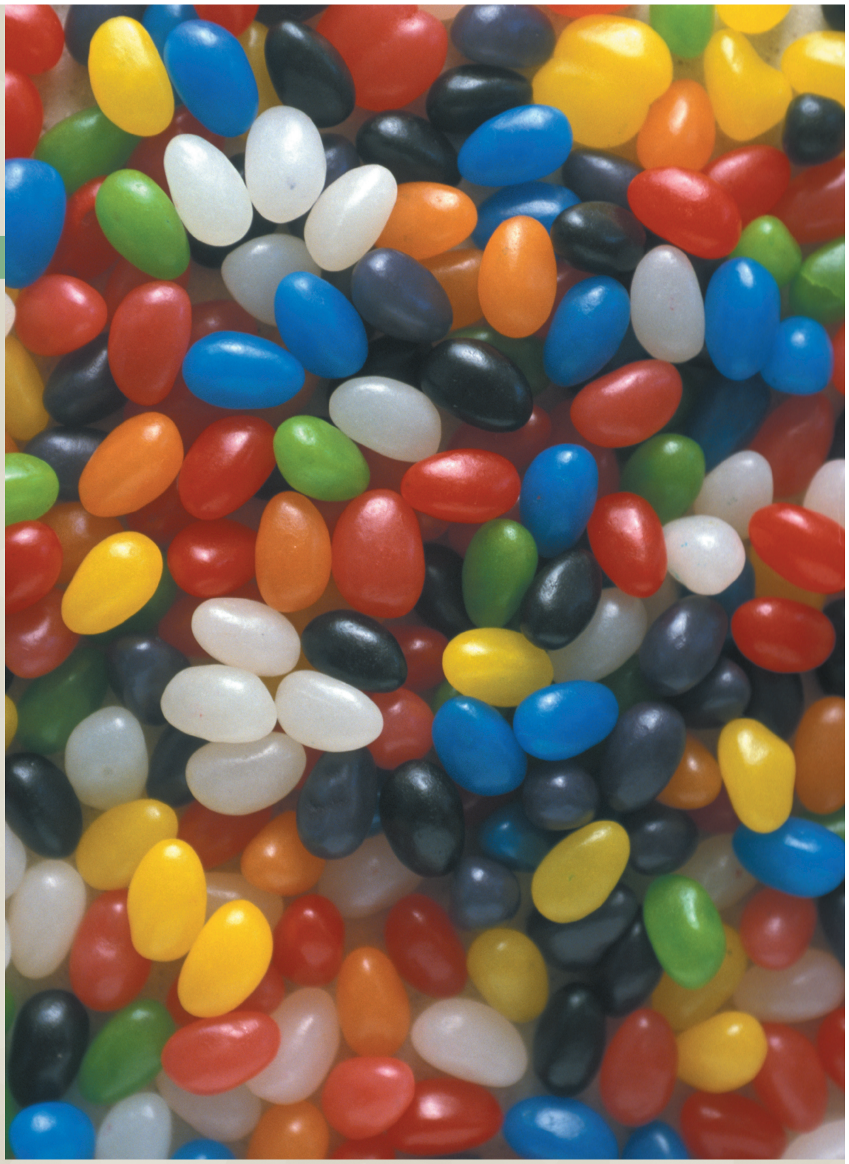
ORGANIC CHEMISTRY

12 Alcohols, Phenols, Thiols, and Ethers



Sugar-free jelly beans

Learning Goals

1. Rank selected alcohols by relative water solubility, boiling points, or melting points.
2. Write the names and draw the structures for common alcohols.
3. Discuss the biological, medical, or environmental significance of several alcohols.
4. Classify alcohols as primary, secondary, or tertiary.
5. Write equations representing the preparation of alcohols by the hydration of an alkene.
6. Write equations representing the preparation of alcohols by hydrogenation (reduction) of aldehydes or ketones.
7. Write equations showing the dehydration of an alcohol.
8. Write equations representing the oxidation of alcohols.
9. Discuss the role of oxidation and reduction reactions in the chemistry of living systems.
10. Discuss the use of phenols as germicides.
11. Write names and draw structures for common ethers and discuss their use in medicine.
12. Write equations representing the dehydration reaction between two alcohol molecules.
13. Write names and draw structures for simple thiols and discuss their biological significance.

Outline

Chemistry Connection

Polyols for the Sweet Tooth

Do you crave sweets, but worry about the empty calories in sugary treats? If so, you are not alone. Research tells us that, even as babies, we demonstrate preference for sweet tastes over all others. But there are many reasons to reduce our intake of refined sugars, in particular sucrose or table sugar. Too many people eat high-calorie, low-nutrition snacks rather than more nutritious foods. This can lead to obesity, a problem that is very common in our society. In addition, sucrose is responsible for tooth decay. Lactic acid, one of the products of the metabolism of sucrose by bacteria on our teeth, dissolves the tooth enamel, which results in a cavity. For those with diabetes, glucose intolerance, or hypoglycemia, sucrose in the diet makes it difficult to maintain a constant blood sugar level.

The food chemistry industry has invested billions of dollars in the synthesis of sugar substitutes. We recognize names such as aspartame (Equal or Nutrasweet), saccharin (Sweet & Low), and SPLENDA®, because they are the most common non-nutritive sweeteners worldwide. We also buy products, including candies, soft drinks, and gums, which are advertised to be "sugar-free." But you might be surprised to find that many of these products are not free of calories. A check of the nutritional label may reveal that these products contain sorbitol, mannitol, or one or more other members of a class of compounds called sugar alcohols, or *polyols* (*poly*—many; *ols*—alcohol or hydroxyl groups).

Sugar alcohols are found in many foods, including fruits, vegetables, and mushrooms. Others are made by hydrogenation or fermentation of carbohydrates from wheat or corn. But all are natural products. Compared to sucrose, they range in sweetness from about half to nearly the same; they also have fewer calories per gram than sucrose (about one-third to one-half the calories). Polyols also cause a cooling sensation in the mouth. This cooling is caused by a negative heat of solution (they must absorb heat from the surroundings in order to dissolve) and is used to advantage in breath freshening mints and gums.

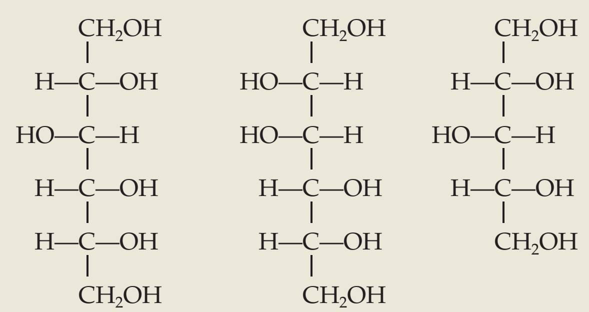
Sorbitol, the most commonly used sugar alcohol, is about 0.6 times the sweetness of sucrose. While sucrose contains four calories per gram, sorbitol is only about 2.6 C/g. Discovered in 1872 in the berries of Mountain Ash trees, sorbitol has a smooth mouthfeel, which makes it ideal as a texturizing agent in foods. It also has a pleasant, cool, sweet flavor and acts as a humectant, keeping foods from losing moisture. No acceptable daily intake (ADI) has been specified for sorbitol, which is an indication that it is considered to be a very safe food additive. However, it has been observed that ingestion of more than 50–80 g/day may have a laxative effect.

Mannitol, a structural isomer of sorbitol, is found naturally in asparagus, olives, pineapple, and carrots. For use in the food industry, it is extracted from seaweed. Mannitol has about 0.7 times the sweetness of sucrose and only about 1.6 C/g. As for sorbitol, no ADI has been specified; but ingestion of more than 20 g/day may cause diarrhea and bloating.

Xylitol was discovered in 1891 and has been used as a sweetener since the 1960s. Found in many fruits and vegetables, it has about the same sweetness as sucrose, but only one-third of the caloric value. Its high cooling effect, as well as sweetness, contribute to its popularity as a sweetening agent in hard candies and gums, as well as in oral health products. In fact, extensive studies suggest that use of xylitol-sweetened gum (7–10 g of xylitol per day) between meals results in a 30–60% decrease in dental cavities.

While polyols give us the sweetness that we enjoy without all of the calories, cavities, and blood sugar peaks of sucrose, they are not without a negative side. Some studies have reported weight gain by individuals who overeat these "sugar-free" foods. The American Diabetes Association has reported that these foods are "acceptable in moderate amounts but should not be eaten in excess." In fact, some diabetics have suffered elevated blood sugar after overeating foods containing polyols. Finally, as we noted above, when ingested in excess, sugar alcohols may cause bloating and diarrhea.

The use of these natural products continues to be investigated by the food and pharmaceutical industries. As we learn more about them, sugar alcohols continue to be versatile food additives. Using them in moderation, we can enjoy the benefits that they confer, without suffering uncomfortable side effects.



Sorbitol Mannitol Xylitol

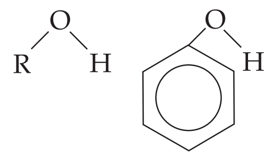
Structures of three of the sugar alcohols used in the food industry.

Introduction

> **An aryl group is an aromatic ring with one hydrogen atom removed.**

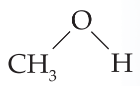
The characteristic functional group of the alcohols and phenols is the hydroxyl group (—OH). Alcohols have the general structure R—OH, in which R is any alkyl group. Phenols are similar in structure but contain an aryl group in place of the alkyl group. Both can be viewed as substituted water molecules in which one of the hydrogen atoms has been replaced by an alkyl or aryl group.

General formulas:



Alcohol Phenol

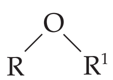
Example:



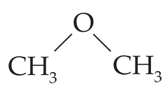
Methanol (methyl alcohol)

Ethers have two alkyl or aryl groups attached to the oxygen atom and may be thought of as substituted alcohols. The functional group characteristic of an ether is R—O—R. Thiols are a family of compounds that contain the sulfhydryl group (—SH). They, too, have a structure similar to that of alcohols.

> **R and R[1] = alkyl or aryl group**



Ethers



Methoxymethane (dimethyl ether)

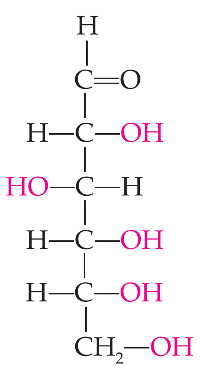
R—SH

Thiol

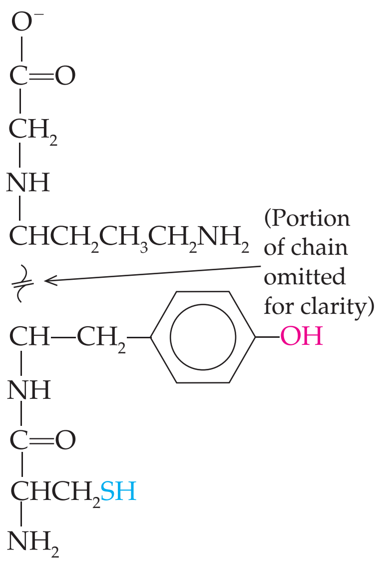
CH_3—SH

Methanethiol

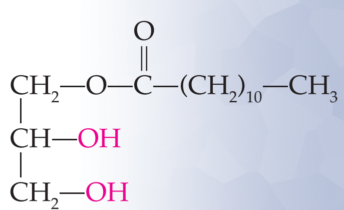
Many important biological molecules, including sugars (carbohydrates), fats (lipids), and proteins, contain hydroxyl and/or thiol groups.



D-Glucose, *a sugar*



Lysine vasopressin (partial structure), *a protein*



Monolaurin, *a lipid*

In biological systems, the hydroxyl group is often involved in a variety of reactions such as oxidation, reduction, hydration, and dehydration. In glycolysis (a metabolic pathway by which glucose is degraded and energy is harvested in the form of ATP), several steps center on the reactivity of the hydroxyl group. The majority of the consumable alcohol in the world (ethanol) is produced by fermentation reactions carried out by yeasts.

> *Glycolysis and fermentation are discussed in Chapter 21.*

The thiol group is found in the structure of some amino acids and is essential for keeping proteins in the proper three-dimensional shape required for their biological function. Thus, these functional groups play a central role in the structure and chemical properties of biological molecules. The thiol group of the amino acid cysteine is highlighted in blue in the structure of lysine vasopressin presented above.

12.1 Alcohols: Structure and Physical Properties

LEARNING GOAL 1

An **alcohol** is an organic compound that contains a **hydroxyl group** (—OH) attached to an alkyl group (Figure 12.1). The R—O—H portion of an alcohol is similar to the structure of water. The oxygen and the two atoms bonded to it lie in the same plane, and the R—O—H bond angle is approximately 104°, which is very similar to the H—O—H bond angle of water.

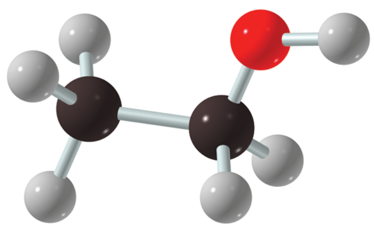


Figure 12.1
Ball-and-stick model of the simple alcohol ethanol.

The hydroxyl groups of alcohols are very polar because the oxygen and hydrogen atoms have significantly different electronegativities. Because the two atoms involved in this polar bond are oxygen and hydrogen, hydrogen bonds can form between alcohol molecules (Figure 12.2).

