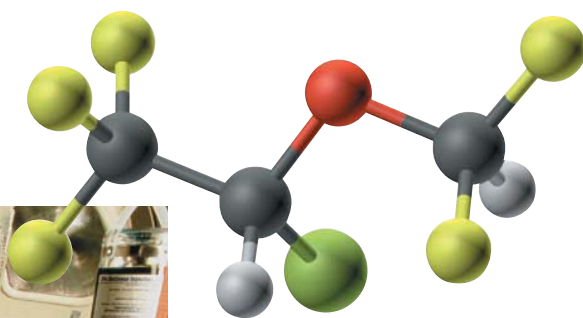


08



Alcohols, Ethers, and Thiols

An anesthesiologist administers isoflurane to a patient before surgery. The discovery that inhaling ethers could make a patient insensitive to pain revolutionized the practice of medicine. Inset: A model of isoflurane, $\text{CF}_3\text{CHClOCHF}_2$, a halogenated ether widely used as an inhalation anesthetic in both human and veterinary medicine. (Alan Levenson/Stone/Getty Images)

KEY QUESTIONS

- 8.1 What Are Alcohols?
- 8.2 What Are the Characteristic Reactions of Alcohols?
- 8.3 What Are Ethers?
- 8.4 What Are Epoxides?
- 8.5 What Are Thiols?
- 8.6 What Are the Characteristic Reactions of Thiols?

HOW TO

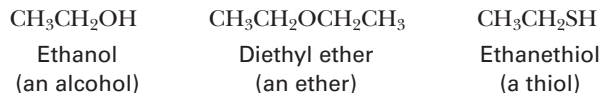
- 8.1 How to Name Cyclic Alcohols
- 8.2 How to Predict Relative Boiling Points of Compounds of Similar Molecular Weight

- 8.3 How to Predict the Position of Equilibrium of an Acid–Base Reaction
- 8.4 How to Complete a Dehydration Reaction
- 8.5 How to Predict the Product of an Epoxidation Reaction

CHEMICAL CONNECTIONS

- 8A Nitroglycerin: An Explosive and a Drug
- 8B Blood Alcohol Screening
- 8C Ethylene Oxide: A Chemical Sterilant

IN THIS CHAPTER, we study the physical and chemical properties of alcohols and ethers, two classes of oxygen-containing compounds we have seen as products of chemical reactions (Sections 5.3B and 7.4). We also study thiols, a class of sulfur-containing compounds. Thiols are like alcohols in structure, except that they contain an —SH group rather than an —OH group.



These three compounds are certainly familiar to you. Ethanol is the fuel additive in gasoline, the alcohol in alcoholic beverages, and an important industrial and laboratory solvent. Diethyl ether was the first inhalation anesthetic used in general surgery. It is also an important industrial and laboratory solvent. Ethanethiol, like other low-molecular-weight thiols, has a stench. Smells such as those from skunks, rotten eggs, and sewage are caused by thiols.

Alcohols are particularly important in both laboratory and biochemical transformations of organic compounds. They can be converted into other types of compounds, such as alkenes, haloalkanes, aldehydes, ketones, carboxylic acids, and esters. Not only can alcohols be converted to these compounds, but they also can be prepared from them. Thus, alcohols play a central role in the interconversion of organic functional groups.

8.1 What Are Alcohols?

A. Structure

Alcohol A compound containing an —OH (hydroxyl) group bonded to an sp^3 hybridized carbon.

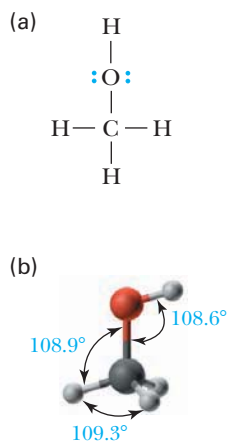


FIGURE 8.1 Methanol, CH_3OH . (a) Lewis structure and (b) ball-and-stick model. The measured $\text{H}-\text{O}-\text{C}$ bond angle in methanol is 108.6° , very close to the tetrahedral angle of 109.5° .

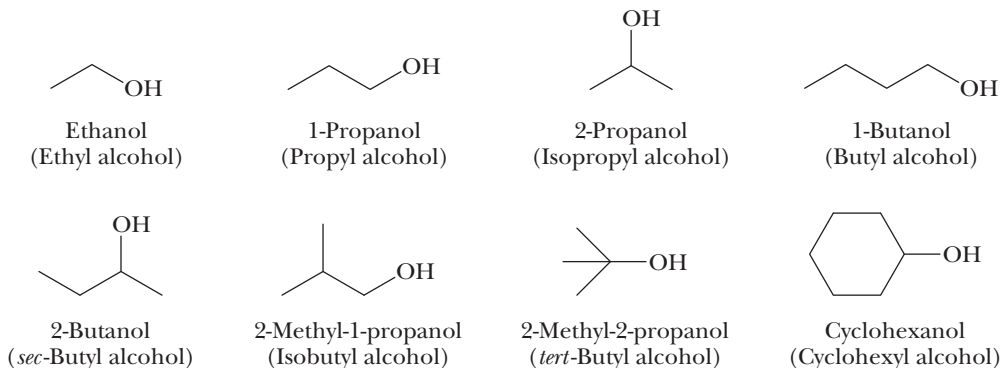
The functional group of an **alcohol** is an —OH (**hydroxyl**) group bonded to an sp^3 hybridized carbon atom (Section 1.7A). The oxygen atom of an alcohol is also sp^3 hybridized. Two sp^3 hybrid orbitals of oxygen form sigma bonds to atoms of carbon and hydrogen. The other two sp^3 hybrid orbitals of oxygen each contain an unshared pair of electrons. Figure 8.1 shows a Lewis structure and ball-and-stick model of methanol, CH_3OH , the simplest alcohol.

B. Nomenclature

We derive the IUPAC names for alcohols in the same manner as those for alkanes, with the exception that the ending of the parent alkane is changed from *-e* to *-ol*. The ending *-ol* tells us that the compound is an alcohol.

1. Select, as the parent alkane, the longest chain of carbon atoms that contains the —OH, and number that chain from the end closer to the —OH group. In numbering the parent chain, the location of the —OH group takes precedence over alkyl groups and halogens.
2. Change the suffix of the parent alkane from *-e* to *-ol* (Section 3.5), and use a number to show the location of the —OH group. For cyclic alcohols, numbering begins at the carbon bearing the —OH group.
3. Name and number substituents and list them in alphabetical order.

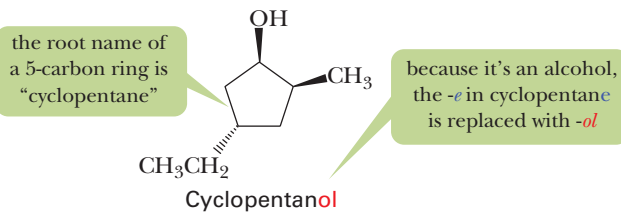
To derive common names for alcohols, we name the alkyl group bonded to —OH and then add the word *alcohol*. Following are the IUPAC names and, in parentheses, the common names of eight low-molecular-weight alcohols:



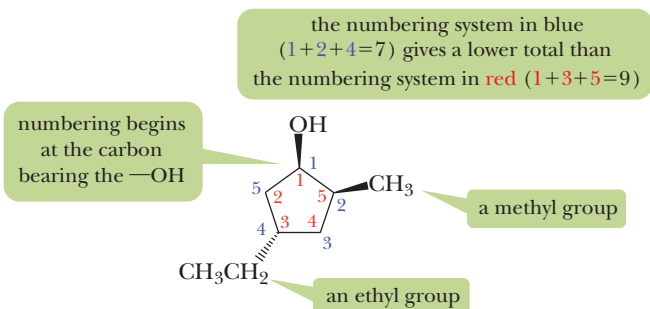
HOW TO 8.1

Name Cyclic Alcohols

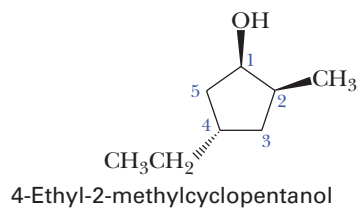
- (a) First, determine the root name of the cycloalkane, and replace the suffix *-e* with *-ol*.



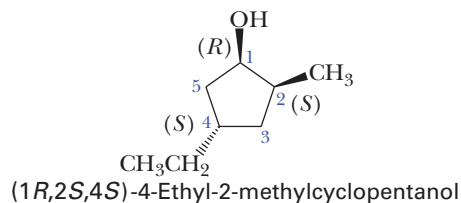
- (b) Name and number the substituents. Numbering begins at the carbon bearing the —OH group and proceeds in the direction that gives the lowest *total* for all substituents.



- (c) Place substituents in alphabetical order preceded by its position on the ring. Position 1 for the —OH group is assumed.

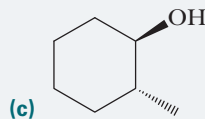
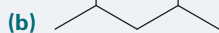


- (d) Don't forget to indicate stereochemistry.



EXAMPLE 8.1

Write the IUPAC name for each alcohol:



STRATEGY

First look for the longest chain of carbons that contains the —OH group. This will allow you to determine the root name. Then identify the atoms or groups of atoms that are not part of that chain of carbons. These are your substituents.

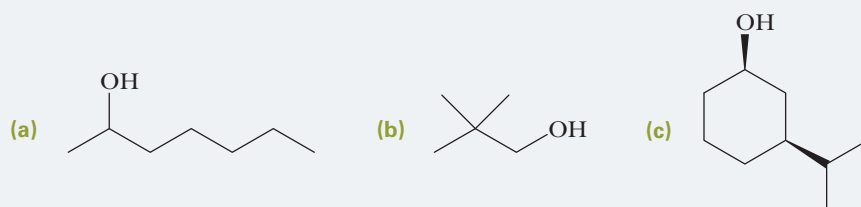
SOLUTION

(a) 1-Octanol (b) 4-Methyl-2-pentanol (c) *trans*-2-Methylcyclohexanol or (1*R*,2*R*)-2-Methylcyclohexanol

See problems 8.14, 8.15, 8.17

PROBLEM 8.1

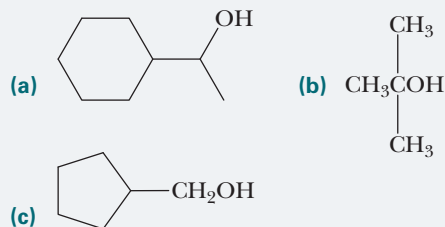
Write the IUPAC name for each alcohol:



We classify alcohols as **primary** (1°), **secondary** (2°), or **tertiary** (3°), depending on whether the —OH group is on a primary, secondary, or tertiary carbon (Section 1.7A).

EXAMPLE 8.2

Classify each alcohol as primary, secondary, or tertiary:

**STRATEGY**

Determine how many carbons are bonded to the carbon bonded to the —OH group (1 carbon = 1°, 2 carbons = 2°, and 3 carbons = 3°).

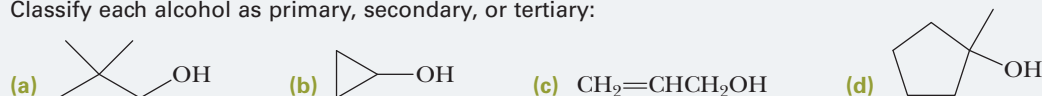
SOLUTION

(a) Secondary (2°) (b) Tertiary (3°) (c) Primary (1°)

See problem 8.13

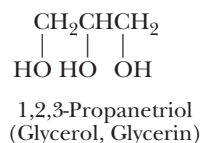
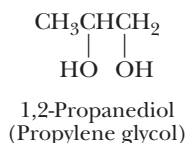
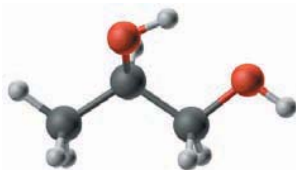
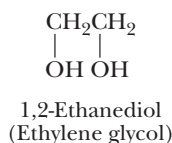
PROBLEM 8.2

Classify each alcohol as primary, secondary, or tertiary:



In the IUPAC system, a compound containing two hydroxyl groups is named as a **diol**, one containing three hydroxyl groups is named as a **triol**, and so on. In IUPAC names for diols, triols, and so on, the final -e of the parent alkane name is retained, as for example, in 1,2-ethanediol.

As with many organic compounds, common names for certain diols and triols have persisted. Compounds containing two hydroxyl groups on different carbons are often referred to as **glycols**. Ethylene glycol and propylene glycol are synthesized from ethylene and propylene, respectively—hence their common names:



Glycol A compound with two hydroxyl ($-\text{OH}$) groups on different carbons.



Charles D. Winters

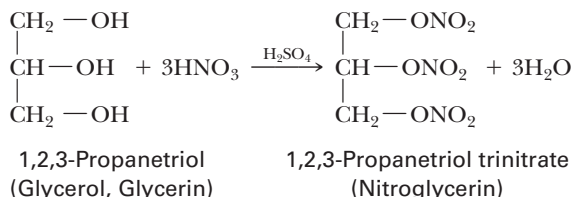
Ethylene glycol is a polar molecule and dissolves readily in water, a polar solvent.

Chemical

Connections 8A

NITROGLYCERIN: AN EXPLOSIVE AND A DRUG

In 1847, Ascanio Sobrero (1812–1888) discovered that 1,2,3-propanetriol, more commonly named glycerin, reacts with nitric acid in the presence of sulfuric acid to give a pale yellow, oily liquid called nitroglycerin:

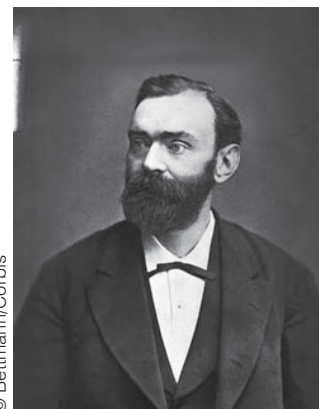


Sobrero also discovered the explosive properties of the compound: When he heated a small quantity of it, it exploded! Soon, nitroglycerin became widely used for blasting in the construction of canals, tunnels, roads, and mines and, of course, for warfare.

One problem with the use of nitroglycerin was soon recognized: It was difficult to handle safely, and accidental explosions occurred frequently. The Swedish chemist Alfred Nobel (1833–1896) solved the problem: He discovered that a claylike substance called diatomaceous earth absorbs nitroglycerin so that it will not explode without a fuse. He gave the name *dynamite* to this mixture of nitroglycerin, diatomaceous earth, and sodium carbonate.

Surprising as it may seem, nitroglycerin is used in medicine to treat angina pectoris, the symptoms of which are sharp chest pains caused by a reduced flow of blood in the coronary artery. Nitroglycerin, which is available in liquid (diluted with alcohol to render

the fortune of Alfred Nobel, 1833–1896, built on the manufacture of dynamite, now funds the Nobel Prizes.



© Bettmann/Corbis

it nonexplosive), tablet, or paste form, relaxes the smooth muscles of blood vessels, causing dilation of the coronary artery. This dilation, in turn, allows more blood to reach the heart.

When Nobel became ill with heart disease, his physicians advised him to take nitroglycerin to relieve his chest pains. He refused, saying he could not understand how the explosive could relieve chest pains. It took science more than 100 years to find the answer. We now know that it is nitric oxide, NO , derived from the nitro groups of nitroglycerin, that relieves the pain.

Question

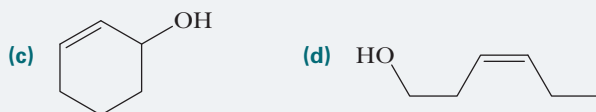
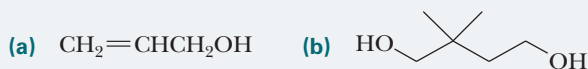
Classify each hydroxyl group in glycerol as either 1°, 2°, or 3°.

We often refer to compounds containing —OH and $\text{C}=\text{C}$ groups as unsaturated alcohols. To name an unsaturated alcohol,

1. Number the parent alkane so as to give the —OH group the lowest possible number.
2. Show the double bond by changing the infix of the parent alkane from *-an-* to *-en-* (Section 3.5), and show the alcohol by changing the suffix of the parent alkane from *-e* to *-ol*.
3. Use numbers to show the location of both the carbon-carbon double bond and the hydroxyl group.

EXAMPLE 8.3

Write the IUPAC name for each alcohol:



STRATEGY

First look for the longest chain of carbons. This will allow you to determine the root name. If the alcohol is unsaturated, the name will follow the general form #-alken-#-ol. If there are two —OH groups, name the compound as an #-,-alkanediol if it is saturated or as an #-,-alken-#,-,-diol if it is unsaturated.

SOLUTION

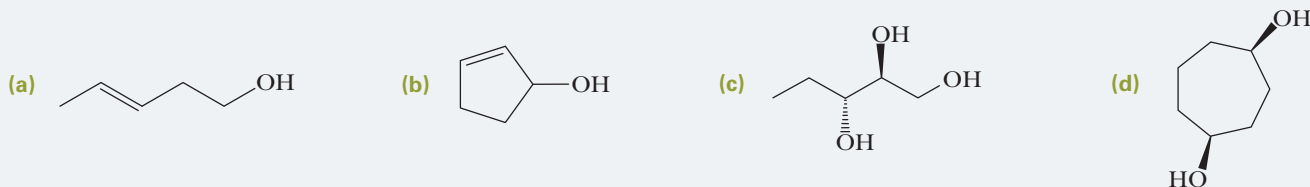
- (a) 2-Propen-1-ol. Its common name is allyl alcohol.
 (b) 2,2-Dimethyl-1,4-butanediol.
 (c) 2-Cyclohexenol.
 (d) *cis*-3-Hexen-1-ol. This unsaturated alcohol is sometimes called leaf alcohol because of its occurrence in leaves of fragrant plants, including trees and shrubs.

in this cyclic alcohol, the location of the —OH group is assumed to be at C-1

See problems 8.14, 8.15, 8.17

PROBLEM 8.3

Write the IUPAC name for each alcohol:



C. Physical Properties

The most important physical property of alcohols is the polarity of their —OH groups. Because of the large difference in electronegativity (Table 1.5) between oxygen and carbon ($3.5 - 2.5 = 1.0$) and between oxygen and hydrogen ($3.5 - 2.1 = 1.4$), both the C—O and O—H bonds of an alcohol are polar covalent, and alcohols are polar molecules, as illustrated in Figure 8.2 for methanol.

