

27

ALCOHOLS, HALOALKANES, AND ETHERS

27.1 | Alcohols: Structure, Properties, and Nomenclature



WHAT'S AHEAD

- 27.1 ► Alcohols: Structure, Properties, and Nomenclature
- 27.2 ► Haloalkanes
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- 27.4 ► Reactions of Alcohols
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- 27.7 ► Substitution versus Elimination

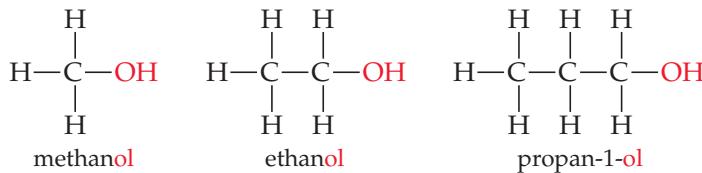
Whether white, red, or something in between, wine is a complex mixture of chemicals. One of the main constituents of wine is, of course, ethanol. Produced by the yeast fermentation of the sugars within the fruits from which it is made, much of the popularity of wine comes from its intoxicating effect. The science of wine and wine making is called *oenology*, and today it helps sustain a multibillion-dollar industry worldwide.

Currently, ethanol is valued more than ever. Its uses are as diverse as a substitute for, or additive in, petrol; as a solvent in the manufacture of varnishes and perfumes; as a fluid in thermometers; in the manufacture of acetic acid; in the preparation of essences and flavorings and as a disinfectant. Ethanol is miscible with water in all proportions. Absolute ethanol contains >99% v/v ethanol and is purified from industrial ethanol by first applying fractional distillation, which produces a liquid that is 95% v/v ethanol, then by azeotropic distillation.

In this section, we take an introductory look at the structure of alcohols, some of their physical properties, and how to name them. By the end of the section, you should be able to:

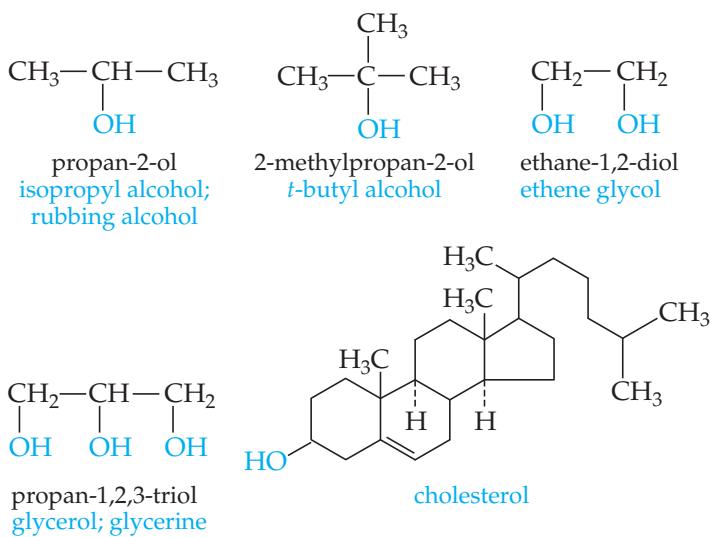
- Have an idea of the solubility of alcohols in water or hydrocarbons
- Be able to name simple alcohols
- Recognize the classification of an alcohol as primary, secondary, or tertiary

Alcohols are hydrocarbon derivatives in which one or more hydrogens have been replaced by a *hydroxyl* group, OH. **Figure 27.1** shows the structural formulas and names of the three simplest straight-chain alcohols together with five other important alcohols. The simple alcohols are named by changing the last letter in the name of the corresponding alkane to *-ol*; for example, ethane becomes ethanol. Where necessary, the location of the OH group is designated by an appropriate numeral prefix that indicates the position of the OH group (Figure 27.1).

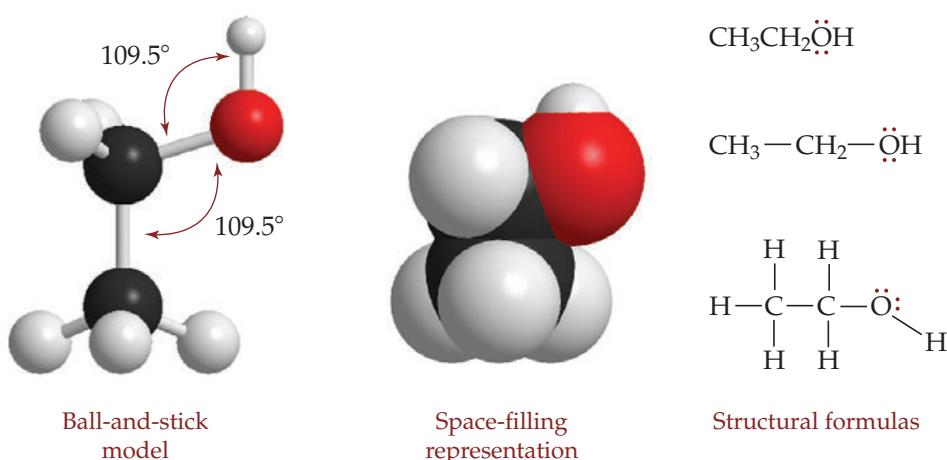


The oxygen atom of the hydroxyl group is sp^3 hybridized, having a tetrahedral arrangement of its bonds and lone pairs (Figure 27.2). Two of the sp^3 hybrid orbitals of the oxygen atom form σ -bonds with carbon and hydrogen. Each of the other two orbitals contain a pair of unshared electrons, or **lone pair**. The bond angles about the oxygen atom of an alcohol are very similar to those around sp^3 carbon centers. Any variation from the ideal 109.5° bond angle is due to the comparatively large size of the lone pairs.

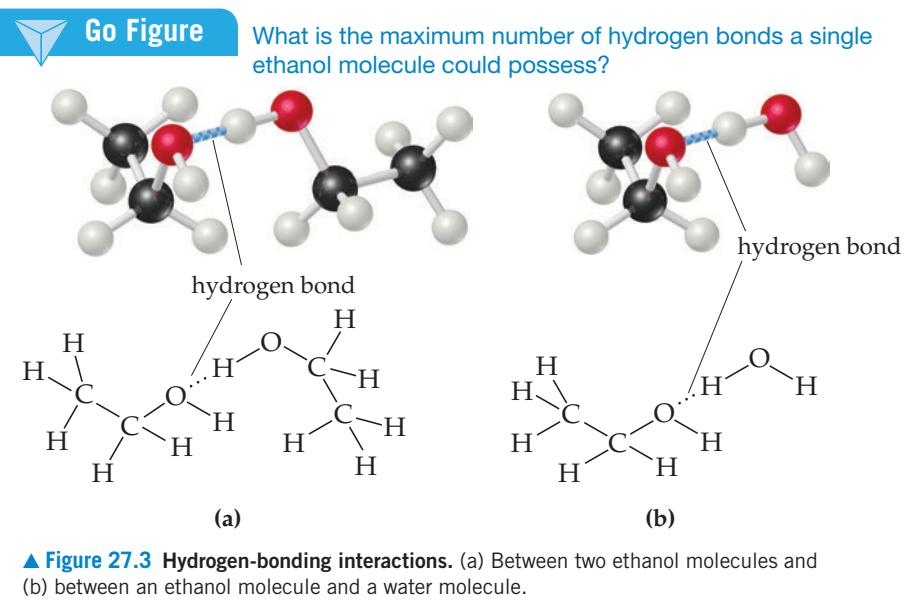
▼ **Figure 27.1** Structural formulas of six important alcohols. Common names are given in blue.



The properties of alcohols are very different from those of the alkanes from which they are derived. For example, methane, ethane and propane are all colorless gases under normal conditions, whereas methanol, ethanol, and propanol are colorless liquids. The reason for the difference in physical properties lies in the fact that the O—H bond is polar, with the difference in electronegativity values between the oxygen and hydrogen atoms being 1.4. As a result, the —OH functional group can participate in intermolecular hydrogen bonding, which increases the attractive forces between the molecules of the alcohol. The strength of a hydrogen bond is approximately 20 kJ/mol, which is considerably weaker than an O—H covalent bond (about 460 kJ/mol); however, it is strong enough to have a significant effect on the alcohol's physical properties. As a result, the boiling points of alcohols are much higher than those of their parent alkanes. The ability of alcohols to form hydrogen bonds is also why they are much more soluble in polar solvents such as water, than in the corresponding



◀ **Figure 27.2** The structure of ethanol.
A number of representations for ethanol are shown.



hydrocarbons (Figure 27.3). For example, the solute–solute, solvent–solvent and solute–solvent forces are not greatly different within a mixture of $\text{CH}_3\text{CH}_2\text{OH}$ and H_2O . As a result, there is no major change in the environments of the molecules as they are mixed.

Liquids that mix completely in another liquid are said to be *miscible*, whereas solids that dissolve in a liquid are said to be *soluble* in that liquid. Pairs of liquids, such as ethanol and water, that mix in all proportions are miscible; those that do not mix are *immiscible*. For example, hexane (C_6H_{14}) is immiscible in water. The attraction between the polar water molecules and the nonpolar hexane molecules is not sufficiently strong to allow the formation of a solution.

The number of carbon atoms in an alcohol affects its solubility in water. As the length of the carbon chain increases, the polar OH group becomes an ever-smaller part of the molecule, and the compound behaves more like a hydrocarbon. The solubility of the alcohol in water decreases correspondingly. By contrast, the solubility of the alcohol in a nonpolar solvent like hexane increases as the nonpolar hydrocarbon chain increases in length. The series of alcohols in Table 27.1 demonstrates that polar liquids tend to be miscible in other polar liquids and nonpolar liquids in nonpolar ones. This phenomenon is simply stated as “*like dissolves like*”.

TABLE 27.1 Solubilities of some alcohols in water and in hexane*

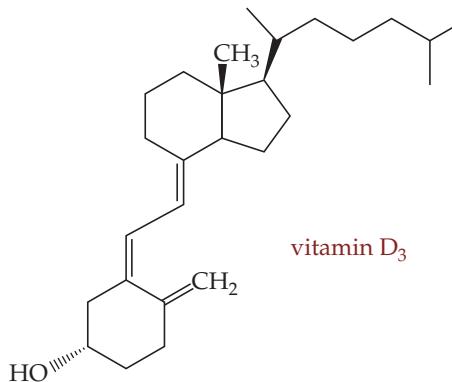
Alcohol	Solubility in H ₂ O	Solubility in C ₆ H ₁₄
CH ₃ OH (methanol)	∞	0.12
CH ₃ CH ₂ OH (ethanol)	∞	∞
CH ₃ CH ₂ CH ₂ OH (propan-1-ol)	∞	∞
CH ₃ CH ₂ CH ₂ CH ₂ OH (butan-1-ol)	0.11	∞
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ OH (pentan-1-ol)	0.030	∞
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ OH (hexan-1-ol)	0.0058	∞
CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ OH (heptan-1-ol)	0.0008	∞

* Expressed in mol alcohol/100 g solvent at 20 °C. The infinity symbol indicates that the alcohol is completely miscible with the solvent.

CHEMISTRY AND LIFE

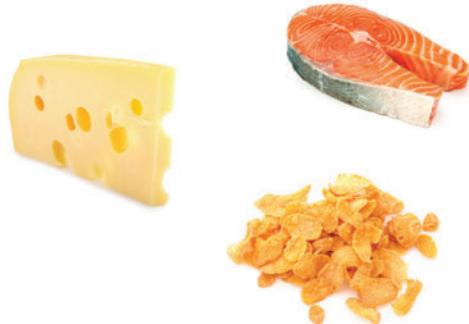
Vitamin D

Vitamin D, an alcohol, is a steroid hormone derived from cholesterol. The biologically active form of the hormone is vitamin D₃ whose primary function is to regulate calcium and phosphorus homeostasis and maintain bone density in the body. Food provides us with a precursor molecule which is converted to vitamin D₃ under the skin by the action of sunlight. Hence it is sometimes called the sunshine vitamin (**Figure 27.4**). Milk is fortified with vitamin D as a dietary safeguard in countries where outdoor exposure is often limited. Recent evidence suggests there is a need, for children especially, to spend more time outdoors. The “stay out of the sun” campaigns, in conjunction with the great popularity of computer games, have been linked to an increased risk of vitamin D deficiency and the resulting underdevelopment of bone in children, called *rickets*. Rickets is characterized by improper mineralization during the development of bones and results in soft bones, curved spines, and knock-knees. Nevertheless, a sensible approach to sun exposure is also required.



Food sources:

- Cheese
- Margarine
- Butter
- Fortified milk
- Healthy cereals
- Fatty fish



▲ **Figure 27.4** Vitamin D and its food sources.

Sample Exercise 27.1

Predicting Solubility Patterns in Organic Compounds

Predict whether the following compounds are more likely to dissolve in water or hexane (C₆H₁₄) solvent: cyclohexanol (C₆H₁₁OH), acetic acid (CH₃COOH), chloroform (CHCl₃), heptane (C₇H₁₆), and glycerol (Figure 27.1).

SOLUTION

Analyze We are asked to differentiate between various compounds by their solubility or miscibility in either hexane or water.

Plan *Like dissolves in like.*

Solve Although cyclohexanol contains an OH group, the addition of the C₆ ring system would make its properties comparable with 1-hexanol. Given the choice of solvents, cyclohexanol dissolves better in hexane because the molecule is more “alkane-like”.

Acetic acid is a very polar compound, containing little alkane character. This compound dissolves better in water as a solvent.

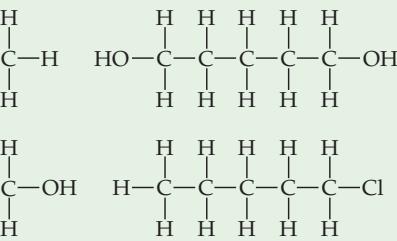
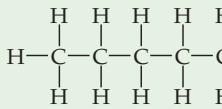
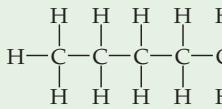
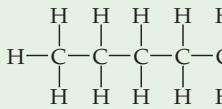
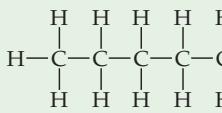
Chloroform is a moderately polar liquid because of its tetrahedral geometry. Chlorine atoms are poor hydrogen-bonding groups, however, and so this compound would be more miscible with hexane.

Heptane is an alkane, so it is nonpolar. This compound is miscible with hexane.

Glycerol is a small organic compound containing three OH groups. It is very soluble in water.

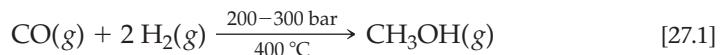
► Practice Exercise

Arrange the following substances in order of increasing solubility in water:



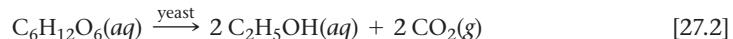
Common Alcohols

Figure 27.5 shows several commercial products that consist entirely or in part of an alcohol. Let's consider how some of the more important alcohols are formed and used. The simplest alcohol, methanol, has many important industrial uses and is produced on a large scale. Carbon monoxide and hydrogen are heated together under pressure in the presence of a metal oxide catalyst:



Because methanol has a very high octane rating as a car fuel, it is used as a petroleum additive and as a fuel in its own right.

Ethanol is a product of the fermentation of carbohydrates such as sugar and starch. In the absence of air, yeast cells convert carbohydrates into a mixture of ethanol and CO₂, as shown in Equation 27.2. In the process, yeast derives energy necessary for growth.



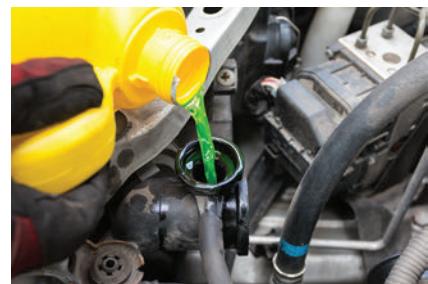
This reaction is conducted under carefully controlled conditions to produce beer, wine, and other beverages in which ethanol is the active ingredient.

Many polyhydroxyl alcohols (those containing more than one OH group) are known. The simplest of these is ethane-1,2-diol (ethylene glycol, HOCH₂CH₂OH). This substance is the major ingredient in car radiator coolant. Another common polyhydroxyl alcohol is propane-1,2,3-triol (glycerol, HOCH₂CH(OH)CH₂OH). This is a viscous liquid that dissolves readily in water and is widely used as a skin softener in cosmetic preparations. It is also used in foods and confectionary to keep them moist.