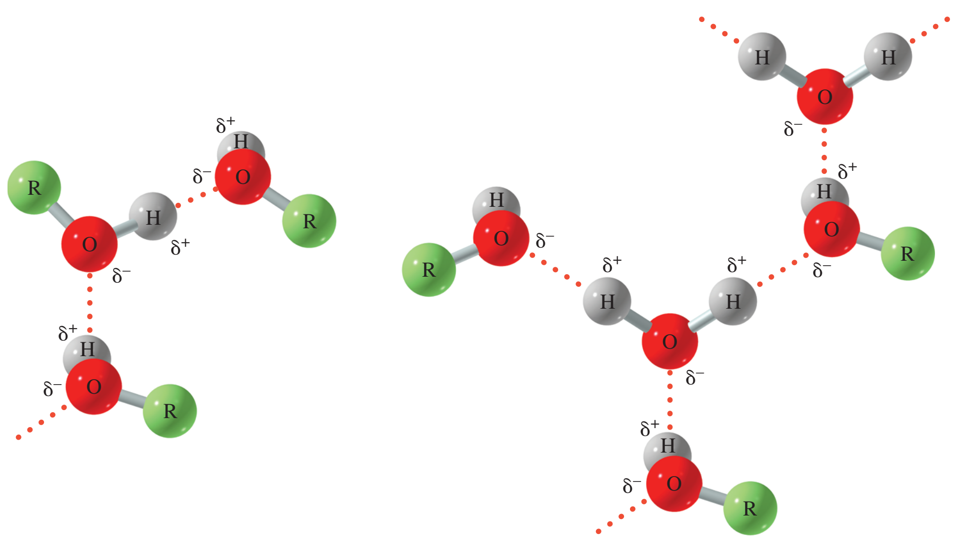
Electronegativity is discussed in Section 3.1. Hydrogen bonding is described in detail in Section 5.2.

As a result of this intermolecular hydrogen bonding, alcohols boil at much higher temperatures than hydrocarbons of similar molecular weight. These higher boiling points are caused by the large amount of heat needed to break the hydrogen bonds that attract the alcohol molecules to one another. Compare the boiling points of butane and propanol, which have similar molecular weights:

$CH_3CH_2CH_2CH_3$	$CH_3CH_2CH_2OH$
Butane	1-Propanol
M.W. = 58	M.W. = 60
b.p. = −0.5°C	b.p. = 97.2°C

Alcohols of one to four carbon atoms are very soluble in water, and those with five or six carbons are moderately soluble in water. This is due to the ability of the alcohol to form intermolecular hydrogen bonds with water molecules (see Figure 12.2b). As the nonpolar, or hydrophobic, portion of an alcohol (the carbon chain) becomes larger relative to the polar, hydrophilic, region (the hydroxyl group), the water solubility of an alcohol decreases. As a result alcohols of seven carbon atoms or more are nearly insoluble in water. The term *hydrophobic,* which literally means

Figure 12.2
(a) Hydrogen bonding between alcohol molecules. (b) Hydrogen bonding between alcohol molecules and water molecules.



(a) (b)

"water fearing," is used to describe a molecule or a region of a molecule that is nonpolar and, thus, more soluble in nonpolar solvents than in water. Similarly, the term *hydrophilic,* meaning water loving, is used to describe a polar molecule or region of a molecule that is more soluble in the polar solvent water than in a nonpolar solvent.

An increase in the number of hydroxyl groups along a carbon chain will increase the influence of the polar hydroxyl group. It follows, then that diols and triols are more water soluble than alcohols with only a single hydroxyl group.

The presence of polar hydroxyl groups in large biological molecules—for instance, proteins and nucleic acids—allows intramolecular hydrogen bonding that keeps these molecules in the shapes needed for biological function.

Intermolecular **hydrogen bonds are attractive forces between two molecules.** ***Intramolecular*** **hydrogen bonds are attractive forces between polar groups within the same molecule.**

12.2 Alcohols: Nomenclature

I.U.P.A.C. Names

2 LEARNING GOAL

In the I.U.P.A.C. Nomenclature System, alcohols are named according to the following steps:

- Determine the name of the *parent compound,* the longest continuous carbon chain containing the —OH group.
- Replace the *-e* ending of the alkane chain with the *-ol* ending of the alcohol. Following this pattern, an alkane becomes an alkanol. For instance, ethan*e* becomes ethan*ol,* and propan*e* becomes propan*ol.*
- Number the parent chain to give the carbon bearing the hydroxyl group the lowest possible number.
- Name and number all substituents, and add them as prefixes to the "alkanol" name.
- Alcohols containing two hydroxyl groups are named *-diols.* Those bearing three hydroxyl groups are called *-triols.* A number giving the position of each of the hydroxyl groups is needed in these cases.

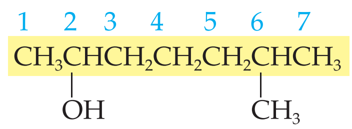
The way to determine the parent compound was described in Section 10.2.

Using I.U.P.A.C. Nomenclature to Name an Alcohol — EXAMPLE 12.1

2 LEARNING GOAL

Name the following alcohol using I.U.P.A.C. nomenclature.

Solution



Parent compound: heptane (becomes heptanol)
Position of —OH: carbon-2 (*not* carbon-6)
Substituents: 6-methyl
Name: 6-Methyl-2-heptanol

Using I.U.P.A.C. Nomenclature to Name Alcohols — EXAMPLE 12.2

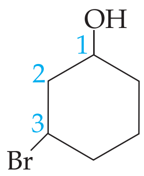
2 LEARNING GOAL

Name the following cyclic alcohol using I.U.P.A.C. nomenclature.

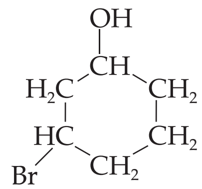
Continued—

EXAMPLE 12.2 —*Continued*

Solution



Remember that this line structure represents a cyclic molecule composed of six carbon atoms and associated hydrogen atoms, as follows:



Parent compound: cyclohexane (becomes cyclohexanol)
Position of —OH: carbon-1 (*not* carbon-3)
Substituents: 3-bromo (*not* 5-bromo)
Name: 3-Bromocyclohexanol (it is assumed that the —OH is on carbon-1 in cyclic structures)

Common Names

See Section 10.2 for the names of the common alkyl groups.

The common names for alcohols are derived from the alkyl group corresponding to the parent compound. The name of the alkyl group is followed by the word *alcohol*. For some alcohols, such as ethylene glycol and glycerol, historical names are used. The following examples provide the I.U.P.A.C. and common names of several alcohols:

CH_3CHCH_3 (with OH on C-2)	$HOCH_2CH_2OH$	CH_3CH_2OH
2-Propanol (isopropyl alcohol)	1,2-Ethanediol (ethylene glycol)	Ethanol (ethyl alcohol) (grain alcohol)

Question 12.1

Use the I.U.P.A.C. Nomenclature System to name each of the following compounds.

a. $CH_3CHCH_2CH_2CH_2OH$ (with CH_3 on C-2)

b. $CH_3CHCH_2CHCH_3$ (with OH on C-2 and CH_2CH_3 on C-4)

c. $CH_2—CH—CH_2$ (with OH on each carbon)
(Common name: Glycerol)

d. $CH_3CH_2CH—CHCH_2CH_2OH$ (with Cl on C-3 and CH_3 on C-4)

Question 12.2

Give the common name and the I.U.P.A.C. name for each of the following compounds.

a. $CH_3CH_2CH_2CH_2CH_2CH_2CH_2OH$

b. CH_3CHCH_3
   |
   OH

c. CH_3
   |
   CH_3CHCH_2OH

12.3 Medically Important Alcohols

Methanol

3 LEARNING GOAL

Methanol (methyl alcohol), CH_3OH, is a colorless and odorless liquid that is used as a solvent and as the starting material for the synthesis of methanal (formaldehyde). Methanol is often called *wood alcohol* because it can be made by heating wood in the absence of air. In fact, ancient Egyptians produced methanol by this process and, mixed with other substances, used it for embalming. It was not until 1661 that Robert Boyle first isolated pure methanol, which he called *spirit of box*, because he purified it by distillation from boxwood. Methanol is toxic and can cause blindness and perhaps death if ingested. Methanol may also be used as fuel, especially for "formula" racing cars.

Figure 12.3
Champagne, a sparkling wine, results when fermentation is carried out in a sealed bottle. Under these conditions, the CO_2 produced during fermentation is trapped in the wine.

Ethanol

Ethanol (ethyl alcohol), CH_3CH_2OH, is a colorless and odorless liquid and is the alcohol in alcoholic beverages. It is also widely used as a solvent and as a raw material for the preparation of other organic chemicals.

The ethanol used in alcoholic beverages comes from the **fermentation** of carbohydrates (sugars and starches). The beverage produced depends on the starting material and the fermentation process: scotch (grain), bourbon (corn), burgundy wine (grapes and grape skins), and chablis wine (grapes without red skins) (Figure 12.3). The following equation summarizes the fermentation process:

$$\underset{\text{(glucose)}}{\underset{\text{Sugar}}{C_6H_{12}O_6}} \xrightarrow[\text{enzyme action}]{\text{Several steps involving}} \underset{\text{(ethyl alcohol)}}{\underset{\text{Ethanol}}{2CH_3CH_2OH}} + 2CO_2$$

Fermentation reactions are described in detail in Section 21.4 and in A Human Perspective: Fermentations: The Good, the Bad, and the Ugly.

The alcoholic beverages listed have quite different alcohol concentrations. Wines are generally 12–13% alcohol because the yeasts that produce the ethanol are killed by ethanol concentrations of 12–13%. To produce bourbon or scotch with an alcohol concentration of 40–45% ethanol (80 or 90 proof), the original fermentation products must be distilled.

Distillation is the separation of compounds in a mixture based on differences in boiling points.

The sale and use of pure ethanol (100% ethanol) are regulated by the federal government. To prevent illegal use of pure ethanol, it is *denatured* by the addition of a denaturing agent, which makes it unfit to drink but suitable for many laboratory applications.

A Medical Perspective

Fetal Alcohol Syndrome

The first months of pregnancy are a time of great joy and anticipation but are not without moments of anxiety. On her first visit to the obstetrician, the mother-to-be is tested for previous exposure to a number of infectious diseases that could damage the fetus. She is provided with information about diet, weight gain, and drugs that could harm the baby. Among the drugs that should be avoided are alcoholic beverages.

The use of alcoholic beverages by a pregnant woman can cause *fetal alcohol syndrome (FAS).* A *syndrome* is a set of symptoms that occur together and are characteristic of a particular disease. In this case, physicians have observed that infants born to women with chronic alcoholism showed a reproducible set of abnormalities including mental retardation, poor growth before and after birth, and facial malformations.

Mothers who report only social drinking may have children with *fetal alcohol effects,* a less severe form of fetal alcohol syndrome. This milder form is characterized by a reduced birth weight, some learning disabilities, and behavioral problems.

How does alcohol consumption cause these varied symptoms? No one is exactly sure, but it is well known that the alcohol consumed by the mother crosses the placenta and enters the bloodstream of the fetus. Within about fifteen minutes, the concentration of alcohol in the blood of the fetus is as high as that of the mother! However, the mother has enzymes to detoxify the alcohol in her blood; the fetus does not. Now consider that alcohol can cause cell division to stop or be radically altered. It is thought that even a single night on the town could be enough to cause FAS by blocking cell division during a critical developmental period.

This raises the question "How much alcohol can a pregnant woman safely drink?" As we have seen, the severity of the symptoms seems to increase with the amount of alcohol consumed by the mother. However, it is virtually impossible to do the scientific studies that would conclusively determine the risk to the fetus caused by different amounts of alcohol. There is some evidence that suggests that there is a risk associated with drinking even one ounce of absolute (100%) alcohol each day. Because of these facts and uncertainties, the American Medical Association and the U.S. Surgeon General recommend that pregnant women completely abstain from alcohol.

The American Medical Association recommends abstaining from alcohol during pregnancy.

For Further Understanding

In July 2004, the U.S. Centers for Disease Control issued a new document entitled *Fetal Alcohol Syndrome: Guidelines for Referral and Diagnosis,* which can be found at the following Web address: http://www.cdc.gov/ncbddd/fas/documents/FAS_guidelines_accessible.pdf. Refer to this document when answering the following questions.

What is the estimate of the number of babies born each year with fetal alcohol syndrome and why is a more accurate number so difficult to determine?

What are some of the issues, practical and ethical, involved in intervention efforts to prevent fetal alcohol syndrome?

2-Propanol

2-Propanol (isopropyl alcohol),

$$\begin{array}{c} CH_3\underset{\displaystyle \overset{|}{OH}}{CH}CH_3 \end{array}$$

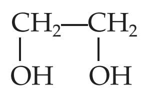
was commonly called *rubbing alcohol* because patients with high fevers were often given alcohol baths to reduce body temperature. Rapid evaporation of the alcohol results in skin cooling. This practice is no longer commonly used.

It is also used as a disinfectant (Figure 12.4), an astringent (skin-drying agent), an industrial solvent, and a raw material in the synthesis of organic chemicals. It is colorless, has a very slight odor, and is toxic when ingested.