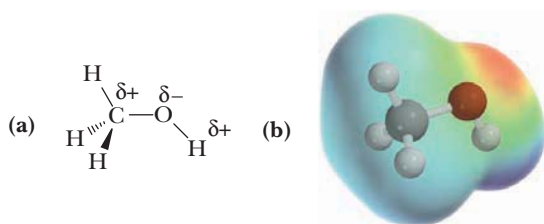


FIGURE 8.2

Polarity of the C—O—H bond in methanol. (a) There are partial positive charges on carbon and hydrogen and a partial negative charge on oxygen. (b) An electron density map showing the partial negative charge (in red) around oxygen and a partial positive charge (in blue) around hydrogen of the —OH group.

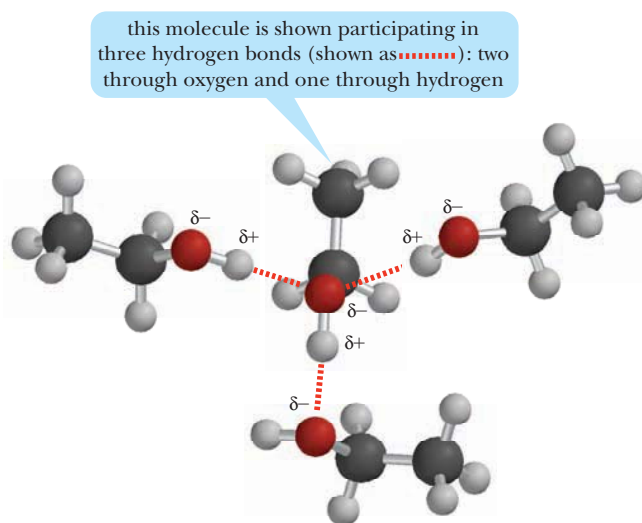
TABLE 8.1 Boiling Points and Solubilities in Water of Five Groups of Alcohols and Alkanes of Similar Molecular Weight

Structural Formula	Name	Molecular Weight	Boiling Point (°C)	Solubility in Water
CH ₃ OH	methanol	32	65	infinite
CH ₃ CH ₃	ethane	30	-89	insoluble
CH ₃ CH ₂ OH	ethanol	46	78	infinite
CH ₃ CH ₂ CH ₃	propane	44	-42	insoluble
CH ₃ CH ₂ CH ₂ OH	1-propanol	60	97	infinite
CH ₃ CH ₂ CH ₂ CH ₃	butane	58	0	insoluble
CH ₃ CH ₂ CH ₂ CH ₂ OH	1-butanol	74	117	8 g/100 g
CH ₃ CH ₂ CH ₂ CH ₂ CH ₃	pentane	72	36	insoluble
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ OH	1-pentanol	88	138	2.3 g/100 g
HOCH ₂ CH ₂ CH ₂ CH ₂ OH	1,4-butanediol	90	230	infinite
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃	hexane	86	69	insoluble

Table 8.1 lists the boiling points and solubilities in water for five groups of alcohols and alkanes of similar molecular weight. Notice that, of the compounds compared in each group, the alcohol has the higher boiling point and is the more soluble in water.

Alcohols have higher boiling points than alkanes of similar molecular weight, because alcohols are polar molecules and can associate in the liquid state by a type of dipole-dipole intermolecular attraction called **hydrogen bonding** (Figure 8.3). The strength of hydrogen bonding between alcohol molecules is approximately 8.4 to 21 kJ/mol (2 to 5 kcal/mol). For comparison, the strength of the O—H covalent bond in an alcohol molecule is approximately 460 kJ/mol (110 kcal/mol). As we see by comparing these numbers, an O---H hydrogen bond is considerably weaker than an O—H covalent bond. Nonetheless, it is sufficient to have a dramatic effect on the physical properties of alcohols.

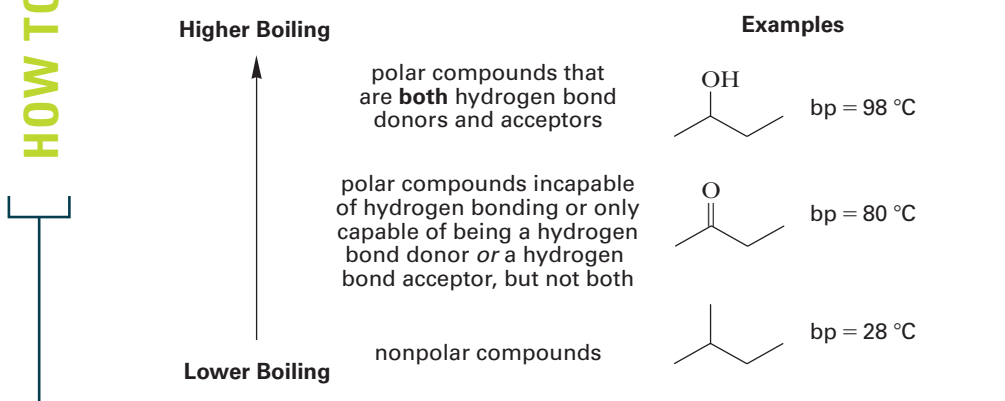
Hydrogen bonding The attractive force between a partial positive charge on hydrogen and partial negative charge on a nearby oxygen, nitrogen, or fluorine atom.

**FIGURE 8.3**

The association of ethanol molecules in the liquid state. Each O—H can participate in up to three hydrogen bonds (one through hydrogen and two through oxygen).

Predict Relative Boiling Points of Compounds of Similar Molecular Weight

- HOW TO 8.2**
- (a) Look for features that make a compound's boiling point higher than another's such as greater polarity, the ability to form hydrogen bonds with that compound's molecules (true for compounds containing N—H or O—H bonds), and greater surface area.
- (b) Boiling will typically follow the trend:



Because of hydrogen bonding between alcohol molecules in the liquid state, extra energy is required to separate each hydrogen-bonded alcohol molecule from its neighbors—hence the relatively high boiling points of alcohols compared with those of alkanes. The presence of additional hydroxyl groups in a molecule further increases the extent of hydrogen bonding, as can be seen by comparing the boiling points of 1-pentanol (138 °C) and 1,4-butanediol (230 °C), both of which have approximately the same molecular weight.

Because of increased dispersion forces (Section 3.8B) between larger molecules, boiling points of all types of compounds, including alcohols, increase with increasing molecular weight. (Compare, for example, the boiling points of ethanol, 1-propanol, 1-butanol, and 1-pentanol.)

Alcohols are much more soluble in water than are alkanes, alkenes, and alkynes of comparable molecular weight. Their increased solubility is due to hydrogen bonding between alcohol molecules and water. Methanol, ethanol, and 1-propanol are soluble in water in all proportions. As molecular weight increases, the physical properties of alcohols become more like those of hydrocarbons with comparable molecular weight. Alcohols with higher molecular weight are much less soluble in water because of the increase in size of the hydrocarbon portion of their molecules.

8.2 What Are the Characteristic Reactions of Alcohols?

In this section, we study the acidity and basicity of alcohols, their dehydration to alkenes, their conversion to haloalkanes, and their oxidation to aldehydes, ketones, or carboxylic acids.

A. Acidity of Alcohols

Alcohols have about the same pK_a values as water (15.7), which means that aqueous solutions of alcohols have about the same pH as that of pure water. The pK_a of methanol, for example, is 15.5:

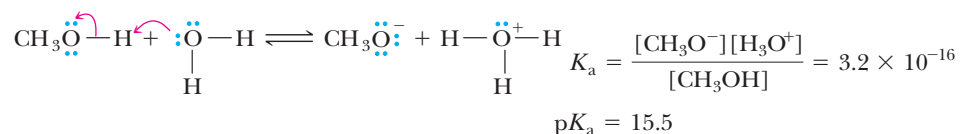



TABLE 8.2 pK_a Values for Selected Alcohols in Dilute Aqueous Solution*

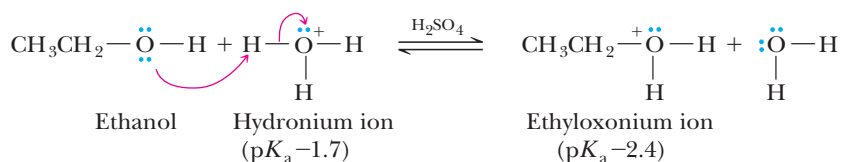
Compound	Structural Formula	pK_a	
hydrogen chloride	HCl	-7	<p>Stronger acid</p>  <p>Weaker acid</p>
acetic acid	CH ₃ COOH	4.8	
methanol	CH ₃ OH	15.5	
water	H ₂ O	15.7	
ethanol	CH ₃ CH ₂ OH	15.9	
2-propanol	(CH ₃) ₂ CHOH	17	
2-methyl-2-propanol	(CH ₃) ₃ COH	18	

*Also given for comparison are pK_a values for water, acetic acid, and hydrogen chloride.

Table 8.2 gives the acid ionization constants for several low-molecular-weight alcohols. Methanol and ethanol are about as acidic as water. Higher-molecular-weight, water-soluble alcohols are slightly weaker acids than water. Even though alcohols have some slight acidity, they are not strong enough acids to react with weak bases such as sodium bicarbonate or sodium carbonate. (At this point, it would be worthwhile to review Section 2.4 and the discussion of the position of equilibrium in acid–base reactions.) Note that, although acetic acid is a “weak acid” compared with acids such as HCl, it is still 10^{10} times stronger as an acid than alcohols are.

B. Basicity of Alcohols

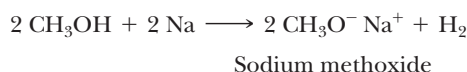
In the presence of strong acids, the oxygen atom of an alcohol is a weak base and reacts with an acid by proton transfer to form an oxonium ion:



Thus, alcohols can function as both weak acids and weak bases.

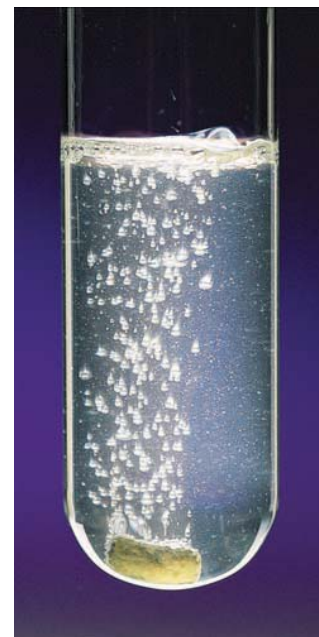
C. Reaction with Active Metals

Like water, alcohols react with Li, Na, K, Mg, and other active metals to liberate hydrogen and to form metal alkoxides. In the following oxidation–reduction reaction, Na is oxidized to Na^+ and H^+ is reduced to H_2 :



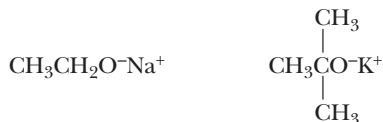
To name a metal alkoxide, name the cation first, followed by the name of the anion. The name of an alkoxide ion is derived from a prefix showing the number of carbon atoms and their arrangement (*meth-*, *eth-*, *isoprop-*, *tert-but-*, and so on) followed by the suffix *-oxide*.

Alkoxide ions are somewhat stronger bases than is the hydroxide ion. In addition to sodium methoxide, the following metal salts of alcohols are commonly used in organic



Methanol reacts with sodium metal to give sodium methoxide along with the evolution of hydrogen gas.

reactions requiring a strong base in a nonaqueous solvent; sodium ethoxide in ethanol and potassium *tert*-butoxide in 2-methyl-2-propanol (*tert*-butyl alcohol):

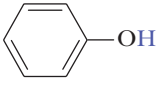


Sodium ethoxide Potassium *tert*-butoxide

As we saw in Chapter 7, alkoxide ions can also be used as nucleophiles in substitution reactions.

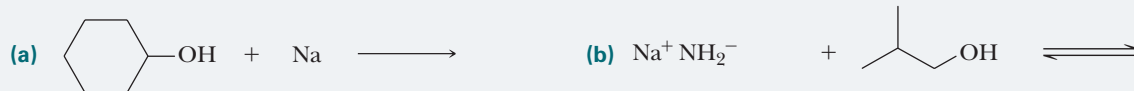
Predict the Position of Equilibrium of an Acid–Base Reaction

- HOW TO 8.3**
- Identify the two acids and two bases in the equilibrium.
 - The position of equilibrium lies on the side with the weaker acid and weaker base.
 - Following are common types of compounds encountered in organic chemistry and their relative acidities.

		Example
Higher acidity ↑ Lower acidity	mineral acids	HCl, H ₂ SO ₄
	carboxylic acids	RCOOH
	phenols	
	water	H ₂ O
	alcohols	ROH
	alkynes (terminal)	R—C≡C—H
	ammonia and amines	NH ₃ , RNH ₂ , R ₂ NH
	alkenes and alkanes	R ₂ C=CH ₂ , RH

EXAMPLE 8.4

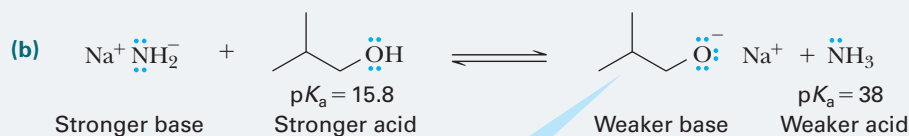
Write balanced equations for the following reactions. If the reaction is an acid–base reaction, predict its position of equilibrium.



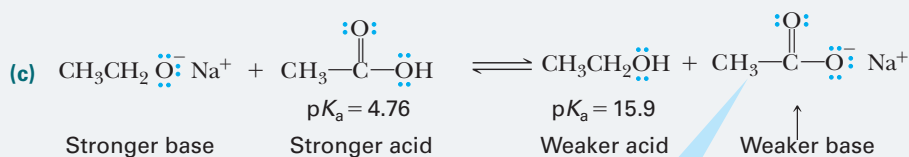
STRATEGY

First determine what type of reaction is occurring. When elemental sodium is used, an oxidation–reduction reaction takes place, producing a sodium alkoxide and hydrogen gas. In acid–base reactions, the position of the equilibrium resides on the side with the weaker acid and weaker base (i.e., the more stable species).

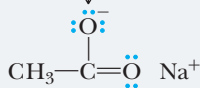
SOLUTION



the right side of the equation contains the more stable species, especially when comparing the alkoxide anion with NH_2^- because the oxygen in the alkoxide anion is more electronegative and better able to hold a negative charge than the nitrogen in NH_2^-



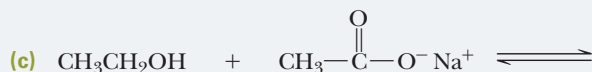
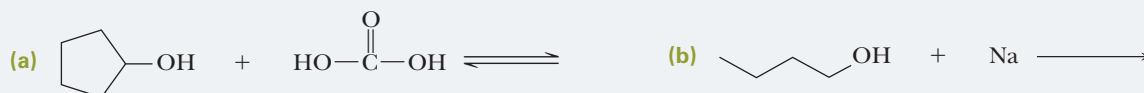
the right side of the equation contains the more stable species, especially when comparing the conjugate base of the carboxylic acid (known as a carboxylate anion) with the ethoxide anion because the negative charge in the carboxylate anion can be delocalized by resonance



See problems 8.28–8.32, 8.34, 8.35

PROBLEM 8.4

Write balanced equations for the following reactions. If the reaction is an acid–base reaction, predict its position of equilibrium.



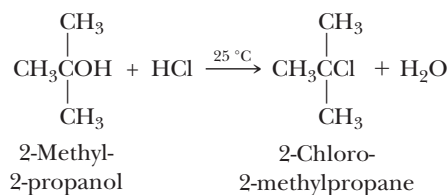
D. Conversion to Haloalkanes

The conversion of an alcohol to an alkyl halide involves substituting halogen for —OH at a saturated carbon. The most common reagents for this conversion are the halogen acids and SOCl_2 .

Reaction with HCl, HBr, and HI

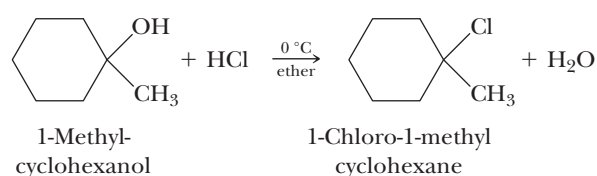
Water-soluble tertiary alcohols react very rapidly with HCl, HBr, and HI. Mixing a tertiary alcohol with concentrated hydrochloric acid for a few minutes at room temperature

converts the alcohol to a water-insoluble chloroalkane that separates from the aqueous layer.



