\ddot{\text{Cl}}:$$
$$\quad\quad\; |$$
$$\quad\quad\; \text{H}$$

<div align="center">Butane   sec-Butyl radical</div>

The resulting free radicals react with chlorine to give the corresponding alkyl chlorides. Butyl radical gives only 1-chlorobutane; *sec*-butyl radical gives only 2-chlorobutane.

$$\text{CH}_3\text{CH}_2\text{CH}_2\dot{\text{C}}\text{H}_2 + \text{Cl}_2 \longrightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl} + \cdot\ddot{\text{Cl}}:$$

<div align="center">n-Butyl radical   1-Chlorobutane
(n-butyl chloride)</div>

$$\text{CH}_3\dot{\text{C}}\text{HCH}_2\text{CH}_3 + \text{Cl}_2 \longrightarrow \text{CH}_3\text{CHCH}_2\text{CH}_3 + \cdot\ddot{\text{Cl}}:$$
$$\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad | $$
$$\quad\quad\quad\quad\quad\quad\quad\quad\quad \text{Cl}$$

<div align="center">sec-Butyl radical   2-Chlorobutane
(sec-butyl chloride)</div>
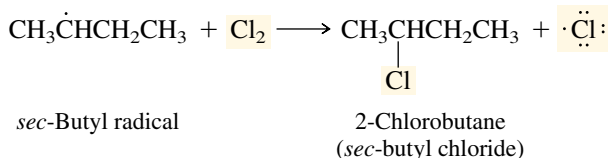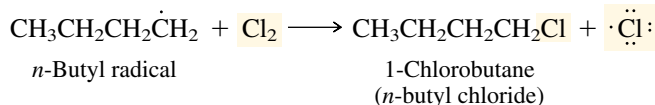
If every collision of a chlorine atom with a butane molecule resulted in hydrogen abstraction, the *n*-butyl/*sec*-butyl radical ratio and, therefore, the 1-chloro/2-chlorobutane ratio, would be given by the relative numbers of hydrogens in the two equivalent methyl groups of $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$ (six) compared with those in the two equivalent methylene groups (four). The product distribution expected on a *statistical* basis would be 60% 1-chlorobutane and 40% 2-chlorobutane. The *experimentally observed* product distribution, however, is 28% 1-chlorobutane and 72% 2-chlorobutane. *sec*-Butyl radical is therefore formed in greater amounts, and *n*-butyl radical in lesser amounts, than expected statistically.

The reason for this behavior stems from the greater stability of secondary compared with primary free radicals. The transition state for the step in which a chlorine atom abstracts a hydrogen from carbon has free-radical character at carbon.

$$\overset{\delta\cdot}{\text{Cl}}\text{---}\overset{}{\text{H}}\text{---}\overset{\delta\cdot}{\text{CH}}_2\text{CH}_2\text{CH}_2\text{CH}_3$$

$$\overset{\delta\cdot}{\text{Cl}}\text{---}\overset{}{\text{H}}\text{---}\overset{\delta\cdot}{\text{CH}}\text{CH}_2\text{CH}_3$$
with CH₃ above

<div align="center">Transition state for abstraction   Transition state for abstraction
of a primary hydrogen   of a secondary hydrogen</div>

A secondary hydrogen is abstracted faster than a primary hydrogen because the transition state with secondary radical character is more stable than the one with primary radical character. The same factors that stabilize a secondary radical stabilize a transition state with secondary radical character more than one with primary radical character. Hydrogen atom abstraction from a CH_2 group occurs faster than from a CH_3 group. We can calculate how much faster a *single* secondary hydrogen is abstracted compared with a *single* primary hydrogen from the experimentally observed product distribution.
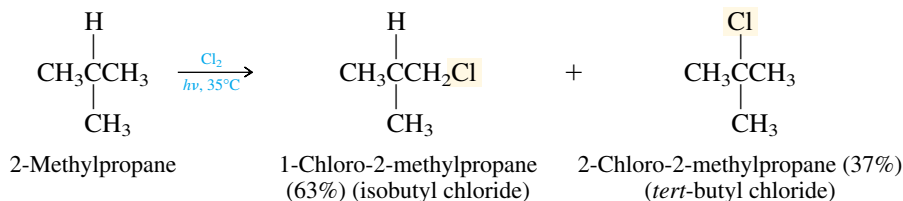
$$\frac{72\% \text{ 2-chlorobutane}}{28\% \text{ 1-chlorobutane}} = \frac{\text{rate of secondary H abstraction} \times 4 \text{ secondary hydrogens}}{\text{rate of primary H abstraction} \times 6 \text{ primary hydrogens}}$$

$$\frac{\text{Rate of secondary H abstraction}}{\text{Rate of primary H abstraction}} = \frac{72}{28} \times \frac{6}{4} = \frac{3.9}{1}$$

A single secondary hydrogen in butane is abstracted by a chlorine atom 3.9 times as fast as a single primary hydrogen.