Figure 12.4
Isopropyl alcohol, or rubbing alcohol, is used as a disinfectant before and after an injection or blood test.

1,2-Ethanediol

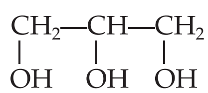
1,2-Ethanediol (ethylene glycol),



is used as automobile antifreeze. When added to water in the radiator, the ethylene glycol solute lowers the freezing point and raises the boiling point of the water. Ethylene glycol has a sweet taste but is extremely poisonous. For this reason, color additives are used in antifreeze to ensure that it is properly identified.

1,2,3-Propanetriol

1,2,3-Propanetriol (glycerol),

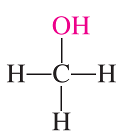


is a viscous, sweet-tasting, nontoxic liquid. It is very soluble in water and is used in cosmetics, pharmaceuticals, and lubricants. Glycerol is obtained as a by-product of the hydrolysis of fats.

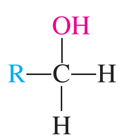
12.4 Classification of Alcohols

4 LEARNING GOAL

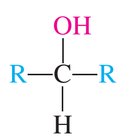
Alcohols are classified as **primary (1°), secondary (2°),** or **tertiary (3°),** depending on the number of alkyl groups attached to the **carbinol carbon,** the carbon bearing the hydroxyl (—OH) group. If no alkyl groups are attached, the alcohol is methyl alcohol; if there is a single alkyl group, the alcohol is a primary alcohol; an alcohol with two alkyl groups bonded to the carbon bearing the hydroxyl group is a secondary alcohol, and if three alkyl groups are attached, the alcohol is a tertiary alcohol.



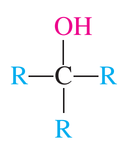
Methyl alcohol



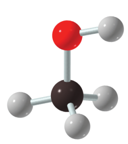
1° Alcohol



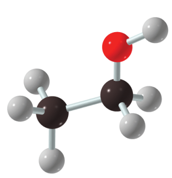
2° Alcohol



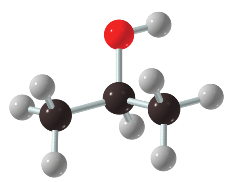
3° Alcohol



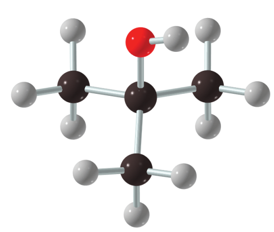
Methanol
(methyl alcohol)



Ethanol
(1° alcohol)



2-Propanol
(2° alcohol)



2-Methyl-2-propanol
(3° alcohol)

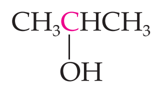
EXAMPLE 12.3 Classifying Alcohols

LEARNING GOAL 4

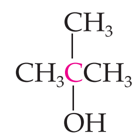
Classify each of the following alcohols as primary, secondary, or tertiary.

Solution

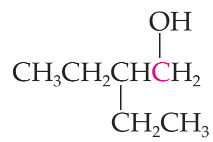
In each of the structures shown below, the carbinol carbon is shown in red:



This alcohol, 2-propanol, is a secondary alcohol because there are two alkyl groups attached to the carbinol carbon.



This alcohol, 2-methyl-2-propanol, is a tertiary alcohol because there are three alkyl groups attached to the carbinol carbon.

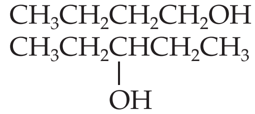


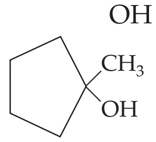
This alcohol, 2-ethyl-1-butanol, is a primary alcohol because there is only one alkyl group attached to the carbinol carbon.

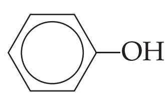
Question 12.3

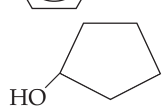
Classify each of the following alcohols as 1°, 2°, 3°, or aromatic (phenol).

a. $CH_3CH_2CH_2CH_2OH$

b. 

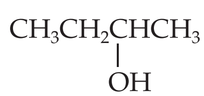
c. 

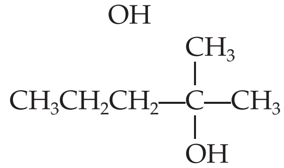
d. 

e. 

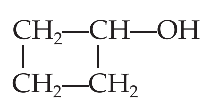
Question 12.4

Classify each of the following alcohols as 1°, 2°, or 3°.

a. 

b. 

c. $CH_3CH_2—OH$

d. 

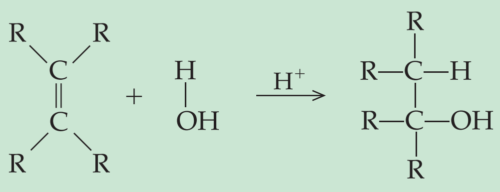
12.5 Reactions Involving Alcohols

Preparation of Alcohols

5 LEARNING GOAL

As we saw in the last chapter, the most important reactions of alkenes are *addition reactions*. Addition of a water molecule to the carbon-carbon double bond of an alkene produces an alcohol. This reaction, called **hydration,** requires a trace of acid (H^+) as a catalyst, as shown in the following equation:

Hydration of alkenes is described in Section 11.5.



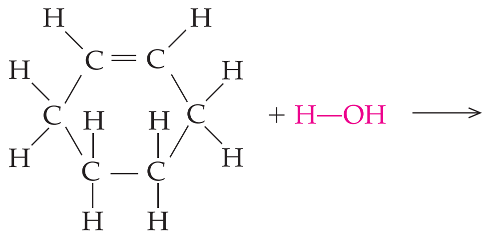
Alkene Water Alcohol

EXAMPLE 12.4 Writing an Equation Representing the Preparation of an Alcohol by the Hydration of an Alkene

Write an equation representing the preparation of cyclohexanol from cyclohexene.

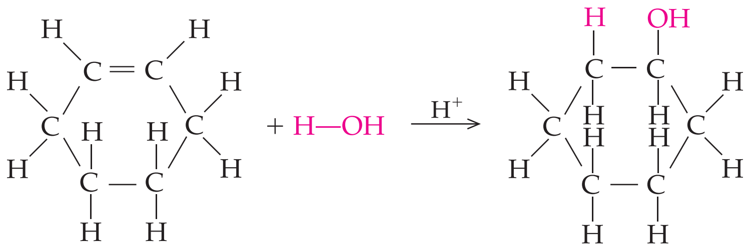
Solution

Begin by writing the structure of cyclohexene. Recall that cyclohexene is a six-carbon cyclic alkene. Now add the water molecule to the equation.



Cyclohexene Water

You will recognize that the hydration reaction involves the addition of a water molecule to the carbon-carbon double bond. Recall that the reaction requires a trace of acid as a catalyst. Complete the equation by adding the catalyst and product, cyclohexanol.



Cyclohexene Water Cyclohexanol

Question 12.5

Write a balanced equation showing the hydration of each of the following alkenes. Remember that Markovnikov's rule must be applied in the case of unsymmetrical alkenes.

a. $CH_3CH{=}CH_2$
b. $CH_2{=}CH_2$
c. $CH_3CH_2CH{=}CHCH_2CH_3$

Question 12.6

Using the I.U.P.A.C Nomenclature System, name the reactants and products for each of the reactions in Question 12.5.

Question 12.7

Classify each of the alcohols produced in the reactions of Question 12.5 as primary (1°), secondary (2°), or tertiary (3°).

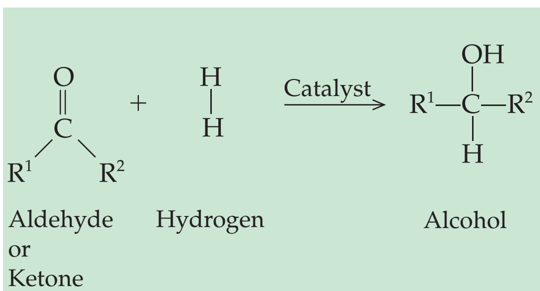
Question 12.8

Which of the alkenes in Question 12.5 can be found as both *cis* and *trans* isomers?

LEARNING GOAL 6

Alcohols may also be prepared via the hydrogenation (reduction) of aldehydes and ketones. This reaction, summarized as follows, is discussed in Section 13.4, and is similar to the hydrogenation of alkenes.

In an aldehyde, R^1 and R^2 may be either alkyl groups or H. In ketones, R^1 and R^2 are both alkyl groups.



EXAMPLE 12.5 Writing an Equation Representing the Preparation of an Alcohol by the Hydrogenation (Reduction) of an Aldehyde

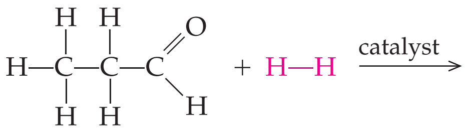
Write an equation representing the preparation of 1-propanol from propanal.

Solution

Begin by writing the structure of propanal. Propanal is a three-carbon aldehyde. Aldehydes are characterized by the presence of a carbonyl group (—C=O) attached to the end of the carbon chain of the molecule. After you have drawn the structure of propanal, add diatomic hydrogen to the equation.

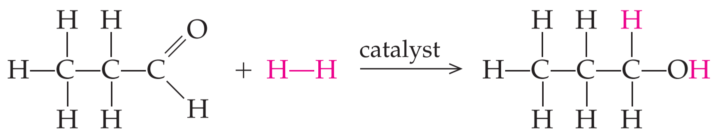
Continued—

EXAMPLE 12.5 —*Continued*



Propanal Hydrogen

Notice that the general equation reveals this reaction to be another example of a hydrogenation reaction. As the hydrogens are added to the carbon-oxygen double bond, it is converted to a carbon-oxygen single bond, as the carbonyl oxygen becomes a hydroxyl group.



Propanal Hydrogen 1-Propanol

Writing an Equation Representing the Preparation of an Alcohol by the Hydrogenation (Reduction) of a Ketone

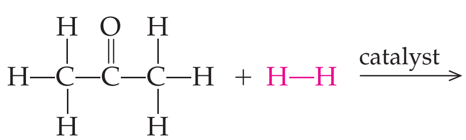
EXAMPLE 12.6

6 LEARNING GOAL

Write an equation representing the preparation of 2-propanol from propanone.

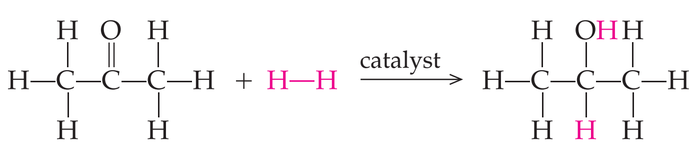
Solution

Begin by writing the structure of propanone. Propanone is a three-carbon ketone. Ketones are characterized by the presence of a carbonyl group (—C=O) located anywhere within the carbon chain of the molecule. In the structure of propanone, the carbonyl group must be associated with the center carbon. After you have drawn the structure of propanone, add diatomic hydrogen to the equation.



Propanone Hydrogen

Notice that this reaction is another example of a hydrogenation reaction. As the hydrogens are added to the carbon-oxygen double bond, it is converted to a carbon-oxygen single bond, as the carbonyl oxygen becomes a hydroxyl group.



Propanone Hydrogen 2-Propanol

Question 12.9

Write an equation representing the reduction of butanone. *Hint:* Butanone is a four-carbon ketone.

Question 12.10

Classify the alcohol product of the reaction in Question 12.9 as a primary (1°), secondary (2°), or tertiary (3°) alcohol, and provide its I.U.P.A.C. name.

Question 12.11

Write an equation representing the reduction of butanal. Provide the structures and names for the reactants and products. *Hint:* Butanal is a four-carbon aldehyde.

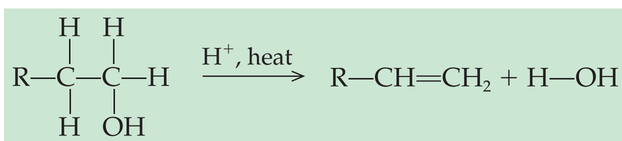
Question 12.12

Classify the alcohol product of the reaction in Question 12.11 as a primary (1°), secondary (2°), or tertiary (3°) alcohol, and provide its I.U.P.A.C. name.

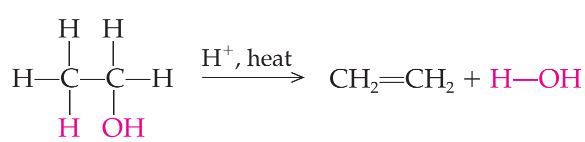
Dehydration of Alcohols

LEARNING GOAL 7

Alcohols undergo **dehydration** (lose water) when heated with concentrated sulfuric acid (H_2SO_4) or phosphoric acid (H_3PO_4). Dehydration is an example of an **elimination reaction,** that is, a reaction in which a molecule loses atoms or ions from its structure. In this case, the —OH and —H are "eliminated" from adjacent carbons in the alcohol to produce an alkene and water. We have just seen that alkenes can be hydrated to give alcohols. Dehydration is simply the reverse process: the conversion of an alcohol back to an alkene. This is seen in the following general reaction and the examples that follow:



Alcohol Alkene Water

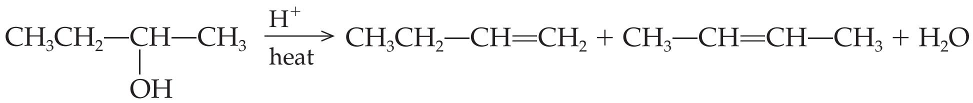


Ethanol (ethyl alcohol) Ethene (ethylene)

$$CH_3CH_2CH_2OH \xrightarrow{H^+,\ heat} CH_3CH{=}CH_2 + H_2O$$

1-Propanol (propyl alcohol) Propene (propylene)

In some cases, dehydration of alcohols produces a mixture of products, as seen in the following example:



2-Butanol — 1-Butene (minor product) — 2-Butene (major product)

Notice in the equation shown above and in Example 12.7, the major product is the more highly substituted alkene. In 1875 the Russian chemist Alexander Zaitsev developed a rule to describe such reactions. **Zaitsev's rule** states that in an elimination reaction, the alkene with the greatest number of alkyl groups on the double bonded carbons (the more highly substituted alkene) is the major product of the reaction.

