The bristlecone pine is the oldest living organism on Earth. The waxy coating on its needles contains a mixture of organic compounds called alkanes, the subject of this chapter.

Jeff Foott/Getty Images

Alkanes: The Nature of Organic Compounds

OWL

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There are more than 37 million known organic compounds.
Each of these compounds has its own physical properties, such as melting point, and each has its own chemical reactivity. Chemists have learned through years of experience that organic compounds can be classified into families according to their structural features and that the members of a given family often have similar chemical reactivity. Instead of 37 million compounds with random reactivity, there are a few dozen families of compounds whose chemistry is reasonably predictable. We'll study the chemistry of specific families of organic molecules throughout this book, beginning in this chapter with a look at the simplest family, the *alkanes*.

WHY THIS CHAPTER?

Alkanes are relatively unreactive and are rarely involved in chemical reactions, but they nevertheless provide a useful way to introduce some important general ideas. In this chapter, we'll use alkanes to introduce the basic approach to naming organic compounds and to take an initial look at some of the three-dimensional aspects of molecules, a topic of particular importance in understanding biological organic chemistry.

2.1 | Functional Groups

The structural features that make it possible to classify compounds into families are called *functional groups*. A **functional group** is a group of atoms within a molecule that has a characteristic chemical behavior. Chemically, a given functional group behaves almost the same way in every molecule it's a part of. For example, compare ethylene, a plant hormone that causes fruit to ripen, with menthene, a much more complicated molecule found in peppermint oil. Both substances contain a carbon–carbon double-bond functional group, and both therefore react with Br_2 in the same way to give products in which a Br atom has added to each of the double-bond carbons (Figure 2.1). This example is typical: *the chemistry of every organic molecule, regardless of size and complexity, is determined by the functional groups it contains.*
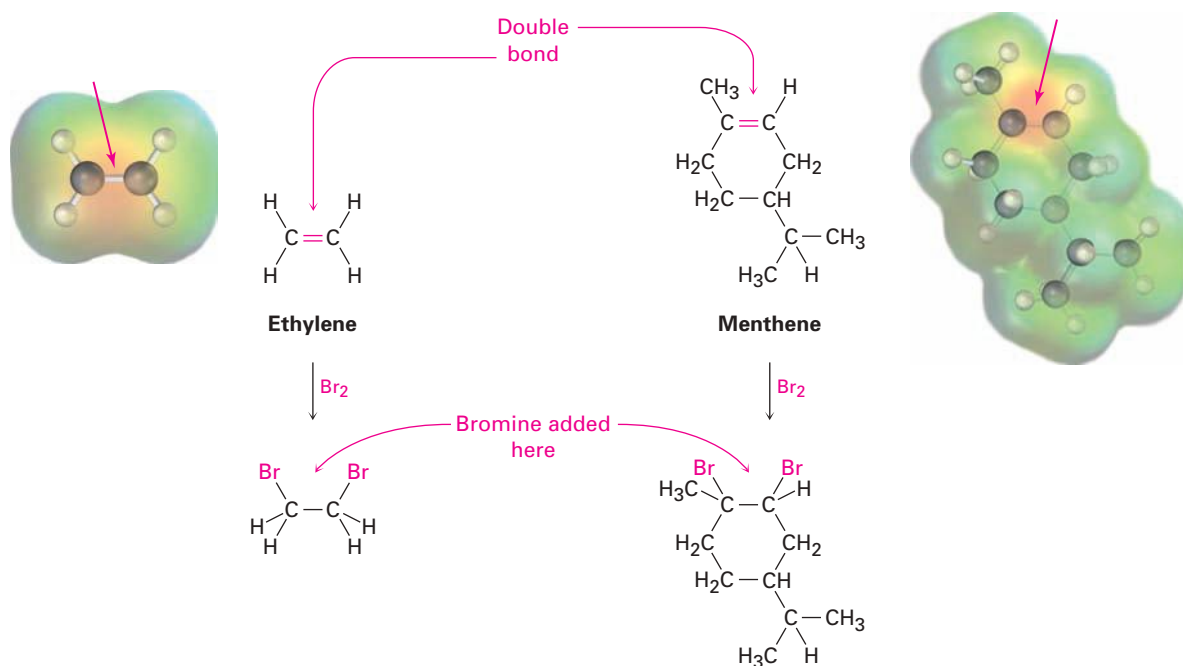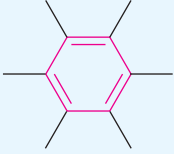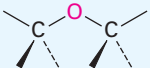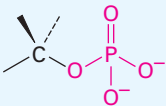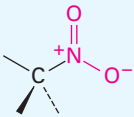

Figure 2.1 The reactions of ethylene and menthene with bromine. In both molecules, the carbon–carbon double-bond functional group reacts with Br_2 in the same way. The size and complexity of the molecules are not important.

Look at Table 2.1, which lists many of the common functional groups and gives simple examples of their occurrence. Some functional groups have only carbon–carbon double or triple bonds; others have halogen atoms; and still others contain oxygen, nitrogen, sulfur, or phosphorus. Much of the chemistry you'll be studying in subsequent chapters is the chemistry of these functional groups.
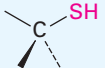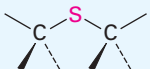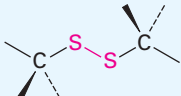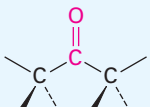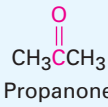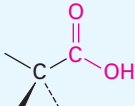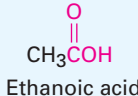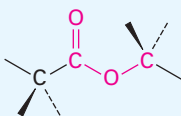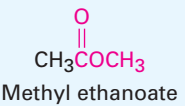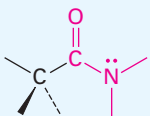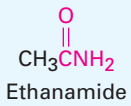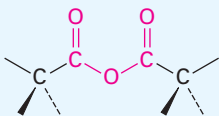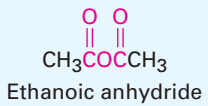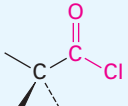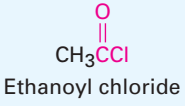
Table **2.1**	Structure of Some Common Functional Groups		
Name	**Structure***	**Name ending**	**Example**
Alkene (double bond)	$C=C$	*-ene*	$H_2C=CH_2$ Ethene
Alkyne (triple bond)	$-C\equiv C-$	*-yne*	$HC\equiv CH$ Ethyne
Arene (aromatic ring)		None	Benzene
Halide	X (X = F, Cl, Br, I)	None	CH_3Cl Chloromethane
Alcohol	OH	*-ol*	CH_3OH Methanol
Ether	C–O–C	*ether*	CH_3OCH_3 Dimethyl ether
Monophosphate		*phosphate*	$CH_3OPO_3{}^{2-}$ Methyl phosphate
Amine	N:	*-amine*	CH_3NH_2 Methylamine
Imine (Schiff base)	:N	None	$\begin{matrix}NH\\\|\\CH_3CCH_3\end{matrix}$ Acetone imine
Nitrile	$-C\equiv N$	*-nitrile*	$CH_3C\equiv N$ Ethanenitrile
Nitro		None	CH_3NO_2 Nitromethane

*The bonds whose connections aren't specified are assumed to be attached to carbon or hydrogen atoms in the rest of the molecule.

Table **2.1**	Structure of Some Common Functional Groups *(continued)*		
Name	**Structure***	**Name ending**	**Example**
Thiol		*-thiol*	CH_3SH Methanethiol
Sulfide		*sulfide*	CH_3SCH_3 Dimethyl sulfide
Disulfide		*disulfide*	CH_3SSCH_3 Dimethyl disulfide
Carbonyl			
Aldehyde		*-al*	CH_3CH Ethanal
Ketone		*-one*	CH_3CCH_3 Propanone
Carboxylic acid		*-oic acid*	CH_3COH Ethanoic acid
Ester		*-oate*	CH_3COCH_3 Methyl ethanoate
Amide		*-amide*	CH_3CNH_2 Ethanamide
Carboxylic acid anhydride		*-oic anhydride*	CH_3COCCH_3 Ethanoic anhydride
Carboxylic acid chloride		*-oyl chloride*	CH_3CCl Ethanoyl chloride

*The bonds whose connections aren't specified are assumed to be attached to carbon or hydrogen atoms in the rest of the molecule.

Functional Groups with Carbon–Carbon Multiple Bonds

Alkenes, alkynes, and arenes (aromatic compounds) all contain carbon–carbon multiple bonds. *Alkenes* have a double bond, *alkynes* have a triple bond, and *arenes* have alternating double and single bonds in a six-membered ring of carbon atoms. Because of their structural similarities, these compounds also have chemical similarities.