Cholesterol is classed as a steroid but here we will look at it as a biochemically important alcohol. The OH group forms only a small component of this rather large molecule, so cholesterol is virtually insoluble in water (0.2 g per 100 cm³ of H₂O) and has a waxy feel. Cholesterol is an essential component of our bodies; when present in excessive amounts, however, it may precipitate from solution. If it precipitates in the gall bladder, it may form crystalline lumps called *gallstones*. Cholesterol may also precipitate against the walls of veins and arteries and thus contribute to high blood pressure and other cardiovascular problems. The amount of cholesterol in our blood is determined not only by how much cholesterol we eat but also by total energy intake. There is evidence that excessive caloric intake leads the body to synthesize excessive amounts of cholesterol.

Naming Alcohols

Alcohol nomenclature is based on selecting the longest chain containing the OH group. This chain is numbered to give the OH group the lowest possible number. Alcohols that are *normal*—that is, they contain the OH functional group on the first carbon of a straight-chain alkyl group—are listed in Table 27.1. Sometimes, you may see these compounds named as *n*-butanol, *n*-hexanol, and so on. In these cases, the *n* stands for normal.



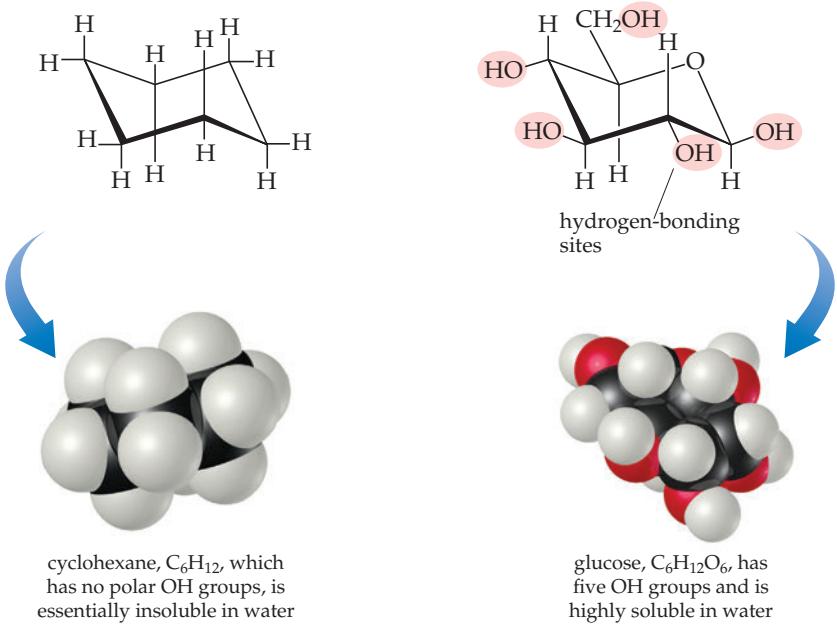
▲ **Figure 27.5** Everyday alcohols. Many of the products we use every day—from rubbing alcohol and throat lozenges to hair spray and radiator coolant—are composed either entirely or mainly of alcohols.

CHEMISTRY AND LIFE The Solubility Nexus

The solubility of organic molecules is an important issue, especially in the area of medicine. Not only must a drug be effective, but it must have sufficient solubility in water for aqueous administration in the blood. These two criteria are seldom satisfied collectively and are complicated further by the need for a drug candidate to pass through hydrophobic cell membranes and/or the blood-brain barrier.

One way to enhance the solubility of a substance in water is to increase the number of polar groups it contains. For example, increasing the number of OH groups along a carbon chain of a solute increases the extent of hydrogen bonding between that solute

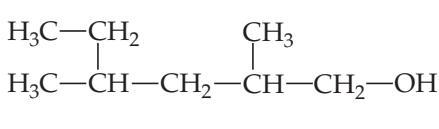
and water, thereby increasing solubility. Glucose ($C_6H_{12}O_6$) has five OH groups, which makes the molecule very soluble in water (83 g dissolves in 100 cm³ of water at 17.5 °C). Glucose is shown in **Figure 27.6** and is compared structurally with cyclohexane, its hydrocarbon analogue. The solubility of cyclohexane in water is extremely low due to its inability to hydrogen-bond to water. The second approach to increasing polarity is to add charge. As we will see in Chapters 29 and 31, negative charge can be added through *carboxylate groups* and positive charge through *ammonium salts*. Both are proven and common ways to make drugs soluble in water.



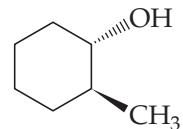
▲ **Figure 27.6** Hydrogen bonding and aqueous solubility. The presence of OH groups capable of hydrogen bonding with water enhances the aqueous solubility of organic molecules.

It is more appropriate, however, to use IUPAC nomenclature, which names these compounds using a positional prefix—for example, butan-1-ol, hexan-1-ol. Note that methanol and ethanol do not need a prefix.

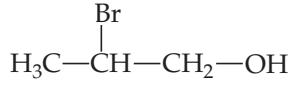
The names of some simple alcohols are given here. Each molecule contains extra functionality or branching, yet all the names are derived from the name of the alcohol. Their names illustrate, to some extent, the hierarchy of nomenclature.



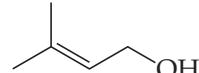
2,4-dimethylhexan-1-ol



(1*S*,2*S*)-2-methylcyclohexanol
is better than
trans-2-methylcyclohexanol



2-bromopropan-1-ol



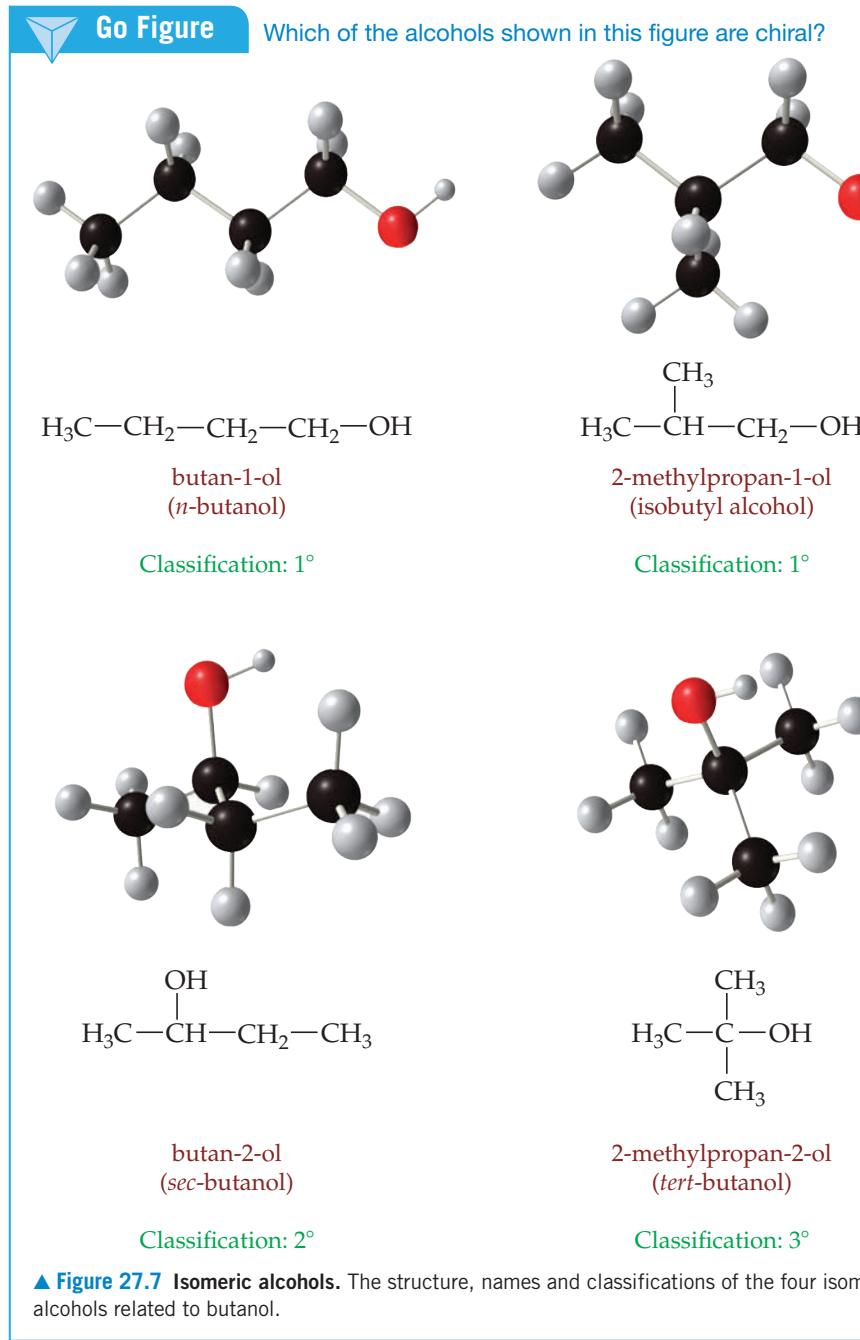
3-methyl-2-buten-1-ol

Systematic naming using the IUPAC conventions does not distinguish between, for example, 1-hexanol and hexan-1-ol as the most satisfactory way to name a functionalized

alcohol. Both methods unambiguously describe the position of the OH group and could be used. The latter naming style is better suited to molecules that contain an alkene as well as the OH group. In such cases, “*an*” would be replaced by “*en*” to represent the incorporation of the alkene. Compounds of this type are called *unsaturated alcohols*.

The 2-methylcyclohexanol example illustrated earlier demonstrates two nomenclature principles. The alcohol functional group, when bonded to a cyclic structure, is assigned position 1, based on the arguments we used to discuss the nomenclature of cycloalkenes (Section 26.2). Although *trans* satisfactorily describes the orientation of the OH and CH₃ groups, it does not unambiguously describe the molecule (there is another enantiomer with a *trans* arrangement—can you draw it?). In this case, the absolute stereochemistry at each position should be described.

The OH group is not always located at position 1. **Figure 27.7** illustrates the different C₄H₁₀O alcohols that are possible, as well as their systematic and common names. Alcohols, like alkanes, are classified as primary, secondary or tertiary. We discuss this in more detail in the following section.





Sample Exercise 27.2

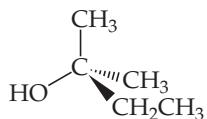
Naming Alcohols

Systematically name the following alcohols, taking stereochemistry into account where appropriate.

(a)



(b)



SOLUTION

Analyze We are given two structures and asked to name them.

Plan Name each compound using the longest chain possessing the OH group. Assign stereochemistry based first on symmetry then on the Cahn–Ingold–Prelog rules in Chapter 25.

Solve

(a) This example has no stereochemical consequence because a plane of symmetry exists within the molecule. The compound is derived from cyclopentane. Its systematic name is 1-methylcyclopentanol.

(b) This example also has no stereochemical consequences because a plane of symmetry exists within the molecule. The compound is derived from butanol, as the longest chain bearing the OH group is four carbons long. Its systematic name is 2-methylbutan-2-ol.

► Practice Exercise

Draw the structures corresponding to the following names:

(a) (*R*)-4-methylpentan-2-ol (b) (*Z*)-3-penten-1-ol

Alcohols containing two or three OH groups are called **diols** and **triols**, respectively. Common examples are shown in Figure 27.1.



Sample Exercise 27.3

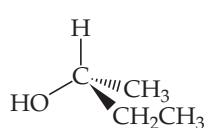
Classifying Alcohols

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

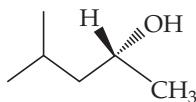
(a)



(b)



(c)



SOLUTION

Analyze We are given the structures of three alcohols and asked to classify them.

Plan Locate the carbon bearing the OH group and determine the number of carbons attached to this carbon.

Solve

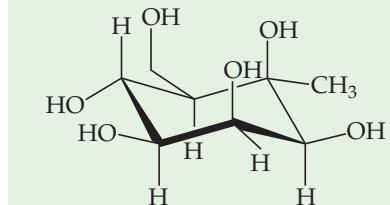
(a) The carbon bearing the OH group has three carbons attached to it: two from the ring and one from the methyl group. Therefore, this is a tertiary alcohol.

(b) The carbon bearing the OH group has two carbons attached to it, one from the methyl group and the other from the ethyl group. This compound can be classed as a secondary alcohol.

(c) The carbon bearing the OH group has two other carbons attached. Hence it too is secondary.

► Practice Exercise

Classify all alcohol functional groups in the following molecule as 1°, 2° or 3°.



Classifying Alcohols

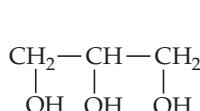
The classification and notation used to distinguish between types of alcohols are:

- Primary (1°) alcohol:** The carbon atom bearing the OH group is bonded to only one other carbon atom.
- Secondary (2°) alcohol:** The carbon atom bearing the OH group is bonded to two carbon atoms.
- Tertiary (3°) alcohol:** The carbon atom bearing the OH group is bonded to three carbon atoms.

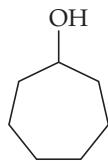
Figure 27.7 illustrates this classification within a series of butanol isomers. There is a big difference in reactivity between 1° , 2° , and 3° alcohols. An important part of your understanding of the chemistry of alcohols is the ability to recognize an alcohol's class and to use this knowledge to predict the product of a reaction. Each classification of alcohol—namely primary, secondary and tertiary—reacts differently to a range of reactants. As we see in the following chapters, this classification allows us to predict the type of product and/or the necessary reagents with which to undertake certain functional-group manipulations.

Self-Assessment Exercises

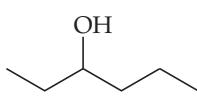
- 27.1** Which of the following molecules would you expect to be miscible in water?



(a)



(b)



(c)

- (a) Cyclopent-1-en-3-ol
- (b) Cyclopent-1-en-4-ol
- (c) Cyclopent-3-enol
- (d) (R)-Cyclopent-3-enol

- 27.3** Which of the structures in self-assessment exercise 27.1 contains a primary alcohol?

- 27.2** Give the full systematic name of the following alcohol:



Exercises

- 27.4** Suppose the hydrogens on the OH group of glycerol (Figure 27.1) were replaced with methyl groups, CH_3 . Would you expect the solubility in water of the resulting molecules to be higher than, lower than or about the same as the solubility of glycerol?
- 27.5** Write the structural formulae for as many alcohols as you can think of that have the empirical formula $\text{C}_3\text{H}_6\text{O}$.

- 27.6** Explain why propan-1-ol is miscible with water yet hexan-1-ol is not.
- 27.7** Write the condensed structural formula for each of the following compounds: (a) butan-2-ol, (b) 1,2-ethanediol, (c) diethyl ether.
- 27.8** Classify the isomeric alcohols with molecular formula $\text{C}_4\text{H}_{10}\text{O}$ as primary, secondary or tertiary.

27.1 (a) 27.2 (c) 27.3 (a)

Answers to Self-Assessment Exercises



27.2 | Haloalkanes



A class of haloalkanes you may be familiar with are the **chlorofluorocarbons**, or CFCs. Compounds of this category were typically used as refrigerants, as propellants in aerosols, and as industrial solvents. They were usually marketed under the name *Freon*. CFCs are odorless, non-toxic, non-flammable, and non-corrosive compounds and so found great industrial utility. During the mid-1970s, however, research into CFCs showed they had a harmful effect on the environment. Being relatively chemically inert means that CFCs can persist in the atmosphere for a long time. Thus, they are not broken down in the troposphere but find their way into the stratosphere, where they are decomposed by the action of ultraviolet (UV) radiation. In this process, a reaction sequence is initiated that depletes the ozone layer—a thin layer of the Earth's atmosphere that acts as a shield against excess UV radiation. The attributed result is not only a greater prevalence in skin cancer, but also a higher risk of global warming as chlorofluorocarbons are also much more effective as greenhouse gases than carbon dioxide. In the late 1980s, the United Nations Environment Program put in place a number of agreements to phase out the use of CFCs by 1996. For their work in this area and for their forewarning of the implications, Sherwood Rowland, Mario Molina, and Paul Crutzen were awarded the 1995 Nobel Prize in Chemistry.

In this section, we will introduce haloalkanes with some examples and names. By the end of the section, you should be able to:

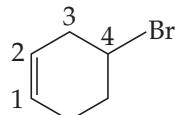
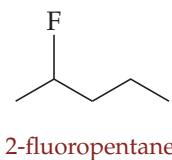
- Write the name of simple haloalkanes

Aliphatic or cyclic hydrocarbons containing a halogen directly bonded to an sp^3 hybridized carbon are called **haloalkanes**. They are generally written as:



Haloalkanes are also commonly referred to as alkyl halides.