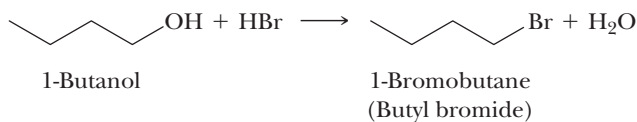
Low-molecular-weight, water-soluble primary and secondary alcohols do not react under these conditions.

Water-insoluble tertiary alcohols are converted to tertiary halides by bubbling gaseous HX through a solution of the alcohol dissolved in diethyl ether or tetrahydrofuran (THF):



Water-insoluble primary and secondary alcohols react only slowly under these conditions.

Primary and secondary alcohols are converted to bromoalkanes and iodoalkanes by treatment with concentrated hydrobromic and hydroiodic acids. For example, heating 1-butanol with concentrated HBr gives 1-bromobutane:

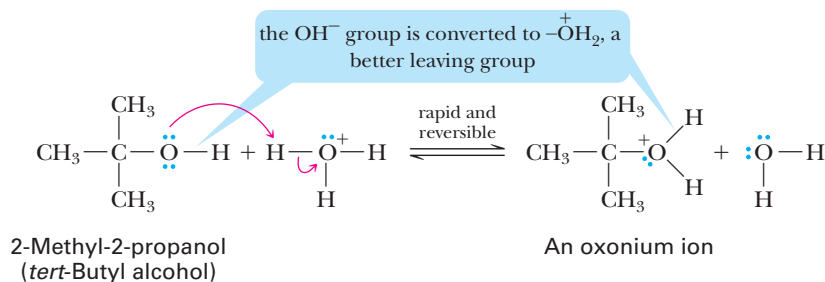


On the basis of observations of the relative ease of reaction of alcohols with HX ($3^\circ > 2^\circ > 1^\circ$), it has been proposed that the conversion of tertiary and secondary alcohols to haloalkanes by concentrated HX occurs by an $\text{S}_{\text{N}}1$ mechanism (Section 7.4) and involves the formation of a carbocation intermediate. *Note:* Recall that secondary carbocations are subject to rearrangement to more stable tertiary carbocations (Section 5.4).

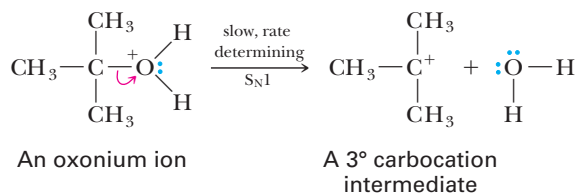
Mechanism

Reaction of a Tertiary Alcohol with HCl: An $\text{S}_{\text{N}}1$ Reaction

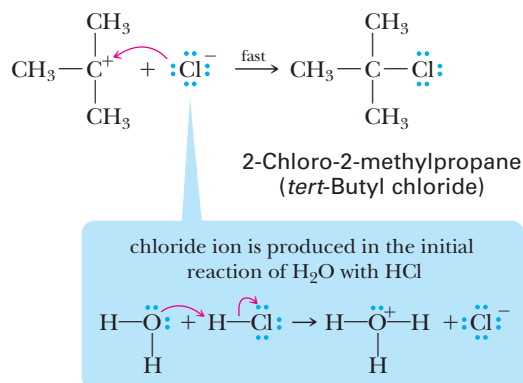
STEP 1: Add a proton. Rapid and reversible proton transfer from the acid to the OH group gives an oxonium ion. The result of this proton transfer is to convert the leaving group from OH^- , a poor leaving group, to H_2O , a better leaving group:



STEP 2: Break a bond to form a stable molecule or ion. Loss of water from the oxonium ion gives a 3° carbocation intermediate:



STEP 3: Reaction of an electrophile and a nucleophile to form a new covalent bond. Reaction of the 3° carbocation intermediate (an electrophile) with chloride ion (a nucleophile) gives the product:

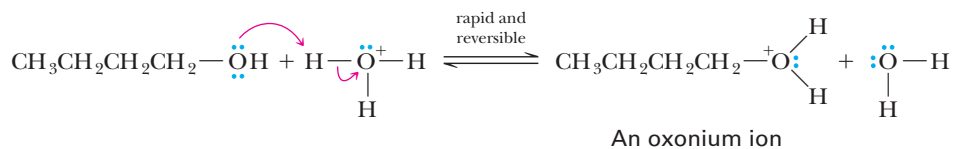


Primary alcohols react with HX by an S_N2 mechanism. In the rate-determining step, the halide ion displaces H₂O from the carbon bearing the oxonium ion. The displacement of H₂O and the formation of the C—X bond are simultaneous.

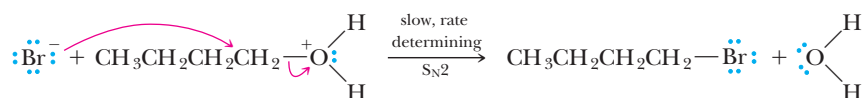
Mechanism

Reaction of a Primary Alcohol with HBr: An S_N2 Reaction

STEP 1: Add a proton. Rapid and reversible proton transfer to the OH group which converts the leaving group from OH[−], a poor leaving group, to H₂O, a better leaving group:

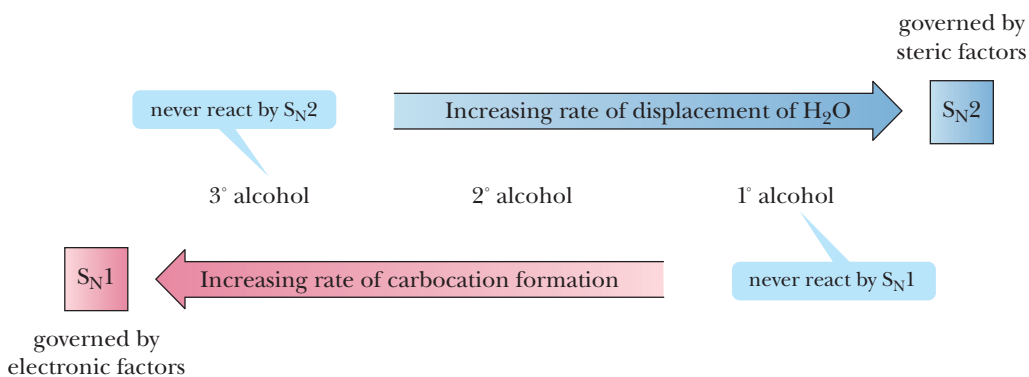


STEP 2: Reaction of an electrophile and a nucleophile to form a new covalent bond and break a bond to form a stable molecule or ion. The nucleophilic displacement of H₂O by Br[−] gives the bromoalkane:



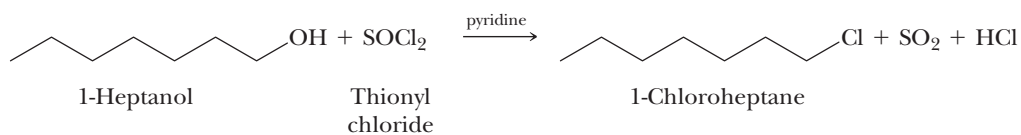
Why do tertiary alcohols react with HX by formation of carbocation intermediates, whereas primary alcohols react by direct displacement of —OH (more accurately, by displacement of —OH_2^+)? The answer is a combination of the same two factors involved in nucleophilic substitution reactions of haloalkanes (Section 7.5B):

- Electronic factors** Tertiary carbocations are the most stable (require the lowest activation energy for their formation), whereas primary carbocations are the least stable (require the highest activation energy for their formation). Therefore, tertiary alcohols are most likely to react by carbocation formation; secondary alcohols are intermediate, and primary alcohols rarely, if ever, react by carbocation formation.
- Steric factors** To form a new carbon–halogen bond, halide ion must approach the substitution center and begin to form a new covalent bond to it. If we compare the ease of approach to the substitution center of a primary oxonium ion with that of a tertiary oxonium ion, we see that approach is considerably easier in the case of a primary oxonium ion. Two hydrogen atoms and one alkyl group screen the back side of the substitution center of a primary oxonium ion, whereas three alkyl groups screen the back side of the substitution center of a tertiary oxonium ion.



Reaction with Thionyl Chloride

The most widely used reagent for the conversion of primary and secondary alcohols to alkyl chlorides is thionyl chloride, SOCl_2 . The by-products of this nucleophilic substitution reaction are HCl and SO_2 , both given off as gases. Often, an organic base such as pyridine (Section 10.1) is added to react with and neutralize the HCl by-product:

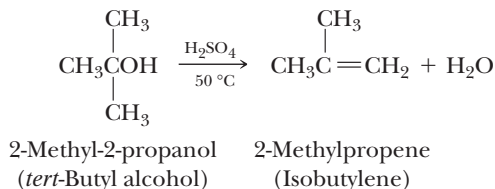
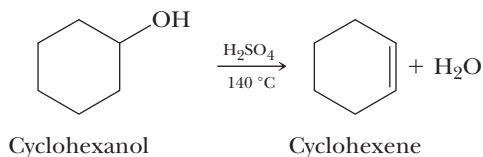
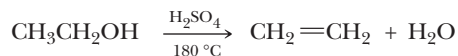


E. Acid-Catalyzed Dehydration to Alkenes

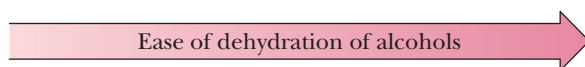
Dehydration Elimination of a molecule of water from a compound.

An alcohol can be converted to an alkene by **dehydration**—that is, by the elimination of a molecule of water from adjacent carbon atoms. In the laboratory, the dehydration of an alcohol is most often brought about by heating it with either 85% phosphoric acid or concentrated sulfuric acid. Primary alcohols are the most difficult to dehydrate and generally require heating in concentrated sulfuric acid at temperatures as high as 180°C . Secondary alcohols undergo acid-catalyzed dehydration at somewhat lower temperatures. The

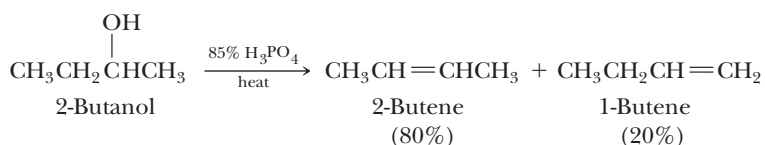
acid-catalyzed dehydration of tertiary alcohols often requires temperatures only slightly above room temperature:



Thus, the ease of acid-catalyzed dehydration of alcohols occurs in this order:



When isomeric alkenes are obtained in the acid-catalyzed dehydration of an alcohol, the more stable alkene (the one with the greater number of substituents on the double bond; see Section 5.3B) generally predominates; that is, the acid-catalyzed dehydration of alcohols follows Zaitsev's rule (Section 7.7):

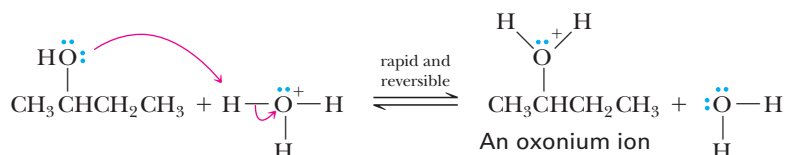


On the basis of the relative ease of dehydration of alcohols ($3^\circ > 2^\circ > 1^\circ$), chemists propose a three-step mechanism for the acid-catalyzed dehydration of secondary and tertiary alcohols. This mechanism involves the formation of a carbocation intermediate in the rate-determining step and therefore is an E1 mechanism.

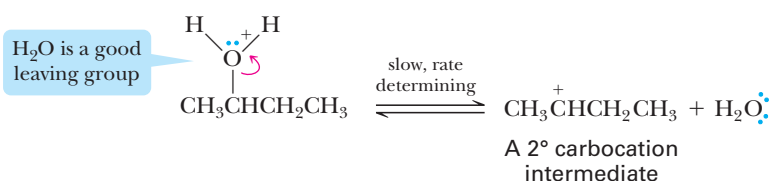
Mechanism

Acid-Catalyzed Dehydration of 2-Butanol: An E1 Mechanism

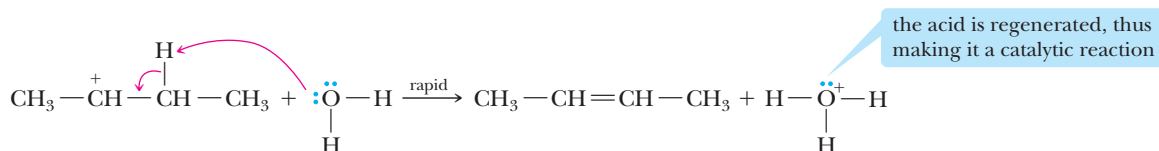
STEP 1: Add a proton. Proton transfer from H_3O^+ to the OH group of the alcohol gives an oxonium ion. A result of this step is to convert OH^- , a poor leaving group, into H_2O , a better leaving group:



STEP 2: Break a bond to form a stable molecule or ion. Breaking of the C—O bond gives a 2° carbocation intermediate and H₂O:



STEP 3: Take away a proton. Proton transfer from the carbon adjacent to the positively charged carbon to H₂O gives the alkene and regenerates the catalyst. The sigma electrons of a C—H bond become the pi electrons of the carbon-carbon double bond:



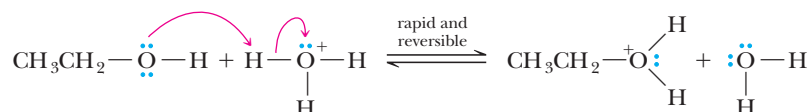
Because the rate-determining step in the acid-catalyzed dehydration of secondary and tertiary alcohols is the formation of a carbocation intermediate, the relative ease of dehydration of these alcohols parallels the ease of formation of carbocations.

Primary alcohols react by the following two-step mechanism, in which Step 2 is the rate-determining step.

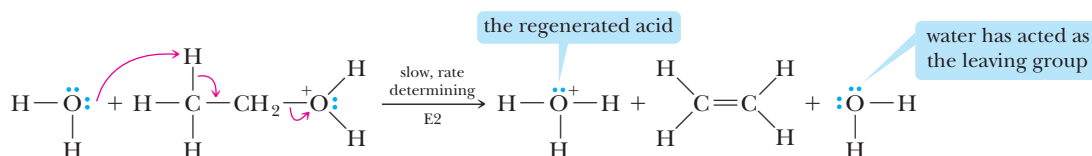
Mechanism

Acid-Catalyzed Dehydration of a Primary Alcohol: An E2 Mechanism

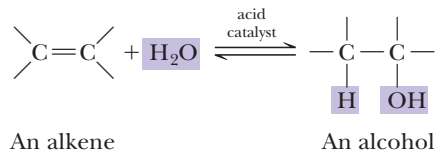
STEP 1: Add a proton. Proton transfer from H₃O⁺ to the OH group of the alcohol gives an oxonium ion:



STEP 2: Take a proton away and break a bond to form a stable molecule or ion. Simultaneous proton transfer to solvent and loss of H₂O gives the alkene:



In Section 5.3B, we discussed the acid-catalyzed hydration of alkenes to give alcohols. In the current section, we discussed the acid-catalyzed dehydration of alcohols to give alkenes. In fact, hydration–dehydration reactions are reversible. Alkene hydration and alcohol dehydration are competing reactions, and the following equilibrium exists:

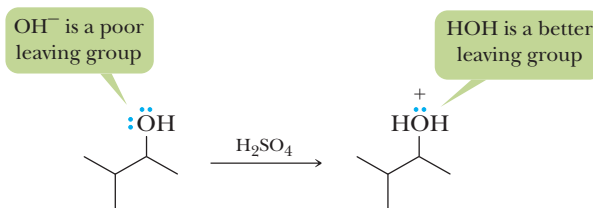


How, then, do we control which product will predominate? Recall that LeChâtelier's principle states that a system in equilibrium will respond to a stress in the equilibrium by counteracting that stress. This response allows us to control these two reactions to give the desired product. Large amounts of water (achieved with the use of dilute aqueous acid) favor alcohol formation, whereas a scarcity of water (achieved with the use of concentrated acid) or experimental conditions by which water is removed (for example, heating the reaction mixture above 100 °C) favor alkene formation. Thus, depending on the experimental conditions, it is possible to use the hydration–dehydration equilibrium to prepare either alcohols or alkenes, each in high yields.

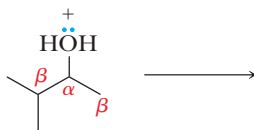
Complete a Dehydration Reaction

HOW TO 8.4

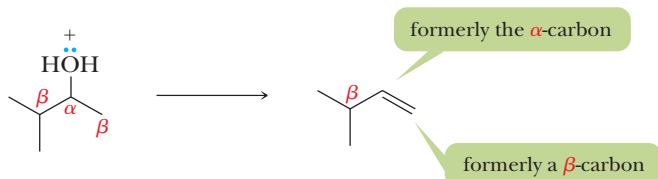
- (a) A dehydration reaction is very similar to a dehydrohalogenation reaction (Section 7.7) except that the hydroxyl group must be protonated to generate a better leaving group.



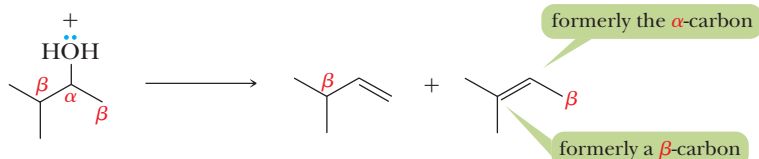
- (b) Label the carbon bonded to the leaving group as “ α ” (alpha).
 (c) Label any carbon bonded to the α -carbon as “ β ” (beta). *Note:* Only do so if the β -carbon is bonded to a hydrogen atom.