Alkene

Alkyne

**Arene
(aromatic ring)**
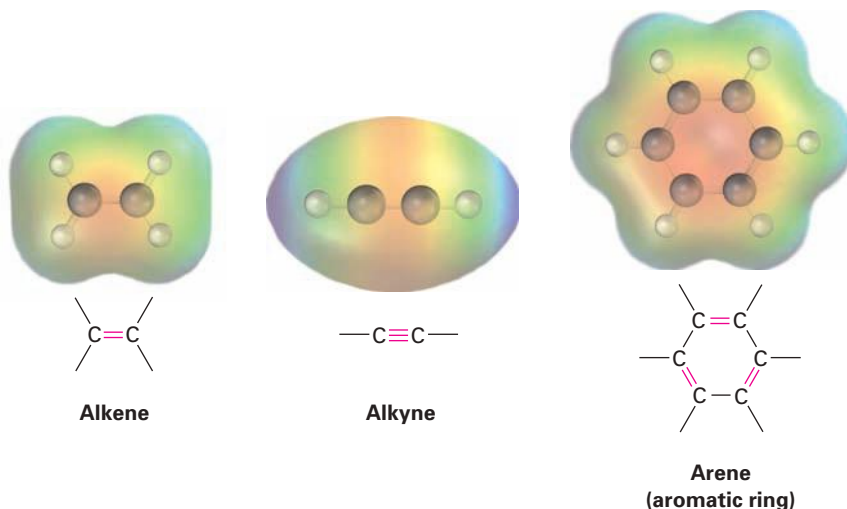
Functional Groups with Carbon Singly Bonded to an Electronegative Atom

Alkyl halides (haloalkanes), alcohols, ethers, alkyl phosphates, amines, thiols, sulfides, and disulfides all have a carbon atom singly bonded to an electronegative atom—halogen, oxygen, nitrogen, or sulfur. Alkyl halides have a carbon atom bonded to halogen ($-X$), alcohols have a carbon atom bonded to the oxygen of a hydroxyl group ($-OH$), ethers have two carbon atoms bonded to the same oxygen, organophosphates have a carbon atom bonded to the oxygen of a phosphate group ($-OPO_3^{2-}$), amines have a carbon atom bonded to a nitrogen, thiols have a carbon atom bonded to the sulfur of an $-SH$ group, sulfides have two carbon atoms bonded to the same sulfur, and disulfides have carbon atoms bonded to two sulfurs that are joined together. In all cases, the bonds are polar, with the carbon atom bearing a partial positive charge ($\delta+$) and the electronegative atom bearing a partial negative charge ($\delta-$).

**Alkyl halide
(haloalkane)**

Alcohol

Ether

Phosphate

Amine   **Thiol**   **Sulfide**   **Disulfide**
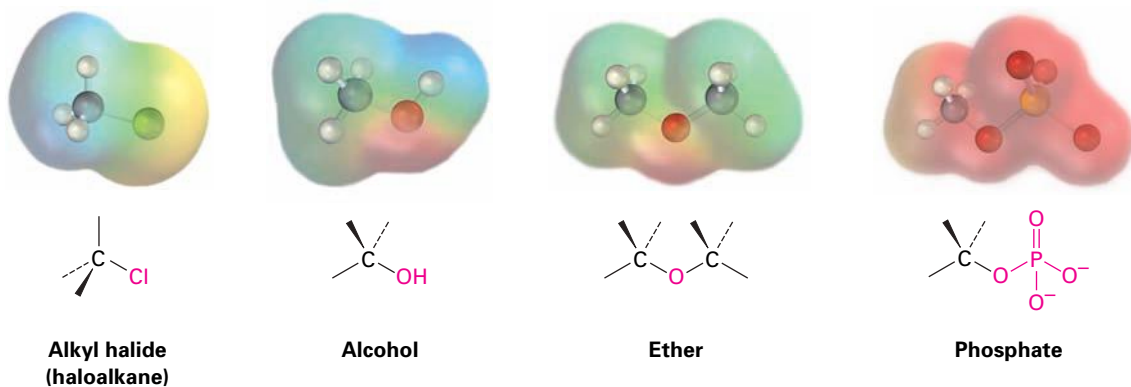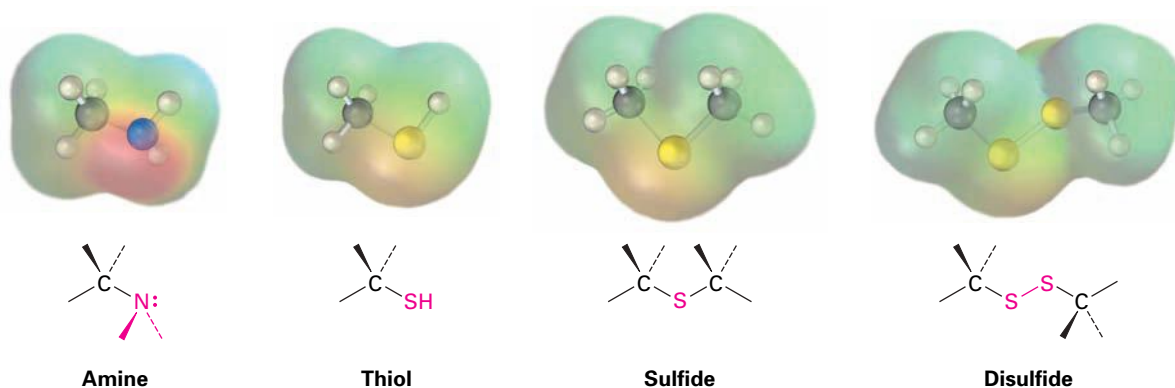
Functional Groups with a Carbon–Oxygen Double Bond (Carbonyl Groups)

The *carbonyl group,* C=O (pronounced car-bo-**neel**) is common to many of the families listed in Table 2.1. Carbonyl groups are present in the great majority of organic compounds and in practically all biological molecules. These compounds behave similarly in many respects but differ depending on the identity of the atoms bonded to the carbonyl-group carbon. Aldehydes have at least one hydrogen bonded to the C=O, ketones have two carbons bonded to the C=O, carboxylic acids have one carbon and one –OH group bonded to the C=O, esters have one carbon and one ether-like oxygen bonded to the C=O, amides have one carbon and one nitrogen bonded to the C=O, acid chlorides have one carbon and one chlorine bonded to the C=O, and so on. The carbonyl carbon atom bears a partial positive charge ($\delta+$), and the oxygen bears a partial negative charge ($\delta-$).
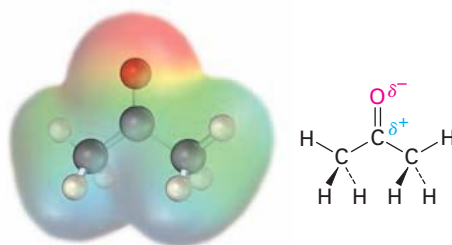
Acetone—a typical carbonyl compound

Aldehyde   **Ketone**   **Carboxylic acid**   **Ester**

Thioester   **Amide**   **Acid chloride**
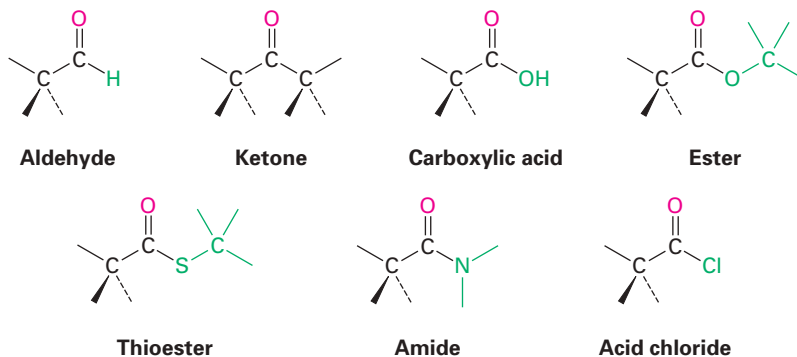
Problem 2.1   Identify the functional groups in the following molecules:

(a)

Acrylic acid
(2 functional groups)

(b)

Aspirin
(3 functional groups)

(c)

Glucose
(6 functional groups)
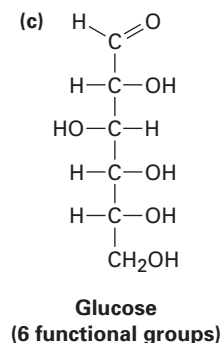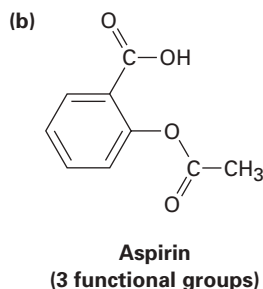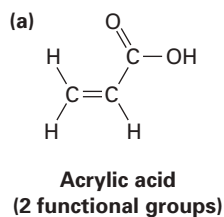
Problem 2.2   Propose structures for simple molecules that contain the following functional groups:

(a) Alcohol   (b) Aromatic ring   (c) Carboxylic acid
(d) Amine   (e) Both ketone and amine (f) Two double bonds

Problem 2.3   Identify the functional groups in the following model of arecoline, a veterinary drug used to control worms in animals. Convert the drawing into a line-bond structure (gray = C, red = O, blue = N, ivory = H).
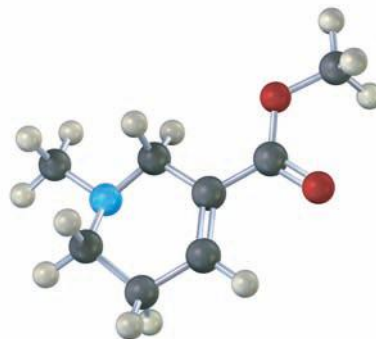
2.2 Alkanes and Alkyl Groups: Isomers

Before beginning a systematic study of the different functional groups, let's look first at the simplest family of molecules—the *alkanes*—to develop some general ideas that apply to all families. We saw in Section 1.7 that the C–C single bond in ethane results from σ (head-on) overlap of carbon sp^3 hybrid orbitals. If we imagine joining three, four, five, or even more carbon atoms by C–C single bonds, we generate the large family of molecules called **alkanes**.

Methane   **Ethane**   **Propane**   **Butane**   . . . and so on

Alkanes are often described as *saturated hydrocarbons:* **hydrocarbons** because they contain only carbon and hydrogen atoms; **saturated** because they have only C–C and C–H single bonds and thus contain the maximum possible number of hydrogens per carbon. They have the general formula C_nH_{2n+2}, where n is any integer. Alkanes are also occasionally called **aliphatic** compounds, a word derived from the Greek *aleiphas,* meaning "fat." We'll see in Chapter 16 that animal fats contain long carbon chains similar to alkanes.

$$
\begin{array}{l}
\overset{\displaystyle O}{\overset{\displaystyle \|}{CH_2OCCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3}} \\
\overset{\displaystyle O}{\overset{\displaystyle \|}{CHOCCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3}} \\
\overset{\displaystyle O}{\overset{\displaystyle \|}{CH_2OCCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3}}
\end{array}
$$

A typical animal fat

Think about the ways that carbon and hydrogen might combine to make alkanes. With one carbon and four hydrogens, only one structure is possible: methane, CH_4. Similarly, there is only one possible combination of two carbons with six hydrogens (ethane, CH_3CH_3) and only one possible combination of three carbons with eight hydrogens (propane, $CH_3CH_2CH_3$). If larger numbers of carbons and hydrogens combine, however, more than one kind of molecule can form. For example, there are two ways that molecules with the formula C_4H_{10} can form: the four carbons can be in a row (butane), or they can branch (isobutane). Similarly, there are three ways in which C_5H_{12} molecules can form, and so on for larger alkanes.