Haloalkane nomenclature is derived from the longest chain bearing the halogen. The position number is taken to be the lowest possible, bearing all other substituents in mind. Halogen substituents are indicated by the prefixes fluoro-, chloro-, bromo- and iodo-. The derived name places these substituents in alphabetical order:



4-bromocyclohexene

We should also note here that the halogen functional group is second only to alkyl groups as the lowest functional group in the nomenclature hierarchy. All other substituents take precedence in deriving a compound's name, and the numbering used is determined by the location of the other group. For example, 2-chloroethanol is named as the alcohol and not the haloalkane. 4-Bromocyclohexene is named by taking into account the position of the double bond before the halogen.

Many haloalkanes have common names. Some examples are:



methylene chloride
(dichloromethane)

chloroform
(trichloromethane)

vinyl chloride
(chloroethene)

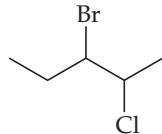
Compounds such as dichloromethane and chloroform are useful solvents in organic synthesis. Compounds of the form CHX_3 are often called **haloforms**, of which chloroform is an example. Perfluorinated compounds (in which all hydrogens are replaced by fluorine) are also very useful. One example we are all familiar with is Teflon™ (polytetrafluoroethylene, $(\text{CF}_2\text{CF}_2)_n$) with its application in non-stick cookware among others.

Having properties very different from both water and hydrocarbons, perfluorinated compounds have been used as solvents since they are easily partitioned from both water and most organic solvents. The polar structure also has application in medicine. For example, perfluorocarbons are able to dissolve oxygen at levels greater than blood. As a result, they are undergoing trials in dramatic experiments as blood substitutes in cases where trauma results in severe blood loss with no time to match blood types.

Haloalkanes have a wealth of chemistry associated with them. We have already seen how they can be formed from alkenes and alkanes. Later in this chapter we will explore two reaction types in detail—nucleophilic substitution (Section 27.5) and β -elimination (Section 27.6)—in which haloalkanes are reactants. Later, in Chapter 28, we will explore the use of haloalkanes for the preparation of Grignard reagents.

Self-Assessment Exercises

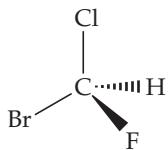
27.9 Write the systematic name of:



- (a) 3-bromo-4-chloropentane
- (b) 4-chloro-3-bromopentane
- (c) 2-chloro-3-bromopentane
- (d) 3-bromo-2-chloropentane

Exercises

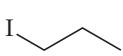
27.10 Give the full name, including stereochemical descriptor of:



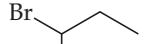
27.11 Name and classify the following haloalkanes as primary, secondary or tertiary.



(a)



(b)

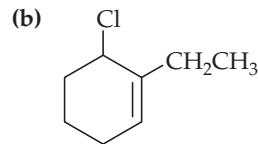
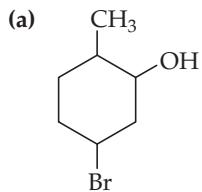


(c)



(d)

27.12 Give the IUPAC name for the following structures:



27.9 (d)

Answers to Self-Assessment Exercise



27.3 | Ethers: Structure, Properties, and Nomenclature



Diethyl ether, originally called just “ether”, was used in medicine for the treatment of some illnesses more than 200 years ago. However, it was not until 1846, when Boston dentist William T G Morton administered its vapors to a patient and extracted a tooth, apparently painlessly, that its potential for use in surgery was quickly realized, and the era of modern anesthetics began. The word anesthesia comes from the Greek for “without sensation”. Nowadays, there are many safer anesthetics and ether is no longer used.

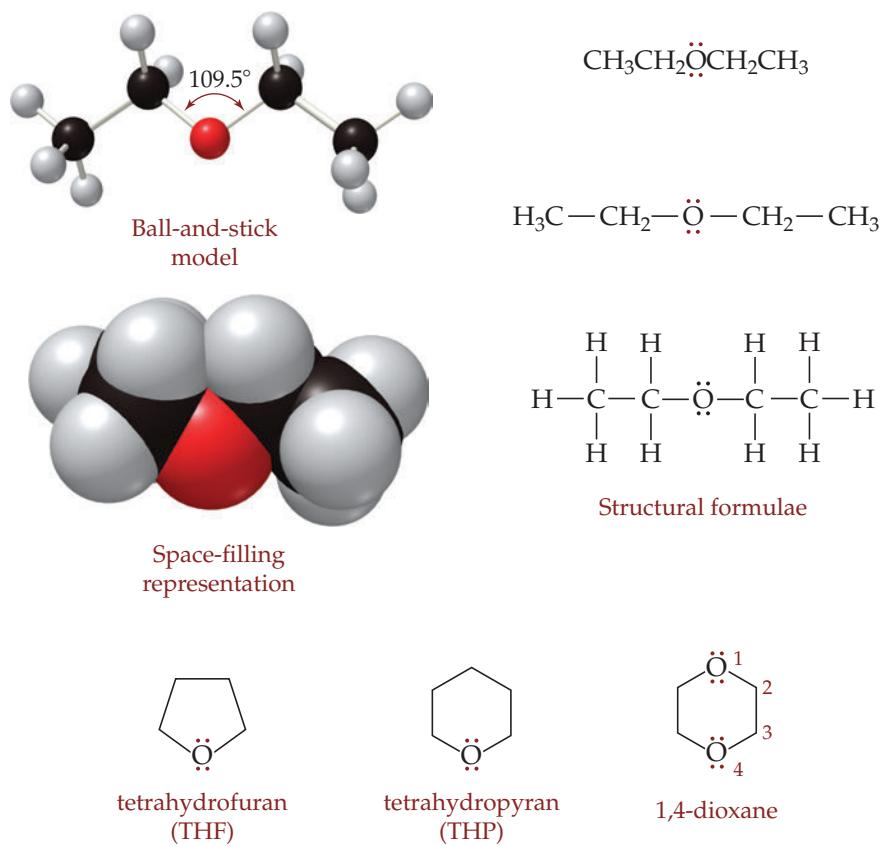
In this section, we introduce you to the ether functional group and its nomenclature. By the end of this section, you should be able to:

- Name alkyl ethers

We can think of alcohols as compounds in which one hydrogen atom and one hydrocarbon group are bonded to an oxygen atom. Compounds in which two hydrocarbon groups are bonded to one oxygen atom are called **ethers**. As for alcohols, the oxygen atom is sp^3 hybridized with the two C—O bonds subtending an angle of approximately 109.5° . Two of the sp^3 hybrid orbitals of the oxygen atom form σ -bonds with two carbon atoms adjacent to them. Each of the other two hybridized orbitals contains a pair of unshared electrons. **Figure 27.8** illustrates the Lewis structure and other molecular model representations of diethyl ether, the most commonly used of all the ethers.

Ethers are polar molecules, but because of the steric hindrance due to the alkyl groups attached, only weak dipole–dipole interactions exist between molecules. As a result of having alkyl groups bonded to the central oxygen atom, there is no opportunity for hydrogen bonding or other strong electrostatic interactions, so the physical properties of ethers are closer to those of alkanes than to those of alcohols. This moderate polarity is, however, advantageous as it allows ethers to dissolve a wider range of organic compounds than hexane would as a comparative solvent.

Ethers resemble hydrocarbons in their inertness to chemical reactions. As a consequence, ethers make excellent solvents in which to undertake chemical reactions. Two commonly used solvents are diethyl ether and tetrahydrofuran (THF). Diethyl ether, as we have already seen, is an acyclic ether (Figure 27.8), whereas THF (**Figure 27.9**) is a cyclic ether derived, as the name suggests, from furan, that has a structure given here.

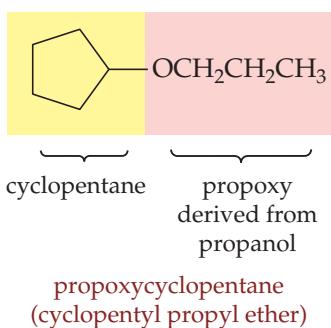
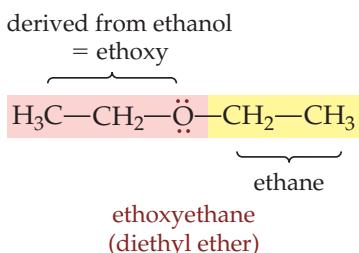


◀ Figure 27.8 The structure of diethyl ether. A number of representations for diethyl ether are shown.

◀ Figure 27.9 Cyclic ethers. Simple cyclic ethers such as tetrahydrofuran (THF) and 1,4-dioxane are excellent solvents. Tetrahydropyran (THP) are useful reagents in organic synthesis.

TABLE 27.2 Physical properties of the constitutional isomers butan-1-ol and diethyl ether

Compound	Structure	Melting point	Boiling point	Density g/cm ³
butan-1-ol	CH ₃ CH ₂ CH ₂ CH ₂ OH	-90 °C	118 °C	0.81
diethyl ether	CH ₃ CH ₂ OCH ₂ CH ₃	-116 °C	35 °C	0.70



▲ **Figure 27.10 Ether nomenclature.**

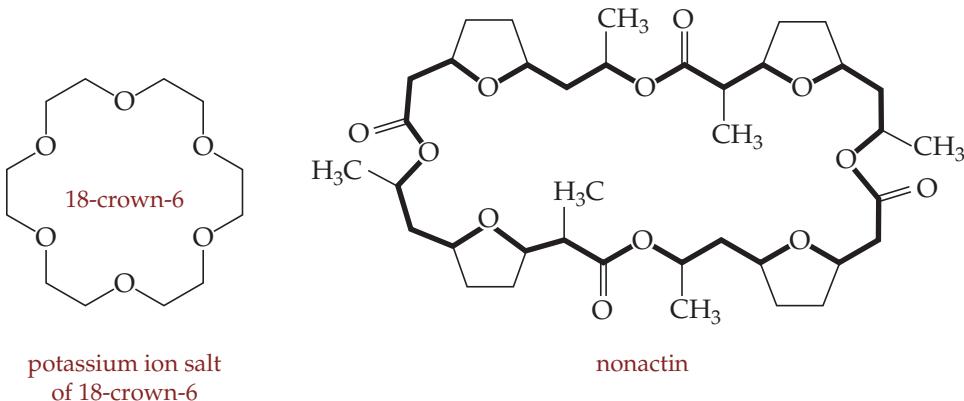
Systematic names are derived from the longest alkyl chain present that is attached to the ether oxygen and the residual alkoxy group. Examples of common names are shown in brackets.

Naming Ethers

Ayclic ethers are named systematically by selecting the longest chain and adding to it the name of the attached **alkoxy** (-OR) **group**. Common names are used more freely with this class of compounds, as the IUPAC method leads to lengthy names quite quickly. These common ether names are derived from the two alkyl groups that are attached to the ether oxygen. **Figure 27.10** illustrates how to derive the systematic and common names of acyclic ethers.

Cyclic ethers, such as tetrahydrofuran, are **heterocyclic compounds** whose names are derived in some instances from the parent heterocycle. Heterocyclic compounds are derivatives of cyclic hydrocarbons in which one of the ring carbons is replaced with another atom, usually O or N, but many other hetero atoms have also been incorporated (for example, S, Se, P). Figure 27.9 showed the structure of the most common cyclic ethers.

Cyclic polyethers such as 18-crown-6 (**Figure 27.11**) are useful in organic synthesis as phase transfer catalysts and metal ion complexation agents. Discovered and developed by Charles Pedersen in the 1960s, **crown ethers** are a synthetic analogue of naturally occurring antibiotics such as nonactin.

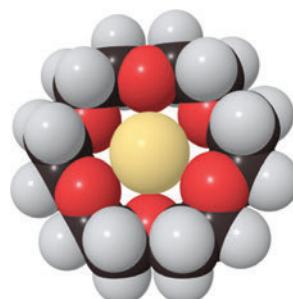


▲ **Figure 27.11 Macrocyclic ethers.** Naturally occurring cyclic ethers like nonactin can transport ions across biological membranes. In doing so, they act as potent antibiotics. Crown ethers such as 18-crown-6 are synthetic analogues of nonactin that are also useful for the separation of heavy metal salts from waterways, as catalysts of reactions involving carbanions and as phase transfer catalysts.

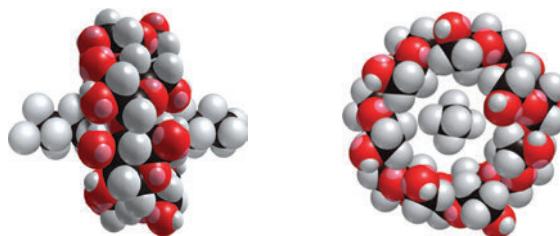
A CLOSER LOOK Crown Ethers

Supramolecular chemistry, also known as “chemistry beyond the molecule”, is a multidisciplinary science that came to prominence in the late 1980s. This was in part due to the award of the 1987 Nobel Prize in Chemistry to Charles Pedersen (1904–1989), Donald Cram (1919–2001) and Jean-Marie Lehn (b 1939), three of the founders and early developers of supramolecular chemistry. This field began with Pedersen’s pioneering work on crown ethers and their metal ion complexes (Figure 27.12). The potential of supramolecular chemistry to bridge the gap between chemistry and biology, thereby finding applications in medicine, materials and environmental science, biotechnology and nanotechnology, has seen interest in this field grow rapidly over the past 10–15 years.

Supramolecular chemistry is seen by some as either a molecular art form or as *molecular engineering*. During its development throughout the 1980s and 1990s, supramolecular chemistry was used as a tool to create the most unlikely molecular topologies. For example, rotaxanes (*rota*, wheel; *axa*, axle) are a chemical curiosity containing two molecular components (Figure 27.13). The molecular shapes of the two components differ, one resembling a wheel and the other an axle. The axle component is threaded through the center of the wheel component, and is usually terminated by bulky groups to stop the wheel falling off. The use of the bulky stoppers means that the wheel and axle components are mechanically interlocked—they cannot be removed from each other without breaking a covalent bond. Rotaxanes are being investigated as molecular electronic switching and optical binary devices due to their ability to undergo conformational isomerism.



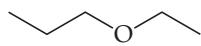
▲ Figure 27.12 18-crown-6 complex of K^+ .



▲ Figure 27.13 Rotaxanes are mechanically interlocked molecules. In this illustration, the axle component, a simple alkane, is threaded through the wheel or ring component, a cyclodextrin.

Self-Assessment Exercise

- 27.13** What is the systematic name of the following structure?

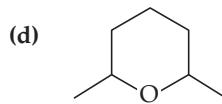
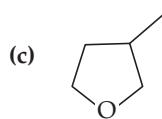
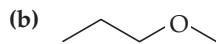
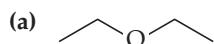


- (a) Ethyl propyl ether
- (b) Propyl ethyl ether
- (c) Propoxy ethane
- (d) Ethoxy propane

Exercises

- 27.14** Explain why the boiling point of ethanol (78°C) is much higher than that of its isomer, dimethyl ether (-25°C), and why the boiling point of CH_2F_2 (-52°C) is far above that of CF_4 (-128°C).

- 27.15** Give names for the following ethers (ignore stereochemistry):



- 27.16** Write the structures for all the isomeric ethers with molecular formula $\text{C}_5\text{H}_{12}\text{O}$ and give a name for each.
27.17 List two criteria that would make a liquid a good solvent in which to undertake chemical reactions.
27.18 What properties of 18-crown-6 make it possible to complex metal ions such as Na^+ or K^+ ?

27.13 (d)

Answers to Self-Assessment Exercise



27.4 | Reactions of Alcohols

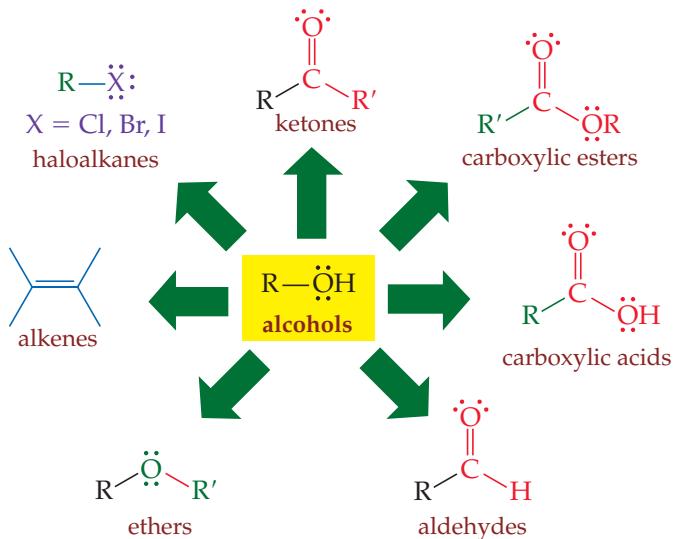


In this section, we start to examine some of the reactions that alcohols can undergo and begin to see how functional groups may be interconverted. Some reactions show a visible change. For instance, when sodium metal reacts with ethanol to form a solution of sodium ethoxide, the metal dissolves and bubbles of hydrogen are evolved. Other reactions take place entirely within the solution phase, but a knowledge of the chemistry involved allows us to predict the outcome of the reaction.