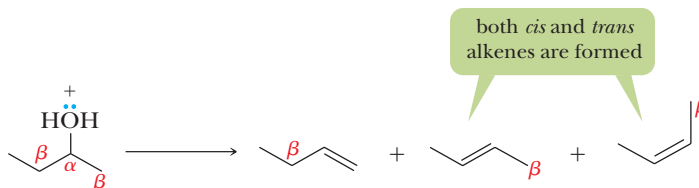
- (d) Remove the leaving group (H_2O) and a β -hydrogen from the molecule and place a new double bond between the α and β carbons. This forms a dehydration product.



- (e) Repeat step (d) above for any other β -carbons to form a different dehydration product.

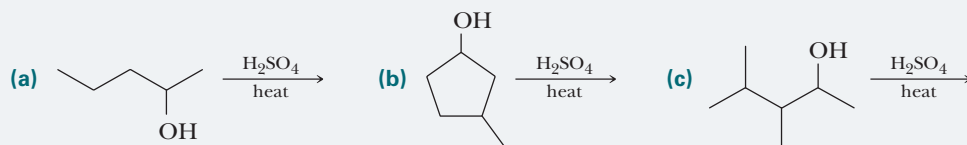


- (f) When forming an alkene by E1 elimination, consider the fact that both *cis* and *trans* isomers of the alkene are possible.



EXAMPLE 8.5

For each of the following alcohols, draw structural formulas for the alkenes that form upon acid-catalyzed dehydration, and predict which alkene is the major product from each alcohol. Be aware that rearrangements may occur because carbocations are formed in the reactions.

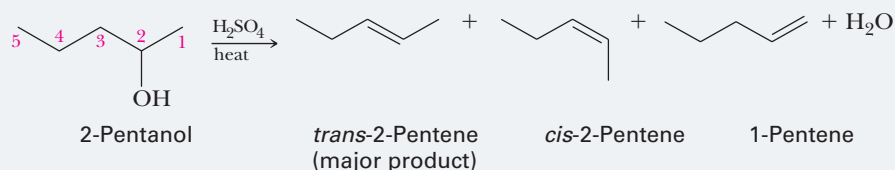


STRATEGY

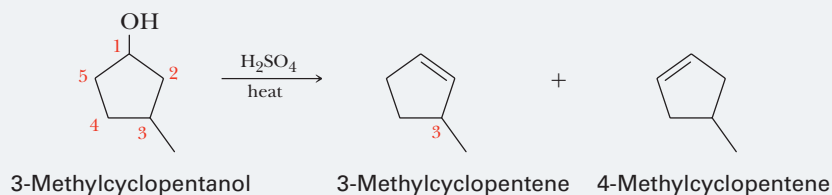
Label the carbon bonded to the —OH group as α . This is where the carbocation will form in the mechanism of the reaction. Consider whether a rearrangement (Section 5.4) will occur, and if so, relabel the new carbocation as α . Then label any carbons next to the α -carbon as β . If the β -carbon is bonded to at least one hydrogen, remove that hydrogen and the —OH and draw a C—C double bond between the α - and β -carbons. Start over and repeat this process for any other β -carbons that meet this criteria. Each time you are able to do this will result in an elimination product.

SOLUTION

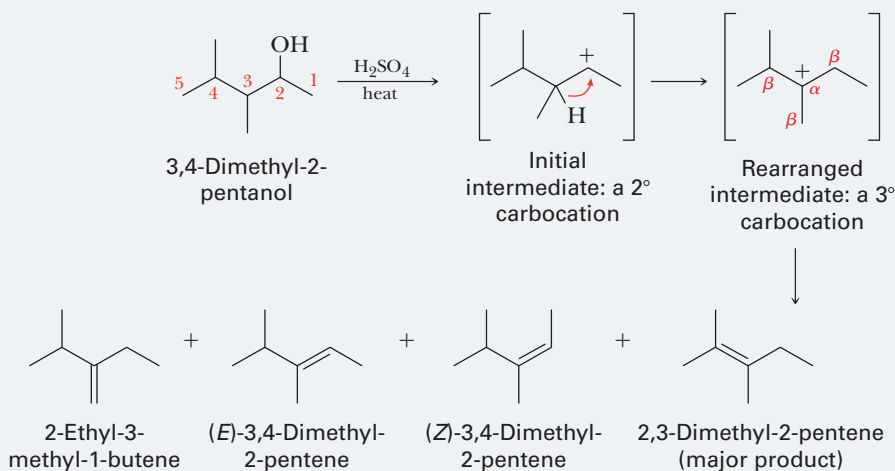
- (a) The elimination of H_2O from carbons 2 and 3 gives 2-pentene, which can form as *cis–trans* isomers; the elimination of H_2O from carbons 1 and 2 gives 1-pentene. *trans*-2-Pentene, with two alkyl groups (an ethyl and a methyl) on the double bond and with *trans* being more stable than *cis* (Section 5.6), is the major product. 1-Pentene, with only one alkyl group (a propyl group) on the double bond, is a minor product:



- (b) The elimination of H_2O from carbons 1 and 2 gives 3-methylcyclopentene; the elimination of H_2O from carbons 1 and 5 gives 4-methylcyclopentene. Because both products are disubstituted alkenes (two carbons bonded to each C—C double bond), they will be formed in approximately equal amounts. Note also that C_3 becomes a stereocenter in 3-methylcyclopentene.



- (c) This reaction initially forms a 2° carbocation intermediate, which rearranges via a 1,2-hydride shift (Section 5.4) to form the more stable 3° carbocation. This new carbocation has three β hydrogens and a C—C double bond and can form in three places. 2,3-Dimethyl-2-pentene is the product with the more substituted double bond and is therefore the most stable and major product.



See problems 8.41–8.45

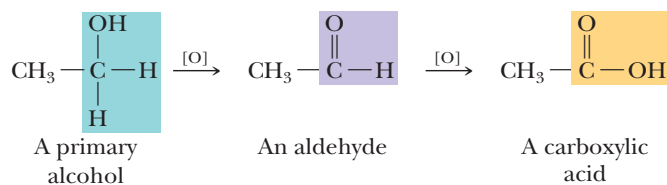
PROBLEM 8.5

For each of the following alcohols, draw structural formulas for the alkenes that form upon acid-catalyzed dehydration, and predict which alkene is the major product:

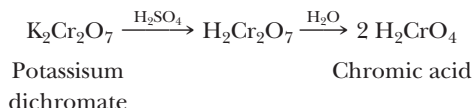
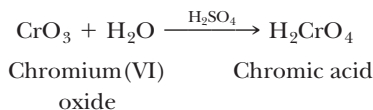


F. Oxidation of Primary and Secondary Alcohols

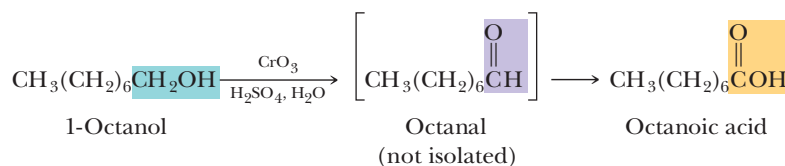
The oxidation of a primary alcohol gives an aldehyde or a carboxylic acid, depending on the experimental conditions. Secondary alcohols are oxidized to ketones. Tertiary alcohols are not oxidized. Following is a series of transformations in which a primary alcohol is oxidized first to an aldehyde and then to a carboxylic acid. The fact that each transformation involves oxidation is indicated by the symbol O in brackets over the reaction arrow:



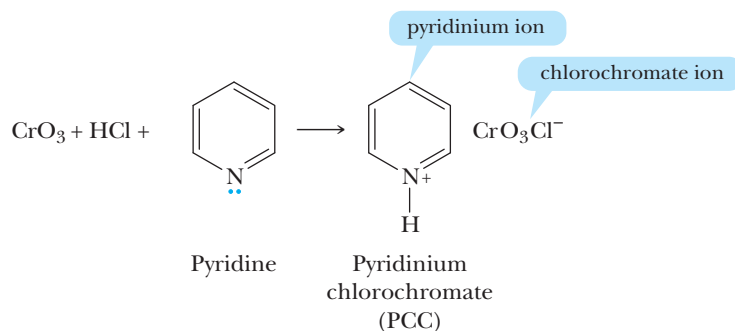
The reagent most commonly used in the laboratory for the oxidation of a primary alcohol to a carboxylic acid and a secondary alcohol to a ketone is chromic acid, H_2CrO_4 . Chromic acid is prepared by dissolving either chromium(VI) oxide or potassium dichromate in aqueous sulfuric acid:



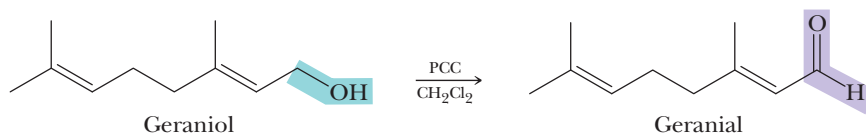
The oxidation of 1-octanol by chromic acid in aqueous sulfuric acid gives octanoic acid in high yield. These experimental conditions are more than sufficient to oxidize the intermediate aldehyde to a carboxylic acid:



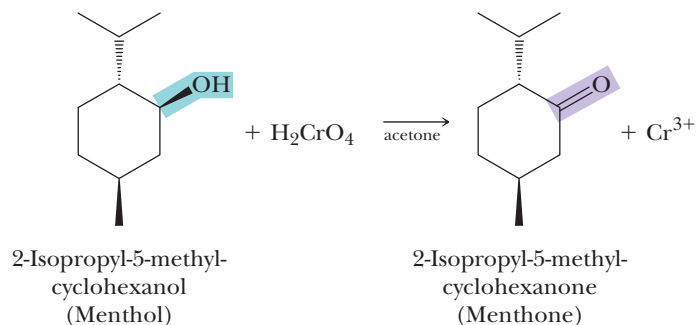
The form of Cr(VI) commonly used for the oxidation of a primary alcohol to an aldehyde is prepared by dissolving CrO_3 in aqueous HCl and adding pyridine to precipitate **pyridinium chlorochromate (PCC)** as a solid. PCC oxidations are carried out in aprotic solvents, most commonly dichloromethane, CH_2Cl_2 :



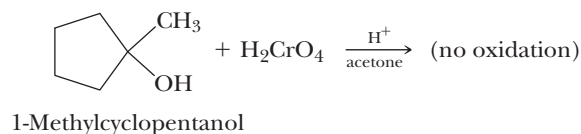
PCC is selective for the oxidation of primary alcohols to aldehydes. It is less reactive than the previously discussed oxidation with chromic acid in aqueous sulfuric acid, and the reaction is run stoichiometrically so that no PCC remains once all the alcohol molecules have been converted to aldehyde. PCC also has little effect on carbon-carbon double bonds or other easily oxidized functional groups. In the following example, geraniol is oxidized to geranial without affecting either carbon-carbon double bond:



Secondary alcohols are oxidized to ketones by both chromic acid and PCC:



Tertiary alcohols are resistant to oxidation, because the carbon bearing the —OH is bonded to three carbon atoms and therefore cannot form a carbon–oxygen double bond:



Note that the essential feature of the oxidation of an alcohol is the presence of at least one hydrogen on the carbon bearing the OH group. Tertiary alcohols lack such a hydrogen; therefore, they are not oxidized.

EXAMPLE 8.6

Draw the product of the treatment of each of the following alcohols with PCC:

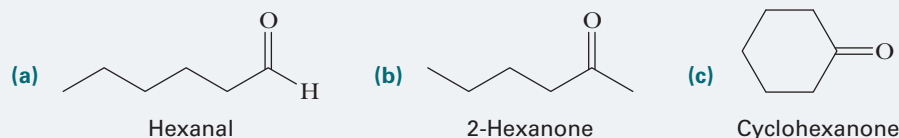
- (a) 1-Hexanol (b) 2-Hexanol (c) Cyclohexanol

STRATEGY

In oxidation reactions of alcohols, identify the type of alcohol as 1° , 2° , or 3° . Tertiary alcohols remain unreactive. Secondary alcohols are oxidized to ketones. Primary alcohols are oxidized to aldehydes when PCC is used as the oxidizing agent, and to carboxylic acids when chromic acid is used as the oxidizing agent.

SOLUTION

1-Hexanol, a primary alcohol, is oxidized to hexanal. 2-Hexanol, a secondary alcohol, is oxidized to 2-hexanone. Cyclohexanol, a secondary alcohol, is oxidized to cyclohexanone.



See problems 8.34, 8.35, 8.38, 8.41–8.46

PROBLEM 8.6

Draw the product of the treatment of each alcohol in Example 8.6 with chromic acid.

8.3 What Are Ethers?

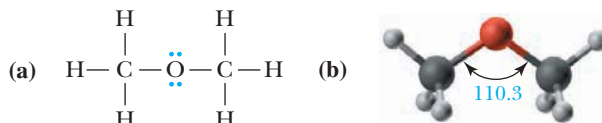
A. Structure

Ether A compound containing an oxygen atom bonded to two carbon atoms.

The functional group of an **ether** is an atom of oxygen bonded to two carbon atoms. Figure 8.4 shows a Lewis structure and a ball-and-stick model of dimethyl ether, CH_3OCH_3 , the simplest ether. In dimethyl ether, two sp^3 hybrid orbitals of oxygen form sigma bonds to carbon atoms. The other two sp^3 hybrid orbitals of oxygen each contain an unshared pair of electrons. The $\text{C}-\text{O}-\text{C}$ bond angle in dimethyl ether is 110.3° , close to the predicted tetrahedral angle of 109.5° .

FIGURE 8.4

Dimethyl ether, CH_3OCH_3 . (a) Lewis structure and (b) ball-and-stick model.

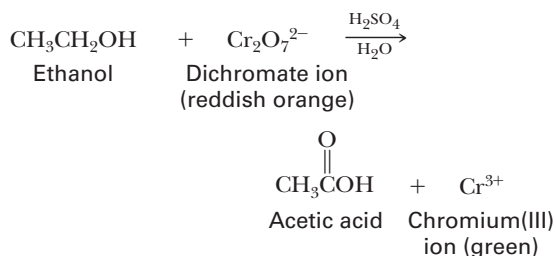


Chemical

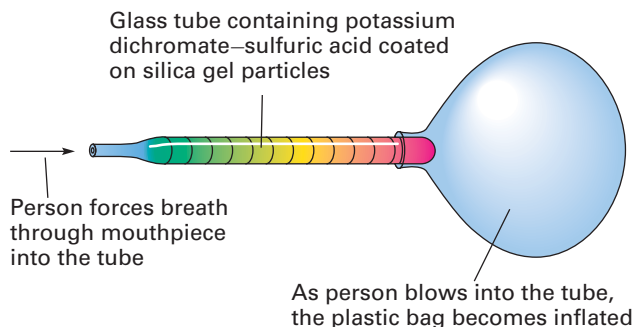
Connections 8B

BLOOD ALCOHOL SCREENING

Potassium dichromate oxidation of ethanol to acetic acid is the basis for the original breath alcohol screening test used by law enforcement agencies to determine a person's blood alcohol content. The test is based on the difference in color between the dichromate ion (reddish orange) in the reagent and the chromium(III) ion (green) in the product. Thus, color change can be used as a measure of the quantity of ethanol present in a breath sample:



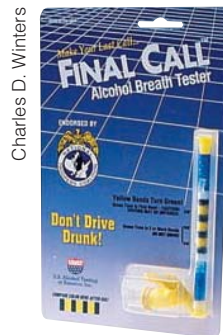
In its simplest form, a breath alcohol screening test consists of a sealed glass tube containing a potassium dichromate-sulfuric acid reagent impregnated on silica gel. To administer the test, the ends of the tube are broken off, a mouthpiece is fitted to one end, and the other end is inserted into the neck of a plastic bag. The person being tested then blows into the mouthpiece until the plastic bag is inflated.



As breath containing ethanol vapor passes through the tube, reddish-orange dichromate ion is reduced to green chromium(III) ion. The concentration of ethanol in the breath is then estimated by measuring how far the green color extends along the length of the tube. When it extends beyond the halfway point, the person is judged as having a sufficiently high blood alcohol content to warrant further, more precise testing.

The Breathalyzer, a more precise testing device, operates on the same principle as the simplified screening test. In a Breathalyzer test, a measured volume of breath is bubbled through a solution of potassium dichromate in aqueous sulfuric acid, and the color change is measured spectrophotometrically.

Both tests measure alcohol in the breath. The legal definition of being under the influence of alcohol is based on *blood* alcohol content, not breath alcohol content. The chemical correlation between these two measurements is that air deep within the lungs is in equilibrium with blood passing through the pulmonary arteries, and an equilibrium is established between blood alcohol and breath alcohol. It has been determined by tests in persons drinking alcohol that 2100 mL of breath contains the same amount of ethanol as 1.00 mL of blood.



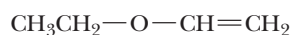
A device for testing the breath for the presence of ethanol. When ethanol is oxidized by potassium dichromate, the reddish-orange color of dichromate ion turns to green as it is reduced to chromium(III) ion.

Questions

Although methanol* and isopropyl alcohol are much more toxic than ethanol and would rarely be found in one's breath, would these two compounds also give a positive alcohol screening test? If so, what would be the products of these reactions?

*Methanol is indeed much more toxic than ethanol, as many found out during Prohibition when they drank wood alcohol instead of ethanol. Methanol causes damage to the nerve sheaths, and one symptom of methanol poisoning is intense pain in response to light.