CH_4

Methane, CH_4

CH_3CH_3

Ethane, C_2H_6

$CH_3CH_2CH_3$

Propane, C_3H_8

$CH_3CH_2CH_2CH_3$

Butane, C_4H_{10}

$$\overset{\displaystyle CH_3}{\overset{\displaystyle |}{CH_3CHCH_3}}$$

Isobutane, C_4H_{10}
(2-methylpropane)

Pentane, C_5H_{12} 2-Methylbutane, C_5H_{12} 2,2-Dimethylpropane, C_5H_{12}

$CH_3CH_2CH_2CH_2CH_3$

$$CH_3CH_2CHCH_3$$
with CH_3 above

$$CH_3CCH_3$$
with CH_3 above and CH_3 below

Compounds like butane, whose carbons are connected in a row, are called **straight-chain alkanes, or normal (*n*) alkanes**, whereas compounds with branched carbon chains, such as isobutane (2-methylpropane), are called **branched-chain alkanes**.

Compounds like the two C_4H_{10} molecules and the three C_5H_{12} molecules, which have the same formula but different structures, are called *isomers,* from the Greek *isos + meros,* meaning "made of the same parts." **Isomers** have the same numbers and kinds of atoms but differ in the way the atoms are arranged. Compounds like butane and isobutane, whose atoms are connected differently, are called **constitutional isomers**. We'll see shortly that other kinds of isomerism are also possible, even among compounds whose atoms are connected in the same order.

A given alkane can be arbitrarily drawn in many ways. The straight-chain, four-carbon alkane called butane, for instance, can be represented by any of the structures shown in Figure 2.2. These structures don't imply any particular three-dimensional geometry for butane; they only indicate the connections among atoms. In practice, chemists rarely draw all the bonds in a molecule and usually refer to butane by the *condensed structure,* $CH_3CH_2CH_2CH_3$ or $CH_3(CH_2)_2CH_3$. In such representations, the C–C and C–H bonds are "understood" rather than shown. If a carbon has three hydrogens bonded to it, we write CH_3; if a carbon has two hydrogens bonded to it, we write CH_2, and so on. Still more simply, butane can even be represented as n-C_4H_{10}, where n signifies *normal,* straight-chain butane.
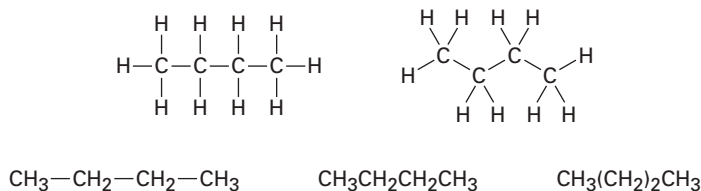
Figure 2.2 Some representations of butane (n-C_4H_{10}). The molecule is the same regardless of how it's drawn. These structures imply only that butane has a continuous chain of four carbon atoms.

CH_3—CH_2—CH_2—CH_3 $CH_3CH_2CH_2CH_3$ $CH_3(CH_2)_2CH_3$

Straight-chain alkanes are named according to the number of carbon atoms they contain, as shown in Table 2.2. With the exception of the first four compounds—methane, ethane, propane, and butane—whose names have historical origins, the alkanes are named based on Greek numbers, according to the number of carbons. The suffix *-ane* is added to the end of each name to identify the molecule as an alkane. Thus, pent*ane* is the five-carbon alkane, hex*ane* is the six-carbon alkane, and so on.

If a hydrogen atom is removed from an alkane, the partial structure that remains is called an **alkyl group**. Alkyl groups are named by replacing the *-ane* ending of the parent alkane with an *-yl* ending. For example, removal of

Table **2.2**		Names of Straight-Chain Alkanes				
Number of carbons (n)	Name	Formula (C_nH_{2n+2})		Number of carbons (n)	Name	Formula (C_nH_{2n+2})
1	Methane	CH_4		9	Nonane	C_9H_{20}
2	Ethane	C_2H_6		10	Decane	$C_{10}H_{22}$
3	Propane	C_3H_8		11	Undecane	$C_{11}H_{24}$
4	Butane	C_4H_{10}		12	Dodecane	$C_{12}H_{26}$
5	Pentane	C_5H_{12}		13	Tridecane	$C_{13}H_{28}$
6	Hexane	C_6H_{14}		20	Icosane	$C_{20}H_{42}$
7	Heptane	C_7H_{16}		30	Triacontane	$C_{30}H_{62}$
8	Octane	C_8H_{18}				

a hydrogen atom from methane, CH_4, generates a *methyl group,* $-CH_3$, and removal of a hydrogen atom from ethane, CH_3CH_3, generates an *ethyl group,* $-CH_2CH_3$. Similarly, removal of a hydrogen atom from the end carbon of any n-alkane gives the series of n-alkyl groups shown in Table 2.3.

Just as n-alkyl groups are generated by removing a hydrogen from an *end* carbon, branched alkyl groups are generated by removing a hydrogen atom from an *internal* carbon. Two 3-carbon alkyl groups and four 4-carbon alkyl groups are possible (Figure 2.3).

Figure 2.3 Alkyl groups generated from straight-chain alkanes.
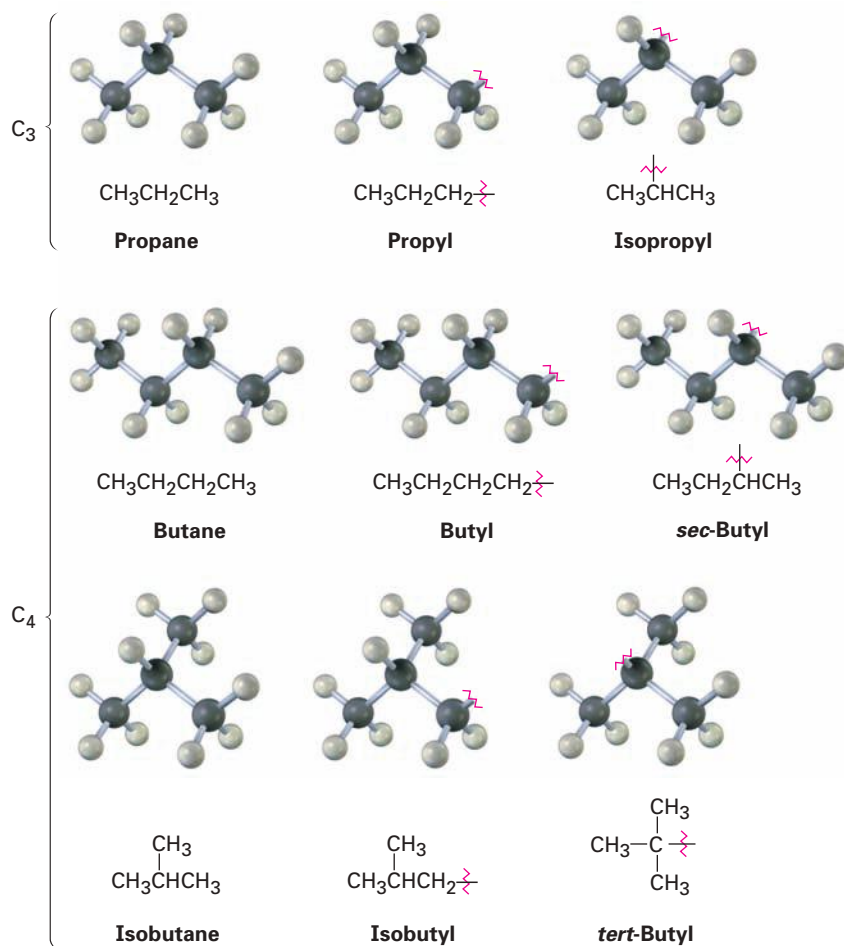

C3

CH3CH2CH3
Propane

CH3CH2CH2
Propyl

CH3CHCH3
Isopropyl

CH3CH2CH2CH3
Butane

CH3CH2CH2CH2
Butyl

CH3CH2CHCH3
***sec*-Butyl**

C4

CH3CHCH3
CH3
Isobutane

CH3CHCH2
CH3
Isobutyl

CH3—C
CH3
CH3
***tert*-Butyl**

Table **2.3**		Some Straight-Chain Alkyl Groups		
Alkane		**Name**	**Alkyl group**	**Name (abbreviation)**
CH_4		Methane	$-CH_3$	Methyl (Me)
CH_3CH_3		Ethane	$-CH_2CH_3$	Ethyl (Et)
$CH_3CH_2CH_3$		Propane	$-CH_2CH_2CH_3$	Propyl (Pr)
$CH_3CH_2CH_2CH_3$		Butane	$-CH_2CH_2CH_2CH_3$	Butyl (Bu)
$CH_3CH_2CH_2CH_2CH_3$		Pentane	$-CH_2CH_2CH_2CH_2CH_3$	Pentyl, or amyl

One further word about naming alkyl groups: the prefixes *sec-* (for secondary) and *tert-* (for tertiary) used for the C_4 alkyl groups in Figure 2.3 refer to the number of other carbon atoms attached to the branching carbon atom. There are four possibilities: primary (1°), secondary (2°), tertiary (3°), and quaternary (4°).

Primary carbon (1°)
is bonded to one
other carbon.

Secondary carbon (2°)
is bonded to two
other carbons.

Tertiary carbon (3°)
is bonded to three
other carbons.

Quaternary carbon (4°)
is bonded to four
other carbons.