> **PROBLEM 4.19**   Assuming the relative rate of secondary to primary hydrogen atom abstraction to be the same in the chlorination of propane as it is in that of butane, calculate the relative amounts of propyl chloride and isopropyl chloride obtained in the free-radical chlorination of propane.

A similar study of the chlorination of 2-methylpropane established that a tertiary hydrogen is removed 5.2 times faster than each primary hydrogen.

H			Cl		
CH₃CCH₃	$\xrightarrow[hv, 35°C]{Cl_2}$	CH₃CCH₂Cl	+	CH₃CCH₃	
CH₃		CH₃		CH₃	
2-Methylpropane		1-Chloro-2-methylpropane (63%) (isobutyl chloride)		2-Chloro-2-methylpropane (37%) (*tert*-butyl chloride)	

In summary then, the chlorination of alkanes is not very selective. The various kinds of hydrogens present in a molecule (tertiary, secondary, and primary) differ by only a factor of 5 in the relative rate at which each reacts with a chlorine atom.

$$R_3CH \quad > \quad R_2CH_2 \quad > \quad RCH_3$$

(tertiary)   (secondary)   (primary)

Relative rate (chlorination)   5.2   3.9   1
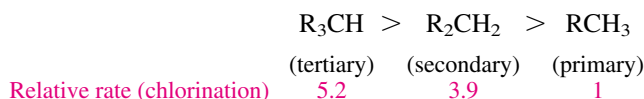
Bromine reacts with alkanes by a free-radical chain mechanism analogous to that of chlorine. There is an important difference between chlorination and bromination, however. Bromination is highly selective for substitution of *tertiary hydrogens*. The spread in reactivity among primary, secondary, and tertiary hydrogens is greater than 10^3.

$$R_3CH \quad > \quad R_2CH_2 \quad > \quad RCH_3$$

(tertiary)   (secondary)   (primary)

Relative rate (bromination)   1640   82   1
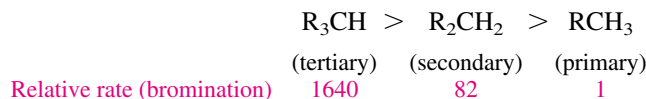
In practice, this means that when an alkane contains primary, secondary, and tertiary hydrogens, it is usually only the tertiary hydrogen that is replaced by bromine.

The yield cited in this reaction is the isolated yield of purified product. Isomeric bromides constitute only a tiny fraction of the crude product.

$$\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{CH_3CCH_2CH_2CH_3}} + Br_2 \xrightarrow[60°C]{hv} \underset{\underset{CH_3}{|}}{\overset{\overset{Br}{|}}{CH_3CCH_2CH_2CH_3}} + HBr$$

2-Methylpentane   Bromine   2-Bromo-2-methylpentane (76% isolated yield)   Hydrogen bromide
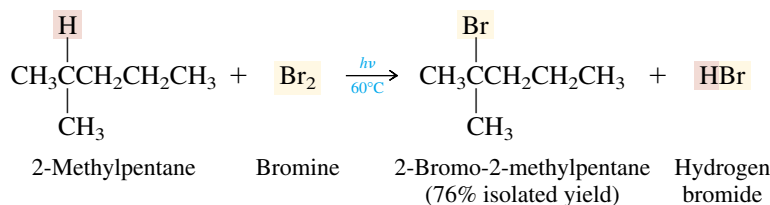
PROBLEM 4.20   Give the structure of the principal organic product formed by free-radical bromination of each of the following:

(a) Methylcyclopentane   (c) 2,2,4-Trimethylpentane

(b) 1-Isopropyl-1-methylcyclopentane

SAMPLE SOLUTION   (a) Write the structure of the starting hydrocarbon, and identify any tertiary hydrogens that are present. The only tertiary hydrogen in methylcyclopentane is the one attached to C-1. This is the one replaced by bromine.

| Methylcyclopentane | 1-Bromo-1-methylcyclopentane |
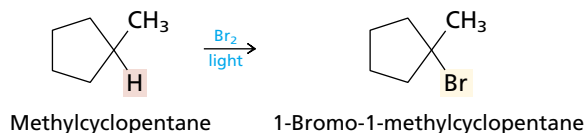
This difference in selectivity between chlorination and bromination of alkanes needs to be kept in mind when one wishes to prepare an alkyl halide from an alkane:

1. Since chlorination of an alkane yields every possible monochloride, it is used only when all the hydrogens in an alkane are equivalent.