Predicting the Products of Alcohol Dehydration

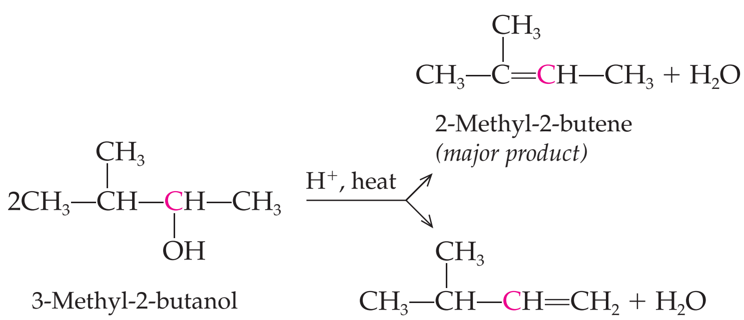
EXAMPLE 12.7

7 LEARNING GOAL

Predict the products of the dehydration of 3-methyl-2-butanol.

Solution

Assuming that no rearrangement occurs, the product(s) of a dehydration of an alcohol will contain a double bond in which one of the carbons was the original carbinol carbon—the carbon to which the hydroxyl group is attached. Consider the following reaction:



3-Methyl-2-butanol

2-Methyl-2-butene *(major product)*

3-Methyl-1-butene *(minor product)*

It is clear that both the major and minor products have a double bond to carbon number 2 in the original alcohol (this carbon is set off in color). Zaitsev's rule tells us that in dehydration reactions with more than one product possible, the more highly branched alkene predominates. In the reaction shown, 2-methyl-2-butene has three alkyl groups at the double bond, whereas 3-methyl-1-butene has only two alkyl groups at the double bond. The more highly branched alkene is more stable and thus is the major product.

Question 12.13

Predict the products obtained on reacting each of the following alkenes with water and a trace of acid:

a. Ethene
b. Propene
c. 2-Butene

Question 12.14

Name the products of the reactions in Question 12.13 using the I.U.P.A.C. Nomenclature System, and classify each of the product alcohols as primary (1°), secondary (2°), or tertiary (3°).

Question 12.15

Predict the products obtained on reacting each of the following alkenes with water and a trace of acid:

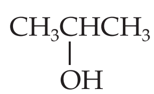
a. 1-Butene
b. 2-Methylpropene

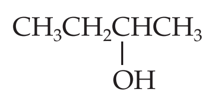
Question 12.16

Name the products of the reactions in Question 12.15 using the I.U.P.A.C. Nomenclature System, and classify each of the product alcohols as primary (1°), secondary (2°), or tertiary (3°).

Question 12.17

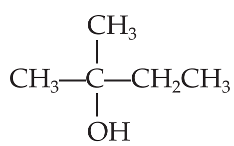
Draw the alkene products that would be produced on dehydration of each of the following alcohols:

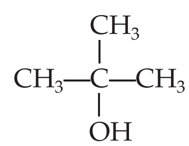
a. 

b. 

Question 12.18

Draw the alkene products that would be produced on dehydration of each of the following alcohols:

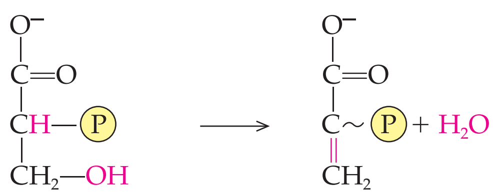
a. 

b. 

This reaction, and the other reactions of glycolysis, are considered in Section 21.3.

The dehydration of 2-phosphoglycerate to phosphoenolpyruvate is a critical step in the metabolism of the sugar glucose. In the following structures, the circled P represents a phosphoryl group (PO_4^{2-}).

The squiggle (~) represents a high energy bond.



2-Phosphoglycerate → Phosphoenolpyruvate

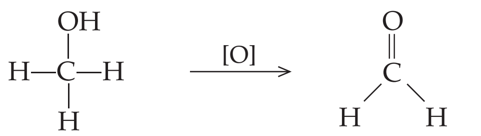
Oxidation Reactions

8 **LEARNING GOAL**

Alcohols may be oxidized with a variety of oxidizing agents to aldehydes, ketones, and carboxylic acids. The most commonly used oxidizing agents are solutions of basic potassium permanganate ($KMnO_4/OH^-$) and chromic acid (H_2CrO_4). The symbol [O] over the reaction arrow is used throughout this book to designate any general oxidizing agent, as in the following reactions:

An *oxidation* reaction involves a gain of oxygen or the loss of hydrogen. A *reduction* reaction involves the loss of oxygen or gain of hydrogen. If two hydrogens are gained or lost for every oxygen gained or lost, the reaction is neither an oxidation nor a reduction.

Oxidation of methanol produces the aldehyde methanal:

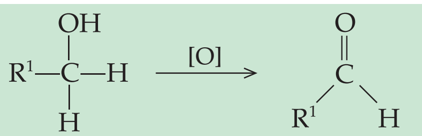


Methanol (methyl alcohol) An alcohol

Methanal (formaldehyde) An aldehyde

Note that the symbol [O] is used throughout this book to designate any oxidizing agent.

Oxidation of a primary alcohol produces an aldehyde:



1° Alcohol

An aldehyde

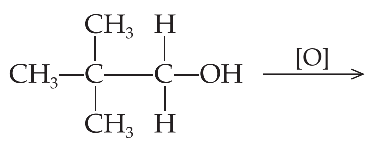
As we will see in Section 13.4, aldehydes can undergo further oxidation to produce carboxylic acids.

Writing an Equation Representing the Oxidation of a Primary Alcohol — EXAMPLE 12.8

Write an equation showing the oxidation of 2,2-dimethylpropanol to produce 2,2-dimethylpropanal.

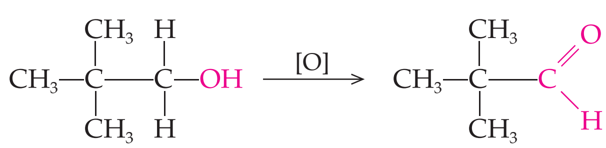
Solution

Begin by writing the structure of the reactant, 2,2-dimethylpropanol and indicate the need for an oxidizing agent by placing the designation [O] over the reaction arrow:



2,2-Dimethylpropanol

Now show the oxidation of the hydroxyl group to the aldehyde carbonyl group.



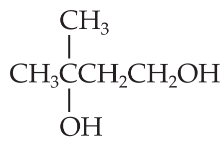
2,2-Dimethylpropanol

2,2-Dimethylpropanal

Question 12.19

Write an equation showing the oxidation of the following primary alcohols:

a.

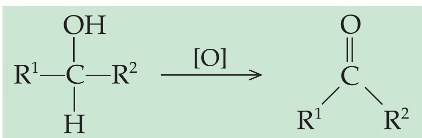


b. CH_3CH_2OH

Question 12.20

Name each of the reactant alcohols and product aldehydes in Question 12.19 using the I.U.P.A.C. Nomenclature System. *Hint:* Refer to the example above, as well as to Section 13.2 to name the aldehyde products.

Oxidation of a secondary alcohol produces a ketone:



2° Alcohol A ketone

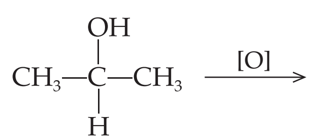
EXAMPLE 12.9 Writing an Equation Representing the Oxidation of a Secondary Alcohol

LEARNING GOAL 8

Write an equation showing the oxidation of 2-propanol to produce propanone.

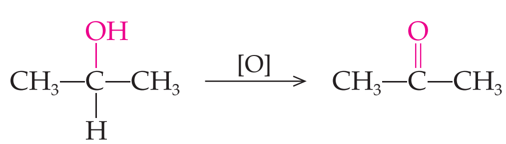
Solution

Begin by writing the structure of the reactant, 2-propanol, and indicate the need for an oxidizing agent by placing the designation [O] over the reaction arrow:



2-Propanol

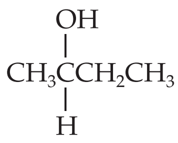
Now show the oxidation of the hydroxyl group to the ketone carbonyl group.



2-Propanol Propanone

Question 12.21

Write an equation showing the oxidation of the following secondary alcohols:

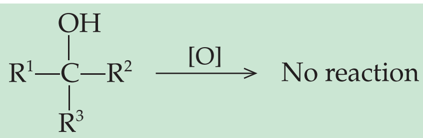
a. 

b. 

Question 12.22

Name each of the reactant alcohols and product ketones in Question 12.21 using the I.U.P.A.C. Nomenclature System. *Hint:* Refer to the example above, as well as to Section 13.2, to name the ketone products.

Tertiary alcohols cannot be oxidized:



3° Alcohol

For the oxidation reaction to occur, the carbon bearing the hydroxyl group must contain at least one C—H bond. Because tertiary alcohols contain three C—C bonds to the carbinol carbon, they cannot undergo oxidation.

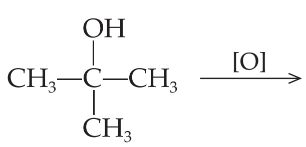
Writing an Equation Representing the Oxidation of a Tertiary Alcohol

EXAMPLE 12.10

Write an equation showing the oxidation of 2-methyl-2-propanol.

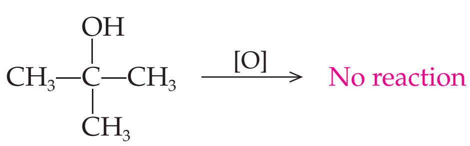
Solution

Begin by writing the structure of the reactant, 2-methyl-2-propanol and indicate the need for an oxidizing agent by placing the designation [O] over the reaction arrow:



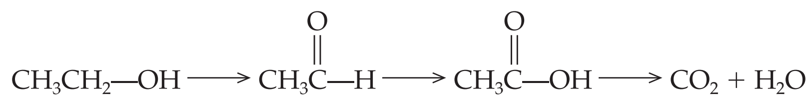
2-Methyl-2-propanol

The structure of 2-methyl-2-propanol reveals that it is a tertiary alcohol. Therefore, no oxidation reaction can occur because the carbon bearing the hydroxyl group is bonded to three other carbon atoms, not to a hydrogen atom.



2-Methyl-2-propanol

When ethanol is metabolized in the liver, it is oxidized to ethanal (acetaldehyde). If too much ethanol is present in the body, an overabundance of ethanal is formed, which causes many of the adverse effects of the "morning-after hangover." Continued oxidation of ethanal produces ethanoic acid (acetic acid), which is used as an energy source by the cell and eventually oxidized to CO_2 and H_2O. These reactions, summarized as follows, are catalyzed by liver enzymes.



Ethanol (ethyl alcohol) Ethanal (acetaldehyde) Ethanoic acid (acetic acid)

12.6 Oxidation and Reduction in Living Systems

LEARNING GOAL 9

Before beginning a discussion of oxidation and reduction in living systems, we must understand how to recognize **oxidation** (loss of electrons) and **reduction** (gain of electrons) in organic compounds. It is easy to determine when an oxidation or a reduction occurs in inorganic compounds because the process is accompanied by a change in charge. For example,

$$Ag^0 \longrightarrow Ag^+ + 1e^-$$

With the loss of an electron, the neutral atom is converted to a positive ion, which is oxidation. In contrast,

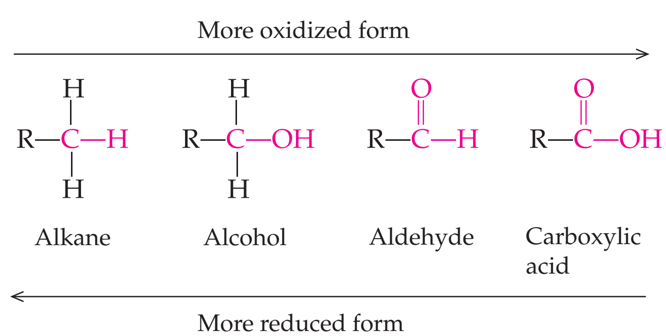
$$:\ddot{\underset{..}{Br}}\cdot + e^- \longrightarrow :\ddot{\underset{..}{Br}}:^-$$

With the gain of one electron, the bromine atom is converted to a negative ion, which is reduction.

When organic compounds are involved, however, there may be no change in charge, and it is often difficult to determine whether oxidation or reduction has occurred. The following simplified view may help.

In organic systems, *oxidation* may be recognized as a gain of oxygen or a loss of hydrogen. A *reduction* reaction may involve a loss of oxygen or gain of hydrogen.