The symbol **R** is used here and throughout this text to represent a *generalized* alkyl group. The R group can be methyl, ethyl, or any of a multitude of others. You might think of **R** as representing the **R**est of the molecule, which isn't specified.
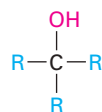
General class of tertiary
alcohols, R_3COH
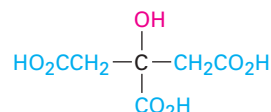
Citric acid—a specific
tertiary alcohol

Worked Example 2.1

Drawing Isomeric Structures

Propose structures for two isomers with the formula C_2H_6O.

Strategy   We know that carbon forms four bonds, oxygen forms two, and hydrogen forms one. Put the pieces together by trial and error, along with intuition.

Solution   There are two possibilities:
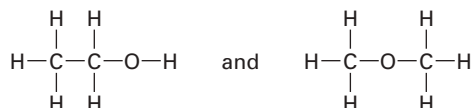
Problem 2.4 Draw structures for the five isomers of C_6H_{14}.

Problem 2.5 Draw structures that meet the following descriptions:
(a) Three isomers with the formula C_8H_{18}
(b) Two isomers with the formula $C_4H_8O_2$

Problem 2.6 Draw the eight possible five-carbon alkyl groups (pentyl isomers).

Problem 2.7 Draw alkanes that meet the following descriptions:
(a) An alkane with two tertiary carbons
(b) An alkane that contains an isopropyl group
(c) An alkane that has one quaternary and one secondary carbon

Problem 2.8 Identify the carbon atoms in the following molecules as primary, secondary, tertiary, or quaternary:

(a)
$$\begin{array}{c} CH_3 \\ | \\ CH_3CHCH_2CH_2CH_3 \end{array}$$

(b)
$$\begin{array}{c} CH_3CHCH_3 \\ | \\ CH_3CH_2CHCH_2CH_3 \end{array}$$

(c)
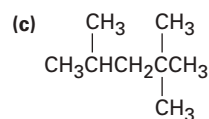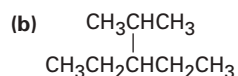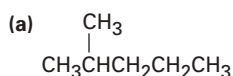$$\begin{array}{c} CH_3 \quad CH_3 \\ | \qquad | \\ CH_3CHCH_2CCH_3 \\ | \\ CH_3 \end{array}$$

2.3 Naming Branched-Chain Alkanes

In earlier times, when few pure organic chemicals were known, new compounds were named at the whim of their discoverer. Thus, urea (CH_4N_2O) is a crystalline substance isolated from urine, and morphine ($C_{17}H_{19}NO_3$) is an analgesic (painkiller) named after Morpheus, the Greek god of dreams. As the science of organic chemistry slowly grew in the 19th century, so too did the number of known compounds and the need for a systematic method of naming them. The system of naming (*nomenclature*) we'll use in this book is that devised by the International Union of Pure and Applied Chemistry (IUPAC, usually spoken as **eye**-you-pac).

A chemical name typically has four parts in the IUPAC system of nomenclature: prefix, parent, locant, and suffix. The prefix specifies the location and identity of various substituent groups in the molecule, the parent selects a main part of the molecule and tells how many carbon atoms are in that part, the locant gives the location of the primary functional group, and the suffix identifies the primary functional group.

Prefix—**Parent**—**Locant**—**Suffix**

Where and what are the substituents? | **How many carbons?** | **Where is the primary functional group?** | **What is the primary functional group?**

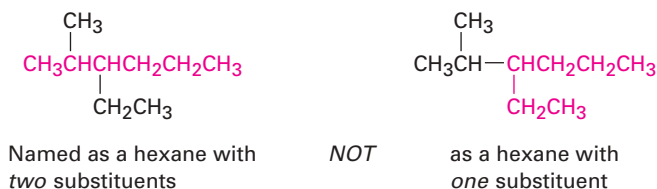As we cover new functional groups in later chapters, the applicable IUPAC rules of nomenclature will be given. In addition, Appendix A gives an overall view of organic nomenclature and shows how compounds that contain more than one functional group are named. For now, let's see how to name branched-chain alkanes. All but the most complex branched-chain alkanes can be named by following four steps.

STEP 1   **Find the parent hydrocarbon**.

(a) Find the longest continuous carbon chain in the molecule and use the name of that chain as the parent name. The longest chain may not always be obvious; you may have to "turn corners."

$$CH_3CH_2CH_2\underset{\underset{CH_2CH_3}{|}}{CH}-CH_3 \qquad \text{Named as a substituted hexane}$$

(b) If two chains of equal length are present, choose the one with the larger number of branch points as the parent.

$$\underset{\underset{CH_2CH_3}{|}}{CH_3\underset{\overset{|}{CH_3}}{CH}CHCH_2CH_2CH_3} \qquad\qquad CH_3\underset{\overset{|}{CH_3}}{CH}-\underset{\underset{CH_2CH_3}{|}}{CH}CH_2CH_2CH_3$$

Named as a hexane with *two* substituents   *NOT*   as a hexane with *one* substituent

STEP 2   **Number the atoms in the main chain**.

Beginning at the end nearer the first branch point, number each carbon atom in the parent chain.
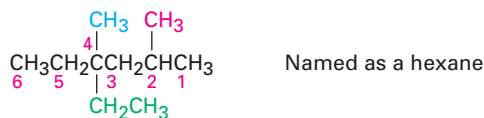
$$\overset{2\quad1}{CH_2CH_3} \\ CH_3-\underset{3}{CH}\underset{\overset{|4}{CH_2CH_2CH_3}}{CH}-CH_2CH_3 \qquad NOT \qquad \overset{6\quad7}{CH_2CH_3}\\ CH_3-\underset{5}{CH}\underset{\overset{|4}{CH_2CH_2CH_3}}{CH}-CH_2CH_3$$
$$\underset{5\quad6\quad7}{} \qquad\qquad\qquad \underset{3\quad2\quad1}{}$$

The first branch occurs at C3 in the proper system of numbering but at C4 in the improper system.

STEP 3   **Identify and number the substituents**.

Assign a number, called a *locant,* to each substituent to specify its point of attachment to the parent chain. If there are two substituents on the same carbon, assign them both the same number. There must always be as many numbers in the name as there are substituents.

$$\overset{9\quad8}{CH_3CH_2} \quad H_3C \quad \overset{}{CH_2CH_3}\\ CH_3-\underset{7}{CH}CH_2CH_2\underset{4}{CH}CHCH_2CH_3 \qquad \text{Named as a nonane}\\ \underset{6\quad5\quad4\quad3\quad2\quad1}{}$$
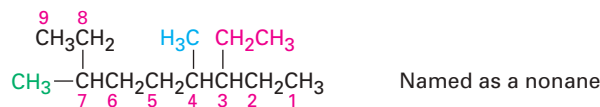
Substituents: On C3, CH_2CH_3 (3-ethyl)
                     On C4, CH_3 (4-methyl)
                     On C7, CH_3 (7-methyl)

$$\overset{CH_3\quad CH_3}{} \\ CH_3CH_2\underset{\overset{|3}{CH_2CH_3}}{CCH_2}\underset{2}{CH}CH_3 \qquad \text{Named as a hexane}\\ \underset{6\quad5}{} \quad \underset{2\quad1}{}$$

Substituents: On C2, CH_3 (2-methyl)
                     On C4, CH_3 (4-methyl)
                     On C4, CH_2CH_3 (4-ethyl)

STEP 4   **Write the name as a single word**.

Use hyphens to separate the various prefixes and commas to separate numbers. If two or more different side chains are present, cite them in alphabetical order. If two or more identical side chains are present, use the appropriate multiplier prefixes *di-*, *tri-*, *tetra-*, and so forth. Don't use these prefixes for alphabetizing, though. Full names for some examples follow:

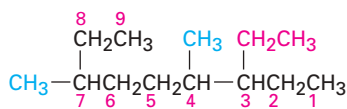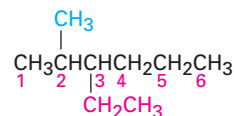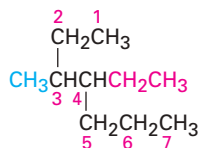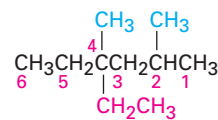$$\begin{array}{c} 2\quad1 \\ CH_2CH_3 \\ | \\ CH_3CH_2CH_2CH-CH_3 \\ 6\quad5\quad4\quad3\quad\quad\end{array}$$

3-Methylhexane

$$\begin{array}{c} 8\quad9\qquad\qquad\qquad \\ CH_2CH_3\quad CH_3\ CH_2CH_3 \\ |\qquad\quad|\qquad| \\ CH_3-CHCH_2CH_2CH-CHCH_2CH_3 \\ 7\quad6\quad5\quad4\quad\ 3\quad2\quad1 \end{array}$$
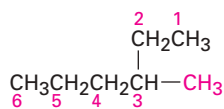
3-Ethyl-4,7-dimethylnonane

$$\begin{array}{c} CH_3 \\ | \\ CH_3CHCHCH_2CH_2CH_3 \\ 1\quad2\ |3\ 4\quad5\quad6 \\ CH_2CH_3 \end{array}$$

3-Ethyl-2-methylhexane

$$\begin{array}{c} 2\quad1 \\ CH_2CH_3 \\ | \\ CH_3CHCHCH_2CH_3 \\ 3\ 4| \\ CH_2CH_2CH_3 \\ 5\quad6\quad7 \end{array}$$

4-Ethyl-3-methylheptane

$$\begin{array}{c} CH_3\ CH_3 \\ 4|\quad\ | \\ CH_3CH_2CCH_2CHCH_3 \\ 6\quad5\ |3\quad2\quad1 \\ CH_2CH_3 \end{array}$$