2. Bromination is normally used only to prepare tertiary alkyl bromides from alkanes.

Selectivity is not an issue in the conversion of alcohols to alkyl halides. Except for certain limitations to be discussed in Section 8.15, the location of the halogen substituent in the product corresponds to that of the hydroxyl group in the starting alcohol.

4.20 SUMMARY

Chemical reactivity and functional group transformations involving the preparation of alkyl halides from alcohols and from alkanes are the main themes of this chapter. Although the conversions of an alcohol or an alkane to an alkyl halide are both classified as substitutions, they proceed by very different mechanisms.

Section 4.1   Alcohols and alkyl halides may be named using either **substitutive** or **functional class** nomenclature. In substitutive nomenclature alkyl halides are named as halogen derivatives of alkanes. The parent is the longest continuous chain that bears the halogen substituent, and in the absence of other substituents the chain is numbered from the direction that gives the lowest number to the carbon that bears the halogen. The functional class names of alkyl halides begin with the name of the alkyl group and end with the halide as a separate word.

$CH_3CHCH_2CH_2CH_2CH_3$ Substitutive name: 2-Bromohexane
| Functional class name: 1-Methylpentyl bromide
Br
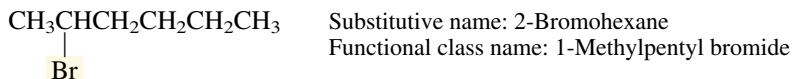
Section 4.2   The substitutive names of alcohols are derived by replacing the -*e* ending of an alkane with -*ol*. Functional class names of alcohols begin with the name of the alkyl group and end in the word "alcohol."

$CH_3CHCH_2CH_2CH_2CH_3$ Substitutive name: 2-Hexanol
| Functional class name: 1-Methylpentyl alcohol
OH
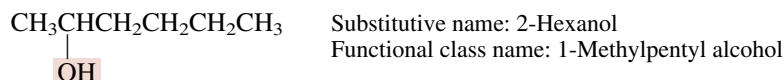
Section 4.3   Alcohols (X = OH) and alkyl halides (X = F, Cl, Br, or I) are classified as primary, secondary, or tertiary according to the degree of substitution at the carbon that bears the functional group.

$$\underset{\text{Primary}}{RCH_2X} \qquad \underset{\text{Secondary}}{\underset{|}{\underset{X}{RCHR'}}} \qquad \underset{\text{Tertiary}}{\overset{\overset{R''}{|}}{\underset{|}{\underset{X}{RCR'}}}}$$
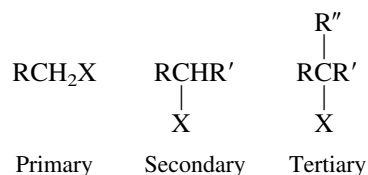
Section 4.4   The halogens (especially fluorine and chlorine) and oxygen are more electronegative than carbon, and the carbon–halogen bond in alkyl halides and the carbon–oxygen bond in alcohols are polar. Carbon is the positive end of the dipole and halogen or oxygen the negative end.

Section 4.5   Dipole/induced-dipole and dipole–dipole attractive forces make alcohols higher boiling than alkanes of similar molecular weight. The attractive force between —OH groups is called **hydrogen bonding.**

$$\underset{H}{\overset{R}{\diagdown}}O\text{---}H\text{—}O\overset{R}{\diagup}$$
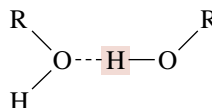
Hydrogen bonding between the hydroxyl group of an alcohol and water makes the water-solubility of alcohols greater than that of hydrocarbons. Low-molecular-weight alcohols [CH_3OH, CH_3CH_2OH, $CH_3CH_2CH_2OH$, and $(CH_3)_2CHOH$] are soluble in water in all proportions. Alkyl halides are insoluble in water.