Consider the following compounds. An alkane may be oxidized to an alcohol by gaining an oxygen. A primary or secondary alcohol may be oxidized to an aldehyde or ketone, respectively, by the loss of hydrogen. Finally, an aldehyde may be oxidized to a carboxylic acid by gaining an oxygen.



Thus, the conversion of an alkane to an alcohol, an alcohol to a carbonyl compound, and a carbonyl compound (aldehyde) to a carboxylic acid are all examples of oxidations. Conversions in the opposite direction are reductions.

Oxidation and reduction reactions also play an important role in the chemistry of living systems. In living systems these reactions are catalyzed by the action of various enzymes called *oxidoreductases.* These enzymes require compounds called *coenzymes* to accept or donate hydrogen in the reactions that they catalyze.

A Human Perspective

Alcohol Consumption and the Breathalyzer Test

Ethanol has been used widely as a beverage, a medicinal, and a solvent in numerous pharmaceutical preparations. Such common usage often overshadows the fact that ethanol is a toxic substance. Ethanol consumption is associated with a variety of long-term effects, including cirrhosis of the liver, death of brain cells, and alcoholism. Alcohol consumed by the mother can even affect the normal development of her unborn child and result in fetal alcohol syndrome. For these reasons, over-the-counter cough and cold medications that were once prepared in ethanol are now manufactured in alcohol-free form.

Short-term effects, linked to the social use of ethanol, center on its effects on behavior, reflexes, and coordination. Blood alcohol levels of 0.05–0.15% seriously inhibit coordination. Blood levels in excess of 0.10% are considered evidence of intoxication in most states. Blood alcohol levels in the range of 0.30–0.50% produce unconsciousness and the risk of death.

Driving under the influence of alcohol impairs coordination and reflexes.

The loss of some coordination and reflex action is particularly serious when the affected individual attempts to drive a car. Law enforcement has come to rely on the "breathalyzer" test to screen for individuals suspected of driving while intoxicated. Those with a positive breathalyzer test are then given a more accurate blood test to establish their guilt or innocence.

The suspect is required to exhale into a solution that will react with the unmetabolized alcohol in the breath. The partial pressure of the alcohol in the exhaled air has been demonstrated to be proportional to the blood alcohol level. The solution is an acidic solution of dichromate ion, which is yellow-orange. The alcohol reduces the chromium in the dichromate ion from +6 to +3, the Cr^{3+} ion, which is green. The intensity of the green color is measured, and it is proportional to the amount of ethanol that was oxidized. The reaction is:

$$16H^+ + \underset{\text{Yellow-orange}}{2Cr_2O_7^{2-}} + 3CH_3CH_2OH \longrightarrow 3CH_3COOH + \underset{\text{Green}}{4Cr^{3+}} + 11H_2O$$

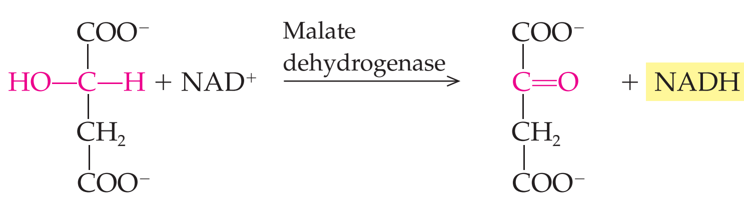
The breathalyzer test is a technological development based on a scientific understanding of the chemical reactions that ethanol may undergo—a further example of the dependence of technology on science.

For Further Understanding

Explain why the intensity of the green color in the reaction solution is proportional to the level of alcohol in the breath.

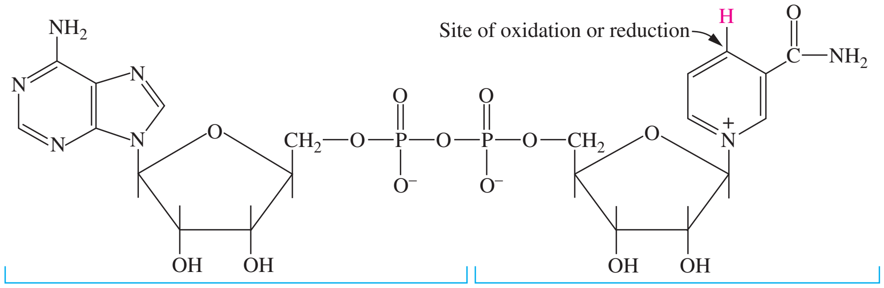
Draw a graph that represents this relationship.

Nicotinamide adenine dinucleotide, NAD^+, is a coenzyme commonly involved in biological oxidation–reduction reactions (Figure 12.5). Now consider the final reaction of the citric acid cycle, an energy-harvesting pathway essential to life. In this reaction, catalyzed by the enzyme malate dehydrogenase, malate is oxidized to produce oxaloacetate:



Malate   Oxaloacetate

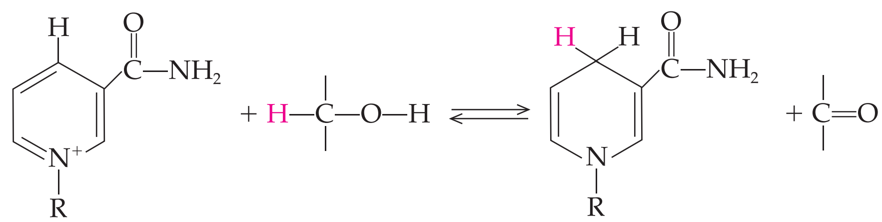
Figure 12.5
Nicotinamide adenine dinucleotide.



Nicotinamide adenine dinucleotide (NAD^+)

NAD^+ actually accepts a hydride anion, H^-, hydrogen with two electrons.

NAD^+ participates by accepting hydrogen from the malate. As malate is oxidized, NAD^+ is reduced to NADH.



NAD^+
Oxidized form

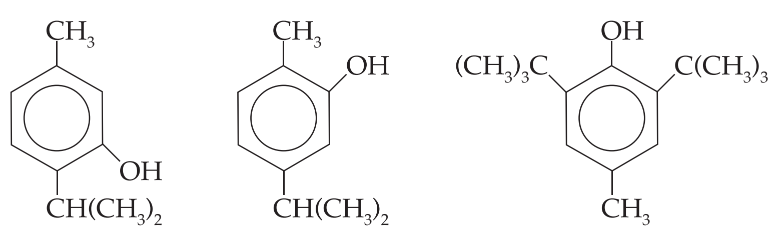
NADH
Reduced form

We will study many other biologically important oxidation-reduction reactions in upcoming chapters.

LEARNING GOAL 10

12.7 Phenols

Phenols are compounds in which the hydroxyl group is attached to a benzene ring (Figure 12.6). Like alcohols, they are polar compounds because of the polar hydroxyl group. Thus, the simpler phenols are somewhat soluble in water. They are found in flavorings and fragrances (mint and savory) and are used as preservatives (butylated hydroxytoluene, BHT). Examples include:



Thymol (mint)   Carvacrol (savory)   Butylated hydroxytoluene, BHT (food preservative)

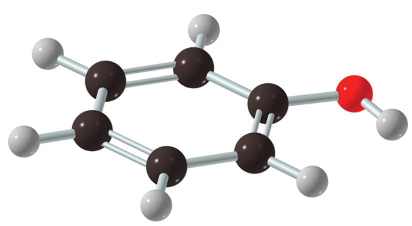
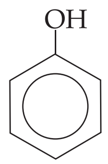


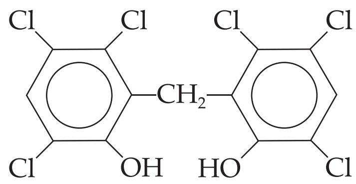
Figure 12.6
Ball-and-stick model of phenol. Keep in mind that this model is not completely accurate because it cannot show the cloud of shared electrons above and below the benzene ring. Review Section 11.6 for a more accurate description of the benzene ring.

Phenols are also widely used in health care as germicides. In fact, carbolic acid, a dilute solution of phenol, was used as an antiseptic and disinfectant by Joseph Lister in his early work to decrease postsurgical infections. He used carbolic acid to bathe surgical wounds and to "sterilize" his instruments. Other derivatives of phenol that are used as antiseptics and disinfectants include hexachlorophene, hexylresorcinol, and *o*-phenylphenol. The structures of these compounds are shown below:

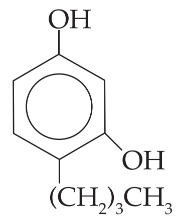
A dilute solution of phenol must be used because concentrated phenol causes severe burns and because phenol is not highly soluble in water.



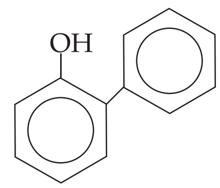
Phenol
(carbolic acid;
phenol dissolved
in water;
antiseptic)



Hexachlorophene
(antiseptic)



Hexylresorcinol
(antiseptic)



o-Phenylphenol
(antiseptic)

12.8 Ethers

Ethers have the general formula R—O—R, and thus they are structurally related to alcohols (R—O—H). The C—O bonds of ethers are polar, so ether molecules are polar (Figure 12.7). However, ethers do not form hydrogen bonds to one another because there is no —OH group. Therefore, they have much lower boiling points than alcohols of similar molecular weight but higher boiling points than alkanes of similar molecular weight. Compare the following examples:

$CH_3CH_2CH_2CH_3$	CH_3—O—CH_2CH_3	$CH_3CH_2CH_2OH$
Butane	Methoxyethane	1-Propanol
(butane)	(ethyl methyl ether)	(propyl alcohol)
M.W. = 58	M.W. = 60	M.W. = 60
b.p. = −0.5°C	b.p. = 7.9°C	b.p. = 97.2°C

In the I.U.P.A.C. system of naming ethers, the —OR substituent is named as an alkoxy group. This is analogous to the name *hydroxy* for the —OH group. Thus, CH_3—O— is methoxy, CH_3CH_2—O— is ethoxy, and so on.

11 **LEARNING GOAL**

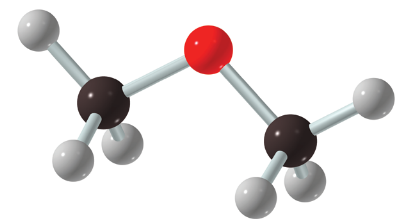


Figure 12.7
Ball-and-stick model of the ether, methoxymethane (dimethyl ether).

An alkoxy group is an alkyl group bonded to an oxygen atom (—OR).

Using I.U.P.A.C. Nomenclature to Name an Ether — EXAMPLE 12.11

Name the following ether using I.U.P.A.C. nomenclature.

Solution

O—CH_3

$CH_3CH_2CHCH_2CH_2CH_2CH_2CH_2CH_3$

1 2 3 4 5 6 7 8 9

Parent compound: nonane
Position of alkoxy group: carbon-3 (*not* carbon-7)
Substituents: 3-methoxy
Name: 3-Methoxynonane

Question 12.23

Name the following ethers using I.U.P.A.C. nomenclature:

a. CH_3CH_2—O—$CH_2CH_2CH_3$
b. CH_3—O—$CH_2CH_2CH_3$

Question 12.24

Name the following ethers using I.U.P.A.C. nomenclature:

a. $CH_3CH_2—O—CH_2CH_2CH_2CH_2CH_3$
b. $CH_3CH_2CH_2CH_2—O—CH_2CH_2CH_3$

In the common system of nomenclature, ethers are named by placing the names of the two alkyl groups attached to the ether oxygen as prefixes in front of the word *ether.* The names of the two groups can be placed either alphabetically or by size (smaller to larger), as seen in the following examples:

$CH_3—O—CH_3$	$CH_3—O—CH_2CH_3$	$CH_3CH_2—O—CH(CH_3)_2$
Dimethyl ether or methyl ether	Ethyl methyl ether or methyl ethyl ether	Ethyl isopropyl ether

EXAMPLE 12.12 Naming Ethers Using the Common Nomenclature System

LEARNING GOAL 11

Write the common name for each of the following ethers.

Solution

	$CH_3CH_2—O—CH_2CH_3$	$CH_3—O—CH_2CH_2CH_3$
Alkyl Groups:	two ethyl groups	methyl and propyl
Name:	Diethyl ether	Methyl propyl ether

Notice that there is only one correct name for methyl propyl ether because the methyl group is smaller than the propyl group and it would be first in an alphabetical listing also.

Question 12.25

Write the common name for each of the following ethers:

a. $CH_3CH_2—O—CH_2CH_2CH_3$
b. $CH_3—O—CH_2CH_2CH_3$

Question 12.26

Write the common name for each of the following ethers:

a. $CH_3CH_2—O—CH_2CH_2CH_2CH_2CH_3$
b. $CH_3CH_2CH_2CH_2—O—CH_2CH_2CH_3$

Chemically, ethers are moderately inert. They do not react with reducing agents or bases under normal conditions. However, they are extremely volatile and highly flammable (easily oxidized in air) and hence must always be treated with great care.

Ethers may be prepared by a dehydration reaction (removal of water) between two alcohol molecules, as shown in the following general reaction. The reaction requires heat and acid.

$$\underset{\text{Alcohol}}{R^1—OH} + \underset{\text{Alcohol}}{R^2—OH} \xrightarrow[\text{heat}]{H^+} \underset{\text{Ether}}{R^1—O—R^2} + \underset{\text{Water}}{H_2O}$$

Writing an Equation Representing the Synthesis of an Ether via a Dehydration Reaction

EXAMPLE 12.13

12 LEARNING GOAL

Write an equation showing the synthesis of dimethyl ether.