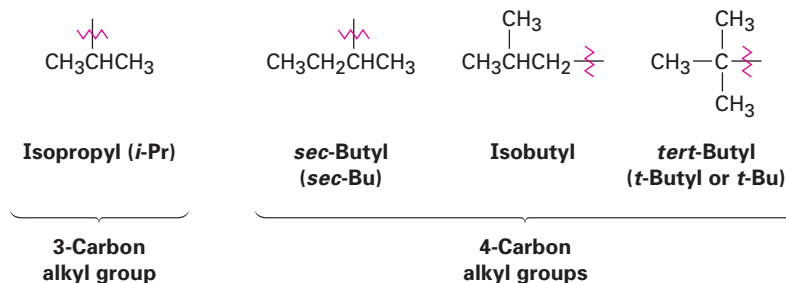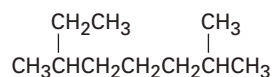**4-Ethyl-2,4-dimethylhexane**

For historical reasons, a few simple branched-chain alkyl groups also have nonsystematic, common names, as noted in Figure 2.3.

$$CH_3CHCH_3$$

Isopropyl (*i*-Pr)

$$CH_3CH_2CHCH_3$$

***sec*-Butyl (*sec*-Bu)**

$$\begin{array}{c} CH_3 \\ | \\ CH_3CHCH_2- \end{array}$$

Isobutyl

$$\begin{array}{c} CH_3 \\ | \\ CH_3-C- \\ | \\ CH_3 \end{array}$$

***tert*-Butyl (*t*-Butyl or *t*-Bu)**

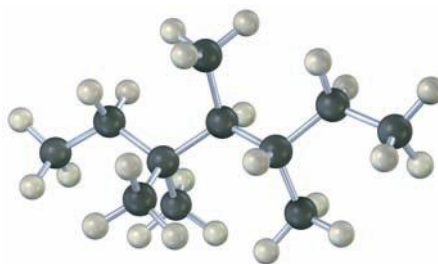|	
3-Carbon alkyl group	**4-Carbon alkyl groups**

When writing the name of an alkane that contains one of these alkyl groups, the nonhyphenated prefix iso- is considered part of the alkyl-group name for alphabetizing purposes, but the hyphenated and italicized prefixes *sec*- and *tert*- are not. Thus, isopropyl and isobutyl are listed alphabetically under *i*, but *sec*-butyl and *tert*-butyl are listed under *b*.

Worked Example 2.2   **Naming an Alkane**

What is the IUPAC name of the following alkane?

$$\begin{array}{c} CH_2CH_3\qquad\quad CH_3 \\ |\qquad\qquad\quad\ | \\ CH_3CHCH_2CH_2CH_2CHCH_3 \end{array}$$

Strategy   The molecule has a chain of eight carbons (octane) with two methyl substituents. Numbering from the end nearer the first methyl substituent indicates that the methyls are at C2 and C6.

Solution

$$\overset{7\quad 8}{CH_2CH_3} \qquad CH_3$$
$$CH_3CHCH_2CH_2CH_2CHCH_3$$
$$\underset{6\ \ 5\quad 4\quad 3\quad 2\ \ 1}{}$$

2,6-Dimethyloctane

Worked Example 2.3

Drawing a Structure from a Name

Draw the structure of 3-isopropyl-2-methylhexane.

Strategy   First, look at the parent name (hexane) and draw its carbon structure.

C–C–C–C–C–C   **Hexane**

Next, find the substituents (3-isopropyl and 2-methyl), and place them on the proper carbons.

CH₃CHCH₃ ⟵——— **An isopropyl group at C3**

C—C—C—C—C—C
1   2| 3   4   5   6
CH₃ ⟵——————— **A methyl group at C2**

Finally, add hydrogens to complete the structure.

Solution

CH₃CHCH₃
CH₃CHCHCH₂CH₂CH₃
CH₃

3-Isopropyl-2-methylhexane

Problem 2.9   Give IUPAC names for the following alkanes:

(a) The three isomers of C_5H_{12}

(b)
CH₃
CH₃CH₂CHCHCH₃
CH₂CH₃

(c)
CH₃   CH₃
CH₃CHCH₂CHCH₃

(d)
CH₃   CH₂CH₃
CH₃—C—CH₂CH₂CHCH₃
CH₃

Problem 2.10   Draw structures corresponding to the following IUPAC names:
(a) 3,4-Dimethylnonane   (b) 3-Ethyl-4,4-dimethylheptane
(c) 2,2-Dimethyl-4-propyloctane   (d) 2,2,4-Trimethylpentane
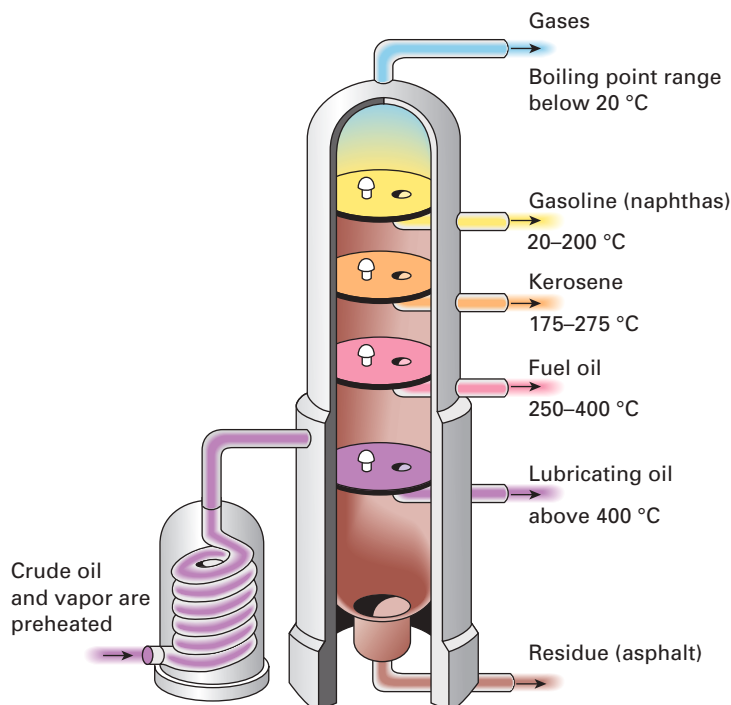
Problem 2.11   Name the following alkane:

2.4 | Properties of Alkanes

Many alkanes occur naturally in the plant and animal world. For example, the waxy coating on cabbage leaves contains nonacosane ($C_{29}H_{60}$), and the wood oil of the Jeffrey pine common to the Sierra Nevada mountains of California contains heptane (C_7H_{16}). By far the major sources of alkanes, however, are the world's natural gas and petroleum deposits. Laid down eons ago, these natural deposits are derived from the decomposition of plant and animal matter, primarily of marine origin. *Natural gas* consists chiefly of methane but also contains ethane, propane, and butane. *Petroleum* is a complex mixture of hydrocarbons that must first be separated into various fractions and then further refined before it can be used.

Petroleum refining begins by fractional distillation of crude oil into three principal cuts, according to their boiling points (bp): straight-run gasoline (bp 20–200 °C), kerosene (bp 175–275 °C), and heating oil, or diesel fuel (bp 250–400 °C). Finally, distillation under reduced pressure yields lubricating oils and waxes, and leaves an undistillable tarry residue of asphalt (Figure 2.4).

Figure 2.4 Fractional distillation separates petroleum into fractions according to boiling point. The temperature in the tower decreases with increasing height, allowing condensation of the vapors and collection of different components.

Alkanes are sometimes referred to as *paraffins,* a word derived from the Latin *parum affinis,* meaning "slight affinity." This term aptly describes their behavior, for alkanes show little chemical affinity for other substances and are inert to most laboratory reagents. They do, however, react under appropriate conditions with oxygen, chlorine, and a few other substances.

The reaction of an alkane with O_2 occurs during combustion in an engine or furnace when the alkane is used as a fuel. Carbon dioxide and water are formed as products, and a large amount of heat is released. For example, methane reacts with oxygen according to the equation:

$$CH_4 + 2\,O_2 \longrightarrow CO_2 + 2\,H_2O + \text{890 kJ (213 kcal)}$$

The reaction of an alkane with Cl_2 occurs when a mixture of the two is irradiated with ultraviolet light (denoted $h\nu$, where ν is the lowercase Greek letter nu). Depending on the relative amounts of the two reactants and on the time allowed for reaction, a sequential replacement of the alkane hydrogen atoms by chlorine occurs, leading to a mixture of chlorinated products. Methane, for instance, reacts with chlorine to yield a mixture of chloromethane (CH_3Cl), dichloromethane (CH_2Cl_2), trichloromethane ($CHCl_3$), and tetrachloromethane (CCl_4).

$$CH_4 \;+\; Cl_2 \;\xrightarrow{h\nu}\; CH_3Cl \;+\; HCl$$
$$\xrightarrow{Cl_2}\; CH_2Cl_2 \;+\; HCl$$
$$\xrightarrow{Cl_2}\; CHCl_3 \;+\; HCl$$
$$\xrightarrow{Cl_2}\; CCl_4 \;+\; HCl$$

2.5 Conformations of Ethane

We know from Section 1.7 that a carbon–carbon single bond results from the head-on overlap of two atomic orbitals. Because the amount of this orbital overlap is the same regardless of the geometric arrangements of other atoms attached to the carbons, *rotation* is possible around carbon–carbon single bonds. In ethane, for instance, rotation around the C–C bond occurs freely, constantly changing the geometric relationships between the hydrogens on one carbon and those on the other (Figure 2.5). The different arrangements of atoms that result from bond rotation are called **conformations**, and molecules that have different arrangements are called conformational isomers, or *conformers*. Unlike constitutional isomers, however, different conformers can't usually be isolated because they interconvert too rapidly.

Figure 2.5 Two conformations of ethane. Rotation around the C–C single bond interconverts the different conformations.

Chemists represent different conformations in two ways, as shown in Figure 2.6. A **sawhorse representation** views the C–C bond from an oblique angle and indicates spatial relationships by showing all the C–H bonds. A **Newman projection** views the C–C bond directly end-on and represents the two carbon atoms by a circle. Bonds attached to the front carbon are represented by lines to a dot in the center of the circle, and bonds attached to the rear carbon are represented by lines to the edge of the circle.