Section 4.6   **Brønsted acids** are proton donors; **Brønsted bases** are proton acceptors. Strong acids transfer protons to alcohols to form **alkyloxonium ions.** An alkyloxonium ion is the **conjugate acid** of an alcohol.

$$\underset{\substack{\text{Alcohol}\\\text{(base)}}}{\overset{R}{\underset{H}{\diagdown}}\ddot{O}\colon} + H\text{—}\overset{..}{\underset{..}{Cl}}\colon \;\rightleftharpoons\; \underset{\substack{\text{Alkyloxonium ion}\\\text{(conjugate acid)}}}{\overset{R}{\underset{H}{\diagdown}}\overset{+}{\ddot{O}}\text{—}H} \;+\; \overset{..}{\underset{..}{\ddot{Cl}}}\colon^{-}$$
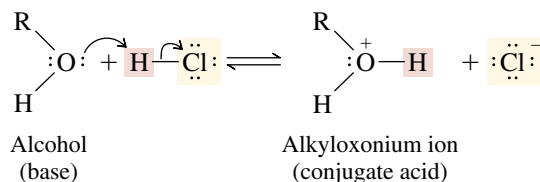
Section 4.7   Proton transfer from a Brønsted acid to the oxygen of water is a single-step process and is very fast. It is a **bimolecular, concerted** process.

Section 4.8   See Table 4.4

Section 4.9   Secondary and tertiary alcohols react with hydrogen halides by a mechanism that involves formation of a carbocation intermediate in the rate-determining step.

$$(1)\quad \underset{\text{Alcohol}}{ROH} \;+\; \underset{\substack{\text{Hydrogen}\\\text{halide}}}{HX} \;\overset{\text{fast}}{\rightleftharpoons}\; \underset{\substack{\text{Alkyloxonium}\\\text{ion}}}{\overset{+}{ROH_2}} \;+\; \underset{\substack{\text{Halide}\\\text{anion}}}{X^-}$$
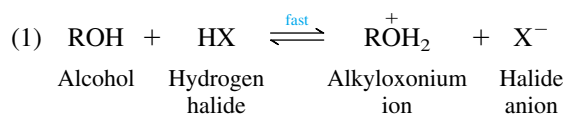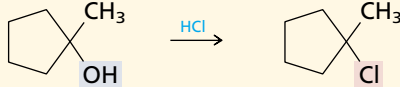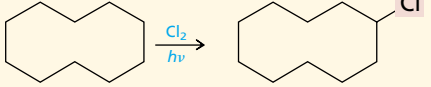
| TABLE 4.4	Conversions of Alcohols and Alkanes to Alkyl Halides

Reaction (section) and comments	General equation and specific example(s)
Reactions of alcohols with hydrogen halides (Section 4.8) Alcohols react with hydrogen halides to yield alkyl halides. The reaction is useful as a synthesis of alkyl halides. The reactivity of hydrogen halides decreases in the order HI > HBr > HCl > HF. Alcohol reactivity decreases in the order tertiary > secondary > primary > methyl.	ROH + HX $\longrightarrow$ RX + H_2O Alcohol Hydrogen Alkyl Water halide halide 1-Methylcyclopentanol $\xrightarrow{HCl}$ 1-Chloro-1-methylcyclopentane (96%)
Reaction of alcohols with thionyl chloride (Section 4.14) Thionyl chloride is a synthetic reagent used to convert alcohols to alkyl chlorides.	ROH + $SOCl_2$ $\longrightarrow$ RCl + SO_2 + HCl Alcohol Thionyl Alkyl Sulfur Hydrogen chloride chloride dioxide chloride $CH_3CH_2CH_2CH_2CH_2OH \xrightarrow[\text{pyridine}]{SOCl_2} CH_3CH_2CH_2CH_2CH_2Cl$ 1-Pentanol 1-Chloropentane (80%)
Reaction of alcohols with phosphorus tribromide (Section 4.14) As an alternative to converting alcohols to alkyl bromides with hydrogen bromide, the inorganic reagent phosphorus tribromide is sometimes used.	$3ROH$ + PBr_3 $\longrightarrow$ $3RBr$ + H_3PO_3 Alcohol Phosphorus Alkyl Phosphorous tribromide bromide acid $CH_3CHCH_2CH_2CH_3 \xrightarrow{PBr_3} CH_3CHCH_2CH_2CH_3$ with OH with Br 2-Pentanol 2-Bromopentane (67%)

Free-radical halogenation of alkanes (Sections 4.15 through 4.19) Alkanes react with halogens by substitution of a halogen for a hydrogen on the alkane. The reactivity of the halogens decreases in the order $F_2 > Cl_2 > Br_2 > I_2$. The ease of replacing a hydrogen decreases in the order tertiary > secondary > primary > methyl. Chlorination is not very selective and so is used only when all the hydrogens of the alkane are equivalent. Bromination is highly selective, replacing tertiary hydrogens much more readily than secondary or primary ones.	RH + X_2 $\longrightarrow$ RX + HX
	 Alkane Halogen Alkyl Hydrogen
	                         halide halide
	