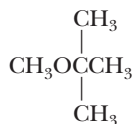
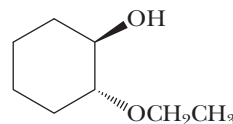
In ethyl vinyl ether, the ether oxygen is bonded to one sp^3 hybridized carbon and one sp^2 hybridized carbon:



Ethyl vinyl ether

**B. Nomenclature**

In the IUPAC system, ethers are named by selecting the longest carbon chain as the parent alkane and naming the —OR group bonded to it as an **alkoxy** (*alkyl* + *oxygen*) **group**. Common names are derived by listing the alkyl groups bonded to oxygen in alphabetical order and adding the word *ether*.

Ethoxyethane
(Diethyl ether)2-Methoxy-2-methylpropane
(methyl *tert*-butyl ether, MTBE)(1*R*,2*R*)-2-Ethoxycyclohexanol
(*trans*-2-Ethoxycyclohexanol)

Chemists almost invariably use common names for low-molecular-weight ethers. For example, although ethoxyethane is the IUPAC name for $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$, it is rarely called that, but rather is called diethyl ether, ethyl ether, or, even more commonly, simply ether. The abbreviation for *tert*-butyl methyl ether, used at one time as an octane-improving additive to gasolines, is *MTBE*, after the common name of methyl *tert*-butyl ether.

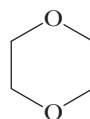
Cyclic ethers are heterocyclic compounds in which the ether oxygen is one of the atoms in a ring. These ethers are generally known by their common names:



Ethylene oxide



Tetrahydrofuran (THF)



1,4-Dioxane

Boston Medical Library in the Francis A. Courtney Library of Medicine



This painting by Robert Hinckley shows the first use of diethyl ether as an anesthetic in 1846.

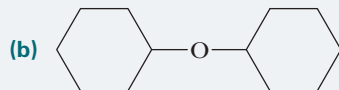
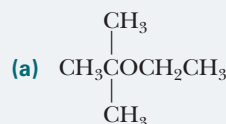
Dr. Robert John Collins was removing a tumor from the patient's neck, and the dentist W. T. G. Morton—who discovered its anesthetic properties—administered the ether.

Alkoxy group An —OR group, where R is an alkyl group.

Cyclic ether An ether in which the oxygen is one of the atoms of a ring.

EXAMPLE 8.7

Write the IUPAC and common names for each ether:



STRATEGY

As with all nomenclature problems, first determine the root name of the compound. In the IUPAC system, —OR groups are named as alkoxy groups. In the common nomenclature system, the alkyl groups bonded to oxygen are named in alphabetical order, followed by the word “ether.”

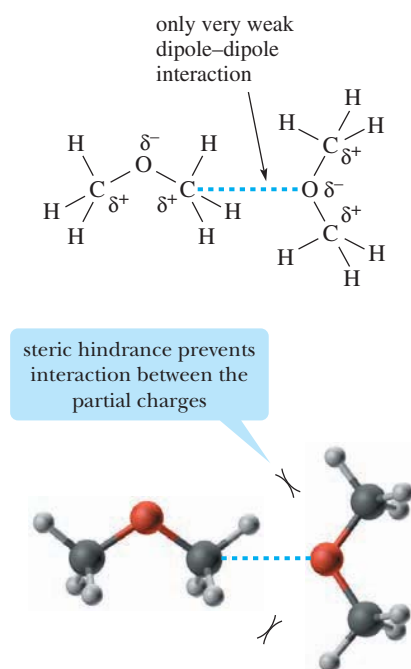
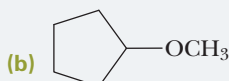
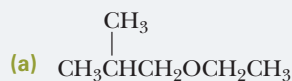
SOLUTION

- (a) 2-Ethoxy-2-methylpropane. Its common name is *tert*-butyl ethyl ether.
 (b) Cyclohexoxycyclohexane. Its common name is dicyclohexyl ether.

See problem 8.16

PROBLEM 8.7

Write the IUPAC and common names for each ether:



C. Physical Properties

Ethers are polar compounds in which oxygen bears a partial negative charge and each carbon bonded to it bears a partial positive charge (Figure 8.5). Because of steric hindrance, however, only weak forces of attraction exist between ether molecules in the pure liquid. Consequently, boiling points of ethers are much lower than those of alcohols of comparable molecular weight (Table 8.3). Boiling points of ethers are close to those of hydrocarbons of comparable molecular weight (compare Tables 3.4 and 8.3).

Because the oxygen atom of an ether carries a partial negative charge, ethers form hydrogen bonds with water (Figure 8.6) and are more soluble in water than are hydrocarbons of comparable molecular weight and shape (compare data in Tables 3.4 and 8.3).

The effect of hydrogen bonding is illustrated dramatically by comparing the boiling points of ethanol (78 °C) and its constitutional isomer dimethyl ether (−24 °C). The difference in boiling points between these two compounds is due to the polar O—H group in the alcohol, which is capable of forming

FIGURE 8.5

Ethers are polar molecules, but because of steric hindrance, only weak attractive interactions exist between their molecules in the pure liquid.

TABLE 8.3 Boiling Points and Solubilities in Water of Some Alcohols and Ethers of Comparable Molecular Weight

Structural Formula	Name	Molecular Weight	Boiling Point (°C)	Solubility in Water
$\text{CH}_3\text{CH}_2\text{OH}$	ethanol	46	78	infinite
CH_3OCH_3	dimethyl ether	46	−24	7.8 g/100 g
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	1-butanol	74	117	7.4 g/100 g
$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$	diethyl ether	74	35	8 g/100 g
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	1-pentanol	88	138	2.3 g/100 g
$\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	1,4-butanediol	90	230	infinite
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OCH}_3$	butyl methyl ether	88	71	slight
$\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3$	ethylene glycol dimethyl ether	90	84	infinite

dimethyl ether in water. The partially negative oxygen of the ether is the hydrogen-bond acceptor, and a partially positive hydrogen of a water molecule is the hydrogen-bond donor

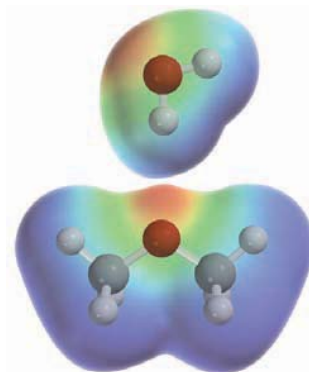
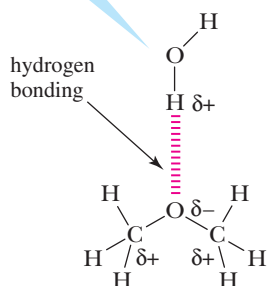


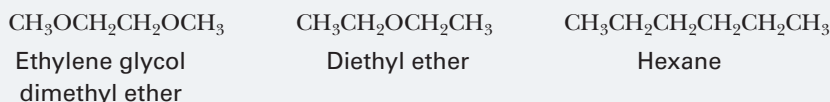
FIGURE 8.6
Ethers are hydrogen-bond acceptors only. They are not hydrogen-bond donors.

intermolecular hydrogen bonds. This hydrogen bonding increases the attractive force between molecules of ethanol; thus, ethanol has a higher boiling point than dimethyl ether:



EXAMPLE 8.8

Arrange these compounds in order of increasing solubility in water:

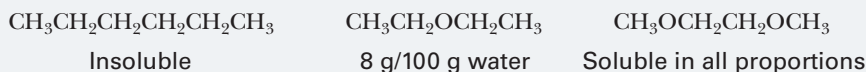


STRATEGY

Look for features that make organic compounds more soluble in water. These are, from most significant to least significant, (1) the ability to form hydrogen bonds with water, (2) polarity, and (3) low molecular weight.

SOLUTION

Water is a polar solvent. Hexane, a nonpolar hydrocarbon, has the lowest solubility in water. Both diethyl ether and ethylene glycol dimethyl ether are polar compounds, due to the presence of their polar C—O—C groups, and each interacts with water as a hydrogen-bond acceptor. Because ethylene glycol dimethyl ether has more sites within its molecules for hydrogen bonding, it is more soluble in water than diethyl ether:



See problems 8.23–8.25

PROBLEM 8.8

Arrange these compounds in order of increasing boiling point:



D. Reactions of Ethers

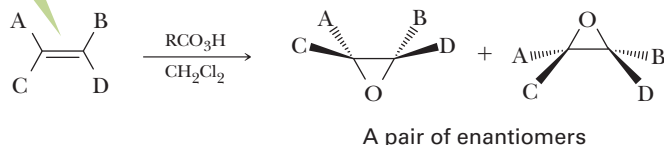
Ethers, R—O—R, resemble hydrocarbons in their resistance to chemical reaction. They do not react with oxidizing agents, such as potassium dichromate or potassium permanganate. They are not affected by most acids or bases at moderate temperatures. Because of their good solvent properties and general inertness to chemical reaction, ethers are excellent solvents in which to carry out many organic reactions.

Predict the Product of an Epoxidation Reaction

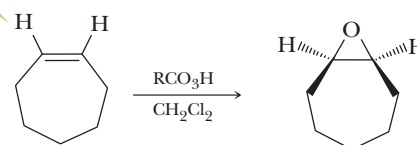
HOW TO 8.5

The key feature of an epoxidation reaction of an alkene and a peroxycarboxylic acid is the formation of an epoxide with retention of stereochemistry about the reacting C—C double bond. This means that the relative stereochemistry of all groups about the double bond must be the same in the product epoxide as shown in the acyclic and cyclic examples.

groups that are *trans* in the alkene, such as groups C and B, will be *trans* in the epoxide



because the vinylic hydrogens are *cis* in the reactant, they must remain *cis* in the product



EXAMPLE 8.9

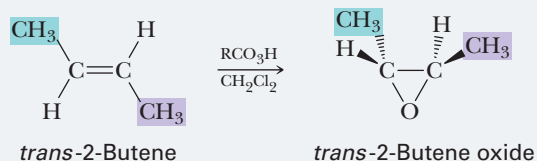
Draw a structural formula of the epoxide formed by treating *trans*-2-butene with a peroxycarboxylic acid.

STRATEGY

To predict the product of a peroxycarboxylic acid and an alkene, convert its C—C double bond to a C—C single bond in which both carbons are bonded to the same oxygen in a three-membered ring.

SOLUTION

The oxygen of the epoxide ring is added by forming both carbon–oxygen bonds from the same side of the carbon–carbon double bond:



See problems 8.43–8.45, 8.47

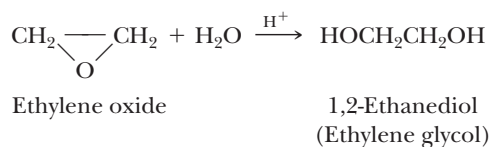
PROBLEM 8.9

Draw the structural formula of the epoxide formed by treating 1,2-dimethylcyclopentene with a peroxycarboxylic acid.

C. Ring-Opening Reactions

Ethers are not normally susceptible to reaction with aqueous acid (Section 8.3D). Epoxides, however, are especially reactive because of the angle strain in the three-membered ring. The normal bond angle about an sp^3 hybridized carbon or oxygen atom is 109.5° . Because of the strain associated with the compression of bond angles in the three-membered epoxide ring from the normal 109.5° to 60° , epoxides undergo ring-opening reactions with a variety of nucleophilic reagents.

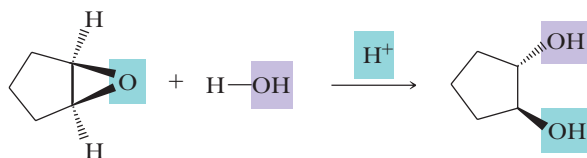
In the presence of an acid catalyst—most commonly, perchloric acid—epoxides are hydrolyzed to glycols. As an example, the acid-catalyzed hydrolysis of ethylene oxide gives 1,2-ethanediol:



Annual production of ethylene glycol in the United States is approximately 10^{10} kg. Two of its largest uses are in automotive antifreeze and as one of the two starting materials for the

production of polyethylene terephthalate (PET), which is fabricated into such consumer products as Dacron[®] polyester, Mylar[®], and packaging films (Section 17.4B).

The acid-catalyzed ring opening of epoxides shows a stereoselectivity typical of S_N2 reactions: The nucleophile attacks anti to the leaving hydroxyl group, and the —OH groups in the glycol thus formed are anti. As a result, the acid-catalyzed hydrolysis of an epoxycycloalkane yields a *trans*-1,2-cycloalkanediol:



Normally, epoxides will not react with H₂O because water is a poor nucleophile. The mechanism below shows how the acid catalyst makes it possible for the epoxide to react with water.

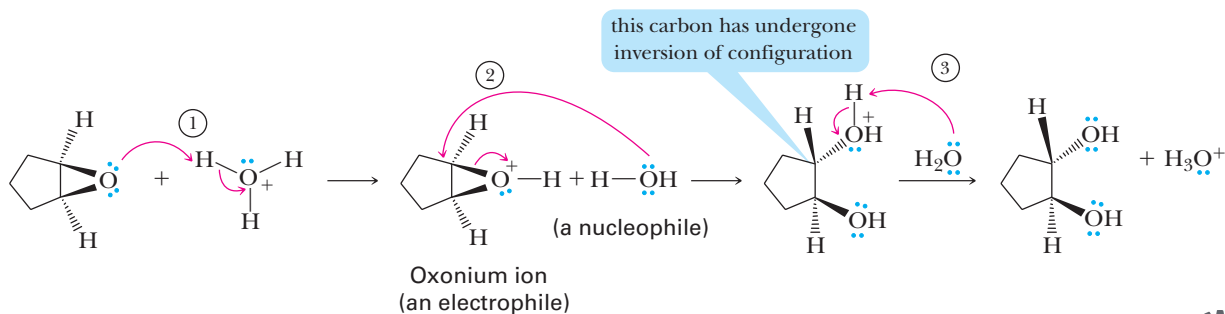
Mechanism

Acid-Catalyzed Epoxide Ring Opening

STEP 1: Add a proton. The reaction is made possible because the acid catalyst protonates the epoxide oxygen, generating a highly reactive oxonium ion.

STEP 2: Reaction of an electrophile and a nucleophile to form a new covalent bond. The positive charge on the oxygen of the three-membered ring makes one of the epoxide carbons susceptible to nucleophilic attack by water. This opens the epoxide with inversion of configuration at the carbon that was attacked.

STEP 3: Take a proton away. Transfer of a proton from the resulting intermediate gives the *trans* glycol and regenerates the acid.



EXAMPLE 8.10

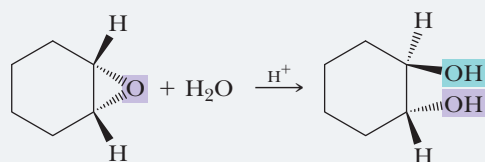
Draw the structural formula of the product formed by treating cyclohexene oxide with aqueous acid. Be certain to show the stereochemistry of the product.

STRATEGY

The acid-catalyzed ring opening of an epoxide always results in a *trans*-1,2,-diol, with the two carbons formerly part of the epoxide bonded to each of the two hydroxyl groups.

SOLUTION

The acid-catalyzed hydrolysis of the three-membered epoxide ring gives a *trans* glycol:

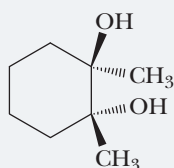


trans-1,2-Cyclohexanediol

See problems 8.26, 8.43–8.45

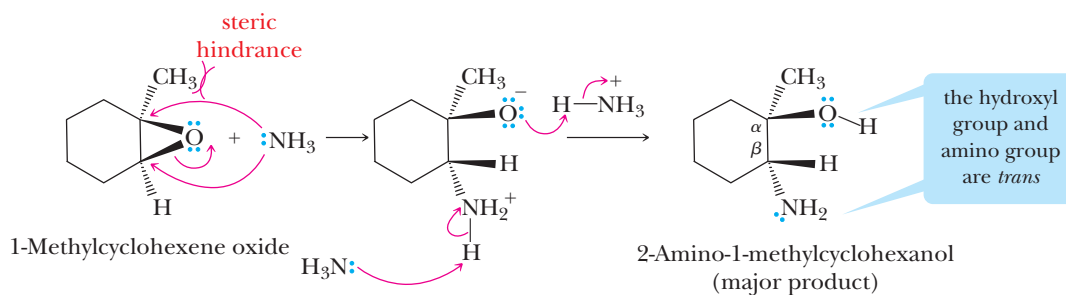
PROBLEM 8.10

Show how to convert 1,2-dimethylcyclohexene to *trans*-1,2-dimethylcyclohexane-1,2-diol.