Figure 2.6 A sawhorse representation and a Newman projection of ethane. The sawhorse representation views the molecule from an oblique angle, while the Newman projection views the molecule end-on. Note that the molecular model of the Newman projection appears at first to have six atoms attached to a single carbon. Actually, the front carbon, with three attached green atoms, is directly in front of the rear carbon, with three attached red atoms.

Sawhorse representation

Newman projection
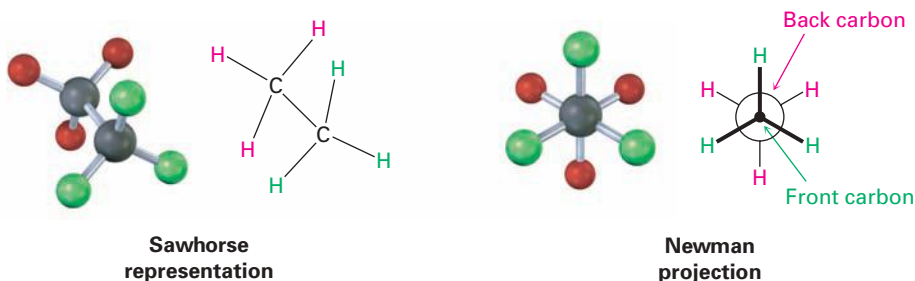
Despite what we've just said, we actually don't observe *perfectly* free rotation in ethane. Experiments show that there is a slight (12 kJ/mol; 2.9 kcal/mol) barrier to rotation and that some conformations are more stable than others. The lowest-energy, most stable conformation is the one in which all six C–H bonds are as far away from one another as possible (**staggered** when viewed end-on in a Newman projection). The highest-energy, least stable conformation is the one in which the six C–H bonds are as close as possible (**eclipsed** in a Newman projection). At any given instant, about 99% of ethane molecules have an approximately staggered conformation, and only about 1% are close to the eclipsed conformation (Figure 2.7).

Figure 2.7 Staggered and eclipsed conformations of ethane. The staggered conformation is lower in energy and more stable by 12.0 kJ/mol.

Ethane—staggered conformation

Rotate rear carbon 60°

Ethane—eclipsed conformation
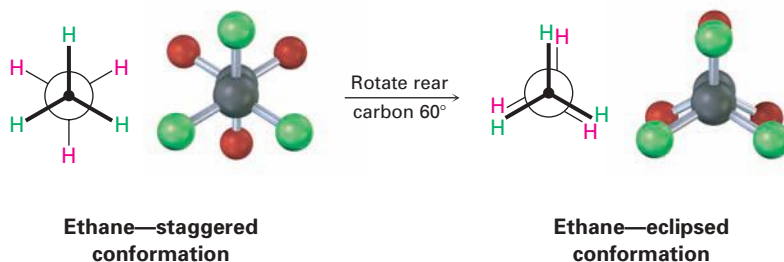
What is true for ethane is also true for propane, butane, and all higher alkanes. The most favored conformation for any alkane is the one in which all bonds have staggered arrangements (Figure 2.8).

Figure 2.8 The most stable conformation of any alkane is the one in which the bonds on adjacent carbons are staggered and the carbon chain is fully extended so that large groups are far away from one another, as in this model of decane.
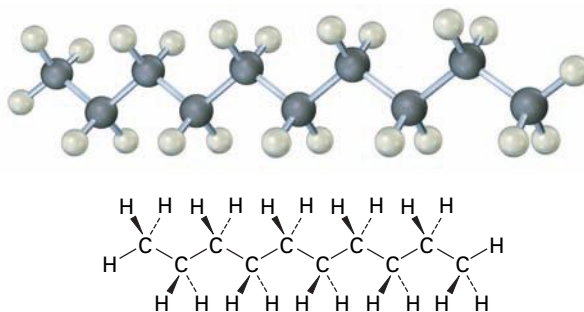
Worked Example 2.4

Drawing a Newman Projection

Sight along the C1–C2 bond of 1-chloropropane and draw Newman projections of the most stable and least stable conformations.

Strategy

The most stable conformation of a substituted alkane is generally a staggered one in which large groups are as far away from one another as possible. The least stable conformation is generally an eclipsed one in which large groups are as close as possible.

Solution
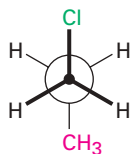
Most stable (staggered)   **Least stable (eclipsed)**
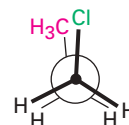
Problem 2.12

Sight along a C–C bond of propane and draw a Newman projection of the most stable conformation. Draw a Newman projection of the least stable conformation.

Problem 2.13

Looking along the C2–C3 bond of butane, there are two different staggered conformations and two different eclipsed conformations. Draw them.

Problem 2.14

Which of the butane conformations you drew in Problem 2.13 do you think is the most stable? Explain.

2.6 Drawing Chemical Structures

In the structures we've been using, a line between atoms has represented the two electrons in a covalent bond. Drawing every bond and every atom is tedious, however, so chemists have devised a shorthand way of drawing **skeletal structures** that greatly simplifies matters. Drawing skeletal structures is straightforward:

- Carbon atoms usually aren't shown. Instead, a carbon atom is assumed to be at the intersection of two lines (bonds) and at the end of each line. Occasionally, a carbon atom might be indicated for emphasis or clarity.
- Hydrogen atoms bonded to carbon aren't shown. Because carbon always has a valence of four, we mentally supply the correct number of hydrogen atoms for each carbon.
- All atoms other than carbon and hydrogen *are* shown.

The following structures give some examples.
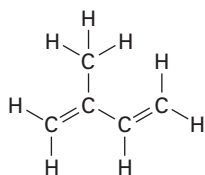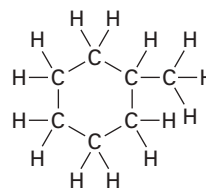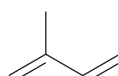
Isoprene, C_5H_8   **Methylcyclohexane, C_7H_{14}**
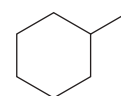
One further comment: although such groupings as $-CH_3$, $-OH$, and $-NH_2$ are usually written with the C, O, or N atom first and the H atom second, the order of writing is sometimes inverted to H_3C-, $HO-$, and H_2N- if needed to make the bonding connections in a molecule clearer. Larger units such as $-CH_2CH_3$ are not inverted, though; we don't write H_3CH_2C- because it would be confusing. There are, however, no well-defined rules that cover all cases; it's largely a matter of preference.

Inverted order to
show C–C bond

H_3C CH_3

HO OH

Inverted order to
show O–C bond

Not inverted

CH_3CH_2 CH_2CH_3

H_2N NH_2

Inverted order to
show N–C bond
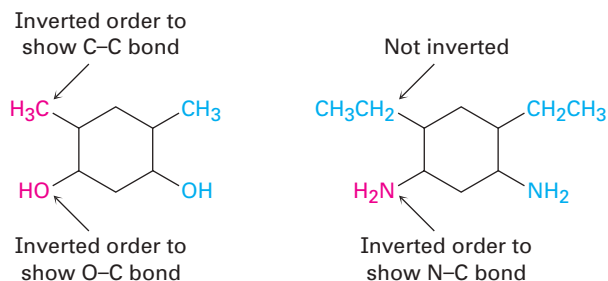
Worked Example 2.5

Interpreting a Skeletal Structure

Carvone, a substance responsible for the odor of spearmint, has the following structure. Tell how many hydrogens are bonded to each carbon, and give the molecular formula of carvone.

Carvone
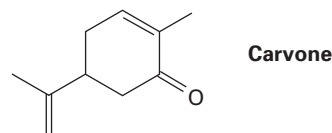
Strategy Remember that the end of a line represents a carbon atom with three hydrogens, CH_3; a two-way intersection is a carbon atom with two hydrogens, CH_2; a three-way intersection is a carbon atom with one hydrogen, CH; and a four-way intersection is a carbon atom with no attached hydrogens.

Solution

0H
1H
2H   3H
3H   0H
0H 1H   O
2H
2H

Carvone, $C_{10}H_{14}O$
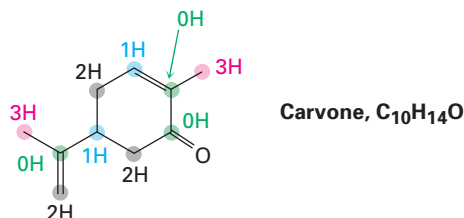
Problem 2.15 Convert the following skeletal structures into molecular formulas, and tell how many hydrogens are bonded to each carbon:

(a)   (b)   O   (c)

N   N
                                            H
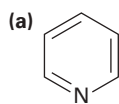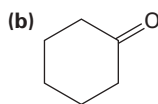
Pyridine   **Cyclohexanone**   **Indole**
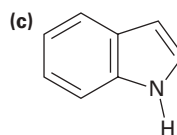
Problem 2.16   Propose skeletal structures for the following molecular formulas:

(a) C_4H_8 **(b)** C_3H_6O **(c)** C_4H_9Cl

Problem 2.17   The following molecular model is a representation of *para*-aminobenzoic acid (PABA), the active ingredient in many sunscreens. Indicate the positions of the multiple bonds, and draw a skeletal structure (gray = C, red = O, blue = N, ivory = H).
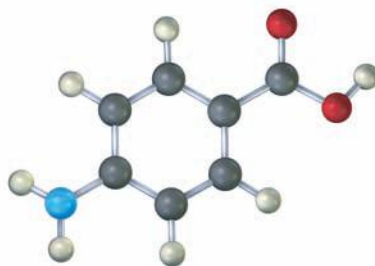
para-Aminobenzoic acid (PABA)

2.7 Cycloalkanes

We've discussed only open-chain alkanes thus far, but compounds with *rings* of carbon atoms are actually more common. Saturated cyclic hydrocarbons are called **cycloalkanes**, or *alicyclic* (*ali*phatic *cyclic*) compounds, and have the general formula $(CH_2)_n$, or C_nH_{2n}. In skeletal drawings, they are represented by polygons.