	 Cyclodecane $\xrightarrow[hv]{Cl_2}$ Cyclodecyl chloride (64%)
	
	 $(CH_3)_2CHC(CH_3)_3 \xrightarrow[hv]{Br_2} (CH_3)_2CC(CH_3)_3$
	                                              with Br
	 2,2,3-Trimethylbutane 2-Bromo-2,3,3-trimethylbutane (80%)

(2) $\overset{+}{R}OH_2$ $\xrightarrow{\text{slow}}$ R^+ + H_2O

　　Alkyloxonium ion   Carbocation   Water

(3) R^+ + X^- $\xrightarrow{\text{fast}}$ RX

　　Carbocation   Halide ion   Alkyl halide
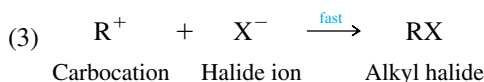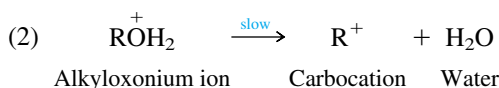
Section 4.10   Carbocations contain a positively charged carbon with only three atoms or groups attached to it. This carbon is sp^2-hybridized and has a vacant $2p$ orbital.
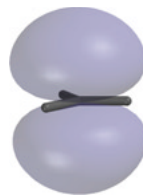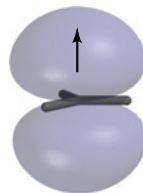
Carbocations are stabilized by alkyl substituents attached directly to the positively charged carbon. Alkyl groups are *electron-releasing* substituents. Stability increases in the order:
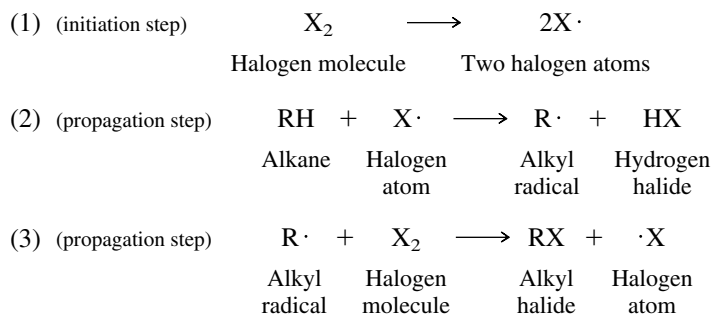
(least stable) $CH_3^+ < R_2CH^+ < R_3C^+$ (most stable)
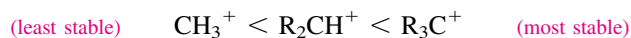
Carbocations are strongly **electrophilic** (Lewis acids) and react with **nucleophiles** (Lewis bases).

Section 4.11   The conversion of an alcohol to an alkyl halide on reaction with a hydrogen halide is a **nucleophilic substitution.** Nucleophilic substitutions (S_N) are classified as S_N1 or S_N2 according to whether the rate-determining step is unimolecular or bimolecular.

Section 4.12   The rates at which alcohols are converted to alkyl halides depends on the rate of carbocation formation: tertiary alcohols are most reactive; primary alcohols and methanol are least reactive.

Section 4.13   Primary alcohols do not react with hydrogen halides by way of carbocation intermediates. The nucleophilic species (Br^-) attacks the alkyloxonium ion and "pushes off" a water molecule from carbon in a bimolecular step. This step is rate-determining, and the mechanism is S_N2.

Section 4.14   See Table 4.4

Section 4.15   See Table 4.4

Section 4.16   Methane reacts with Cl_2 to give chloromethane, dichloromethane, trichloromethane, and tetrachloromethane.

Section 4.17   Chlorination of methane, and halogenation of alkanes generally, proceed by way of **free-radical** intermediates. Alkyl radicals are neutral and have an unpaired electron on carbon.

Like carbocations, free radicals are stabilized by alkyl substituents. The order of free-radical stability parallels that of carbocation stability.