When you finish this section, you should be able to

- Know the conditions to convert an alcohol to an alkoxide
- Recognize two different reagents commonly used to transform alcohols to haloalkanes
- Understand the mechanism of a dehydration reaction

Alcohols are central to organic chemistry. **Figure 27.14** illustrates the relationships between alcohols and the other seven major classes of functional groups introduced in this text.



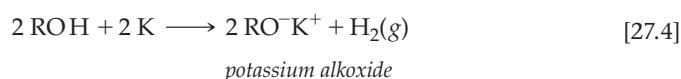
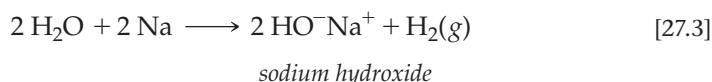
▲ Figure 27.14 Functional group interconversion.

Four of these functional groups, highlighted in red, can be arrived at through oxidation of a suitable alcohol.

In this section we explore further the interconversion of alcohols to alkenes and haloalkanes. Ethers are formed by taking advantage of the high reactivity of the conjugate base of an alcohol, called an **alkoxide**. Alkoxides are as strong a base as hydroxide and also make excellent nucleophiles.

Alkoxides

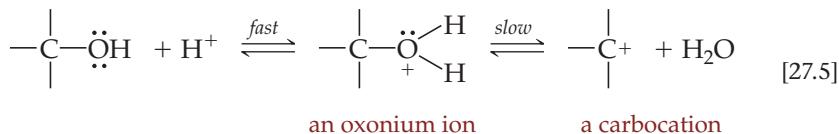
Alcohols react with alkali metals to form alkoxides in the same way that water reacts with alkali metals to form hydroxide. The reaction is irreversible, since the other product of the reaction, hydrogen gas, is evolved.



The name of the alkoxide is derived from the alcohol undergoing reaction. For example, the reaction of ethanol with sodium gives sodium ethoxide, the reaction of *tert*-butanol (2-methyl-2-propanol) with potassium metal yields potassium *tert*-butoxide. Reactions involving alkoxides invariably use the corresponding alcohol as the solvent for ease of preparation.

Basicity of Alcohols

The ability of an alcohol's OH group to accept a proton is an important property that is important in the context of dehydration (loss of $-\text{H}_2\text{O}$). An alcohol can act as a weak base, forming an oxonium ion under acidic conditions. The oxonium ion ($\text{p}K_a \sim -2$) is a slightly better acid than the hydronium ion (H_3O^+ , $\text{p}K_a \sim -1.7$), but of greater importance to organic synthesis is the ability of the oxonium ion to lose water, forming a carbocation intermediate:



As we discussed in the context of Markovnikov's rule, the stability of the carbocation intermediate is an enormous driving force for the reactivity of a species, and even dictates the reaction pathway.

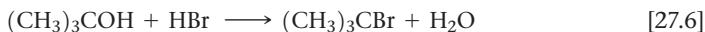
Alcohols to Haloalkanes

Alcohols can be converted into haloalkanes by treatment of a halogenating agent, usually under acidic conditions. In this reaction, the OH group of the alcohol is substituted by a halogen. The reaction is classed as a **nucleophilic substitution (S_N) reaction** and we will see much more of this in the next section.

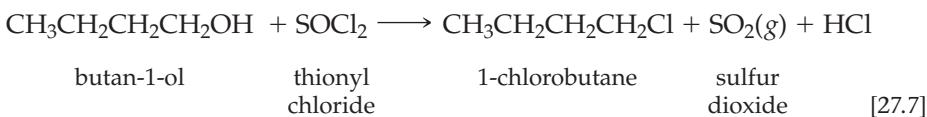
A nucleophilic substitution reaction is any reaction in which one nucleophile is substituted for another.

In using mineral acids (e.g. HCl, HBr, HI) as the halogenating agent, the first stage of substitution is protonation of the alcohol to form an oxonium ion. This is followed by elimination of water to form the intermediate carbocation as indicated in Equation 27.5. This last step is rate-determining, being faster for formation of a 3° carbocation than 2° and 1° .

The stability of the intermediate carbocation is the major factor allowing the substitution reaction to dominate for 3° alcohols. For example, the conversion of 2-methyl-2-propanol to 2-bromo-2-methylpropane using HBr is a reaction that occurs readily at room temperature using HBr.



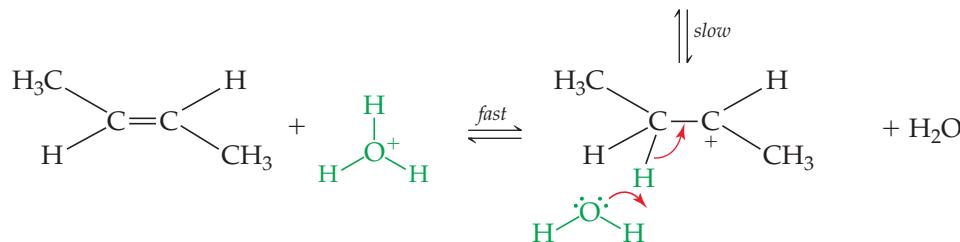
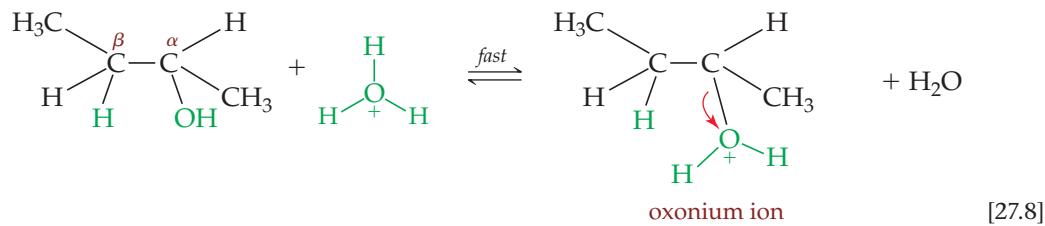
Secondary alcohols also undergo substitution using mineral acids, but they require heating and longer reaction times. Primary alcohols require extreme conditions to substitute using this method, and are impractical. The most efficient way of achieving this conversion is to react the primary alcohol with thionyl chloride:



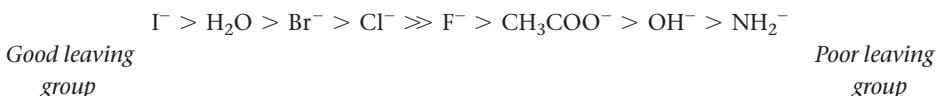
The reason this reaction works well is that one of the products (SO_2) is gaseous, so once it is liberated the reaction goes to completion.

Dehydration of Alcohols

We have already indicated that alcohols can be dehydrated to form alkenes (see Equation 26.15). Equation 27.8 illustrates the accepted mechanism. This acid-catalyzed dehydration process has, as one of its intermediates, an oxonium ion. The rate-determining step is the elimination of water to form the corresponding carbocation. Removal of a small group from a larger molecule, as in this case, is called an *elimination reaction*. Water is classed as a *good leaving group* because of its stability and relatively unreactive nature. Hydroxide ion, however, does not eliminate easily and so is classed as a *poor leaving group*.



Leaving groups can be classified as good or poor based on their reactivity. In general, the better leaving groups are those that are conjugate bases of strong acids. A relative order of leaving group is:



Once water has been eliminated from the oxonium ion in Equation 27.8, the reaction proceeds rapidly to the formation of the alkene by the loss of a proton from a carbon atom located in a neighboring position (called the β -position) to the original C—OH bond. The two electrons that once formed the C_β —H bond will now form the π -bond of the alkene. Without the β -hydrogen atom, the dehydration reaction does not proceed.

The nature of the equilibrium is such that removal of water or distillation of the alkene (which generally will have a lower boiling point than the corresponding alcohol) will maximize the formation of the alkene by driving the equilibrium in the forward direction.

Self-Assessment Exercises

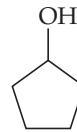
27.19 Can you use an aqueous solution of ethanol to form sodium ethoxide?

- (a) Yes
(b) No

27.20 Which is the reagent of choice to convert butan-1-ol to 1-chlorobutane?

- (a) Cl_2
(b) HCl
(c) SOCl_2

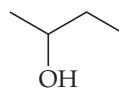
27.21 Which of the following molecules would *not* undergo a dehydration reaction?



(a)



(b)



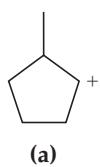
(c)



(d)

Exercises

27.22 Which of the following carbocations is most stable? Which is least stable?



(a)



(b)

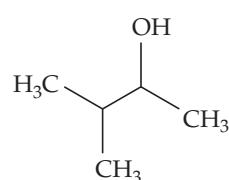


(c)

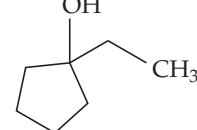
Describe a way of controlling the equilibrium so as to improve the yield of the alcohol.

27.26 What alkenes are formed as the major products from the dehydration of the following alcohols?

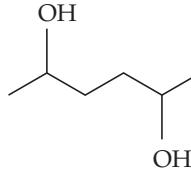
(a)



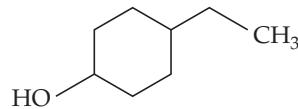
(b)



(c)



(d)



How many sets of stereoisomers are formed in each product case?

27.23 (a) Write a chemical equation for the substitution reaction of butan-2-ol with HBr. (b) Write a stepwise mechanism for this reaction. (c) Would butan-1-ol undergo the substitution reaction more quickly or more slowly than butan-2-ol?

27.24 (a) Which of the following is the *best* leaving group: (i) fluoride, (ii) iodide, (iii) hydroxide, (iv) chloride or (v) bromide? (b) Why, in a polar protic solvent, is iodide a better nucleophile than fluoride?

27.25 The addition of water to an alkene in the presence of H_2SO_4 leads to the formation of an alcohol, as shown in Equation 26.15. This reaction is in equilibrium with the dehydration of the newly formed alcohol to re-form the alkene.

27.19 (b) 27.20 (c) 27.21 (b)

Answers to Self-Assessment Exercises



27.5 | Nucleophilic Substitution Reactions of Haloalkanes

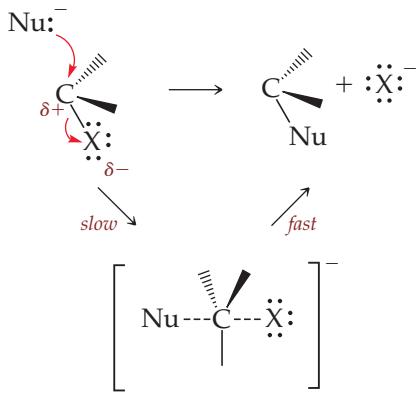


Between 20% and 30% of pharmaceuticals currently on the market have fluorine in their structure. These substances are active in a wide range of physiological situations, including cholesterol regulation (eg Lipitor®), antidepressant medication (eg Prozac®), for treatment of some cancers (fluorouracil), and are also present in many broad-spectrum antibiotics and in inhaled anesthetics (isoflurane). The strong carbon-fluorine bond resists metabolism and delays excretion from the body allowing for longer time periods between doses. The presence of fluorine also makes the substance more lipophilic, a useful property for anesthetics. In contrast, the bond between carbon and chlorine, bromine or iodine, is more reactive than a typical carbon–carbon single bond, which makes these haloalkanes excellent intermediates in chemical synthesis.

By the end of this section, you will be able to:

- Appreciate the scope of reactions undergone by haloalkanes.

The conversion of alcohols to haloalkanes by substitution opens up a large library of functional group manipulation, limited only by imagination. The reactivity of haloalkanes manifests itself from the difference in electronegativity between carbon (2.5) and the halogens (2.6–4.0), which means the carbon bearing the halogen is susceptible to nucleophilic attack.

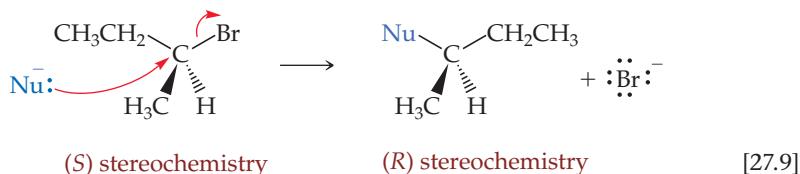


Nucleophilic substitution reactions of haloalkanes proceed by attack of the nucleophile (Nu^-) at the carbon bearing the halogen. The trigonal-bipyramidal transition state formed in this reaction has long $\text{Nu}-\text{C}$ and $\text{C}-\text{X}$ bonds, signifying the strengthening bond formation of the incoming nucleophile and the weakening $\text{C}-\text{X}$ bond of the outgoing halide. One of the driving forces for this reaction is the stability of the halide ion, which is an excellent leaving group.

As you can see in (Figure 27.15), the transition state that leads to the product involves both the haloalkane and the nucleophile in the rate-determining step. As such, this reaction is classed as $\text{S}_{\text{N}}2$ for bimolecular (2), nucleophilic (N) substitution (S) reaction.

▲ Figure 27.15 Nucleophilic substitution reactions.

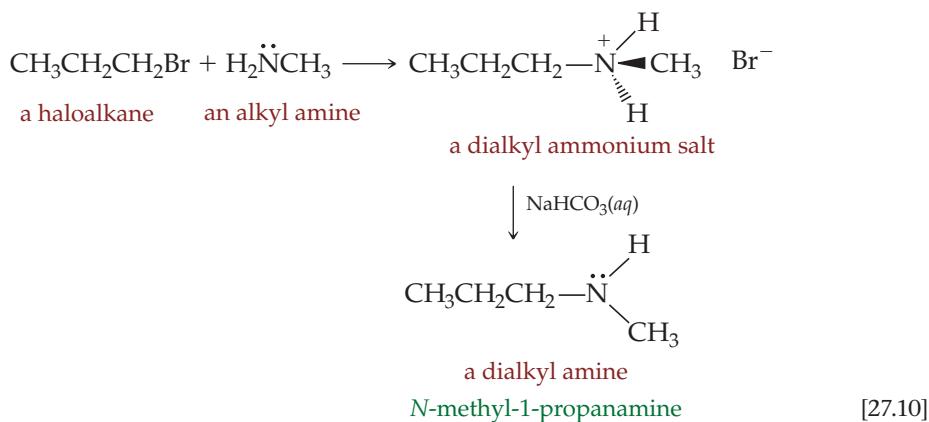
If the starting haloalkane is chiral about the carbon bearing the halogen, then the S_N2 reaction shown in Equation 27.9 usually proceeds with inversion of stereochemistry:



Inversion of stereochemistry can be thought of as the inversion of an umbrella that happens on a windy day (**Figure 27.16**). In this analogy, consider the umbrella canopy as three groups around a tetrahedral center that do not participate in an S_N2 reaction. Upon nucleophilic attack, the canopy is inverted, with some strain, to yield a new conformation.

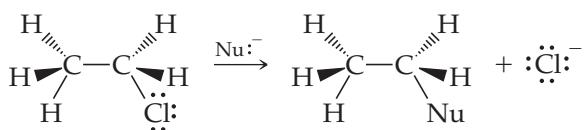
However, the inversion of stereochemistry depends on the nature of the nucleophile and leaving group, the substituents about the stereocenter and the reaction conditions (for example, the solvent used).

Table 27.3 lists common nucleophiles employed in nucleophilic substitution reactions, as well as the classes of organic compound formed by the substitution. We have already investigated some of these in detail. Two nucleophile classes we have yet to discuss in any detail involve amines (which are neutral molecules) and the cyanide ion (CN⁻). The addition of ammonia to a haloalkane, for example, leads initially to an **alkyl ammonium salt**. Such salts are characterized by four groups around nitrogen of which at least one is an alkyl group. Provided the ammonium ion is of the form R₃NH⁺, R₂NH₂⁺ or RNH₃⁺, they are easily transformed into **amines** by the addition of base.



◀ **Figure 27.16** The mechanism of an S_N2 reaction is analogous to an umbrella on a windy day.