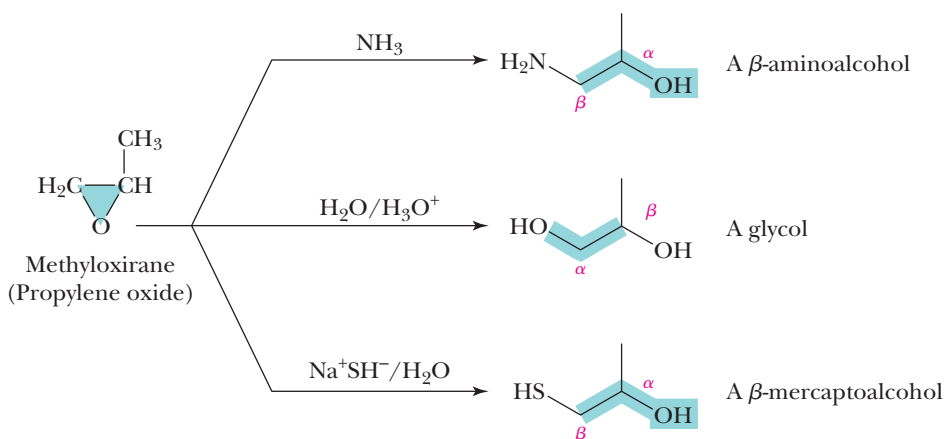


trans-1,2-Dimethylcyclohexane-1,2-diol

Just as ethers are not normally susceptible to reaction with electrophiles, neither are they normally susceptible to reaction with nucleophiles. Because of the strain associated with the three-membered ring, however, epoxides undergo ring-opening reactions with good nucleophiles such as ammonia and amines (Chapter 10), alkoxide ions, and thiols and their anions (Section 8.6). Good nucleophiles attack the ring by an S_N2 mechanism and show a stereoselectivity for attack of the nucleophile at the less hindered carbon of the three-membered ring. The result is an alcohol with the former nucleophile bonded to a carbon β to the newly formed hydroxyl group. An illustration is the reaction of 1-methylcyclohexene oxide with ammonia to give the stereoisomer of 2-amino-1-methylcyclohexanol in which the hydroxyl group and the amino group are *trans*:



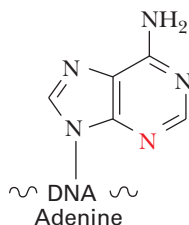
The value of epoxides lies in the number of nucleophiles that bring about ring opening and the combinations of functional groups that can be prepared from them. The following chart summarizes the three most important of these nucleophilic ring-opening reactions (the characteristic structural feature of each ring-opening product is shown in color):



Chemical Connections 8C

ETHYLENE OXIDE: A CHEMICAL STERILANT

Because ethylene oxide is such a highly strained molecule, it reacts with the types of nucleophilic groups present in biological materials. At sufficiently high concentrations, ethylene oxide reacts with enough mol-

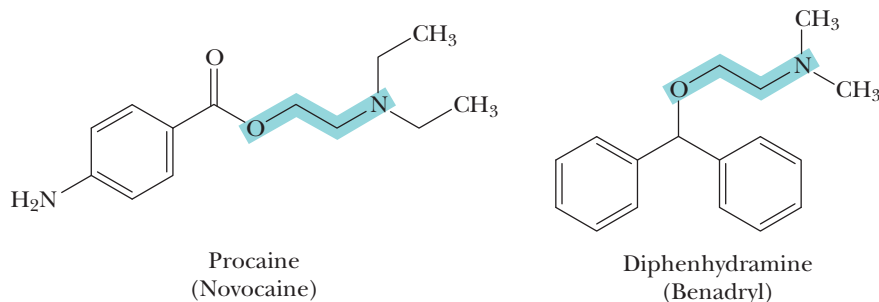


ecules in cells to cause the death of microorganisms. This toxic property is the basis for using ethylene oxide as a chemical sterilant. In hospitals, surgical instruments and other items that cannot be made disposable are now sterilized by exposure to ethylene oxide.

Question

One of the ways that ethylene oxide has been found to kill microorganisms is by reacting with the adenine components of their DNA at the atom indicated in red. Propose a mechanism and an initial product for this reaction. *Hint:* First draw in any lone pairs of electrons in adenine.

Ethylene oxide and substituted ethylene oxides are valuable building blocks for the synthesis of larger organic molecules. Following are structural formulas for two common drugs, each synthesized in part from ethylene oxide:



Stephen J. Krasemann/
Photo Researchers, Inc.



The scent of skunks is a mixture of two thiols, 3-methyl-1-butanethiol and 2-butene-1-thiol.

Thiol A compound containing an —SH (sulfhydryl) group.

Novocaine was the first injectable local anesthetic. Benadryl was the first synthetic antihistamine. The portion of the carbon skeleton of each that is derived from the reaction of ethylene oxide with a nitrogen–nucleophile is shown in color.

In later chapters, after we have developed the chemistry of more functional groups, we will show how to synthesize Novocaine and Benadryl from readily available starting materials. For the moment, however, it is sufficient to recognize that the unit —O—C—C—Nu can be derived by nucleophilic opening of ethylene oxide or a substituted ethylene oxide.

8.5 What Are Thiols?

A. Structure

The functional group of a **thiol** is an —SH (sulfhydryl) group. Figure 8.7 shows a Lewis structure and a ball-and-stick model of methanethiol, CH₃SH, the simplest thiol.

The most outstanding property of low-molecular-weight thiols is their stench. They are responsible for the unpleasant odors such as those from skunks, rotten eggs, and sewage. The scent of skunks is due primarily to two thiols:



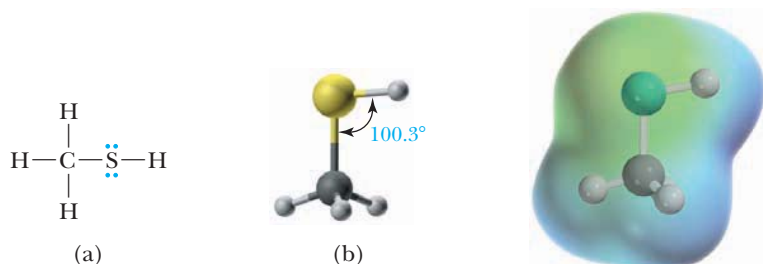
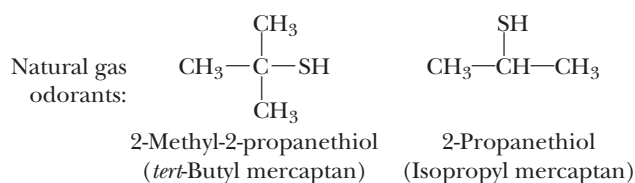


FIGURE 8.7 Methanethiol, CH_3SH . (a) Lewis structure and (b) ball-and-stick model. The $\text{C}-\text{S}-\text{H}$ bond angle is 100.3° , somewhat smaller than the tetrahedral angle of 109.5° .

Methanethiol. The electronegativities of carbon and sulfur are virtually identical (2.5 each), while sulfur is slightly more electronegative than hydrogen (2.5 versus 2.1). The electron density model shows some slight partial positive charge on hydrogen of the $\text{S}-\text{H}$ group and some slight partial negative charge on sulfur.

A blend of low-molecular-weight thiols is added to natural gas as an odorant. The most common of these odorants is 2-methyl-2-propanethiol (*tert*-butyl mercaptan), because it is the most resistant to oxidation and has the greatest soil penetration. 2-Propanethiol is also used for this purpose, usually as a blend with *tert*-butyl mercaptan.

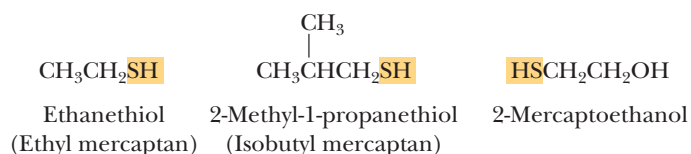


B. Nomenclature

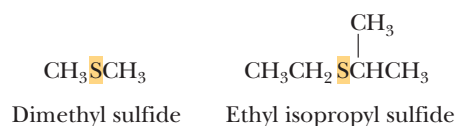
The sulfur analog of an alcohol is called a thiol (thi- from the Greek: *theion*, sulfur) or, in the older literature, a **mercaptan**, which literally means “mercury capturing.” Thiols react with Hg^{2+} in aqueous solution to give sulfide salts as insoluble precipitates. Thiophenol, $\text{C}_6\text{H}_5\text{SH}$, for example, gives $(\text{C}_6\text{H}_5\text{S})_2\text{Hg}$.

In the IUPAC system, thiols are named by selecting as the parent alkane the longest chain of carbon atoms that contains the $-\text{SH}$ group. To show that the compound is a thiol, we add *-thiol* to the name of the parent alkane and number the parent chain in the direction that gives the $-\text{SH}$ group the lower number.

Common names for simple thiols are derived by naming the alkyl group bonded to $-\text{SH}$ and adding the word *mercaptan*. In compounds containing other functional groups, the presence of an $-\text{SH}$ group is indicated by the prefix **mercapto-**. According to the IUPAC system, $-\text{OH}$ takes precedence over $-\text{SH}$ in both numbering and naming:



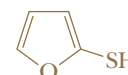
Sulfur analogs of ethers (thioethers) are named by using the word *sulfide* to show the presence of the $-\text{S}-$ group. Following are common names of two sulfides:



Mercaptan A common name for any molecule containing an $-\text{SH}$ group.

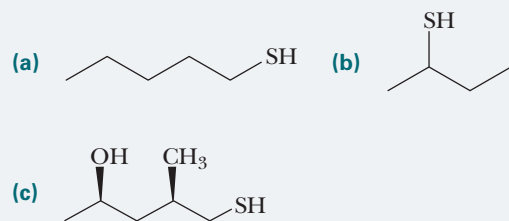


Mushrooms, onions, garlic, and coffee all contain sulfur compounds. One of these present in coffee is



EXAMPLE 8.11

Write the IUPAC name for each compound:



STRATEGY

Identify the root name of the compound. If the compound only contains an —SH group, name it as an alkanethiol. If the compound contains both an —OH group and an —SH group, name the compound as an alcohol with a mercapto substituent. Remember that priority for numbering is given to the —OH group.

SOLUTION

(a) The parent alkane is pentane. We show the presence of the —SH group by adding *thiol* to the name of the par-

ent alkane. The IUPAC name of this thiol is 1-pentanethiol. Its common name is pentyl mercaptan.

(b) The parent alkane is butane. The IUPAC name of this thiol is 2-butanethiol. Its common name is *sec*-butyl mercaptan. It is a chiral molecule due to the stereocenter at C-2. However, the stereochemical configuration was not indicated here.

(c) The parent alkane is pentane. Because —OH receives priority over —SH, the compound is named as an alcohol, with the —OH group receiving priority for numbering as well.

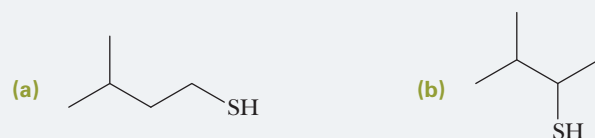


(2*R*,4*R*)-5-Mercapto-4-methylpentan-2-ol

See problems 8.14, 8.15

PROBLEM 8.11

Write the IUPAC name for each thiol:



C. Physical Properties

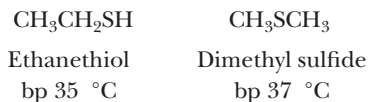
Because of the small difference in electronegativity between sulfur and hydrogen ($2.5 - 2.1 = 0.4$), we classify the S—H bond as nonpolar covalent. Because of this lack of polarity, thiols show little association by hydrogen bonding. Consequently, they have lower boiling points and are less soluble in water and other polar solvents than are alcohols of similar molecular weight. Table 8.4 gives the boiling points of three low-molecular-weight thiols. For comparison, the table also gives the boiling points of alcohols with the same number of carbon atoms.

Earlier, we illustrated the importance of hydrogen bonding in alcohols by comparing the boiling points of ethanol (78 °C) and its constitutional isomer dimethyl ether (24 °C).

TABLE 8.4 Boiling Points of Three Thiols and Three Alcohols with the Same Number of Carbon Atoms

Thiol	Boiling Point (°C)	Alcohol	Boiling Point (°C)
methanethiol	6	methanol	65
ethanethiol	35	ethanol	78
1-butanethiol	98	1-butanol	117

By comparison, the boiling point of ethanethiol is 35 °C, and that of its constitutional isomer dimethyl sulfide is 37 °C:



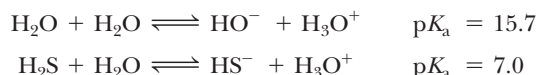
The fact that the boiling points of these constitutional isomers are almost identical indicates that little or no association by hydrogen bonding occurs between thiol molecules.

8.6 What Are the Characteristic Reactions of Thiols?

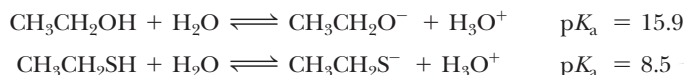
In this section, we discuss the acidity of thiols and their reaction with strong bases, such as sodium hydroxide, and with molecular oxygen.

A. Acidity

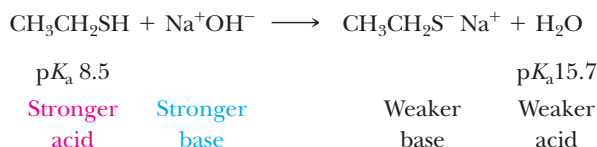
Hydrogen sulfide is a stronger acid than water:



Similarly, thiols are stronger acids than alcohols. Compare, for example, the pK_a 's of ethanol and ethanethiol in dilute aqueous solution:



Thiols are sufficiently strong acids that, when dissolved in aqueous sodium hydroxide, they are converted completely to alkylsulfide salts:

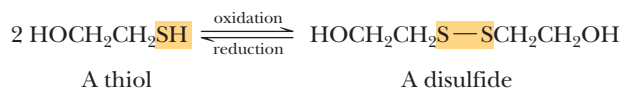


thiols are more acidic than alcohols because sulfides are more stable conjugate bases than are alkoxides. There is more area to delocalize the valence electrons about the negative sulfur atom because sulfur is larger than oxygen.

To name salts of thiols, give the name of the cation first, followed by the name of the alkyl group to which the suffix *-sulfide* is added. For example, the sodium salt derived from ethanethiol is named sodium ethylsulfide.

B. Oxidation to Disulfides

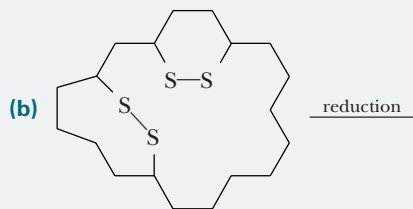
Many of the chemical properties of thiols stem from the fact that the sulfur atom of a thiol is oxidized easily to several higher oxidation states. The most common reaction of thiols in biological systems is their oxidation to disulfides, the functional group of which is a **disulfide** ($-\text{S}-\text{S}-$) bond. Thiols are readily oxidized to disulfides by molecular oxygen. In fact, they are so susceptible to oxidation that they must be protected from contact with air during storage. Disulfides, in turn, are easily reduced to thiols by several reagents. This easy interconversion between thiols and disulfides is very important in protein chemistry, as we will see in Chapter 18:



We derive common names of simple disulfides by listing the names of the groups bonded to sulfur and adding the word *disulfide*, as, for example, $\text{CH}_3\text{S}-\text{SCH}_3$, which is named dimethyldisulfide.

EXAMPLE 8.12

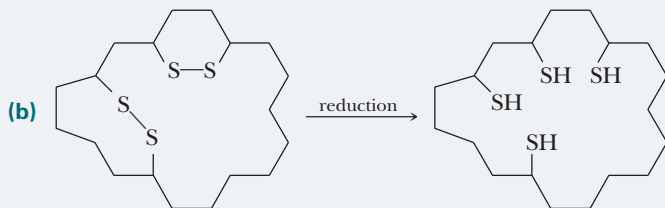
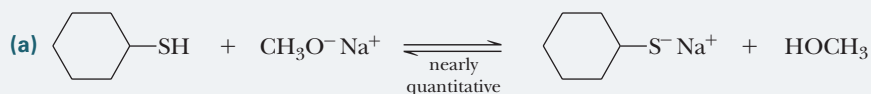
Predict the products of the following reactions. If the reaction is an acid–base reaction, predict its position of equilibrium.



STRATEGY

First determine what type of reaction is occurring. An oxidation reaction of a thiol produces a disulfide bond ($-\text{S}-\text{S}-$). A reduction of a disulfide bond produces two mercapto groups. Thiols can also act as weak acids (although at a $\text{p}K_a$ of 8.5, they are relatively strong for an organic acid).

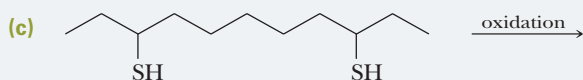
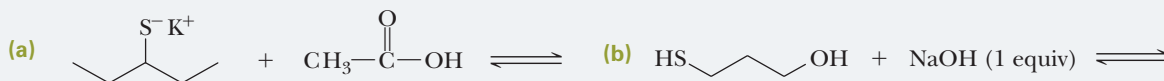
SOLUTION



See problems 8.28–8.30, 8.32

PROBLEM 8.12

Predict the products of the following reactions. If the reaction is an acid–base reaction, predict its position of equilibrium.



SUMMARY OF KEY QUESTIONS

8.1 What Are Alcohols?

- The functional group of an **alcohol** is an $-\text{OH}$ (**hydroxyl group**) bonded to an sp^3 hybridized carbon.
- Alcohols are classified as 1° , 2° , or 3° , depending on whether the $-\text{OH}$ group is bonded to a primary, secondary, or tertiary carbon.
- IUPAC names of alcohols are derived by changing the suffix of the parent alkane from $-e$ to $-ol$. The chain is numbered to give the carbon bearing $-\text{OH}$ the lower number.
- Common names for alcohols are derived by naming the alkyl group bonded to $-\text{OH}$ and adding the word *alcohol*.

- Alcohols are polar compounds with oxygen bearing a partial negative charge and both the carbon and hydrogen bonded to it bearing partial positive charges.
- Because of intermolecular association by hydrogen bonding, the boiling points of alcohols are higher than those of hydrocarbons with comparable molecular weight.
- Because of increased dispersion forces, the boiling points of alcohols increase with increasing molecular weight.
- Alcohols interact with water by **hydrogen bonding** and therefore are more soluble in water than are hydrocarbons of comparable molecular weight.