Section 4.18   The elementary steps (1) through (3) describe a free-radical chain mechanism for the reaction of an alkane with a halogen.
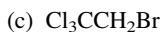
(1) (initiation step) X_2 $\longrightarrow$ $2X\cdot$

Halogen molecule   Two halogen atoms

(2) (propagation step) RH + $X\cdot$ $\longrightarrow$ $R\cdot$ + HX

Alkane   Halogen   Alkyl   Hydrogen
atom   radical   halide

(3) (propagation step) $R\cdot$ + X_2 $\longrightarrow$ RX + $\cdot X$

Alkyl   Halogen   Alkyl   Halogen
radical   molecule   halide   atom

Section 4.19   See Table 4.4

PROBLEMS

4.21 Write structural formulas for each of the following alcohols and alkyl halides:

(a) Cyclobutanol

(b) *sec*-Butyl alcohol

(c) 3-Heptanol

(d) *trans*-2-Chlorocyclopentanol

(e) 2,6-Dichloro-4-methyl-4-octanol

(f) *trans*-4-*tert*-Butylcyclohexanol

(g) 1-Cyclopropylethanol

(h) 2-Cyclopropylethanol

4.22 Name each of the following compounds according to substitutive IUPAC nomenclature:

(a) $(CH_3)_2CHCH_2CH_2CH_2Br$

(b) $(CH_3)_2CHCH_2CH_2CH_2OH$

(c) Cl_3CCH_2Br

(d) $Cl_2CHCHBr$
      |
      Cl

(e) CF_3CH_2OH

(f)

(g)

(h)

(i)
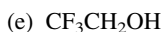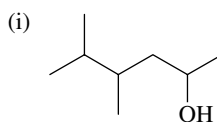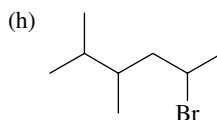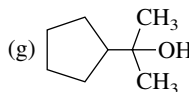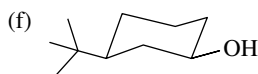
4.23 Write structural formulas, or build molecular models for all the constitutionally isomeric alcohols of molecular formula $C_5H_{12}O$. Assign a substitutive and a functional class name to each one, and specify whether it is a primary, secondary, or tertiary alcohol.

4.24 A hydroxyl group is a somewhat "smaller" substituent on a six-membered ring than is a methyl group. That is, the preference of a hydroxyl group for the equatorial orientation is less pronounced than that of a methyl group. Given this information, write structural formulas or build molecular models for all the isomeric methylcyclohexanols, showing each one in its most stable conformation. Give the substitutive IUPAC name for each isomer.
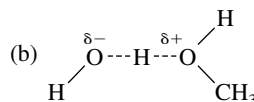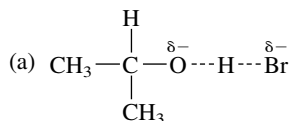
4.25 By assuming that the heat of combustion of the cis isomer was larger than the trans, structural assignments were made many years ago for the stereoisomeric 2-, 3-, and 4-methylcyclohexanols. This assumption is valid for two of the stereoisomeric pairs but is incorrect for the other. For which pair of stereoisomers is the assumption incorrect? Why?
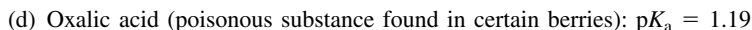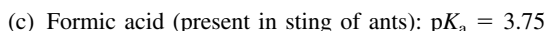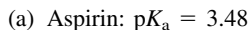
4.26 (a) *Menthol,* used to flavor various foods and tobacco, is the most stable stereoisomer of 2-isopropyl-5-methylcyclohexanol. Draw or make a molecular model of its most stable conformation. Is the hydroxyl group cis or trans to the isopropyl group? To the methyl group?

(b) *Neomenthol* is a stereoisomer of menthol. That is, it has the same constitution but differs in the arrangement of its atoms in space. Neomenthol is the second most stable stereoisomer of 2-isopropyl-5-methylcyclohexanol; it is less stable than menthol but more stable than any other stereoisomer. Write the structure, or make a molecular model of neomenthol in its most stable conformation.

4.27 Each of the following pairs of compounds undergoes a Brønsted acid–base reaction for which the equilibrium lies to the right. Give the products of each reaction, and identify the acid, the base, the conjugate acid, and the conjugate base.