Cyclopropane   **Cyclobutane**   **Cyclopentane**   **Cyclohexane**
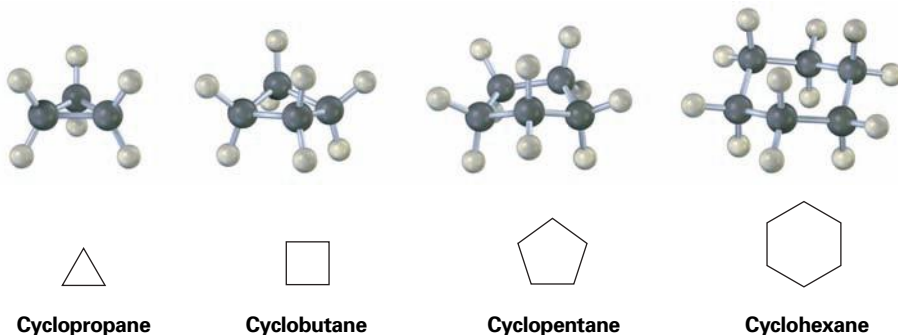
Substituted cycloalkanes are named by rules similar to those for open-chain alkanes. For most compounds, there are only two steps.

STEP 1   **Find the parent.**

Count the number of carbon atoms in the ring and the number in the largest substituent chain. If the number of carbon atoms in the ring is equal to or greater than the number in the substituent, the compound is named as an alkyl-substituted cycloalkane. If the number of carbon atoms in the largest

substituent is greater than the number in the ring, the compound is named as a cycloalkyl-substituted alkane.

Methylcyclopentane   **1-Cyclopropylbutane**
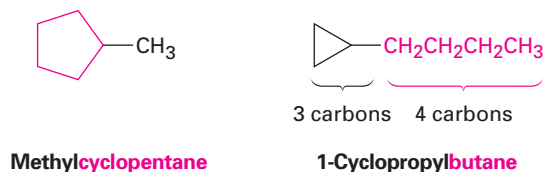
STEP 2   **Number the substituents, and write the name.**

For substituted cycloalkanes, start at a point of attachment and number around the ring. If two or more substituents are present, begin numbering at the group that has alphabetical priority and proceed around the ring so as to give the second substituent the lowest number.

1,3-Dimethylcyclohexane   *NOT*   **1,5-Dimethylcyclohexane**

Lower   Higher

1-Ethyl-2,6-dimethylcycloheptane

Higher

2-Ethyl-1,4-dimethylcycloheptane   *NOT*

Lower   Lower

3-Ethyl-1,4-dimethylcycloheptane

Higher
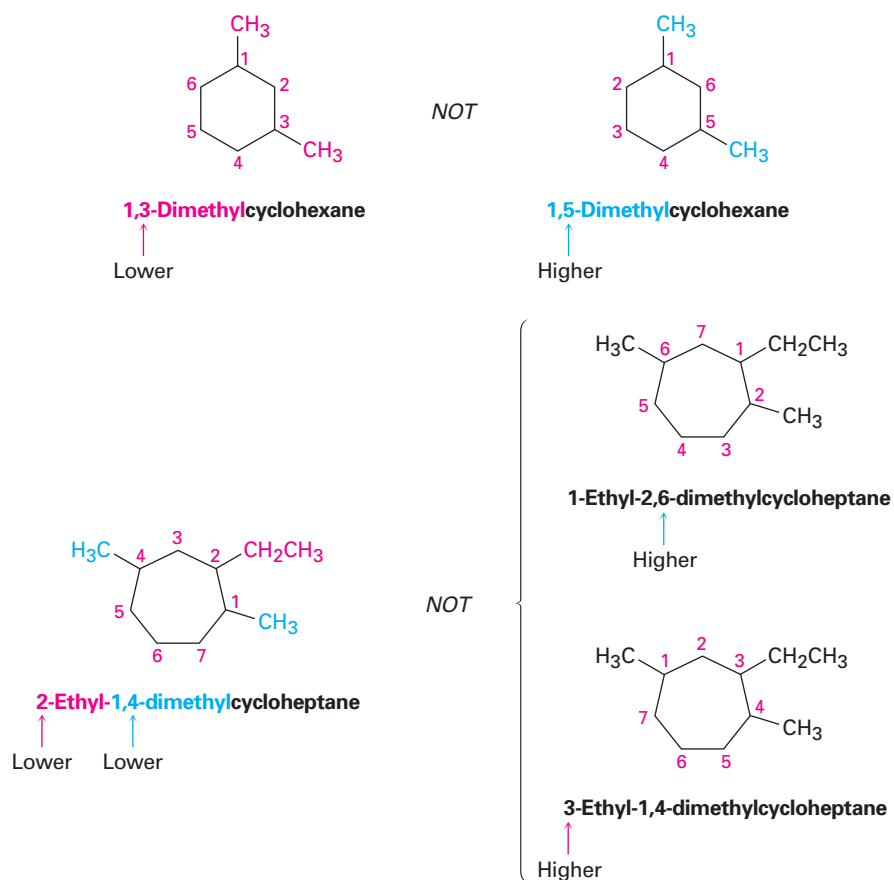
Problem 2.18   Give IUPAC names for the following cycloalkanes:
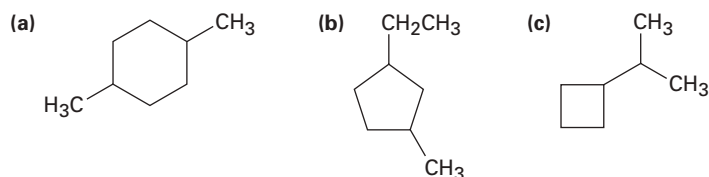
Problem 2.19 Draw structures corresponding to the following IUPAC names:

(a) 1-*tert*-Butyl-2-methylcyclopentane   **(b)** 1,1-Dimethylcyclobutane
(c) 1-Ethyl-4-isopropylcyclohexane   **(d)** 3-Cyclopropylhexane

2.8 Cis–Trans Isomerism in Cycloalkanes

In many respects, the behavior of cycloalkanes is similar to that of open-chain, acyclic alkanes. Both are nonpolar and chemically inert to most reagents. There are, however, some important differences. One difference is that cycloalkanes are less flexible than their open-chain counterparts. Although open-chain alkanes have nearly free rotation around their C–C single bonds, cycloalkanes have much less freedom of motion. Cyclopropane, for example, must be a rigid, planar molecule. No rotation around a C–C bond can take place in cyclopropane without breaking open the ring (Figure 2.9).
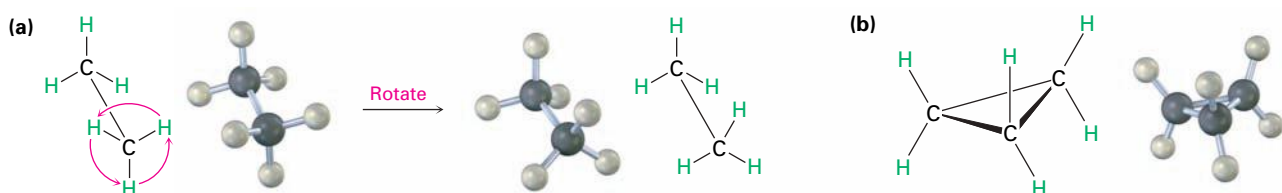
Figure 2.9 **(a)** Rotation occurs around the carbon–carbon bond in ethane, but **(b)** no rotation is possible around the carbon–carbon bonds in cyclopropane without breaking open the ring.

Because of their cyclic structures, cycloalkanes have two sides: a "top" side and a "bottom" side. As a result, isomerism is possible in substituted cycloalkanes. For example, there are two 1,2-dimethylcyclopropane isomers, one with the two methyl groups on the same side of the ring and one with the methyls on opposite sides. Both isomers are stable compounds, and neither can be converted into the other without breaking bonds (Figure 2.10).

cis-1,2-Dimethylcyclopropane   *trans*-1,2-Dimethylcyclopropane
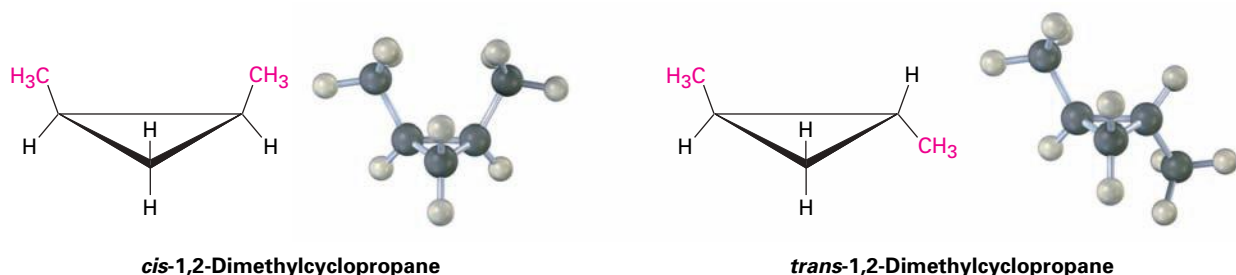
Figure 2.10 There are two different 1,2-dimethylcyclopropane isomers: one with the methyl groups on the same side of the ring (cis) and the other with the methyl groups on opposite sides of the ring (trans). The two isomers do not interconvert.

Unlike the constitutional isomers butane and isobutane (Section 2.2), which have their atoms connected in a different order, the two 1,2-dimethylcyclopropanes have the same order of connections but differ in the spatial orientation of the atoms. Such compounds, which have their atoms connected in the same order but differ in three-dimensional orientation, are called

stereochemical isomers, or **stereoisomers**. More generally, the term **stereochemistry** is used to refer to the three-dimensional aspects of chemical structure and reactivity.