8.2 What Are the Characteristic Reactions of Alcohols?

- Alcohols undergo acid–base reactions, acting both as weak acids and weak bases. The two smallest alcohols, methanol and ethanol, are comparable to water in acidity, while most 2° and 3° alcohols are less acidic than water.
- Alcohols react with **active metals** (e.g., Li, Na, K) to give **alkoxides**.
- Alcohols react with hydrogen halides (HCl, HBr, and HI) to give haloalkanes via substitution reactions. The mechanism of the reaction is either S_N1 or S_N2 depending on the classification (1°, 2°, or 3°) of the alcohol.
- Alcohols react with **thionyl chloride**, SOCl₂, to give chloroalkanes.
- Alcohols undergo **dehydration** in concentrated sulfuric or phosphoric acid. These elimination reactions follow Zaitsev's rule, yielding the more substituted alkene as the major product.
- Alcohols can be **oxidized** to ketones, aldehydes, and carboxylic acids. **Chromic acid** and **pyridinium chlorochromate** (PCC) both oxidize 2° alcohols to ketones. PCC oxidizes 1° alcohols to aldehydes, while chromic acid oxidizes 1° alcohols to carboxylic acids. 3° Alcohols are not oxidized.

8.3 What Are Ethers?

- The functional group of an **ether** is an atom of oxygen bonded to two carbon atoms. Ethers are used as solvents and in medicine as inhalation anesthetics.
 - In the IUPAC name of an ether, the parent alkane is named, and then the —OR group is named as an alkoxy substituent. Common names are derived by naming the two groups bonded to oxygen followed by the word “ether.” Ethers are weakly polar compounds.
- Their boiling points are close to those of hydrocarbons with comparable molecular weight. Because ethers are hydrogen-bond acceptors, they are more soluble in water than are hydrocarbons with comparable molecular weight.
- Ethers are relatively resistant to chemical transformation and, for this reason, are often employed as solvents in chemical reactions.

8.4 What Are Epoxides?

- An **epoxide** is a three-membered cyclic ether in which oxygen is one of the atoms of the three-membered ring.
- Epoxides can be synthesized from the reaction of an alkene with a **peroxycarboxylic acid** (RCO₃H). The reaction proceeds such that the relative stereochemistry about the C—C double bond is retained in the product epoxide.
- Epoxides undergo ring-opening reactions due to the strain of their three-membered rings. In acid-catalyzed hydrolysis, epoxides made from cyclic alkenes are transformed into *trans*-glycols. Good nucleophiles can also open the epoxide ring via nucleophilic attack at the least substituted carbon of the three-membered ring.

8.5 What Are Thiols?

- A **thiol** is the sulfur analog of an alcohol; it contains an —SH (**sulfhydryl group**) in place of an —OH group. Thiols are important compounds in several biological processes.
- Thiols are named in the same manner as alcohols, but the suffix *-e* is retained, and *-thiol* is added. Common names for thiols are derived by naming the alkyl group bonded to —SH and adding the word “**mercaptan**.” In compounds containing functional groups of higher precedence, the presence of —SH is indicated by the prefix **mercapto-**. For thioethers, name the two groups bonded to sulfur, followed by the word “**sulfide**.”
- The S—H bond is nonpolar covalent, and the physical properties of thiols are more like those of hydrocarbons with comparable molecular weight.

8.6 What Are the Characteristic Reactions of Thiols?

- Thiols (pK_a ≈ 8.5) are stronger acids than alcohols and are quantitatively deprotonated by hydroxide.
- Thiols can be oxidized to give a **disulfide** (—S—S—) bond. This process is reversible through reduction.

QUICK QUIZ

Answer true or false to the following questions to assess your general knowledge of the concepts in this chapter. If you have difficulty with any of them, you should review the appropriate section in the chapter (shown in parentheses) before attempting the more challenging end-of-chapter problems.

- Dehydration of an alcohol proceeds either by an E1 or an E2 mechanism. (8.2)
- Epoxides are more reactive than acyclic ethers. (8.3, 8.4)
- Attack of an electrophile on the carbon of an epoxide ring results in opening of the ring. (8.4)
- A hydrogen bond is a form of dipole–dipole interaction. (8.1)
- Alcohols have higher boiling points than thiols with the same molecular weight. (8.1, 8.5)
- Thiols are more acidic than alcohols. (8.2, 8.5)
- Alcohols can act as hydrogen-bond donors but not as hydrogen-bond acceptors. (8.1)
- Alcohols can function as both acids and bases. (8.2)
- Ethers can act as hydrogen-bond donors but not as hydrogen-bond acceptors. (8.3)
- Reduction of a thiol produces a disulfide. (8.6)
- Ethers are more reactive than alcohols. (8.2, 8.3)
- $(\text{CH}_3\text{CH}_2)_2\text{CHOH}$ is classified as a 3° alcohol. (8.1)
- PCC will oxidize a secondary alcohol to a ketone. (8.2)
- PCC will oxidize a primary alcohol to a carboxylic acid. (8.2)
- Alcohols have higher boiling points than ethers with the same molecular weight. (8.1, 8.3)
- A dehydration reaction yields an epoxide as the product. (8.2)
- Alcohols can be converted to alkenes. (8.2)
- Alcohols can be converted to haloalkanes. (8.2)
- In naming alcohols, “alkyl alcohol” is the IUPAC form of the name, while “alkanol” is the common form of the name. (8.1)
- OH is a poor leaving group. (8.2)
- A glycol is any alcohol with at least two hydroxyl groups bonded to different carbons. (8.1)

Answers: (1) T (2) T (3) F (4) T (5) T (6) T (7) F (8) T (9) F (10) F (11) F (12) F (13) T (14) F (15) T (16) F (17) T (18) T (19) F (20) T (21) T

Detailed explanations for many of these answers can be found in the accompanying Solutions Manual.

KEY REACTIONS

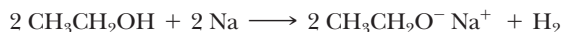
1. Acidity of Alcohols (Section 8.2A)

In dilute aqueous solution, methanol and ethanol are comparable in acidity to water. Secondary and tertiary alcohols are weaker acids than water.



2. Reaction of Alcohols with Active Metals (Section 8.2C)

Alcohols react with Li, Na, K, and other active metals to form metal alkoxides, which are somewhat stronger bases than NaOH and KOH:

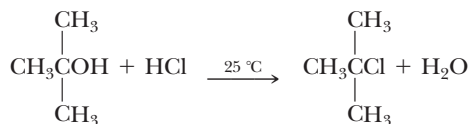


3. Reaction of Alcohols with HCl, HBr, and HI (Section 8.2D)

Primary alcohols react with HBr and HI by an $\text{S}_{\text{N}}2$ mechanism:



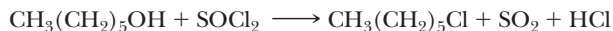
Tertiary alcohols react with HCl, HBr, and HI by an $\text{S}_{\text{N}}1$ mechanism, with the formation of a carbocation intermediate:



Secondary alcohols may react with HCl, HBr, and HI by an $\text{S}_{\text{N}}2$ or an $\text{S}_{\text{N}}1$ mechanism, depending on the alcohol and experimental conditions.

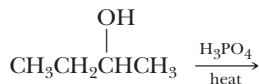
4. Reaction of Alcohols with SOCl_2 (Section 8.2D)

This is often the method of choice for converting an alcohol to an alkyl chloride:



5. Acid-Catalyzed Dehydration of Alcohols (Section 8.2E)

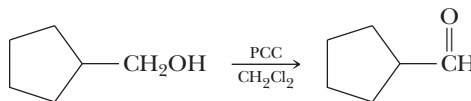
When isomeric alkenes are possible, the major product is generally the more substituted alkene (Zaitsev's rule):



Major product

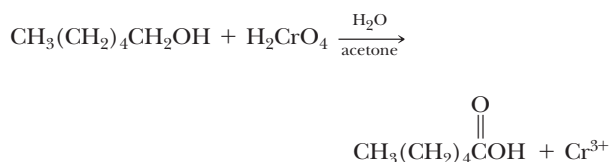
6. Oxidation of a Primary Alcohol to an Aldehyde (Section 8.2F)

This oxidation is most conveniently carried out by using pyridinium chlorochromate (PCC):

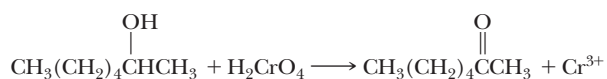


7. Oxidation of a Primary Alcohol to a Carboxylic Acid (Section 8.2F)

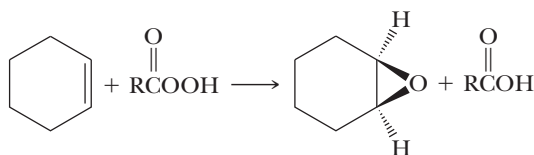
A primary alcohol is oxidized to a carboxylic acid by chromic acid:

**8. Oxidation of a Secondary Alcohol to a Ketone (Section 8.2F)**

A secondary alcohol is oxidized to a ketone by chromic acid and by PCC:

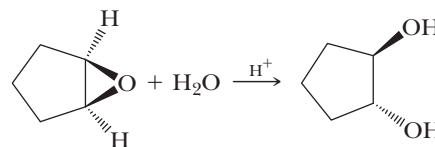
**9. Oxidation of an Alkene to an Epoxide (Section 8.4B)**

The most common method for the synthesis of an epoxide from an alkene is oxidation with a peroxyacetic acid, such as peroxyacetic acid:

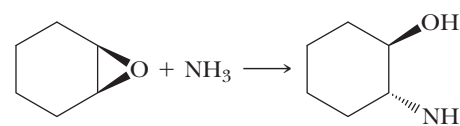
**10. Acid-Catalyzed Hydrolysis of Epoxides (Section 8.4C)**

Acid-catalyzed hydrolysis of an epoxide derived from a cycloalkene gives a *trans* glycol (hydrolysis of

cycloalkene oxide is stereoselective, giving the *trans* glycol):

**11. Nucleophilic Ring Opening of Epoxides (Section 8.4C)**

Good nucleophiles, such as ammonia and amines, open the highly strained epoxide ring by an $\text{S}_{\text{N}}2$ mechanism and show a regioselectivity for attack of the nucleophile at the less hindered carbon of the three-membered ring. The reaction favors the stereoselective formation of the *trans* product:



Cyclohexene oxide *trans*-2-Aminocyclohexanol

12. Acidity of Thiols (Section 8.6A)

Thiols are weak acids, $\text{p}K_{\text{a}}$ 8–9, but are considerably stronger acids than alcohols, $\text{p}K_{\text{a}}$ 16–18.

**13. Oxidation to Disulfides (Section 8.6B)**

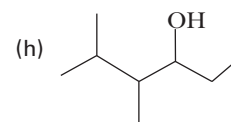
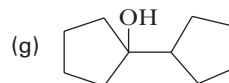
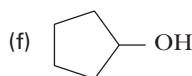
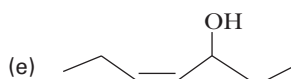
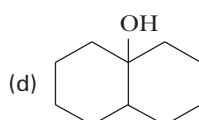
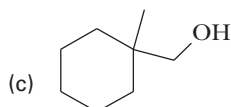
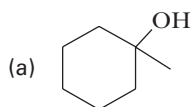
Oxidation of a thiol by O_2 gives a disulfide:

**PROBLEMS**

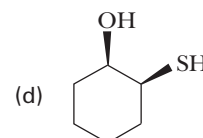
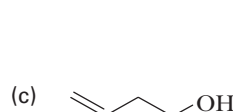
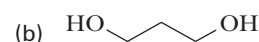
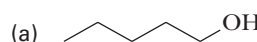
A problem marked with an asterisk indicates an applied “real-world” problem. Answers to problems whose numbers are printed in blue are given in Appendix D.

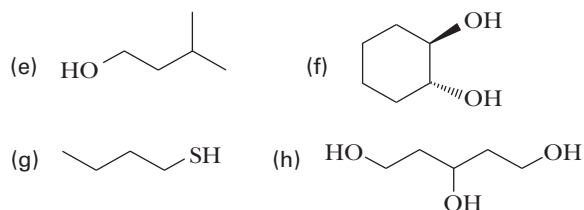
Structure and Nomenclature

8.13 Classify the alcohols as primary, secondary, or tertiary. (See Example 8.2)



8.14 Provide an IUPAC or common name for these compounds: (See Examples 8.1, 8.3, 8.11)





8.15 Draw a structural formula for each alcohol: (See Examples 8.1, 8.3, 8.11)

- Isopropyl alcohol
- Propylene glycol
- (*R*)-5-Methyl-2-hexanol
- 2-Methyl-2-propyl-1,3-propanediol
- 2,2-Dimethyl-1-propanol
- 2-Mercaptoethanol
- 1,4-Butanediol
- (*Z*)-5-Methyl-2-hexen-1-ol

Physical Properties

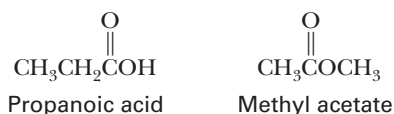
8.18 Arrange these compounds in order of increasing boiling point (values in °C are -42, 78, 117, and 198):

- $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$
- $\text{CH}_3\text{CH}_2\text{OH}$
- $\text{HOCH}_2\text{CH}_2\text{OH}$
- $\text{CH}_3\text{CH}_2\text{CH}_3$

8.19 Arrange these compounds in order of increasing boiling point (values in °C are -42, -24, 78, and 118):

- $\text{CH}_3\text{CH}_2\text{OH}$
- CH_3OCH_3
- $\text{CH}_3\text{CH}_2\text{CH}_3$
- CH_3COOH

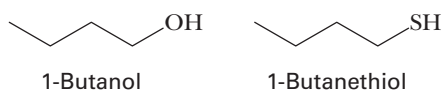
8.20 Propanoic acid and methyl acetate are constitutional isomers, and both are liquids at room temperature:



One of these compounds has a boiling point of 141 °C; the other has a boiling point of 57 °C. Which compound has which boiling point?

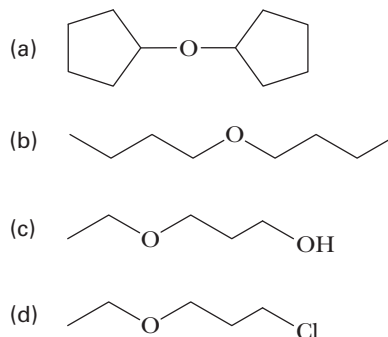
8.21 Draw all possible staggered conformations of ethylene glycol ($\text{HOCH}_2\text{CH}_2\text{OH}$). Can you explain why the conformation in which the —OH groups are closest to each other is more stable than the conformation in which the —OH groups are farthest apart by approximately 4.2 kJ/mol (1 kcal/mol)? (See Example 3.7)

8.22 Following are structural formulas for 1-butanol and 1-butanethiol:



- cis*-3-Penten-1-ol
- trans*-1,4-Cyclohexanediol

8.16 Write names for these ethers: (See Example 8.7)



8.17 Name and draw structural formulas for the eight isomeric alcohols with molecular formula $\text{C}_5\text{H}_{12}\text{O}$. Which are chiral? (See Examples 8.1, 8.3)

One of these compounds has a boiling point of 98.5 °C; the other has a boiling point of 117 °C. Which compound has which boiling point?

8.23 From each pair of compounds, select the one that is more soluble in water: (See Example 8.8)

- CH_2Cl_2 or CH_3OH
- $\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_3$ or $\text{CH}_3\overset{\text{CH}_2}{\parallel}\text{CCH}_3$
- $\text{CH}_3\text{CH}_2\text{Cl}$ or NaCl
- $\text{CH}_3\text{CH}_2\text{CH}_2\text{SH}$ or $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$
- $\text{CH}_3\text{CH}_2\overset{\text{OH}}{\text{C}}\text{HCH}_2\text{CH}_3$ or $\text{CH}_3\text{CH}_2\overset{\text{O}}{\parallel}\text{CCH}_2\text{CH}_3$

8.24 Arrange the compounds in each set in order of decreasing solubility in water: (See Example 8.8)

- Ethanol; butane; diethyl ether
- 1-Hexanol; 1,2-hexanediol; hexane

8.25 Each of the following compounds is a common organic solvent. From each pair of compounds, select the solvent with the greater solubility in water. (See Example 8.8)

- CH_2Cl_2 or $\text{CH}_3\text{CH}_2\text{OH}$
- $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ or $\text{CH}_3\text{CH}_2\text{OH}$
- $\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_3$ or $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$
- $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ or $\text{CH}_3(\text{CH}_2)_3\text{CH}_3$

Synthesis of Alcohols

8.26 Give the structural formula of an alkene or alkenes from which each alcohol or glycol can be prepared: (See Examples 5.5, 8.10)

- (a) 2-Butanol (b) 1-Methylcyclohexanol
 (c) 3-Hexanol (d) 2-Methyl-2-pentanol
 (e) Cyclopentanol (f) 1,2-Propanediol

8.27 The addition of bromine to cyclopentene and the acid-catalyzed hydrolysis of cyclopentene oxide are both stereoselective; each gives a *trans* product. Compare the mechanisms of these two reactions, and show how each mechanism accounts for the formation of the *trans* product.