(a) $HI + HO^- \rightleftharpoons$

(b) $CH_3CH_2O^- + CH_3\overset{\overset{O}{\|}}{C}OH \rightleftharpoons$

(c) $HF + H_2N^- \rightleftharpoons$

(d) $CH_3\overset{\overset{O}{\|}}{C}O^- + HCl \rightleftharpoons$

(e) $(CH_3)_3CO^- + H_2O \rightleftharpoons$

(f) $(CH_3)_2CHOH + H_2N^- \rightleftharpoons$

(g) $F^- + H_2SO_4 \rightleftharpoons$
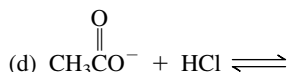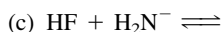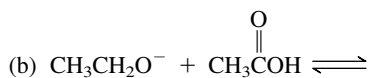
4.28 Transition-state representations are shown for two acid–base reactions. For each one, write the equation for the reaction it represents in the direction for which the equilibrium lies to the right. Label the acid, the base, the conjugate acid, and the conjugate base, and use curved arrows to show the flow of electrons.
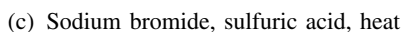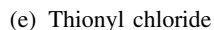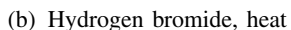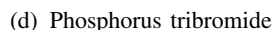
(a)
$$CH_3 - \overset{\overset{H}{|}}{\underset{\underset{CH_3}{|}}{C}} - \overset{\delta-}{O} \cdots H \cdots \overset{\delta-}{Br}$$

(b)
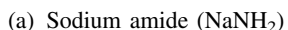$$\underset{H}{\overset{\delta-}{O}} \cdots H \cdots \overset{\delta+}{\underset{CH_3}{O}}\overset{H}{}$$

4.29 Calculate K_a for each of the following acids, given its pK_a. Rank the compounds in order of decreasing acidity.
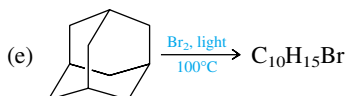
(a) Aspirin: pK_a = 3.48

(b) Vitamin C (ascorbic acid): pK_a = 4.17

(c) Formic acid (present in sting of ants): pK_a = 3.75

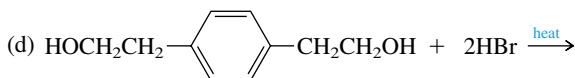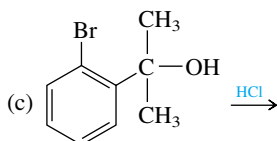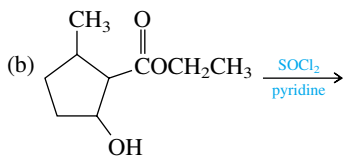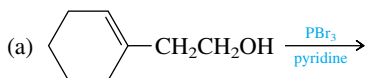(d) Oxalic acid (poisonous substance found in certain berries): pK_a = 1.19

4.30 The pK_a's of methanol (CH_3OH) and methanethiol (CH_3SH) are 16 and 11, respectively. Which is more basic, $KOCH_3$ or $KSCH_3$?

4.31 Write a chemical equation for the reaction of 1-butanol with each of the following:

(a) Sodium amide ($NaNH_2$)

(b) Hydrogen bromide, heat

(c) Sodium bromide, sulfuric acid, heat

(d) Phosphorus tribromide

(e) Thionyl chloride

4.32 Each of the following reactions has been described in the chemical literature and involves an organic starting material somewhat more complex than those we have encountered so far. Nevertheless, on the basis of the topics covered in this chapter, you should be able to write the structure of the principal organic product of each reaction.

(a) [cyclohexene]—CH$_2$CH$_2$OH $\xrightarrow[\text{pyridine}]{\text{PBr}_3}$

(b) [cyclopentane with CH$_3$, COCH$_2$CH$_3$ (C=O), OH] $\xrightarrow[\text{pyridine}]{\text{SOCl}_2}$

(c) [benzene with Br, C(CH$_3$)$_2$—OH] $\xrightarrow{\text{HCl}}$

(d) HOCH$_2$CH$_2$—[benzene]—CH$_2$CH$_2$OH + 2HBr $\xrightarrow{\text{heat}}$

(e) [adamantane] $\xrightarrow[\text{100°C}]{\text{Br}_2, \text{light}}$ C$_{10}$H$_{15}$Br

4.33 Select the compound in each of the following pairs that will be converted to the corresponding alkyl bromide more rapidly on being treated with hydrogen bromide. Explain the reason for your choice.