TABLE 27.3 Common nucleophilic substitution reactions based on the reaction:

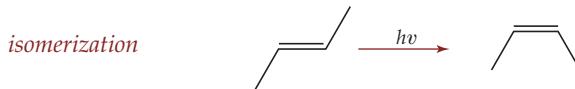


Nucleophile	Product	Class of compound
$:\ddot{\text{O}}\text{H}$	$\text{CH}_3\text{CH}_2\text{OH}$	an alcohol
$:\ddot{\text{O}}\text{R}$	$\text{CH}_3\text{CH}_2\text{OR}$	an ether
$:\ddot{\text{I}}\text{:}$	$\text{CH}_3\text{CH}_2\text{I}$	an alkyl iodide
$:\text{CN}$	$\text{CH}_3\text{CH}_2\text{CN}$	a nitrile
$:\text{NH}_3$	$\text{CH}_3\text{CH}_2\text{NH}_3^+\text{X}^-$	an alkyl ammonium salt
$\ddot{\text{O}}\text{H}_2$	$\text{CH}_3\text{CH}_2\text{OH}$	an alcohol

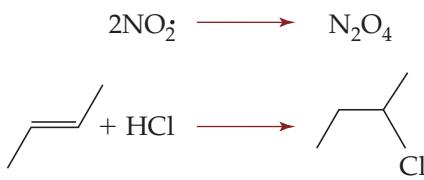
A CLOSER LOOK Molecularity

The molecularity of a reaction describes the number of atoms or molecules of reactant taking part in an elementary reaction. Remember that an overall reaction mechanism is composed of several elementary reactions. Most elementary reactions involve one (*unimolecular*) or two (*bimolecular*) species. Though most reactions are monitored by the loss of reactants or the formation of products, ultimately it is the molecularity of the rate-determining step that defines the observed kinetics of the overall reaction and hence whether a reaction is unimolecular or bimolecular. Molecularity should not be confused with reaction order.

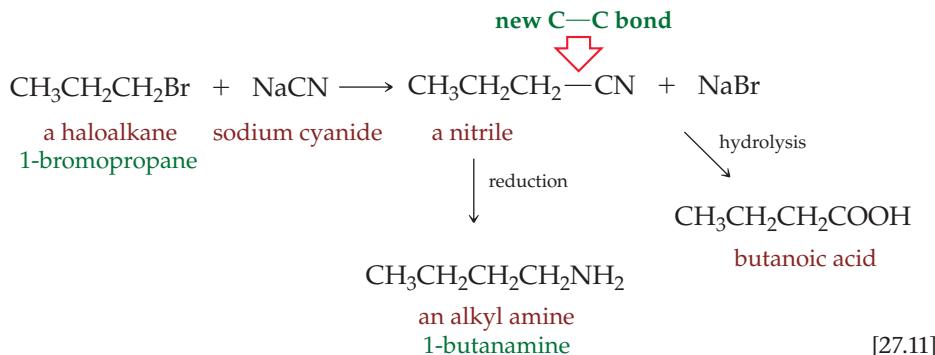
Simple unimolecular reactions include decomposition of chlorine by homolytic bond cleavage or isomerization reactions. In both cases, the rate of reaction depends directly on the concentration of the only reactant. In this case, it is easy to see why this is a unimolecular reaction.



In a bimolecular reaction, two species are required to give rise to the product, for example the dimerization of NO_2 or the addition of HCl to an alkene. In each case, the rate of reaction depends directly on the concentration of the two reactants, which need to collide before reaction can proceed.



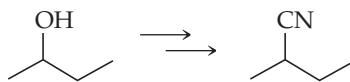
The reaction of cyanide ion (CN^-) with a haloalkane (producing a **nitrile**) is extremely useful in organic synthesis despite the obvious toxicity problems, due to its ability to form a new C—C bond upon substitution. Reduction of the nitrile yields an alkyl amine which differs from the starting haloalkane by the addition of an extra CH_2 group, as well as the change in functional group.



Sample Exercise 27.4

Nucleophilic Substitution Reactions

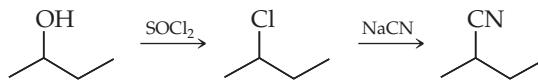
Using 2-butanol as a starting material, design a synthesis of 2-methylbutyronitrile in two steps:



or



Thus the overall two-step reaction sequence is:

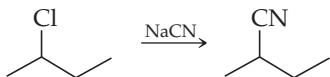


SOLUTION

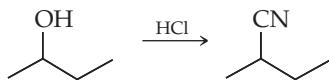
Analyze We are asked to design a substitution reaction for replacing a secondary OH group by CN.

Plan For a synthesis problem like this, it is usually helpful to consider the sequence of steps starting from the product you want. You know from Table 27.3 that nitriles can be synthesized from the haloalkane by substitution.

Solve In the following example the chloride is chosen, although the bromide is just as efficient:

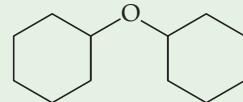


Formation of the alkyl chloride from the alcohol can occur in two ways. Since 2-butanol is a secondary alcohol, reaction with either HCl or thionyl chloride, SOCl_2 , will yield 2-chlorobutane.



► Practice Exercise

Describe how you would prepare this ether from cyclohexanol.



Self-Assessment Exercise

- 27.27 What is the product of the reaction between (S)-2-bromobutane and the hydroxide nucleophile, OH^- ?

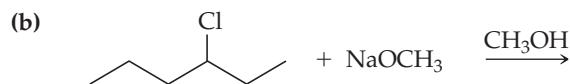
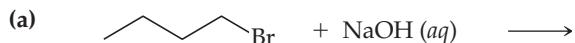
(a) butan-1-ol

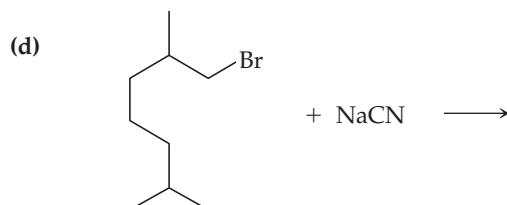
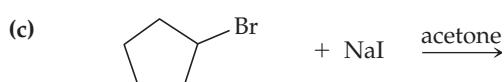
(b) (S)-butan-2-ol

(c) (R)-butan-2-ol

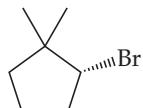
Exercises

- 27.28 Write the structure of the major organic product expected from the following reactions:





27.29 Name the product formed when methoxide reacts with:



27.30 Draw the mechanism of the reaction of chloroethane with cyanide. Use curly arrows where appropriate and show the structure of the trigonal bipyramidal transition state.

27.31 Hydroxide, OH^- , can act as both a base and a nucleophile. Explain the difference between these two terms and give a reaction to illustrate each case.

27.32 Design a synthesis of methoxymethane (CH_3OCH_3) starting from methanol as the only carbon containing compound.

27.27 (c)

Answers to Self-Assessment Exercise



27.6 | Haloalkanes to Alkenes: β -Elimination



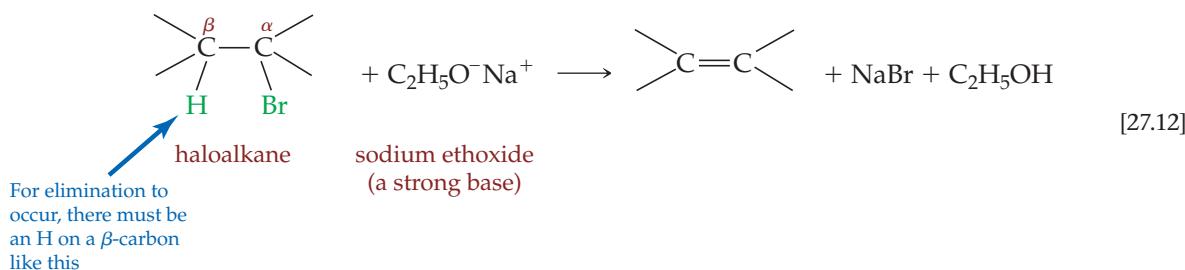
In the laboratory, there is often more than one way to approach the synthesis of a target molecule. The way chosen will depend on a range of factors including availability of starting materials, cost, what byproducts are formed, and the compatibility of the transformation with other functional groups that may be present. We have already seen that alkenes may be formed by the acid catalyzed dehydration of alcohols, they may also be formed from haloalkanes in an elimination reaction.

By the end of this section, you should be able to:

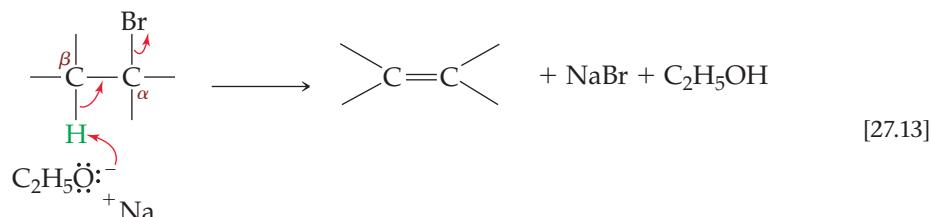
- Recognize which haloalkanes undergo elimination and predict the product formed.

The process of eliminating a good leaving group, as outlined for the dehydration of an alcohol, is quite general. For example, haloalkanes undergo elimination under basic conditions. This process, called a **β -elimination reaction**, involves the *dehydrohalogenation*

of the haloalkane—that is, the loss of a hydrogen atom and a halogen atom from the same molecule. For the reaction to proceed, a hydrogen atom on the carbon atom adjacent to the carbon bearing the halide (that is, the β -carbon) must be present and be removed.

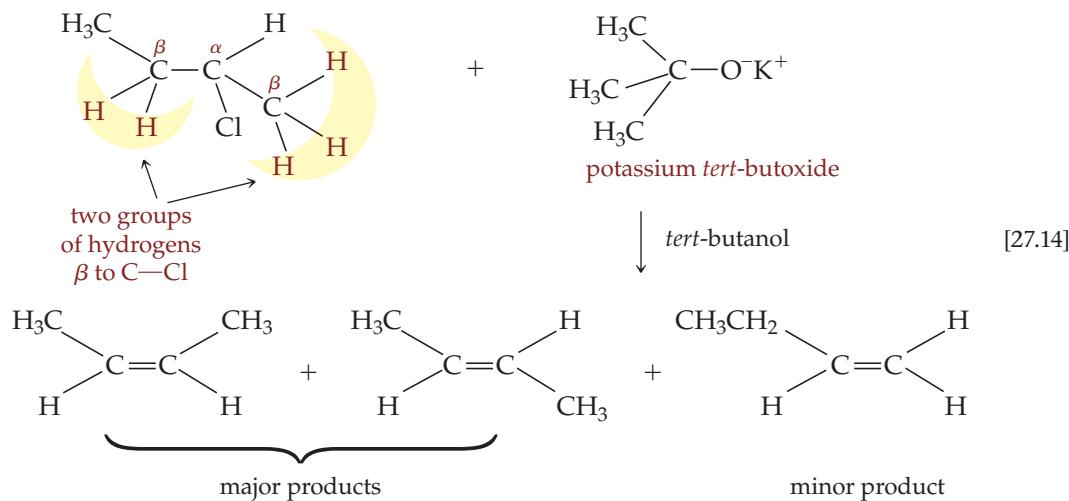


The reaction is not as fast as the corresponding dehydration of an alcohol, requiring the use of a strong base (for example, sodium ethoxide) to proceed. The mechanism can be shown to occur in a single (and essentially irreversible) step:



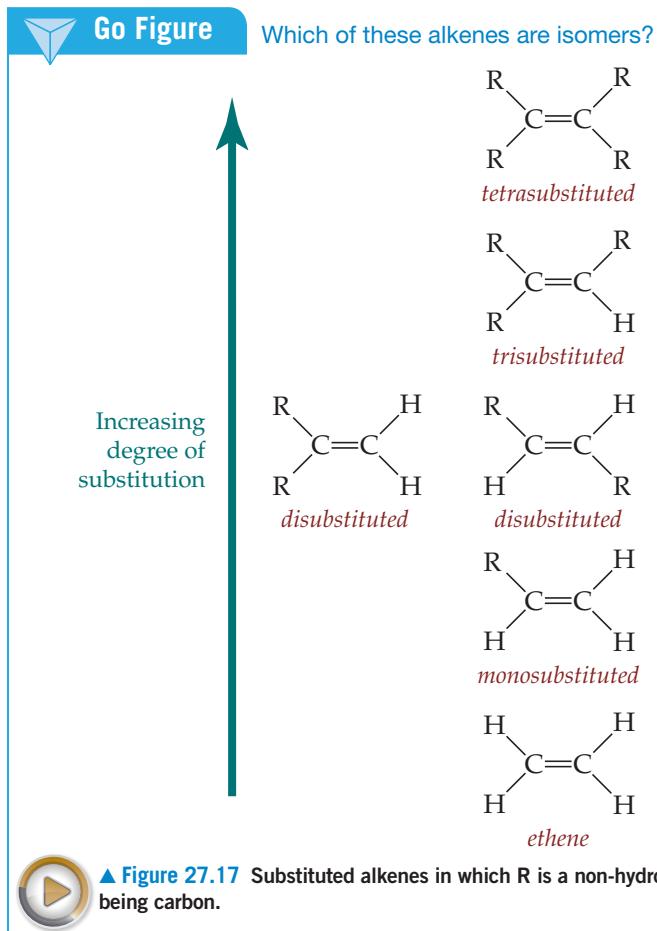
Typically, the hydrogen atoms of hydrocarbons do not react in this way. However, the inductive effect of the halogen atom on the α -carbon draws electron density out of the C—H bond, causing the β -hydrogen to become more acidic by weakening the C—H bond. Because this reaction involves the haloalkane and strong base in the rate-determining step, this **elimination reaction** is known as an **E2** or bimolecular (2) elimination (E) reaction.

Let us now consider the reaction of 2-chlorobutane with potassium *tert*-butoxide, another strong organic base:



In this case, there are two sets of β -hydrogens as highlighted in Equation 27.14. Although β -elimination can lead to the formation of two alkenes, one elimination product is formed in preference to the other.

The major alkene formed by dehydrohalogenation is the one containing the more substituted double bond. This preference is known as **Zaitsev's rule**. The more substituted double bond is the one with the greater number of substituents (excluding hydrogen) attached to the two carbons of the double bond. For example, the but-2-ene formed in Equation 27.14 has two methyl groups connected to the carbons of the double bond, whereas but-1-ene has a single ethyl group connected. Because but-2-ene has two non-hydrogen substituents, it is the more substituted of the two alkenes formed. Figure 27.17 illustrates what is meant by a substituted alkene.



Sample Exercise 27.5

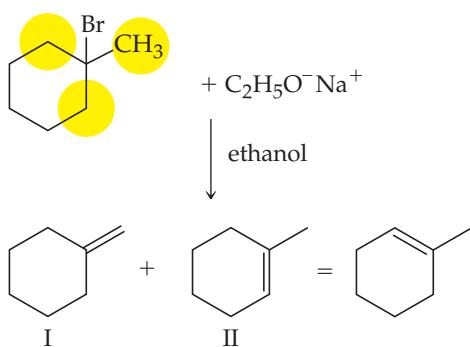
β -Elimination in Haloalkanes

Draw the structural formula for the major product formed when 1-bromo-1-methylcyclohexane is reacted with sodium ethoxide in ethanol. Systematically name the major product.

SOLUTION

Analyze We are asked to determine the product of the reaction of a sterically hindered haloalkane with a strong base.

Plan Begin by structurally identifying the compounds involved. Look for β -hydrogens then determine the types of alkenes possible.

Solve

There are two different sets of β -hydrogens highlighted in yellow, those on the methyl group and two equivalent sets on the cyclohexane ring. Hence two different alkenes, I and II, are formed. The major product will be the one that satisfies the criterion of Zaitsev's rule. The more substituted double bond is found in II, and so it is formed in preference.

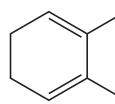
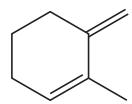
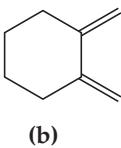
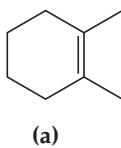
Alkene II is named *1-methylcyclohexene*.

► Practice Exercise

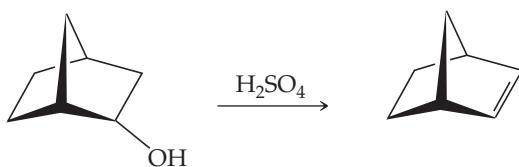
2-Methylpent-2-ene can be formed by the reaction of potassium *tert*-butoxide and which bromoalkane?

Self-Assessment Exercise

- 27.33 What product is formed from the β -elimination reaction of 1,2-dibromo-1,2-dimethylcyclohexane?