Acidity of Alcohols and Thiols

8.28 From each pair, select the stronger acid, and, for each stronger acid, write a structural formula for its conjugate base: (See Examples 8.4, 8.12)

- (a) H₂O or H₂CO₃
 (b) CH₃OH or CH₃COOH
 (c) CH₃COOH or CH₃CH₂SH

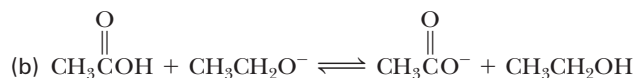
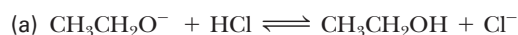
8.29 Arrange these compounds in order of increasing acidity (from weakest to strongest): (See Examples 8.4, 8.12)



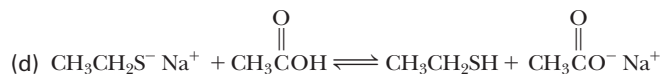
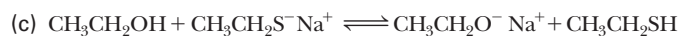
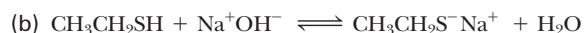
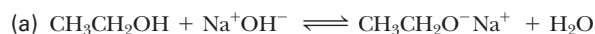
8.30 From each pair, select the stronger base, and, for each stronger base, write the structural formula of its conjugate acid: (See Examples 8.4, 8.12)

- (a) OH⁻ or CH₃O⁻
 (b) CH₃CH₂S⁻ or CH₃CH₂O⁻
 (c) CH₃CH₂O⁻ or NH₂⁻

8.31 Label the stronger acid, stronger base, weaker acid, and weaker base in each of the following equilibria, and then predict the position of each equilibrium (for pK_a values, see Table 2.1): (See Example 8.4)



8.32 Predict the position of equilibrium for each acid-base reaction; that is, does each lie considerably to the left, does each lie considerably to the right, or are the concentrations evenly balanced? (See Examples 8.4, 8.12)



Reactions of Alcohols

8.33 Show how to distinguish between cyclohexanol and cyclohexene by a simple chemical test. (*Hint*: Treat each with Br₂ in CCl₄ and watch what happens.)

8.34 Write equations for the reaction of 1-butanol, a primary alcohol, with these reagents: (See Examples 8.4, 8.6)

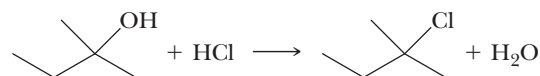
- (a) Na metal
 (b) HBr, heat
 (c) K₂Cr₂O₇, H₂SO₄, heat
 (d) SOCl₂
 (e) Pyridinium chlorochromate (PCC)

8.35 Write equations for the reaction of 2-butanol, a secondary alcohol, with these reagents: (See Examples 8.4, 8.6)

- (a) Na metal (b) H₂SO₄, heat
 (c) HBr, heat (d) K₂Cr₂O₇, H₂SO₄, heat
 (e) SOCl₂ (f) Pyridinium chlorochromate (PCC)

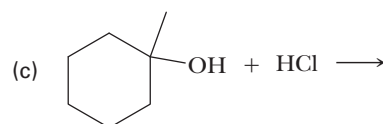
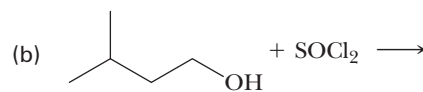
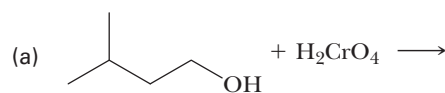
8.36 When (*R*)-2-butanol is left standing in aqueous acid, it slowly loses its optical activity. When the organic material is recovered from the aqueous solution, only 2-butanol is found. Account for the observed loss of optical activity.

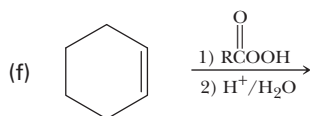
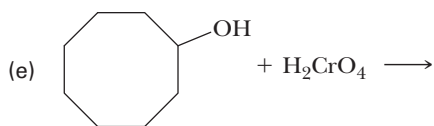
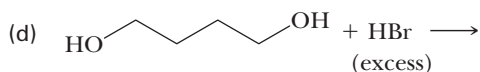
8.37 What is the most likely mechanism of the following reaction?



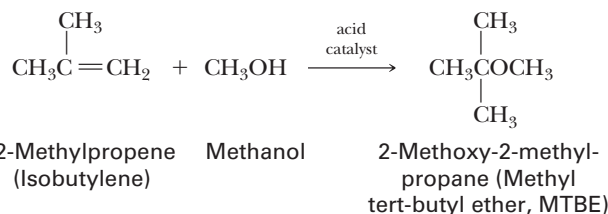
Draw a structural formula for the intermediate(s) formed during the reaction.

8.38 Complete the equations for these reactions: (See Examples 8.6, 8.9)





***8.39** In the commercial synthesis of methyl *tert*-butyl ether (MTBE), once used as an antiknock, octane-improving gasoline additive, 2-methylpropene and methanol are passed over an acid catalyst to give the ether. Propose a mechanism for this reaction. (See Examples 5.5, 5.6)



Syntheses

8.41 Show how to convert (See Examples 8.5, 8.6, 8.10)

- 1-Propanol to 2-propanol in two steps.
- Cyclohexene to cyclohexanone in two steps.
- Cyclohexanol to *trans*-1,2-cyclohexanediol in three steps.
- Propene to propanone (acetone) in two steps.

8.42 Show how to convert cyclohexanol to these compounds: (See Examples 8.5, 8.6)

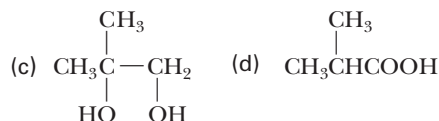
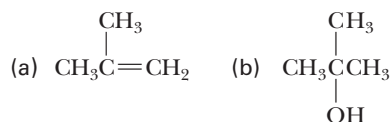
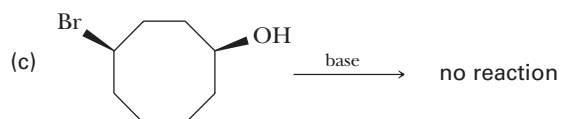
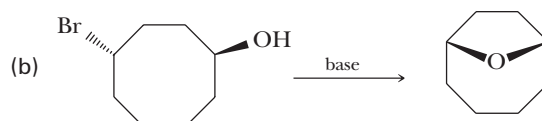
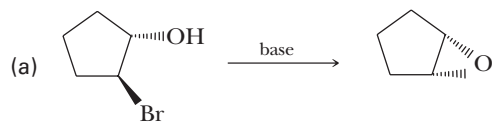
- Cyclohexene
- Cyclohexane
- Cyclohexanone
- Cyclohexene oxide

8.43 Show reagents and experimental conditions that can be used to synthesize these compounds from 1-propanol (any derivative of 1-propanol prepared in an earlier part of this problem may be used for a later synthesis): (See Examples 8.5, 8.6, 8.9, 8.10)

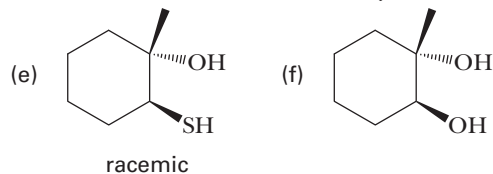
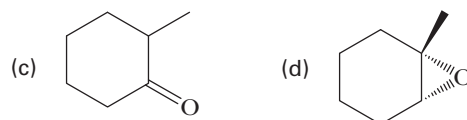
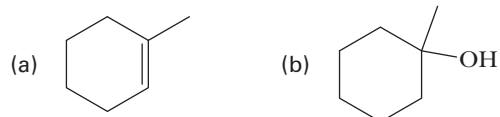
- Propanal
- Propanoic acid
- Propene
- 2-Propanol
- 2-Bromopropane
- 1-Chloropropane
- Propanone
- 1,2-Propanediol

8.44 Show how to prepare each compound from 2-methyl-1-propanol (isobutyl alcohol). For any preparation involving more than one step, show each intermediate compound formed. (See Examples 8.5, 8.6, 8.9, 8.10)

8.40 Cyclic bromoalcohols, upon treatment with base, can sometimes undergo intramolecular $\text{S}_{\text{N}}2$ reactions to form the ethers shown in reactions (a) and (b). Provide a mechanism for reactions (a) and (b). Indicate why equation (c) does not yield a similar reaction.

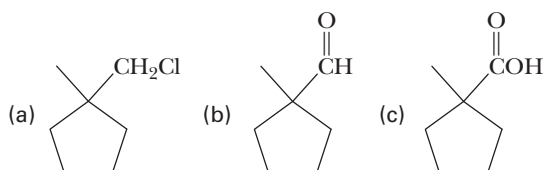
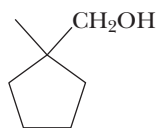


8.45 Show how to prepare each compound from 2-methylcyclohexanol: (See Examples 8.5, 8.6, 8.9, 8.10)

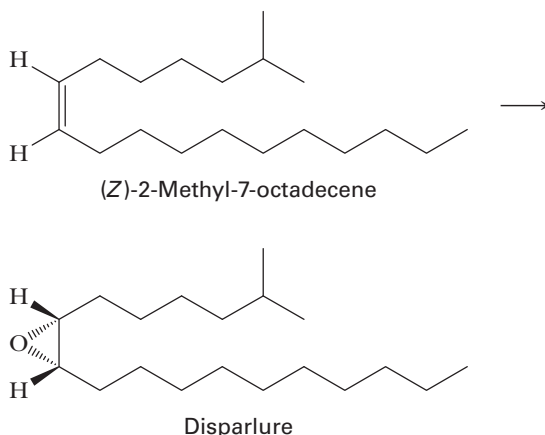


For any preparation involving more than one step, show each intermediate compound formed.

8.46 Show how to convert the alcohol on the left to compounds (a), (b), and (c). (See Example 8.6)



*8.47 Disparlure, a sex attractant of the gypsy moth (*Porthetria dispar*), has been synthesized in the laboratory from the following (*Z*)-alkene: (See Example 8.9)



*8.48 The chemical name for bombykol, the sex pheromone secreted by the female silkworm moth to attract male silkworm moths, is *trans*-10-*cis*-12-hexadecadien-1-ol. (The compound has one hydroxyl group and two carbon-carbon double bonds in a 16-carbon chain.)

- (a) Draw a structural formula for bombykol, showing the correct configuration about each carbon-carbon double bond.
- (b) How many *cis-trans* isomers are possible for the structural formula you drew in part (a)? All possible *cis-trans* isomers have been synthesized in the laboratory, but only the one named bombykol is produced by the female silkworm moth, and only it attracts male silkworm moths.

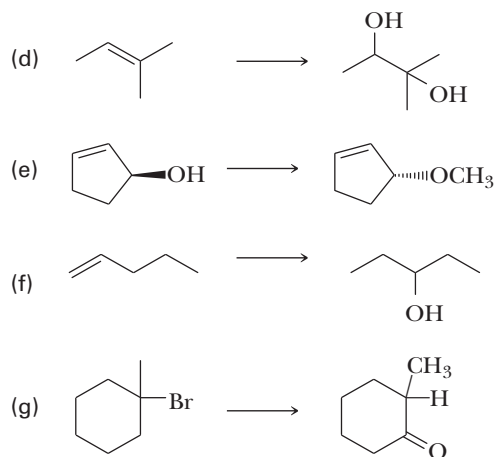
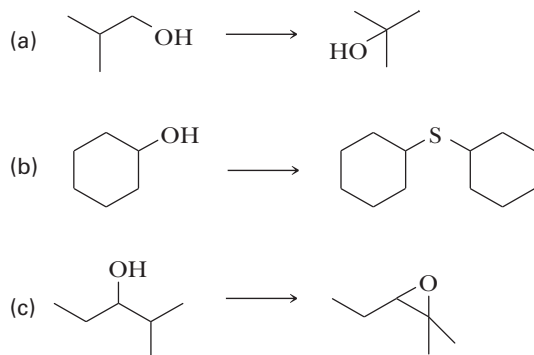


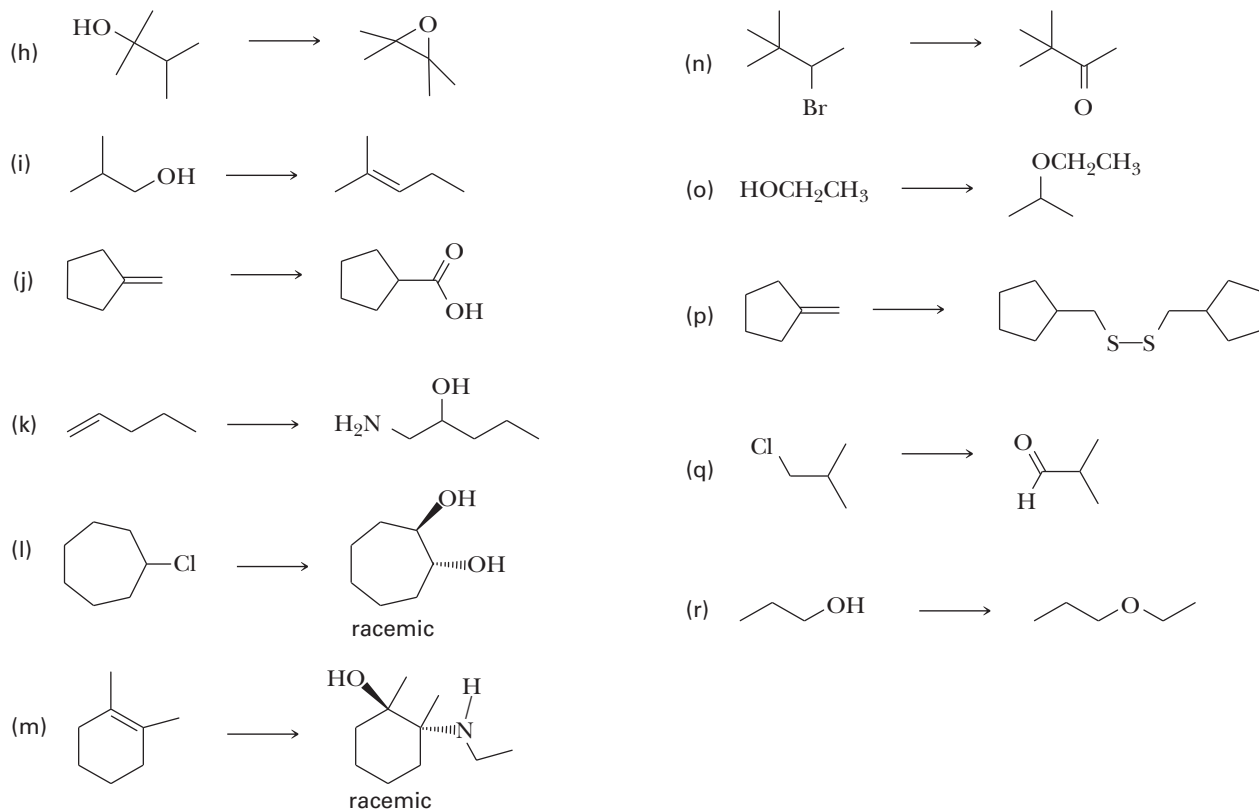
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Gypsy moth caterpillar.

CHEMICAL TRANSFORMATIONS

8.49 Test your cumulative knowledge of the reactions learned thus far by completing the following chemical transformations. Note: Some will require more than one step.

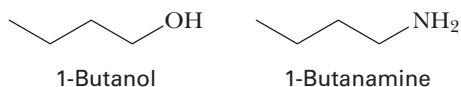




LOOKING AHEAD

8.50 Compounds that contain an N—H group associate by hydrogen bonding.

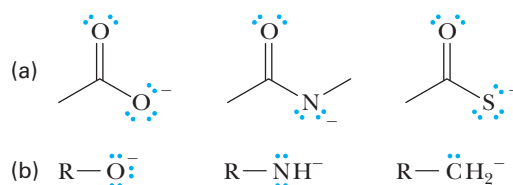
- (a) Do you expect this association to be stronger or weaker than that between compounds containing an O—H group?
- (b) Based on your answer to part (a), which would you predict to have the higher boiling point, 1-butanol or 1-butanamine?



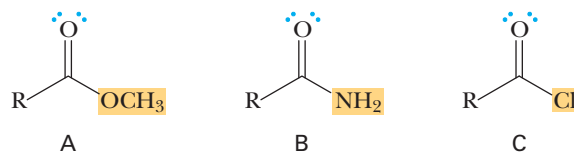
8.51 Draw a resonance structure for methyl vinyl ether in which the oxygen is positively charged. Compared with ethyl methyl ether, how does the resonance structure for methyl vinyl ether influence the reactivity of its oxygen toward an electrophile?



8.52 Rank the members in each set of reagents from most to least nucleophilic:



8.53 In Chapter 15 we will see that the reactivity of the following carbonyl compounds is directly proportional to the stability of the leaving group. Rank the order of reactivity of these carbonyl compounds from most reactive to least reactive based on the stability of the leaving group.



GROUP LEARNING ACTIVITIES

- 8.54** Discuss why primary alcohols (with the exception of ethanol) cannot be prepared by the acid-catalyzed hydration of alkenes. You'll want to discuss the mechanism of acid-catalyzed hydration and consider the reactive species involved.
- 8.55** Discuss why sodium hydroxide is not a good reagent for the synthesis of alkoxides from alcohols. Similarly, could sodium hydroxide be used to synthesize alkylsulfides from thiols? Why or why not? You'll want to discuss the type of reactions that would occur in both reactions as well as what makes a reaction synthetically useful.
- 8.56** One of the following alcohols is used to de-ice airplanes during extreme cold weather. As a group, decide which of the three alcohols would be most suitable for the job by discussing factors that one must consider for such an application.