(a) 1-Butanol or 2-butanol

(b) 2-Methyl-1-butanol or 2-butanol

(c) 2-Methyl-2-butanol or 2-butanol

(d) 2-Methylbutane or 2-butanol

(e) 1-Methylcyclopentanol or cyclohexanol

(f) 1-Methylcyclopentanol or *trans*-2-methylcyclopentanol

(g) 1-Cyclopentylethanol or 1-ethylcyclopentanol

4.34 Assuming that the rate-determining step in the reaction of cyclohexanol with hydrogen bromide to give cyclohexyl bromide is unimolecular, write an equation for this step. Use curved arrows to show the flow of electrons.
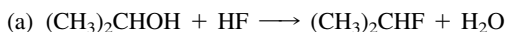
4.35 Assuming that the rate-determining step in the reaction of 1-hexanol with hydrogen bromide to give 1-bromohexane is an attack by a nucleophile on an alkyloxonium ion, write an equation for this step. Use curved arrows to show the flow of electrons.
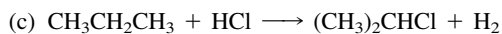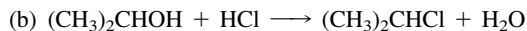
4.36 Two stereoisomers of 1-bromo-4-methylcyclohexane are formed when *trans*-4-methylcyclohexanol reacts with hydrogen bromide. Write structural formulas or make molecular models of:

(a) *trans*-4-Methylcylohexanol

(b) The carbocation intermediate in this reaction

(c) The two stereoisomers of 1-bromo-4-methylcyclohexane

4.37 Basing your answers on the bond dissociation energies in Table 4.3, calculate which of the following reactions are endothermic and which are exothermic:

(a) (CH$_3$)$_2$CHOH + HF $\longrightarrow$ (CH$_3$)$_2$CHF + H$_2$O

(b) $(CH_3)_2CHOH + HCl \longrightarrow (CH_3)_2CHCl + H_2O$

(c) $CH_3CH_2CH_3 + HCl \longrightarrow (CH_3)_2CHCl + H_2$

4.38 By carrying out the reaction at $-78°C$ it is possible to fluorinate 2,2-dimethylpropane to yield $(CF_3)_4C$. Write a balanced chemical equation for this reaction.

4.39 In a search for fluorocarbons having anesthetic properties, 1,2-dichloro-1,1-difluoropropane was subjected to photochemical chlorination. Two isomeric products were obtained, one of which was identified as 1,2,3-trichloro-1,1-difluoropropane. What is the structure of the second compound?

4.40 Among the isomeric alkanes of molecular formula C_5H_{12}, identify the one that on photochemical chlorination yields

(a) A single monochloride

(c) Four isomeric monochlorides

(b) Three isomeric monochlorides

(d) Two isomeric dichlorides

4.41 In both the following exercises, assume that all the methylene groups in the alkane are equally reactive as sites of free-radical chlorination.

(a) Photochemical chlorination of heptane gave a mixture of monochlorides containing 15% 1-chloroheptane. What other monochlorides are present? Estimate the percentage of each of these additional $C_7H_{15}Cl$ isomers in the monochloride fraction.

(b) Photochemical chlorination of dodecane gave a monochloride fraction containing 19% 2-chlorododecane. Estimate the percentage of 1-chlorododecane present in that fraction.

4.42 Photochemical chlorination of 2,2,4-trimethylpentane gives four isomeric monochlorides.

(a) Write structural formulas for these four isomers.

(b) The two primary chlorides make up 65% of the monochloride fraction. Assuming that all the primary hydrogens in 2,2,4-trimethylpentane are equally reactive, estimate the percentage of each of the two primary chlorides in the product mixture.

4.43 Photochemical chlorination of pentane gave a mixture of three isomeric monochlorides. The principal monochloride constituted 46% of the total, and the remaining 54% was approximately a $1 : 1$ mixture of the other two isomers. Write structural formulas for the three monochloride isomers and specify which one was formed in greatest amount. (Recall that a secondary hydrogen is abstracted three times faster by a chlorine atom than a primary hydrogen.)

4.44 Cyclopropyl chloride has been prepared by the free-radical chlorination of cyclopropane. Write a stepwise mechanism for this reaction.

4.45 Deuterium oxide (D_2O) is water in which the protons (^1H) have been replaced by their heavier isotope deuterium (^2H). It is readily available and is used in a variety of mechanistic studies in organic chemistry and biochemistry. When D_2O is added to an alcohol (ROH), deuterium replaces the proton of the hydroxyl group.

$$ROH + D_2O \Longrightarrow ROD + DOH$$
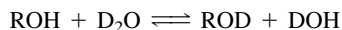
The reaction takes place extremely rapidly, and if D_2O is present in excess, all the alcohol is converted to ROD. This hydrogen–deuterium exchange can be catalyzed by either acids or bases. If D_3O^+ is the catalyst in acid solution and DO^- the catalyst in base, write reasonable reaction mechanisms for the conversion of ROH to ROD under conditions of (a) acid catalysis and (b) base catalysis.