Solution

The alkyl substituents of this ether are two methyl groups. Thus, the alcohol that must undergo dehydration to produce dimethyl ether is methanol.

$$\underset{\text{Methanol}}{CH_3OH} + \underset{\text{Methanol}}{CH_3OH} \xrightarrow{H^+} \underset{\text{Dimethyl ether}}{CH_3{-}O{-}CH_3} + \underset{\text{Water}}{H_2O}$$

Question 12.27

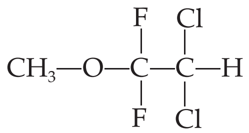
Write an equation showing the dehydration reaction that would produce diethyl ether. Provide structures and names for all reactants and products.

Question 12.28

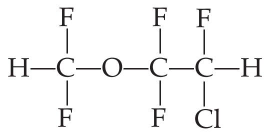
Write an equation showing the dehydration reaction between two molecules of 2-propanol. Provide structures and names for all reactants and products.

Diethyl ether was the first general anesthetic used. The dentist Dr. William Morton is credited with its introduction in the 1800s. Diethyl ether functions as an anesthetic by interacting with the central nervous system. It appears that diethyl ether (and many other general anesthetics) functions by accumulating in the lipid material of the nerve cells, thereby interfering with nerve impulse transmission. This results in analgesia, a lessened perception of pain.

Halogenated ethers are also routinely used as general anesthetics (Figure 12.8). They are less flammable than diethyl ether and are therefore safer to store and work with. *Penthrane* and *Enthrane* (trade names) are two of the more commonly used members of this family:



Penthrane



Enthrane

Figure 12.8
An anesthesiologist administers Penthrane to a surgical patient.

12.9 Thiols

Compounds that contain the sulfhydryl group (—SH) are called **thiols.** They are similar to alcohols in structure, but the sulfur atom replaces the oxygen atom.

Thiols and many other sulfur compounds have nauseating aromas. They are found in substances as different as the defensive spray of the North American striped skunk, onions, and garlic. The structures of the two most common compounds in the defense spray of the striped skunk, *trans*-2-butene-1-thiol and 3-methyl-1-butanethiol, are seen in Figure 12.9. These structures are contrasted with the structures of the two molecules that make up the far more pleasant scent of roses: geraniol, an unsaturated alcohol, and 2-phenylethanol, an aromatic alcohol.

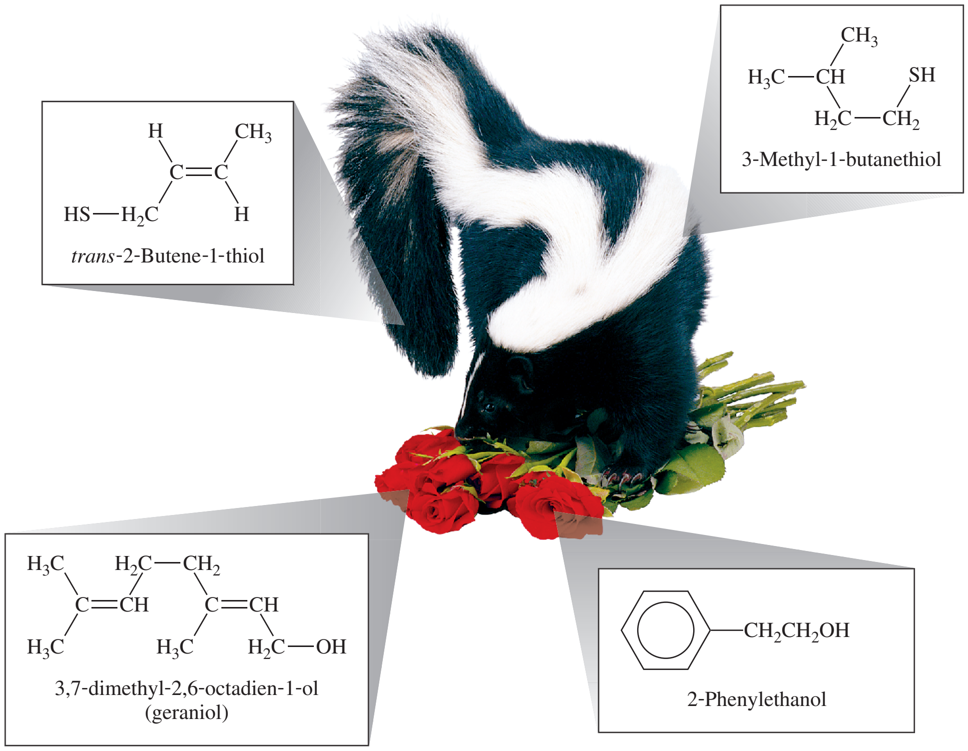


Figure 12.9
This skunk on a bed of roses is surrounded by scent molecules. The two most common compounds in the defense spray of the striped skunk are the thiols *trans*-2-butene-1-thiol and 3-methyl-1-butanethiol. Two alcohols, 2-phenylethanol and geraniol, are the major components of the scent of roses.

LEARNING GOAL 13

The I.U.P.A.C. rules for naming thiols are similar to those for naming alcohols, except that the full name of the alkane is retained. The suffix *-thiol* follows the name of the parent compound.

EXAMPLE 12.14 Naming Thiols Using the I.U.P.A.C. Nomenclature System

Write the I.U.P.A.C. name for the thiols shown below.

Solution

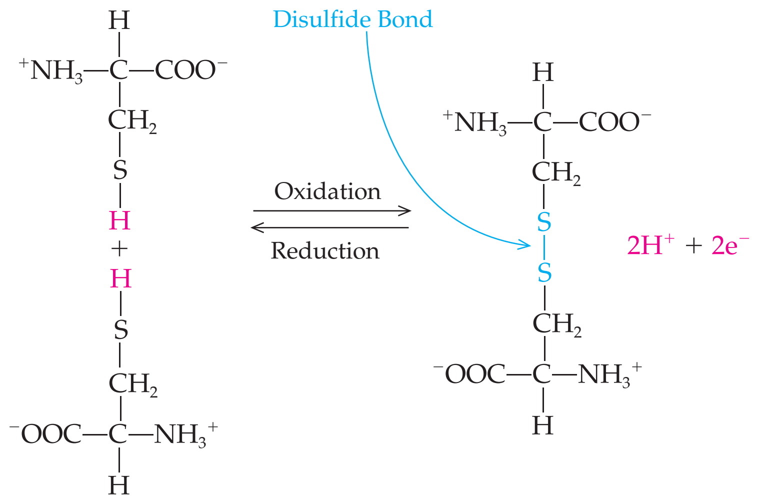
Retain the full name of the parent compound and add the suffix *-thiol.*

	CH_3CH_2—SH	HS—CH_2CH_2—SH
Parent compound:	ethane	ethane
Position of —SH:	carbon-1 (must be)	carbon-1 and carbon-2
Name:	Ethanethiol	1,2-Ethanedithiol

	$CH_3CH(CH_3)CH_2CH_2SH$	$CH_3CH(SH)CH_2CH_2CH_2SH$
Parent Compound:	butane	pentane
Position of —SH:	carbon-1	carbon-1 and carbon-4
Substituent:	3 -methyl	
Name:	3-Methyl-1-butanethiol	1,4-Pentanedithiol

The amino acid cysteine is a thiol that has an important role to play in the structure and shape of many proteins. Two cysteine molecules can undergo oxidation to form cystine. The new bond formed is called a **disulfide** bond (—S—S—) bond.

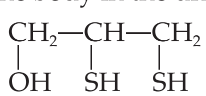
Amino acids are the subunits from which proteins are made. A protein is a long polymer, or chain, of many amino acids bonded to one another.



2 Cysteine   Cystine

If the two cysteines are in different protein chains, the disulfide bond between them forms a bridge joining them together (Figure 12.10). If the two cysteines are in the same protein chain, a loop is formed. An example of the importance of disulfide bonds is seen in the production and structure of the protein hormone insulin, which controls blood sugar levels in the body. Insulin is initially produced as a protein called preproinsulin. Enzymatic removal of 24 amino acids and formation of disulfide bonds between cysteine amino acids produces proinsulin (Figure 12.10). Regions of the protein are identified as the A, B, and C chains. Notice that the A and B chains are covalently bonded to one another by two disulfide bonds. A third disulfide bond produces a hairpin loop in the A chain of the molecule. The molecule is now ready for the final stage of insulin synthesis in which the C chain is removed by the action of protein degrading enzymes (proteases). The active hormone, shown at the bottom of Figure 12.10, consists of the 21 amino acid A chain bonded to the 30 amino acid B chain by two disulfide bonds. Without these disulfide bonds, functional insulin molecules could not exist because there would be no way to keep the two chains together in the proper shape.

British Anti-Lewisite (BAL) is a dithiol used as an antidote in mercury poisoning. It was originally developed as an antidote to a mustard-gas-like chemical warfare agent called Lewisite, which was developed near the end of World War I and never used. By the onset of World War II, Lewisite was considered to be obsolete because of the discovery of BAL, an effective, inexpensive antidote. The two thiol groups of BAL form a water-soluble complex with mercury (or with the arsenic in Lewisite) that is excreted from the body in the urine.

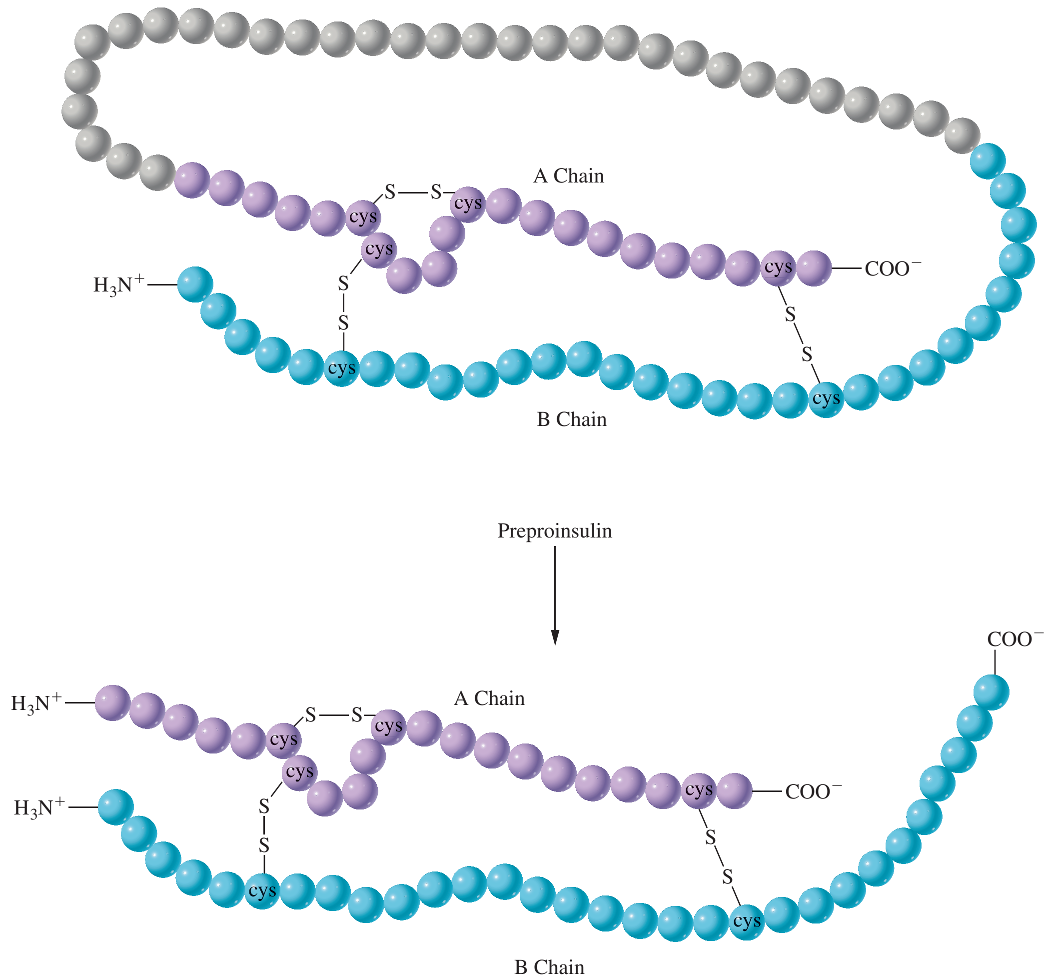


BAL

Coenzyme A is a thiol that serves as a "carrier" of acetyl groups (CH_3CO—) in biochemical reactions. It plays a central role in metabolism by shuttling acetyl groups from one reaction to another. When the two-carbon acetate group is attached to coenzyme A, the product is acetyl coenzyme A (acetyl CoA). The bond between coenzyme A and the acetyl group is a high-energy *thioester bond.* In effect, formation of the high-energy thioester bond "energizes" the acetyl group so that it can participate in other biochemical reactions.