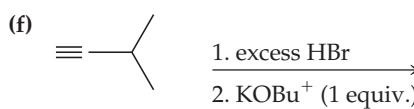
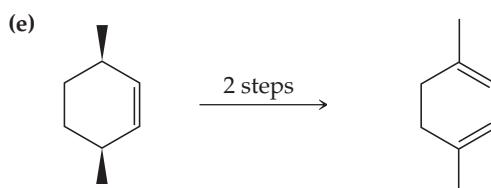
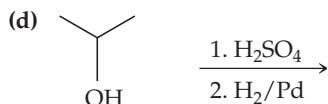
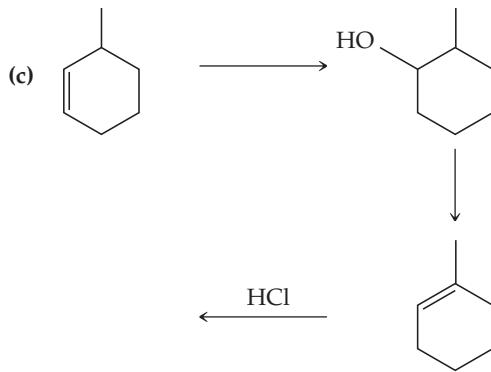
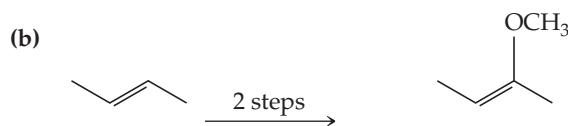
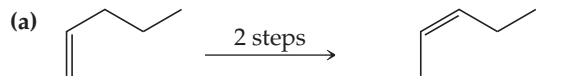
**Exercises**

- 27.34 2-Methylpent-2-ene can be formed by the reaction of potassium *tert*-butoxide and which bromoalkane?
- 27.35 Dec-2-ene can be formed by the reaction of potassium *tert*-butoxide and which two chloroalkanes? Which chloroalkane would you use to maximize your yield?
- 27.36 The dehydration of norborneol yields none of the Zaitsev product. Why is this so? [Hint: Think about the geometry of the products.]



- 27.37 What is the structure of the major alkene product formed when 2-methylpropane is reacted consecutively with Br_2 , in the presence of light, and then potassium *tert*-butoxide? [Hint: You will need to recall the regioselectivity of free-radical bromination, covered in Chapter 24.]

- 27.38 Insert the missing reagents or products in the multi-step reactions shown here.



27.33 (d)



27.7 | Substitution versus Elimination

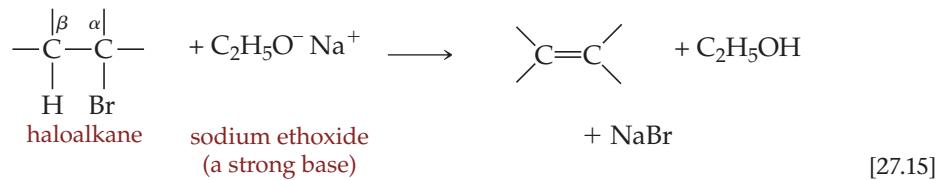


There are many situations in chemistry where two or more reaction pathways compete to give different products. One of the skills we introduce in this section is to recognize the molecular structures, choice of reagents, solvents, and conditions that favor one pathway over a different one. In this way, we optimize the formation of the compound we want and minimize waste. By the end of this section, you should be able to:

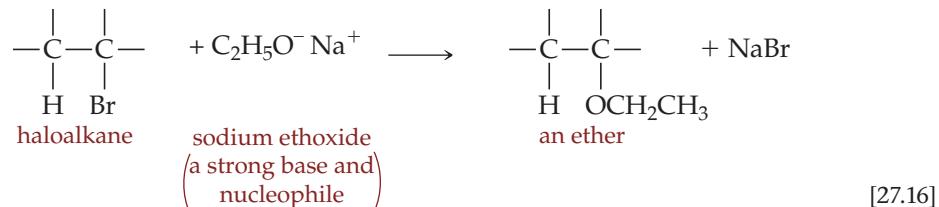
- Identify the features that distinguish substitution and elimination pathways.

We consider four types of reactions in this section, E1, E2, S_N1 and S_N2. We have already encountered two of these formally (E2 and S_N2). As we will see, each reaction type does not operate in isolation, but together they form a competing process. Which direction a reaction proceeds in depends on several factors, including starting material and reagents, type of solvent, and electronic and steric effects.

We have already seen in this chapter that alkoxides are a strong base, able to deprotonate haloalkanes in a β -elimination reaction.



However, as we saw in Section 27.5, alkoxides are able to react with haloalkanes in another way. Instead of providing a means of elimination, alkoxides can also interact with haloalkanes to form ethers. The classic example is the *Williamson ether synthesis*, in which the halide is replaced by the alkoxide in a substitution reaction.



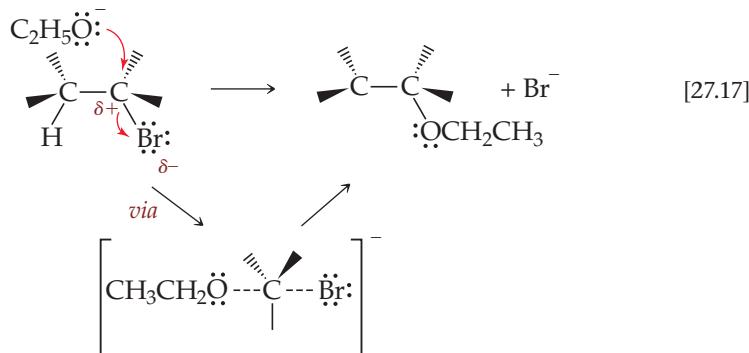
A CLOSER LOOK Nucleophile or Lewis Base?

Whether a reaction follows an elimination or substitution pathway is dependent on whether the added reagent acts as a Lewis base or nucleophile, respectively. Recall that a Lewis base is an electron-pair donor, the same as a nucleophile. In broader definitions, a Lewis base can donate its electron pair to something other than H⁺. By this definition, both a nucleophile and Lewis base can form new covalent bonds. So what's the difference?

The answer is nothing. We usually invoke the term Lewis base when there is a proton abstraction process, as in an elimination reaction, and the term nucleophile in all other cases. So, a Lewis base can be a good nucleophile if there are no sterically bulky groups around the electron donor.

Related Exercise: 27.68

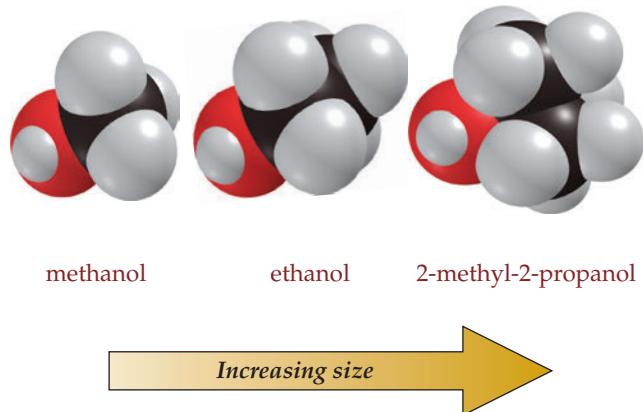
The mechanism for this substitution reaction involves attack of the nucleophilic alkoxide on the weakly electrophilic carbon atom bearing the halide. Note that strong bases are typically good nucleophiles. The carbon atom bearing the halogen is made more electrophilic by the inductive effects of the halogen. This reaction type is called a *nucleophilic substitution (S_N) reaction*. The reaction goes through a trigonal-planar carbon state with elongated bonds for the incoming alkoxide and the outgoing halide. Eventual loss of Br⁻ yields the ether. The reaction shown in Equation 27.17 can be further defined as an S_N2 reaction, since the rate-determining step requires the addition of the alkoxide in concert with the loss of halide.



The β -elimination reaction (Equation 27.12) is in fact in competition with the substitution reaction. Generally, S_N2 reactions are in competition with E2 reactions. Which mechanism predominates in the reaction is dictated by a variety of factors:

1. The size of the alkoxide: the bulkier the alkoxide, the more elimination is favored. **Figure 27.18** illustrates this change in size. Alkoxides such as that generated from 2-methyl-2-propanol (*tert*-butanol) favor E2 because of their large size, while those generated from methanol favor S_N2.
2. The accessibility of the carbon bearing the halogen: the more accessible it is, the more substitution is favored.
3. The accessibility of the hydrogen atom in the β -position: the more accessible it is, the more elimination is favored.

Any alkyl groups positioned off the α -carbon of the haloalkane tend to favor β -elimination. This is particularly true of the larger halogens, Br and I.



▲ **Figure 27.18** Size increases with substitution.

E1 and S_N1 Reactions

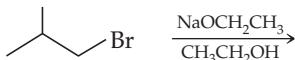
In Section 27.4 we discovered that generating a carbocation intermediate leads rapidly to formation of the alkene. The stability of the carbocation formed in the dehydration is also the driving force for that reaction. That is, the conditions needed to dehydrate a tertiary alcohol are much milder than those needed to dehydrate a primary alcohol, due to the relative stabilities of the intermediate tertiary and primary carbocations, respectively. In this case, the rate-determining step is the loss of water to form the carbocation intermediate as shown in Equation 27.5. As such, this elimination reaction is *unimolecular*



Sample Exercise 27.6

Predicting Substitution or Elimination

What is the major organic product from the following reaction? Indicate whether this is an S_N2 or E2 reaction.

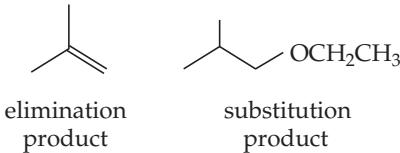


SOLUTION

Analyze We are given the reaction of a haloalkane with a strong base also capable of acting as a good nucleophile. We are asked to determine the product and the mechanism.

Plan We need to consider both elimination and substitution products in our deliberation, as well as the nature of the base and whether a β -hydrogen is present and accessible.

Solve The elimination and substitution products are:



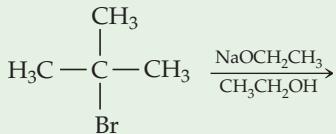
The α -carbon in the starting bromoalkane is essentially unhindered despite the bulk of the two methyl groups nearby and

the bromine atom. This implies that substitution would occur readily. In contrast, the β -hydrogen is more restricted by the same steric groups. This factor suggests that substitution predominates. The substitution follows an S_N2 mechanism.

This practice exercise shows how the yield of alkene may be optimized.

► Practice Exercise

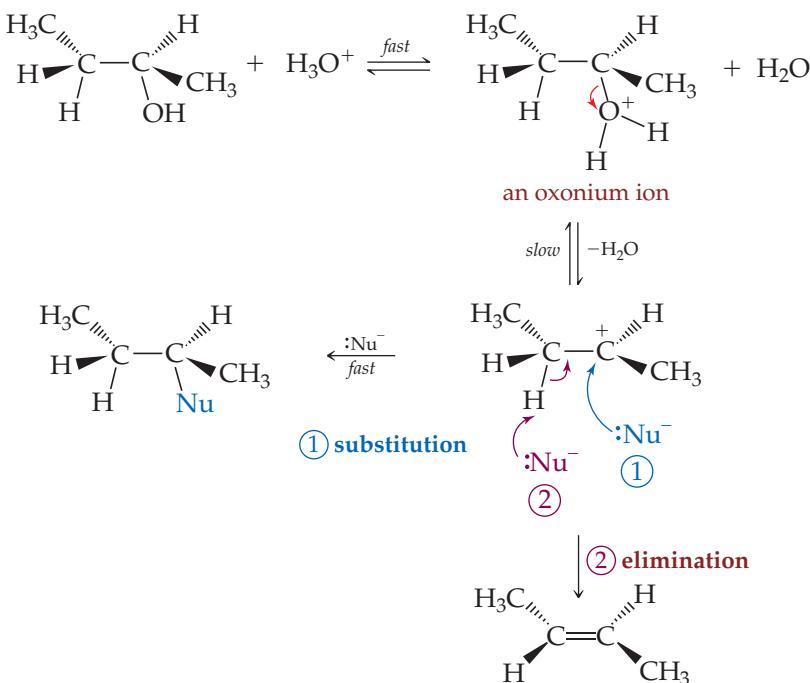
What is the major organic product from the following reaction?



and is designated as an E1 mechanism. A summary of this mechanism and its competing substitution reaction is shown in Figure 27.19.

The β -elimination reaction, shown as route 2 in Figure 27.19, is also in competition with a nucleophilic substitution reaction, shown as route 1 in Figure 27.19. If a nucleophile is present within the reaction mixture, then substitution is also likely. The equilibrium arrows shown in Figure 27.19 between the oxonium ion and the carbocation in fact display this very principle. In this case, water acts as the leaving group in one reaction direction

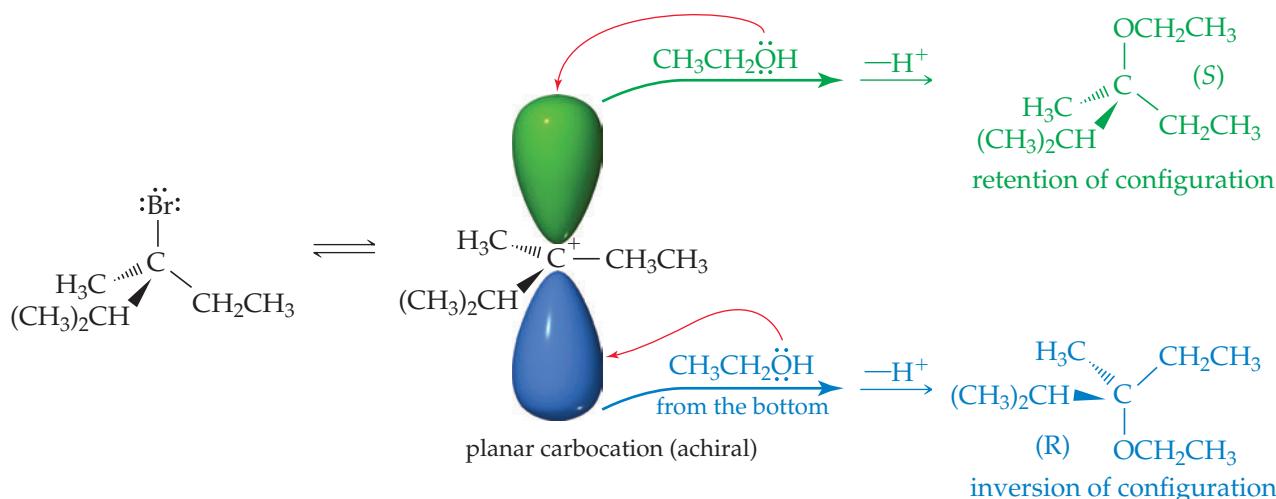
► **Figure 27.19** Substitution and elimination reactions. The rate-determining step is the generation of the carbocation intermediate common to both reactions.



(from top to bottom) and as the nucleophile in the other direction (from bottom to top). The result of the latter reaction leads only to formation of more of the starting alcohol. However, what if another nucleophile, such as Cl^- , is also present? The result is the formation of a haloalkane. Since the rate-determining step is still the same (and unimolecular), this type of substitution is known as an $\text{S}_{\text{N}}1$ reaction.

As opposed to the typical inversion of stereochemistry seen in $\text{S}_{\text{N}}2$ reactions, $\text{S}_{\text{N}}1$ reactions result in, a racemic mix—or at the very least a less optically pure compound than the starting material. This is because in the $\text{S}_{\text{N}}1$ mechanism the carbocation intermediate is sp^2 hybridized and planar (Figure 27.20). A nucleophile can attack the carbocation from either face leading to retention or inversion of stereochemistry.

Table 27.4 summarizes the important parameters for substitution and elimination reactions discussed in this chapter.



▲ Figure 27.20 $\text{S}_{\text{N}}1$ Racemization.

TABLE 27.4 General patterns of reactivity for substitution and elimination reactions at a sp^3 carbon

Property	$\text{S}_{\text{N}}2$	$\text{S}_{\text{N}}1$
Rate of reaction	$1^\circ > 2^\circ \gg 3^\circ$	$3^\circ > 2^\circ \gg 1^\circ$
Reason:	Steric	Carbocation stability
Products	Substitution (major) E2 (minor)	Substitution (major) E1 (major)
Stereochemistry	Stereospecific, inversion	Racemic product
Kinetics	2nd order (substrate, base)	1st order (substrate)
Leaving group	Important	Important
Nucleophile effect on rate	Important	No effect
	E2	E1
Rate of reaction	$3^\circ > 2^\circ \gg 1^\circ$	$3^\circ > 2^\circ \gg 1^\circ$
Cause:	Steric	Carbocation stability
Products	Alkene (major), $\text{S}_{\text{N}}2$ (minor)	Most stable alkene
Kinetics	2nd order (substrate, base)	1st order (substrate)
Leaving group	Important	Important
Effect of base on rate	Strongest base fastest	No base necessary

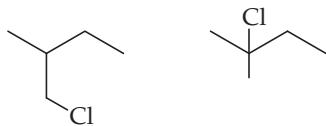
Self-Assessment Exercise

- 27.39** Is the reaction of 1-chloro-2,2-dimethylpropane with hydroxide S_N1, S_N2, E1 or E2?
(a) S_N1

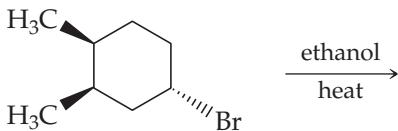
- (b)** S_N2
(c) E1
(d) E2

Exercises

- 27.40** When sodium ethoxide ($\text{NaOCH}_2\text{CH}_3$) reacts with an haloalkane, two types of products are likely. Illustrate this point by drawing the *major* organic products when sodium ethoxide acts as a base or as a nucleophile in its reaction with 2-chlorobutane.
- 27.41** Which of the following haloalkanes gives the *slowest* S_N2 reaction? Why?