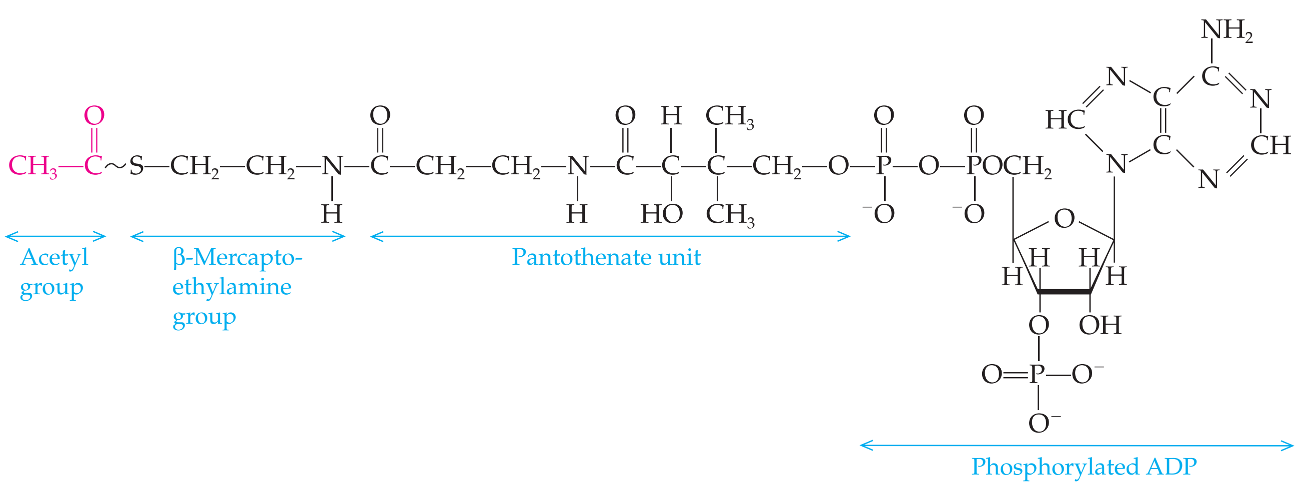
The reactions involving coenzyme A are discussed in detail in Chapters 21, 22, and 23.

A high-energy bond is one that releases a great deal of energy when it is broken.



Insulin

Figure 12.10
Two steps in the synthesis of insulin. Disulfide bonds hold the A and B chains together and form a hairpin loop in the A chain.



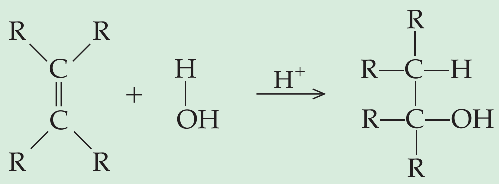
Acetyl coenzyme A
(acetyl CoA)

Acetyl CoA is made and used in the energy-producing reactions that provide most of the energy for life processes. It is also required for the biosynthesis of many biological molecules.

Summary of Reactions

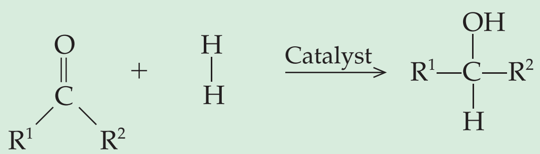
Preparation of Alcohols

Hydration of alkenes:



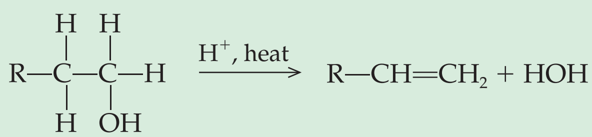
Alkene Water Alcohol

Reduction of an aldehyde or ketone:



Aldehyde or ketone Hydrogen Alcohol

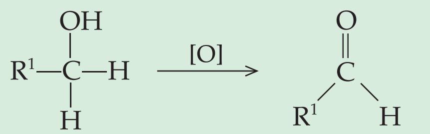
Dehydration of Alcohols



Alcohol Alkene Water

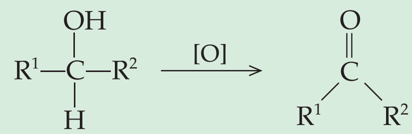
Oxidation Reactions

Oxidation of a primary alcohol:



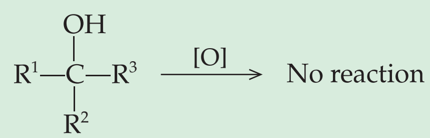
1° Alcohol An aldehyde

Oxidation of a secondary alcohol:



2° Alcohol A ketone

Oxidation of a tertiary alcohol:



3° Alcohol

Dehydration Synthesis of an Ether

$$R^1\text{—OH} + R^2\text{—OH} \xrightarrow[\text{heat}]{H^+} R^1\text{—O—}R^2 + H_2O$$

Alcohol Alcohol Ether Water

SUMMARY

12.1 Alcohols: Structure and Physical Properties

Alcohols are characterized by the *hydroxyl group (—OH)* and have the general formula R—OH. They are very polar, owing to the polar hydroxyl group, and are able to form intermolecular hydrogen bonds. Because of hydrogen bonding between alcohol molecules, they have higher boiling points than hydrocarbons of comparable molecular weight. The smaller alcohols are very water soluble.

12.2 Alcohols: Nomenclature

In the I.U.P.A.C. system, alcohols are named by determining the parent compound and replacing the *-e* ending with *-ol.* The chain is numbered to give the hydroxyl group the lowest possible number. Common names are derived from the alkyl group corresponding to the parent compound.

12.3 Medically Important Alcohols

Methanol is a toxic alcohol that is used as a solvent. Ethanol is the alcohol consumed in beer, wine, and distilled liquors. Isopropanol is used as a disinfectant. Ethylene glycol (1,2-ethanediol) is used as antifreeze, and glycerol (1,2,3-propanetriol) is used in cosmetics and pharmaceuticals.

12.4 Classification of Alcohols

Alcohols may be classified as *primary, secondary,* or *tertiary,* depending on the number of alkyl groups attached to the *carbinol carbon,* the carbon bearing the hydroxyl group. A primary alcohol has a single alkyl group bonded to the *carbinol carbon.* Secondary and tertiary alcohols have two and three alkyl groups, respectively.

12.5 Reactions Involving Alcohols

Alcohols can be prepared by the *hydration* of alkenes or reduction of aldehydes and ketones. Alcohols can undergo *dehydration* to yield alkenes. Primary and secondary alcohols undergo oxidation reactions to yield aldehydes and ketones, respectively. Tertiary alcohols do not undergo oxidation.

12.6 Oxidation and Reduction in Living Systems

In organic and biological systems, *oxidation* involves the gain of oxygen or loss of hydrogen. *Reduction* involves the loss of oxygen or gain of hydrogen. Nicotinamide adenine dinucleotide, NAD^+, is a coenzyme involved in many biological oxidation and reduction reactions.

12.7 Phenols

Phenols are compounds in which the hydroxyl group is attached to a benzene ring; they have the general formula Ar—OH. Many phenols are important as antiseptics and disinfectants.

12.8 Ethers

Ethers are characterized by the R—O—R functional group. Ethers are generally nonreactive but are extremely flammable. Diethyl ether was the first general anesthetic used in medical practice. It has since been replaced by Penthrane and Enthrane, which are less flammable.

12.9 Thiols

Thiols are characterized by the sulfhydryl group (—SH). The amino acid cysteine is a thiol that is extremely important for maintaining the correct shapes of proteins. Coenzyme A is a thiol that serves as a "carrier" of acetyl groups in biochemical reactions.

KEY TERMS

alcohol (12.1)
carbinol carbon (12.4)
dehydration (12.5)
disulfide (12.9)
elimination reaction (12.5)
ether (12.8)
fermentation (12.3)
hydration (12.5)
hydroxyl group (12.1)
oxidation (12.6)
phenol (12.7)
primary (1°) alcohol (12.4)
reduction (12.6)
secondary (2°) alcohol (12.4)
tertiary (3°) alcohol (12.4)
thiol (12.9)
Zaitsev's rule (12.5)

QUESTIONS AND PROBLEMS

Alcohols: Structure and Physical Properties

Foundations

12.29 Describe the relationship between the water solubility of alcohols and their hydrocarbon chain length.

12.30 Explain the relationship between the water solubility of alcohols and the number of hydroxyl groups in the molecule.

Applications

12.31 Arrange the following compounds in order of increasing boiling point, beginning with the lowest:

a. $CH_3CH_2CH_2CH_2CH_3$ **b.** $CH_3CHCH_2CHCH_3$ (OH on C-2 and C-4: | OH | OH)

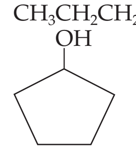
c. $CH_3CHCH_2CH_2CH_3$ (| OH on C-2) **d.** $CH_3CH_2CH_2$—O—CH_2CH_3

12.32 Why do alcohols have higher boiling points than alkanes?

12.33 Which member of each of the following pairs is more soluble in water?

a. CH_3CH_2OH or $CH_3CH_2CH_2CH_2OH$

b. $CH_3CH_2CH_2CH_2CH_3$ or $CH_3CH_2CH_2CH_2$—OH

c.  or CH_3CHCH_3 (| OH on C-2)

12.34 Arrange the three alcohols in each of the following sets in order of increasing solubility in water:

a. $CH_3CH_2CH_2CH_2CH_2OH$ $CH_3CHCH_2CHCH_2CH_3$ (| OH | OH on C-2 and C-4)

$CH_3CHCH_2CHCH_2CH_2OH$ (| OH | OH on C-2 and C-4)

b. Pentyl alcohol 1-Hexanol Ethylene glycol

Alcohols: Nomenclature

Foundations

12.35 Briefly describe the I.U.P.A.C. rules for naming alcohols.

12.36 Briefly describe the rules for determining the common names for alcohols.

Applications

12.37 Give the I.U.P.A.C. name for each of the following compounds:

a. $CH_3CH_2CH_2CH_2CH_2CH_2CH_2OH$

b. CH_3CHCH_3 (| OH on C-2)

c. CH_3—C—CH_3 (central C bearing CH_3 above and CH_2OH below)

12.38 Give the I.U.P.A.C. name for each of the following compounds:

a. $CH_3CH_2CHCH_2CH_2CH_2OH$ (Br | on C-3)

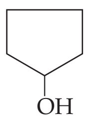
b. CH_3CH—$CCH_2CH_2CH_3$ (OH below C-2; C-3 bearing CH_3 above and CH_3 below)

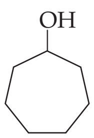
c. $CH_3CH_2CCH_2CH_3$ (central C bearing $CH_2CH_2CH_2CH_3$ above and OH below)

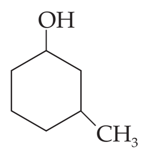
12.39 Draw each of the following, using complete structural formulas:
- **a.** 3-Hexanol
- **b.** 1,2,3-Pentanetriol
- **c.** 2-Methyl-2-pentanol

12.40 Draw each of the following using condensed structural formulas:
- **a.** Cyclohexanol
- **b.** 3,4-Dimethyl-3-heptanol

12.41 Give the I.U.P.A.C. name for each of the following compounds:

a. 

b. 

c. 

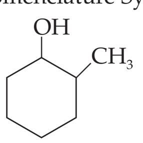
12.42 Draw each of the following alcohols:
- **a.** 1-Iodo-2-butanol
- **b.** 1,2-Butanediol
- **c.** Cyclobutanol

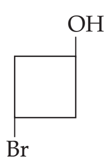
12.43 Give the common name for each of the following compounds:
- **a.** CH_3OH
- **b.** CH_3CH_2OH
- **c.** $CH_2—CH_2$ (each CH_2 bearing OH)
  OH OH
- **d.** $CH_3CH_2CH_2OH$

12.44 Draw the structure of each of the following compounds:
- **a.** Pentyl alcohol
- **b.** Isopropyl alcohol
- **c.** Octyl alcohol
- **d.** Propyl alcohol

12.45 Draw a complete structural formula for each of the following compounds:
- **a.** 4-Methyl-2-hexanol
- **b.** Isobutyl alcohol
- **c.** 1,5-Pentanediol
- **d.** 2-Nonanol
- **e.** 1,3,5-Cyclohexanetriol

12.46 Name each of the following alcohols using the I.U.P.A.C. Nomenclature System:

a. 

b. 

c. $CH_3CHCH_2CHCH_2CHCH_3$
  OH OH OH

d. OH
$CH_3CH_2CHCHCHCH_3$
  OH OH

Medically Important Alcohols

12.47 What is denatured alcohol? Why is alcohol denatured?

12.48 What are the principal uses of methanol, ethanol, and isopropyl alcohol?

12.49 What is fermentation?

12.50 Why do wines typically have an alcohol concentration of 12–13%?

12.51 Why must fermentation products be distilled to produce liquors such as scotch?

12.52 If a bottle of distilled alcoholic spirits—for example, scotch whiskey—is labeled as 80 proof, what is the percentage of alcohol in the scotch?