- 27.42** **(a)** Which is more nucleophilic, methoxide or *tert*-butoxide? Why? **(b)** Show the best way to prepare $\text{CH}_3\text{OCH}(\text{CH}_3)_2$ by an S_N2 reaction.
- 27.43** **(a)** Provide the structure of the major organic products that result in the following reaction (including stereochemistry). **(b)** What mechanism predominates?



- 27.44** When 1-iodo-1-methylcyclohexane is treated with sodium ethoxide, the more highly substituted alkene product

predominates. When potassium *tert*-butoxide is used instead, the less substituted alkene predominates. Why?

- 27.45** **(a)** Which of the following halides is most reactive in an E2 reaction with sodium methoxide? **(b)** Which is least reactive in an E2 reaction?
- (i) $(\text{CH}_3)_3\text{CCH}_2\text{I}$
(ii) $(\text{CH}_3)_2\text{CHCHICH}_3$
(iii) $(\text{CH}_3)_2\text{CHCH}_2\text{Br}$
(iv) $(\text{CH}_3)_2\text{CHCH}_2\text{Cl}$

- 27.46** Supply the missing haloalkane reactant in the following elimination reactions.

- (i) $\text{CH}_3\text{CH}_2\text{ONa} \xrightarrow[\text{heat}]{\text{ethanol}}$
(ii) $\text{CH}_3\text{CH}_2\text{ONa} \xrightarrow[\text{heat}]{\text{ethanol}}$ $\text{CH}_3\text{CH}=\text{CHCH}_2\text{CH}_3$
(iii) $\text{CH}_3\text{CH}_2\text{ONa} \xrightarrow[\text{heat}]{\text{ethanol}}$

27.39 (b)

Answers to Self-Assessment Exercise



Sample Integrative Exercise

Putting Concepts Together

An unknown organic product was characterized by combustion analysis. You find the compound contains 59.96 % carbon and 13.42 % hydrogen and the remainder is oxygen.

- (a)** Determine the empirical formula of the compound. **(b)** If the molar mass is found to be 60.09 g mol^{-1} , draw and name all possible constitutional isomers of the compound and identify the functional groups present. **(c)** Your compound is not very soluble in water and has a boiling point close to room temperature; suggest the identity of the compound. **(d)** How would you synthesize this compound?

SOLUTION

Analyze This question provides some data which we use to obtain the formula of an unknown compound. Using Lewis structures we represent the structure of the possible compounds and, with the aid of some observations of the physical properties, we are asked to suggest the identity of the compound.

Plan Combustion analysis gives the empirical formula of a compound. This, together with a molar mass, enables us to determine the molecular formula from which we can construct all constitutional isomers. This allows us to identify the functional groups present and relate them to likely physical properties of the material.

Solve

- (a)** The percentage of oxygen in the compound is $100\% - (59.96 + 13.42)\% = 26.62\%$. The number of moles of each element in 100 g of the compound is;

$$\text{Moles of C} = \frac{59.96 \text{ g}}{12.01 \text{ g mol}^{-1}} = 4.992 \text{ mol C}$$

$$\text{Moles of H} = \frac{13.12 \text{ g}}{1.008 \text{ g mol}^{-1}} = 13.31 \text{ mol H}$$

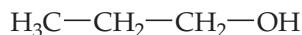
$$\text{Moles of O} = \frac{26.62 \text{ g}}{16.00 \text{ g mol}^{-1}} = 1.664 \text{ mol O}$$

Dividing by the smallest number of moles present (1.664) gives the whole number ratio of the elements.

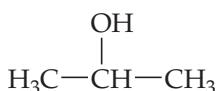
$$\text{Moles of C : H : O} = \frac{4.992 \text{ mol}}{1.664 \text{ mol}} : \frac{13.31 \text{ mol}}{1.664 \text{ mol}} : \frac{1.664 \text{ mol}}{1.664 \text{ mol}} \\ = 3 : 8 : 1$$

So the empirical formula is $\text{C}_3\text{H}_8\text{O}$.

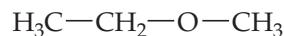
- (b) The molar mass of $\text{C}_3\text{H}_8\text{O}$ is 60.09 g mol⁻¹ which is the same as that determined for the unknown compound so we can conclude the molecular formula of the compound is also $\text{C}_3\text{H}_8\text{O}$. There are three possible constitutional isomers.



1-propanol



2-propanol



methoxyethane

The first two structures are alcohols (a primary alcohol and secondary alcohol, respectively) and the final structure is an ether.

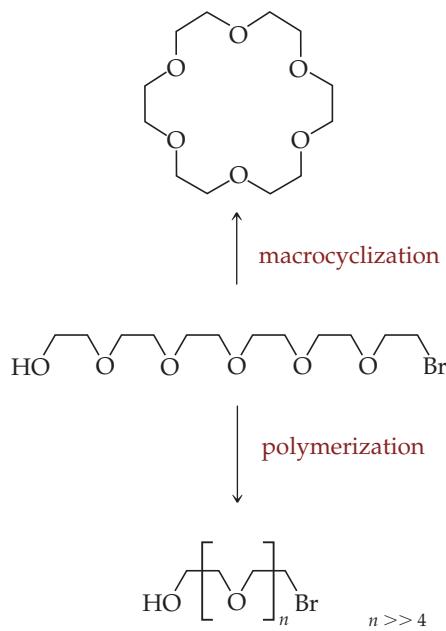
- (c) Boiling point and solubility are directly related to the intermolecular forces present. As all the molecules have the same formula we assume the strength of the dispersion forces are similar in the three cases. Two compounds contain an alcohol functional group which can form hydrogen bonds and the third compound is an ether which, when pure, shows no hydrogen bonds between molecules. As a consequence of the hydrogen bonds the alcohols are likely to display an appreciably higher boiling point and greater solubility in water than the ether. The unknown compound is likely to be methoxyethane.
- (d) A Williamson ether synthesis of iodomethane and ethanol in the presence of sodium metal would form methoxyethane. Note that forming the product from iodoethane and methanol will lead to the formation of ethene as a side product. This occurs through an elimination of HI using the sodium methoxide generated *in situ* as a base.

CHEMISTRY AND LIFE Polymerization versus Macrocyclization

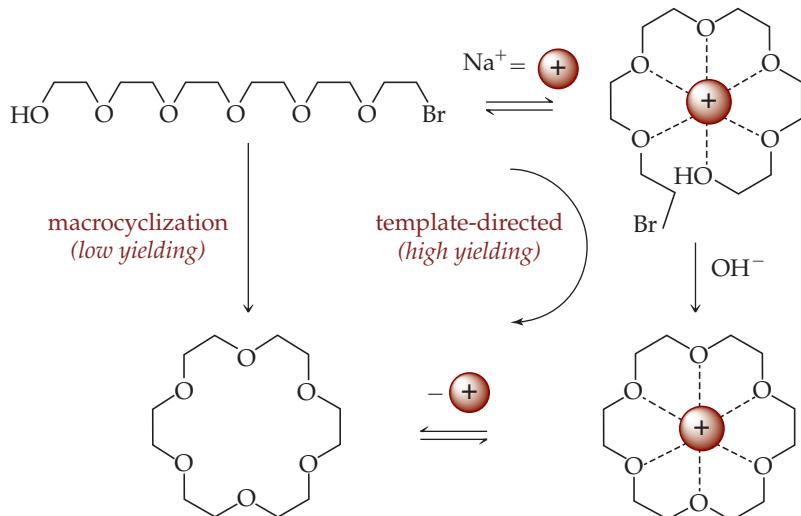
The preparation of cyclic ethers (Section 27.3) has always involved two competing processes: the desired macrocyclization and an unwanted polymerization. FIGURE 27.21 illustrates these two processes using the crown ether, 18-crown-6, as the example. Intramolecular reaction of the OH group on the bromide in the presence of base yields the crown ether, 18-C-6, via substitution. Intermolecular reaction of the OH group on the bromide of a second molecule in the presence of base yields the polyether, also via substitution. Since both processes are competing, the result has always been a low (<20%) isolated yield of the macrocycle. Intramolecular processes are usually faster than intermolecular processes because of the proximity of reactive functional

groups; however, this is true only of small molecules. In the example of crown ether synthesis shown in Figure 27.21 the longer the starting acyclic polyether, the lower the yield of the crown ether.

We can, however, take advantage of the affinity of polyethers for metal cations to bias the reaction outcome. In this case, the spherical cation acts as a *template* to promote the formation of the cyclic crown ether by allowing the polyether to wrap around the cation (FIGURE 27.22). In this orientation, the carbon bearing the bromine atom and the OH group are brought into close proximity, enabling the intramolecular substitution reaction to occur in preference to the polymerization upon the addition of base—for example, hydroxide ion. Removal of the cationic template yields the macrocycle in 60–80% yield. This very practical reaction is analogous to the approach taken by nature in the formation of highly complex and functioning molecules such as DNA, in which a template strand is necessary to build the double helix using DNA polymerases I and II.



▲ Figure 27.21 Competition between (formation of) a crown ether and a polymer.



▲ Figure 27.22 The template effect.

Chapter Summary and Key Terms

SECTION 27.1 Alcohols are hydrocarbon derivatives containing one or more OH groups. Alcohols are more **miscible** with water than ethers of comparable size, due to their ability to hydrogen-bond as a result of the **lone pairs** on oxygen. Alcohols that have two or three OH groups, such as ethene glycol and glycerol, are called **diols** and **triols**, respectively. Alcohols are classed as **primary** (1°), **secondary** (2°) or **tertiary** (3°). Short-chain alcohols are miscible with water.

SECTION 27.2 Haloalkanes are hydrocarbons containing one or more halogens, usually generalized as RX (X = F, Cl, Br, I). They are also commonly referred to as alkyl halides. Compounds of the form CHX_3 are often called **haloforms**, of which chloroform is an example. **Chlorofluorocarbons**, or **CFCs**, are odorless, non-toxic, non-flammable and non-corrosive compounds that were typically used as refrigerants, propellants in aerosols and industrial solvents before being phased out due to their harmful effects on the ozone layer in the atmosphere.

SECTION 27.3 Ethers contain a bridging oxygen atom between two hydrocarbon chains. Cyclic ethers are a subclass of a large group of organic compounds known as **heterocyclic compounds**. Ethers contain both alkyl and **alkoxy** groups. Larger **cyclic polyethers** such as the **crown ethers** are able to complex metal ions within their cavity. Ethers make good solvents.

SECTION 27.4 The reaction of sodium metal with an alcohol leads to an **alkoxide**. Alkoxides are as strong a base as hydroxide. Potassium *tert*-butoxide and sodium ethoxide are examples cited frequently in this chapter. Alcohols act as a weak base, generating an oxonium ion under acidic conditions. Alcohols can be converted into haloalkanes by treatment of a halogenating agent, usually under acidic conditions.

In this reaction, the OH group of the alcohol is substituted by a halogen in a **nucleophilic substitution (S_N) reaction**. Alcohols can also dehydrate to form alkenes.

SECTION 27.5 Nucleophilic substitution reactions of haloalkanes proceed by attack of the nucleophile at the carbon bearing the halogen. Because of the difference in electronegativity between carbon and any of the halides, this bond is polarized such that the carbon becomes mildly electrophilic. If the transition state that leads to the product involves both the haloalkane and the nucleophile in the rate-determining step, the reaction is classed as an S_N2 or bimolecular (2), nucleophilic (N), substitution (S) reaction. The reaction of haloalkanes with **amines** leading to **alkyl ammonium salts**, is one such example. **Nitriles** are formed when haloalkanes are reacted with cyanide.

SECTION 27.6 Alkenes are readily formed from haloalkanes through a process called a **β -elimination reaction**. An **elimination reaction** involves the removal of a small group from a larger molecule. An **E2** reaction is a bimolecular (2) elimination (E) reaction. The alkene that forms in preference is the one that follows **Zaitsev's rule**, which states that the more substituted double bond predominates.

SECTION 27.7 Substitution and elimination reactions are competing reactions. Bimolecular substitution reactions (S_N2) compete against bimolecular elimination reactions (E2); which mechanism predominates in the reaction is dictated by a variety of steric factors. Tertiary alcohols undergo unimolecular reactions in which the rate-determining step is the elimination of water leading to a carbocation intermediate. In this case **E1** or **S_N1** reactions are likely depending on the reaction conditions.

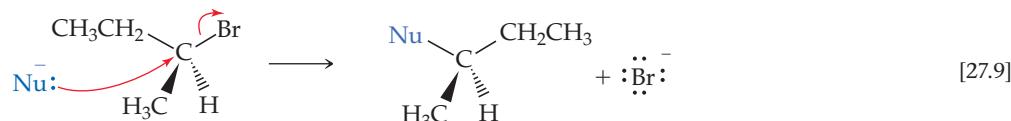
Key Skills

- Understand how to derive the names of simple alcohols, ethers and haloalkanes. Learn the common names for the simplest cases. Learn how to classify alcohols as 1° , 2° or 3° . (Sections 27.1, 27.2 and 27.3)
- Learn the basic functional group manipulation shown in Figure 27.14. (Section 27.4)

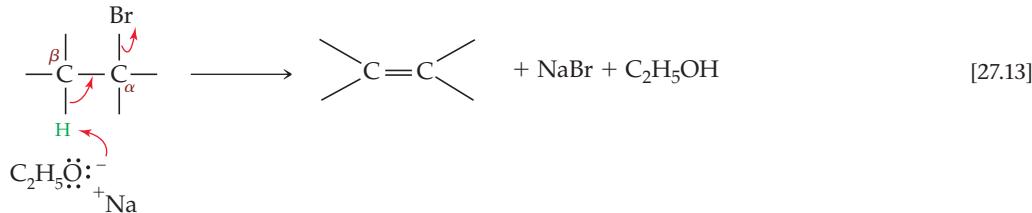
- Be able to explain the difference between S_N1 , S_N2 , E1 and E2 mechanisms and have a qualitative understanding of when one predominates over another to predict reaction outcomes. (Sections 27.5, 27.6 and 24.7)

Key Equations

- Substitution



- β -Elimination



Exercises

Visualizing Concepts

- 27.47** Propan-1-ol ($\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$) and propan-2-ol (also known as isopropyl alcohol ($(\text{CH}_3)_2\text{CHOH}$), whose space-filling models are shown, have boiling points of 97.2°C and 82.5°C , respectively. Explain why the boiling point of propan-1-ol is higher, even though both have the molecular formula of $\text{C}_3\text{H}_8\text{O}$. [Section 27.1]

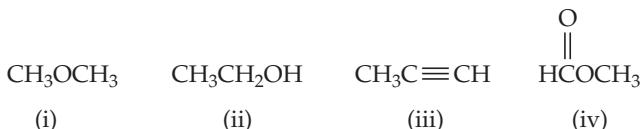


propan-1-ol

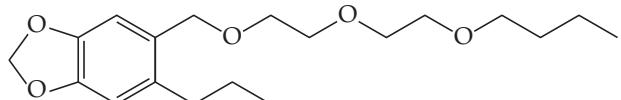


propan-2-ol

- 27.48** What features must a molecule have to participate in hydrogen bonding with other molecules of the same kind? Which of the following compounds would you expect to (a) have the highest boiling point, (b) be least soluble in water? Explain. [Section 27.1]

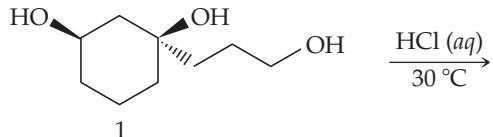


- 27.49** Piperonyl butoxide is used commercially as an additive to pyrethrum-based insecticides to enhance their effect. Copy the structure and highlight the atoms that constitute the cyclic ether and the acyclic polyether. [Section 27.3]

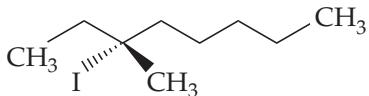


piperonyl butoxide

- 27.50** Draw the carbocation that triol 1 would form under the indicated conditions. Explain your answer. [Section 27.4]



- 27.51** How many distinct alkene products (including stereochemistry) are possible when the iodoalkane shown here undergoes E2 elimination? [Section 27.5]



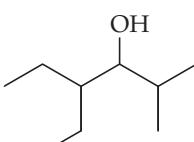
Alcohols: Structure, Properties, and Nomenclature (Section 27.1)

- 27.52** Two oxygen-containing compounds have the same empirical formula. One substance is a gas, the other is a liquid. How is it possible for two substances with the same empirical formula to have markedly different properties?