Classification of Alcohols

Foundations

12.53 Define the term *carbinol carbon.*

12.54 Define the terms *primary, secondary,* and *tertiary alcohol,* and draw a general structure for each.

Applications

12.55 Classify each of the following as a 1°, 2°, or 3° alcohol:
- **a.** 3-Methyl-1-butanol
- **b.** 2-Methylcyclopentanol
- **c.** *t*-Butyl alcohol
- **d.** 1-Methylcyclopentanol
- **e.** 2-Methyl-2-pentanol

12.56 Classify each of the following as a 1°, 2°, or 3° alcohol:

a. $CH_3CH_2CH_2CH_2CH_2CH_2CH_2OH$

b. CH_3CHCH_3
  OH

c. CH_3
$CH_3—C—CH_3$
CH_2OH

d. Br
$CH_3CH_2CHCH_2CH_2CH_2OH$

e. CH_3
$CH_3CH—CCH_2CH_2CH_3$
  OH CH_3

12.57 Classify each of the following as a primary, secondary, or tertiary alcohol:

a. CH_2CH_3
$CH_3CH_2C—OH$
CH_3

b. $CH_3CHCH_2CHCH_3$
  OH Br

c. $CH_3CH_2CH_2OH$

d. CH_3
$CH_3CCH_2CH_2CH_3$
  OH

12.58 Classify each of the following as a primary, secondary, or tertiary alcohol:
- **a.** 2-Methyl-2-butanol
- **b.** 1,2-Dimethylcyclohexanol
- **c.** 2,3,4-Trimethylcyclopentanol
- **d.** 3,3-Dimethyl-2-pentanol

Reactions Involving Alcohols

Foundations

12.59 Write a general equation representing the preparation of an alcohol by hydration of an alkene.

12.60 Write a general equation representing the preparation of an alcohol by hydrogenation of an aldehyde or a ketone.

12.61 Write a general equation representing the dehydration of an alcohol.

12.62 Write a general equation representing the oxidation of a 1° alcohol.

12.63 Write a general equation representing the oxidation of a 2° alcohol.

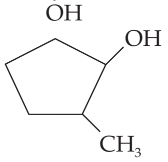
12.64 Write a general equation representing the oxidation of a 3° alcohol.

Applications

12.65 Predict the products formed by the hydration of the following alkenes:
- **a.** 1-Pentene
- **b.** 2-Pentene
- **c.** 3-Methyl-1-butene
- **d.** 3,3-Dimethyl-1-butene

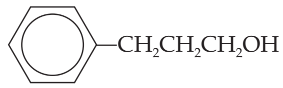
12.66 Draw the alkene products of the dehydration of the following alcohols:
- **a.** 2-Pentanol
- **b.** 3-Methyl-1-pentanol
- **c.** 2-Butanol
- **d.** 4-Chloro-2-pentanol
- **e.** 1-Propanol

12.67 Write an equation showing the hydration of each of the following alkenes. Name each of the products using the I.U.P.A.C. Nomenclature System.
- **a.** 2-Hexene
- **b.** Cyclopentene
- **c.** 1-Octene
- **d.** 1-Methylcyclohexene

12.68 Write an equation showing the dehydration of each of the following alcohols. Name each of the reactants and products using the I.U.P.A.C. Nomenclature System.
- **a.** $CH_3CH(OH)CH_2CH_3$
- **b.** 

12.69 What product(s) would result from the oxidation of each of the following alcohols with, for example, potassium permanganate? If no reaction occurs, write N.R.
- **a.** 2-Butanol
- **b.** 2-Methyl-2-hexanol
- **c.** Cyclohexanol
- **d.** 1-Methyl-1-cyclopentanol

12.70 We have seen that ethanol is metabolized to ethanal (acetaldehyde) in the liver. What would be the product formed, under the same conditions, from each of the following alcohols?
- **a.** CH_3OH
- **b.** $CH_3CH_2CH_2OH$
- **c.** $CH_3CH_2CH_2CH_2OH$

12.71 Give the oxidation products of the following alcohols. If no reaction occurs, write N.R.
- **a.** $CH_3CH_2CH(OH)CH_2CH_3$
- **b.** $CH_3CH_2CH_2OH$
- **c.** $CH_3CH(OH)CH_2CH(CH_3)CH_3$
- **d.** $CH_3—C(OH)(CH_3)—CH_2CH_3$
- **e.** 

12.72 Write an equation, using complete structural formulas, demonstrating each of the following chemical transformations:
- **a.** Oxidation of an alcohol to an aldehyde
- **b.** Oxidation of an alcohol to a ketone
- **c.** Dehydration of a cyclic alcohol to a cycloalkene
- **d.** Hydrogenation of an alkene to an alkane

12.73 Write the reaction, occurring in the liver, that causes the oxidation of ethanol. What is the product of this reaction and what symptoms are caused by the product?

12.74 Write the reaction, occurring in the liver, that causes the oxidation of methanol. What is the product of this reaction and what is the possible result of the accumulation of the product in the body?

12.75 Write an equation for the preparation of 2-butanol from 1-butene. What type of reaction is involved?

12.76 Write a general equation for the preparation of an alcohol from an aldehyde or ketone. What type of reaction is involved?

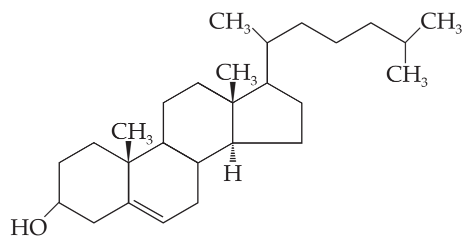
12.77 Show how acetone can be prepared from propene.

$CH_3C(=O)CH_3$

Acetone

12.78 Show how bromocyclopentane can be prepared from cyclopentanol.

12.79 Give the oxidation product for cholesterol.



Cholesterol

12.80 Why is a tertiary alcohol not oxidized?

Oxidation and Reduction in Living Systems

Foundations

12.81 Define the terms *oxidation* and *reduction.*

12.82 How do we recognize oxidation and reduction in organic compounds?

Applications

12.83 Arrange the following compounds from the most reduced to the most oxidized:

$CH_3CH_2C(=O)—OH$ $\quad$ $CH_3CH_2CH_3$

$CH_3CH_2C(=O)—H$ $\quad$ $CH_3CH_2CH_2OH$

12.84 What is the role of the coenzyme nicotinamide adenine dinucleotide (NAD^+) in enzyme-catalyzed oxidation–reduction reactions?

Phenols

Foundations

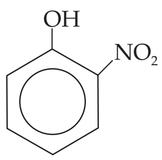
12.85 What are phenols?

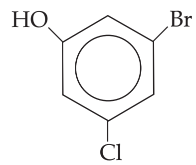
12.86 Describe the water solubility of phenols.

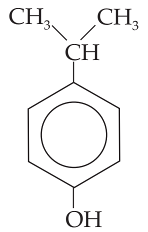
Applications

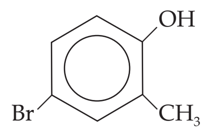
12.87 2,4,6-Trinitrophenol is known by the common name *picric acid.* Picric acid is a solid but is readily soluble in water. In solution it is used as a biological tissue stain. As a solid, it is also known to be unstable and may explode. In this way it is similar to 2,4,6-trinitrotoluene (TNT). Draw the structures of picric acid and TNT. Why is picric acid readily soluble in water whereas TNT is not?

12.88 Name the following aromatic compounds using the I.U.P.A.C. system:

a. 

c. 

b. 

d. 

12.89 List some phenol compounds that are commonly used as antiseptics or disinfectants.

12.90 Why must a dilute solution of phenol be used for disinfecting environmental surfaces?

Ethers

12.91 Draw all of the alcohols and ethers of molecular formula $C_4H_{10}O$.

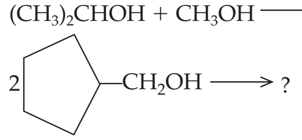
12.92 Name each of the isomers drawn for Problem 12.91.

12.93 Give the I.U.P.A.C. names for Penthrane and Enthrane (see Section 12.8).

12.94 Why have Penthrane and Enthrane replaced diethyl ether as a general anesthetic?

12.95 Ethers may be prepared by the removal of water (dehydration) between two alcohols, as shown. Give the structure(s) of the ethers formed by the reaction of the following alcohol(s) under acidic conditions with heat.

Example: $CH_3OH + HOCH_3 \xrightarrow[\text{Heat}]{H^+,} CH_3OCH_3 + H_2O$

a. $2CH_3CH_2OH \longrightarrow$?
b. $CH_3OH + CH_3CH_2OH \longrightarrow$?
c. $(CH_3)_2CHOH + CH_3OH \longrightarrow$?
d. 

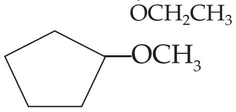
12.96 We have seen that alcohols are capable of hydrogen bonding to each other. Hydrogen bonding is also possible between alcohol molecules and water molecules or between alcohol molecules and ether molecules. Ether molecules *do not* hydrogen bond to each other, however. Explain.

12.97 Name each of the following ethers using the I.U.P.A.C. Nomenclature System:

a. $CH_3CHCH_2CH_2CH_3$ (with OCH_2CH_3 on C-2)

b. $CH_3CH_2CHCH_3$ (with OCH_3 on C-3)

c. $CH_3CH_2CH_2CH$ (with OCH_2CH_3 on the terminal CH)

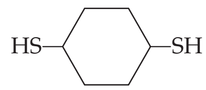
d. 

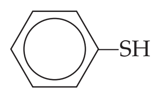
12.98 Draw the structural formula for each of the following ethers:
a. Methyl propyl ether
b. 2-Methoxyoctane
c. Diisopropyl ether
d. 3-Ethoxypentane

Thiols

12.99 Cystine is an amino acid formed from the oxidation of two cysteine molecules to form a disulfide bond. The molecular formula of cystine is $C_6H_{12}O_4N_2S_2$. Draw the structural formula of cystine. (*Hint:* For the structure of cysteine, see page 407.)

12.100 Explain the way in which British Anti-Lewisite acts as an antidote for mercury poisoning.

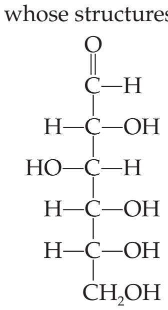
12.101 Give the I.U.P.A.C. name for each of the following thiols.
a. $CH_3CH_2CH_2—SH$
b. $CH_3CHCH_2CH_3$ (with SH on C-2)
c. $CH_3—C—CH_3$ (with CH_2CH_3 and SH on the central C)
d. 

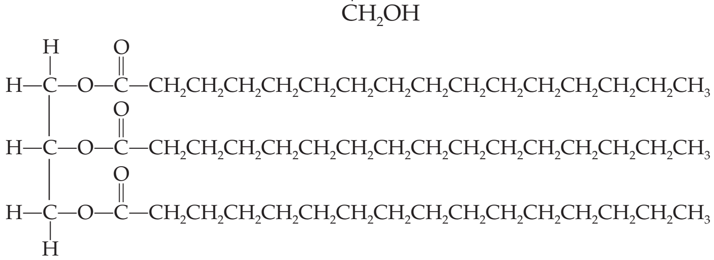
12.102 Give the I.U.P.A.C. name for each of the following thiols.
a. CH_2CHCH_3 (with SH on C-1 and SH on C-2)
b. 

c. $CH_3CHCH_2CH_2CH_3$ (with SH on C-2)
d. $CH_3CH_2CH_2CH_2CH_2CH_2CH_2SH$

CRITICAL THINKING PROBLEMS

1. You are provided with two solvents: water (H_2O) and hexane ($CH_3CH_2CH_2CH_2CH_2CH_3$). You are also provided with two biological molecules whose structures are shown here:

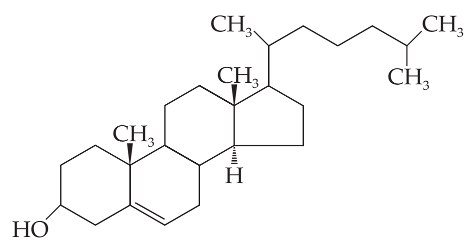




Predict which biological molecule would be more soluble in water and which would be more soluble in hexane. Defend your prediction. Design a careful experiment to test your hypothesis.

Consider the digestion of dietary molecules in the digestive tract. Which of the two biological molecules shown in this problem would be more easily digested under the conditions present in the digestive tract?

2. Cholesterol is an alcohol and a steroid (Chapter 17). Diets that contain large amounts of cholesterol have been linked to heart disease and atherosclerosis, hardening of the arteries. The narrowing of the artery, caused by plaque buildup, is very apparent. Cholesterol is directly involved in this buildup. Describe the various functional groups and principal structural features of the cholesterol molecule. Would you use a polar or nonpolar solvent to dissolve cholesterol? Explain your reasoning.



Cholesterol

3. An unknown compound A is known to be an alcohol with the molecular formula $C_4H_{10}O$. When dehydrated, compound A gave only one alkene product, C_4H_8, compound B. Compound A could not be oxidized. What are the identities of compound A and compound B?

4. Sulfides are the sulfur analogs of ethers, that is, ethers in which oxygen has been substituted by a sulfur atom. They are named in an analogous manner to the ethers with the term *sulfide* replacing *ether.* For example, $CH_3—S—CH_3$ is dimethyl sulfide. Draw the sulfides that correspond to the following ethers and name them:

a. diethyl ether
b. methyl propyl ether
c. dibutyl ether
d. ethyl phenyl ether

5. Dimethyl sulfoxide (DMSO) has been used by many sports enthusiasts as a linament for sore joints; it acts as an anti-inflammatory agent and a mild analgesic (pain killer). However, it is no longer recommended for this purpose because it carries toxic impurities into the blood. DMSO is a sulfoxide—it contains the S═O functional group. DMSO is prepared from dimethyl sulfide by mild oxidation, and it has the molecular formula C_2H_6SO. Draw the structure of DMSO.