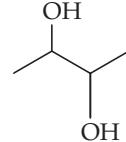
- 27.53** Draw the structures of (a) hexan-2-ol, (b) propane-1,2,3-triol, (c) 4,4-dimethylcyclohexanol, (d) *cis*-1,2-cyclopentanediol, (e) 2-methylpropan-2-ol.

- 27.54** Name the following alcohols, ignoring stereochemistry:

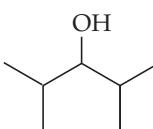
(a)



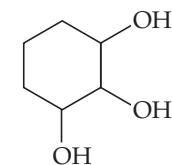
(b)



(c)

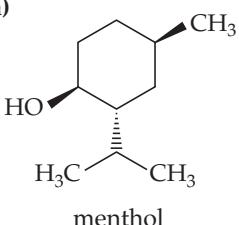


(d)

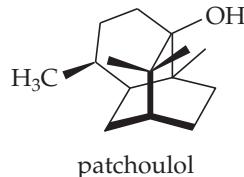


- 27.55** Classify the following alcohols as primary, secondary, or tertiary.

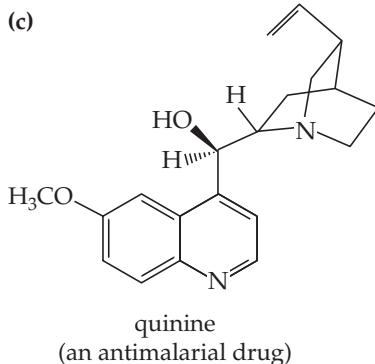
(a)



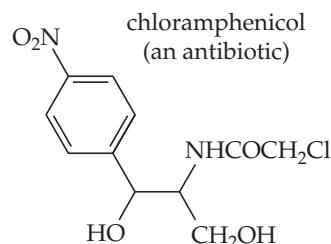
(b)



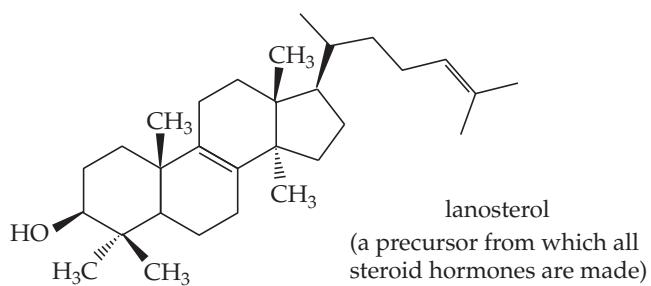
(c)



(d)



(e)

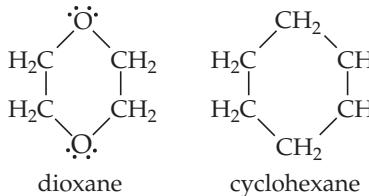


Haloalkanes (Section 27.2)

- 27.56** Eight isomers have the molecular formula $C_5H_{11}Cl$. How many of these are tertiary chloroalkanes?
- 27.57** Describe the carbon–chlorine bond of chloroalkanes as polar or nonpolar. Why?

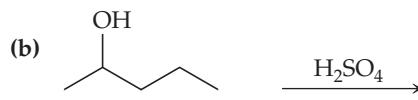
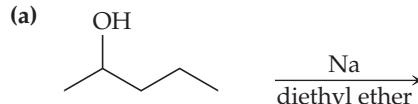
Ethers: Structure, Properties, and Nomenclature (Section 27.3)

- 27.58** Ethene glycol ($HOCH_2CH_2OH$), the major substance in anti-freeze, has a normal boiling point of 198°C . By comparison, ethanol (CH_3CH_2OH) boils at 78°C at one atmospheric pressure. Ethene glycol dimethyl ether ($CH_3OCH_2CH_2OCH_3$) has a normal boiling point of 83°C , and ethyl methyl ether ($CH_3CH_2OCH_3$) has a normal boiling point of 11°C . **(a)** Explain why replacement of a hydrogen on the oxygen by CH_3 generally results in a lower boiling point. **(b)** What are the major factors responsible for the difference in boiling points of the two ethers?
- 27.59** **(a)** Give the empirical formula and structural formula for the cyclic ether containing four carbon atoms in the ring. **(b)** Write the structural formula for a straight-chain compound that is a structural isomer of your answer to part (a).
- 27.60** Why do ethers make good solvents, whereas alcohols usually make poor solvents in which to undertake a chemical reaction? When might an alcohol make an appropriate solvent?
- 27.61** Which would you expect to be more soluble in water, cyclohexane or dioxane? Explain.



Reactions of Alcohols and Haloalkanes (Sections 27.4 and 27.5)

- 27.62** Suggest a possible stable reaction product for each of the following reactions:

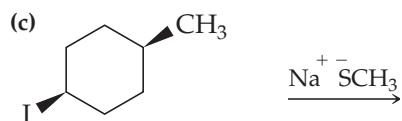
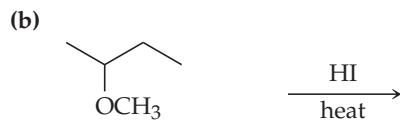
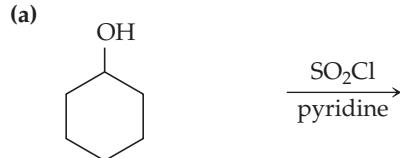


- 27.63** Sodium wire is normally used to “dry” tetrahydrofuran before distillation and use in water-sensitive reactions. **(a)** Write an equation for the reaction of sodium metal with water. **(b)** This reaction is very exothermic and care should be taken as to how “wet” the tetrahydrofuran is. What alternative to water might you use to destroy excess sodium, and what precautions should you take?

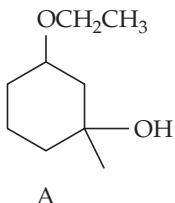
- 27.64** Suggest ways of conducting the following transformations.



- 27.65** Provide the structure of the major organic product of the following reactions.

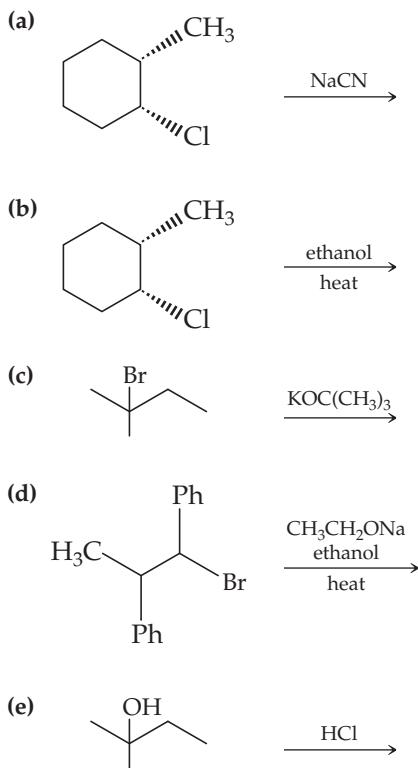


- 27.66** Describe a synthesis of A starting from 3-methylcyclohexene-3-ol.



Haloalkanes to Alkenes: β -Elimination (Section 27.6)

- 27.67** When sodium ethoxide ($\text{NaOCH}_2\text{CH}_3$) reacts with 2-chlorobutane, a haloalkane and three unsaturated products are likely (including stereochemistry). **(a)** Draw them. **(b)** Which ones are likely to be formed in higher yield?
- 27.68** Which base, sodium ethoxide or potassium *tert*-butoxide, would you employ for the efficient dehydrohalogenation of 1-bromo-2-ethylbutane. Why?
- 27.69** **(a)** Define bimolecular. **(b)** Using diagrams, give an example of a bimolecular reaction using diagrams.
- 27.70** What is the major product formed in the following reactions and what mechanisms predominate?

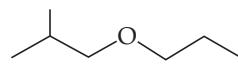


Substitution versus Elimination (Section 27.7)

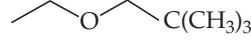
- 27.71** When haloalkanes react with alkoxides a competition exists between elimination and substitution reactions. Which product is formed can be biased by the judicious choice of haloalkane and alkoxide. The following ethers can only be prepared in high yield by the combination of one alkoxide ion and one haloalkane.

What is the correct combination in each case?

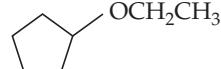
(a)



(b)



(c)



- 27.72** **(a)** What is the substitution product of the following reaction? **(b)** What is the elimination product of this reaction?
 $\text{CH}_3\text{CH}_2\text{Br} + \text{HO}^- \rightarrow$

- 27.73** Which of the following S_N2 reactions is the *fastest*? Why?

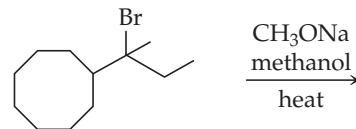
- (a)** $\text{CH}_3\text{CH}_2\text{CH}_2\text{I} + \text{HO}^- \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} + \text{I}^-$
(b) $\text{CH}_3\text{CH}_2\text{CH}_2\text{Br} + \text{HO}^- \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} + \text{Br}^-$
(c) $\text{CH}_3\text{CH}_2\text{CH}_2\text{I} + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} + \text{HI}$
(d) $\text{CH}_3\text{CHICH}_3 + \text{HO}^- \rightarrow \text{CH}_3\text{CHOHCH}_3 + \text{I}^-$

- 27.74** The reaction of a tertiary bromoalkane with iodide follows.
(a) Assuming no other changes, what is the effect of *doubling* the concentration of the haloalkane? **(b)** Assuming no other changes, what is the effect of doubling *only* the concentration of the nucleophile?



- 27.75** When 2-bromo-3-methyl-1-phenylbutane is treated with sodium methoxide, why is the major product 3-methyl-1-phenyl-1-butene?

- 27.76** What is the major organic product of the following reaction? Why?

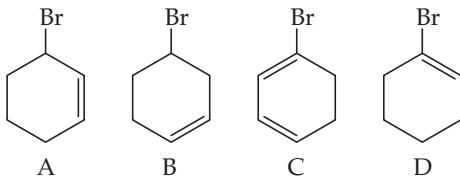


Additional Exercises

- 27.77** Consider the following experimental data for the rate of an elimination reaction for a tertiary bromide. What is the mechanism for the reaction?

Experiment No.	[Bromoalkane]	[Base]	Rate
1	0.01	0.01	1
2	0.02	0.01	2
3	0.01	0.02	1

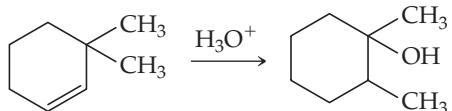
- 27.78** Which of the following bromides forms the most stable carbocation? Why?



- 27.79** **(a)** Dehydrohalogenation of 2-bromobutane in the presence of a strong base proceeds via which mechanistic pathways? **(b)** Why is the E1 not a likely mechanism when 1-chloropentane is heated in ethanol? **(c)** Predict the two most likely mechanisms (substitution and elimination) for the reaction of 2-iodohexane with sodium ethoxide and give the products of these reactions. **(d)** Can primary haloalkanes react by S_N2, S_N1, E2 and E1 mechanisms? Are any of these mechanisms prohibited? What conditions favor a particular mechanism?

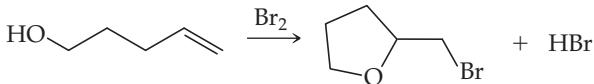
Integrative Exercises

- 27.80** This question relates to the hydration of 3,3-dimethylcyclohexene and the development of an appropriate mechanism to account for the formation of 1,2-dimethoxy-1-cyclohexanol.



(a) Draw a mechanism leading to the first carbocation intermediate. **(b)** The next step involves a methyl migration from carbon 3 to carbon 2. Draw this intermediate and comment on why this is favored. **(c)** Use water as a nucleophile and draw the next step of the mechanism. **(d)** Complete the mechanism to generate the product. What does this mechanism tell you about the requirement of acid?

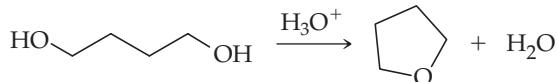
- 27.81** Provide a detailed, step-by-step mechanism for the following reaction.



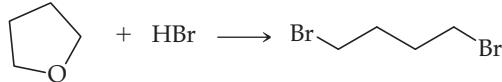
- 27.82** Describe a way of converting but-2-ene into but-2-yne using a bromination as the first step.

- 27.83** Describe a way of converting hex-3-ene into hex-3-yne.

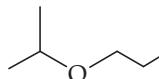
- 27.84** Propose a mechanism for the following reaction:



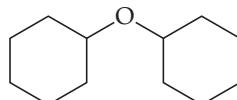
- 27.85** Propose a mechanism for the following reaction:



- 27.86** Starting with propan-1-ol as the only organic material, synthesize isopropyl propyl ether.

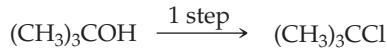


- 27.87** Describe how you would prepare this ether from cyclohexene.

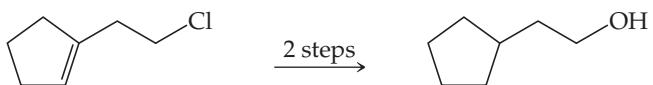


- 27.88** How would you accomplish the following transformations?

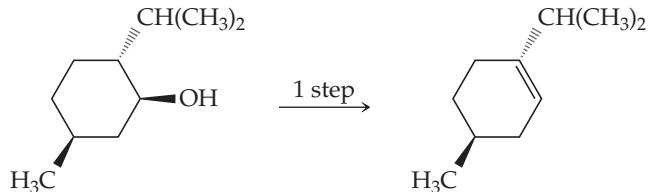
(a)

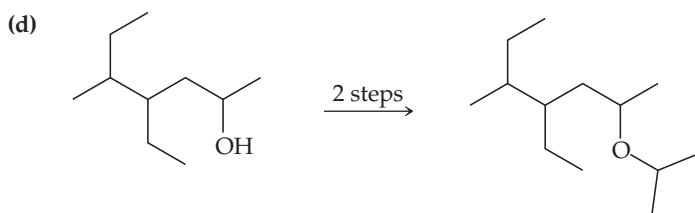


(b)



(c)





- 27.89** Consider the three alkenes: ethene, propene and 2-methylpropene. **(a)** For each alkene, draw the reaction showing the acid-catalyzed hydration to form one major product. Include the carbocation intermediate in each case. **(b)** Write the systematic name of the alcohols produced. Classify the intermediate carbocations and the alcohol products as *primary*, *secondary* or *tertiary*. **(c)** What is the connection between the classification of the carbocations and the alcohols that arise from them?
- 27.90** In the S_N2 reaction of 1-bromobutane with hydroxide ions we imagine a smooth interchange between the leaving

group and the attaching nucleophile, while the S_N1 reaction of 2-bromo-2-methylpropane involves the formation of a carbocation intermediate. Sketch the energy profile (similar to Figure 15.17) for the two mechanisms. Use labels to show which part of your sketch represents a transition state, which an intermediate and which energy changes represents E_a and ΔH for the reaction.

- 27.91** The conversion of 2-methyl-2-propanol to 2-bromo-2-methylpropane using concentrated hydrobromic acid occurs at room temperature. As the reaction proceeds, the reaction mixture separates into two layers. **(a)** Why does this occur? Treatment of the product, 2-bromo-2-methylpropane, with sodium ethoxide gives 2-methylpropene. **(b)** What is the geometry and hybridization observed for the central carbon atom in both the haloalkane and alkene? 2-Methylpropene is a gas at room temperature. **(c)** What is the maximum volume of gas produced, at 25 °C and 101.3 kPa, if 5.0 g of 2-bromo-2-methylpropane reacted completely to form 2-methylpropene?

Design an Experiment

Imagine yourself in a research laboratory where you are going to investigate the factors that affect the outcome of a reaction. The compounds that you want to investigate are the haloalkanes and the competing substitution and elimination reactions they undergo. For each set of experiments that you devise, formulate a research question that the experiments may answer, and give a rationale for how

your experiment may address that question. Variables in the experiment could include: the halide used, the structure of the haloalkane, the reagent employed, the concentrations of the components, the solvent used, and the temperature conditions of the reaction. Think also how you may determine the outcome of the reaction and what changes may be observed during the course of the reaction.