Constitutional isomers (different connections between atoms)

$$CH_3-\overset{\overset{\displaystyle CH_3}{|}}{CH}-CH_3 \quad \text{and} \quad CH_3-CH_2-CH_2-CH_3$$
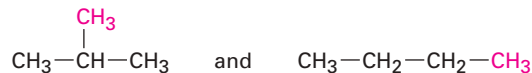
Stereoisomers (same connections but different three-dimensional geometry)

 and
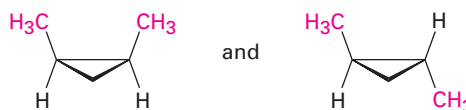
The 1,2-dimethylcyclopropanes are members of a subclass of stereoisomers called **cis–trans isomers**. The prefixes *cis-* (Latin, "on the same side") and *trans-* (Latin, "across") are used to distinguish between them. Cis–trans isomerism is a common occurrence in substituted cycloalkanes and in many cyclic biological molecules.

Worked Example 2.6

Naming Cis–Trans Cycloalkane Isomers

Name the following substances, including the *cis-* or *trans-* prefix:

(a)   **(b)**
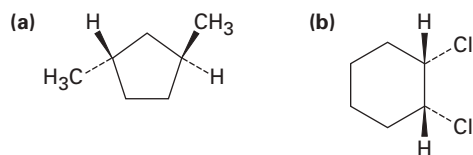
Strategy   In these views, the ring is roughly in the plane of the page, a wedged bond protrudes out of the page, and a dashed bond recedes into the page. Two substituents are cis if they are both out of or both into the page, and they are trans if one is out of and one is into the page.

Solution   **(a)** *trans*-1,3-Dimethylcyclopentane   **(b)** *cis*-1,2-Dichlorocyclohexane

Problem 2.20   Draw *cis*-1-chloro-3-methylcyclopentane.

Problem 2.21   Draw both cis and trans isomers of 1,2-dibromocyclobutane.

Problem 2.22   Prostaglandin $F_{2\alpha}$, a hormone that causes uterine contraction during childbirth, has the following structure. Are the two hydroxyl groups (−OH) on the cyclopentane ring cis or trans to each other? What about the two carbon chains attached to the ring?

Prostaglandin $F_{2\alpha}$
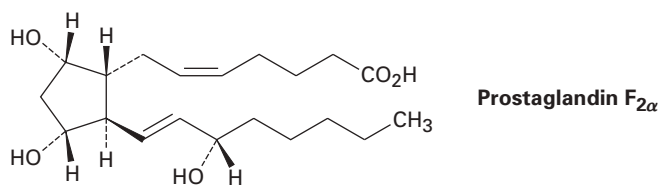
Problem 2.23   Name the following substances, including the *cis*- or *trans*- prefix (red-brown = Br):

(a)

(b)
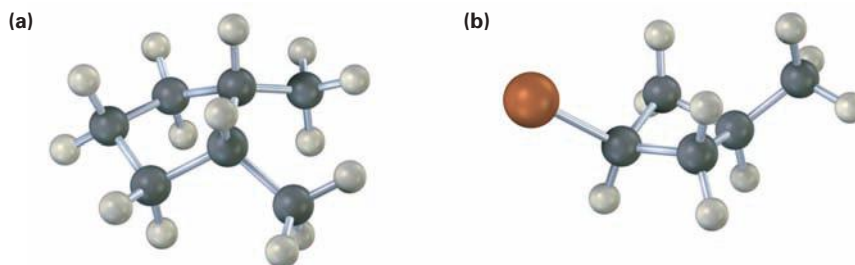
2.9 | Conformations of Some Cycloalkanes

In the early days of organic chemistry, cycloalkanes provoked a good deal of consternation among chemists. The problem was that if carbon prefers to have bond angles of 109.5°, how is it possible for cyclopropane and cyclobutane to exist? After all, cyclopropane must have a triangular shape with bond angles near 60°, and cyclobutane must have a roughly square shape with bond angles near 90°. Nonetheless, these compounds *do* exist and are stable. Let's look at the most common cycloalkanes.

Cyclopropane, Cyclobutane, and Cyclopentane

Cyclopropane is a flat, triangular molecule with C–C–C bond angles of 60°, as indicated in Figure 2.11a. The deviation of bond angles from the normal 109.5° tetrahedral value causes an **angle strain** in the molecule that raises its energy and makes it more reactive than unstrained alkanes. All six of the C–H bonds have an eclipsed, rather than staggered, arrangement with their neighbors.

Cyclobutane and cyclopentane are slightly puckered rather than flat, as indicated in Figure 2.11b–c. This puckering makes the C–C–C bond angles a bit smaller than they would otherwise be and increases the angle strain. At the same time, though, the puckering relieves the unfavorable eclipsing interactions of adjacent C–H bonds that would occur if the rings were flat.

Figure 2.11 The structures of **(a)** cyclopropane, **(b)** cyclobutane, and **(c)** cyclopentane. Cyclopropane is planar, but cyclobutane and cyclopentane are slightly puckered.

(a)   **(b)**   **(c)**

Cyclohexane

Substituted cyclohexanes are the most common cycloalkanes and occur widely in nature. A large number of compounds, including steroids and many pharmaceutical agents, have cyclohexane rings. The flavoring agent menthol, for instance, has three substituents on a six-membered ring.

Menthol
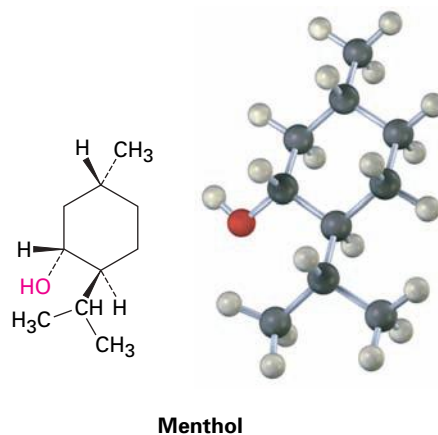
Figure 2.12 The strain-free, chair conformation of cyclohexane. All C–C–C bond angles are close to 109°, and all neighboring C–H bonds are staggered, as evident in the end-on view in **(c)**.

Cyclohexane is not flat. Rather, it is puckered into a strain-free, three-dimensional shape called a **chair conformation** because of its similarity to a lounge chair, with a back, a seat, and a footrest (Figure 2.12). All C–C–C bond angles are near 109°, and all adjacent C–H bonds are staggered.

(a)

(b)

Observer

(c)
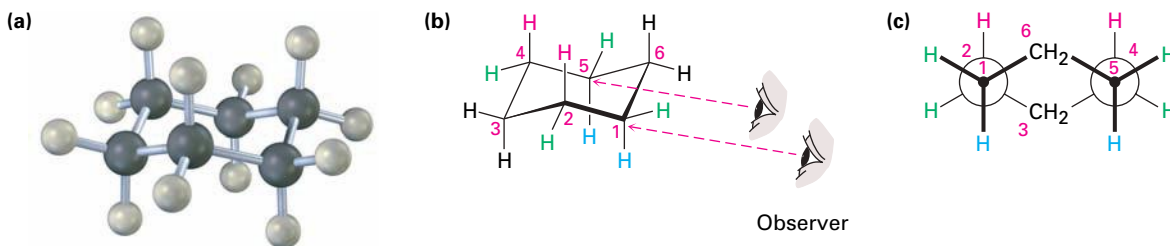
A chair conformation is drawn in three steps.

STEP 1 Draw two parallel lines, slanted downward and slightly offset from each other. This means that four of the cyclohexane carbons lie in a plane.

STEP 2 Place the topmost carbon atom above and to the right of the plane of the other four, and connect the bonds.

STEP 3 Place the bottommost carbon atom below and to the left of the plane of the middle four, and connect the bonds. Note that the bonds to the bottommost carbon atom are parallel to the bonds to the topmost carbon.
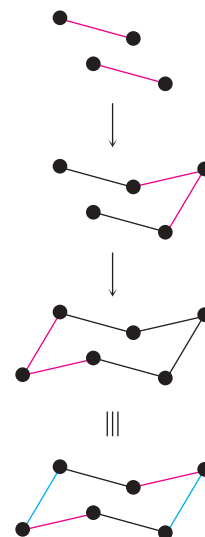
When viewing cyclohexane, it's helpful to remember that the lower bond is in front and the upper bond is in back. If this convention is not defined, an optical illusion can make it appear that the reverse is true. For clarity, all

cyclohexane rings drawn in this book will have the front (lower) bond heavily shaded to indicate nearness to the viewer.

This bond is in back.

This bond is in front.

2.10 Axial and Equatorial Bonds in Cyclohexane

The chair conformation of cyclohexane leads to many consequences. We'll see in Section 14.5, for instance, that simple carbohydrates, such as glucose, adopt a conformation based on the cyclohexane chair and that their chemistry is directly affected as a result.

Cyclohexane
(chair conformation)

Glucose
(chair conformation)
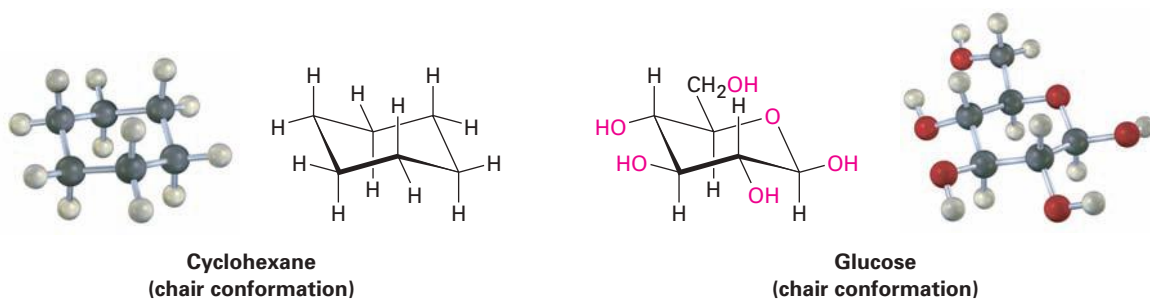
Another consequence of the chair conformation is that there are two kinds of positions for substituents on the cyclohexane ring: *axial* positions and *equatorial* positions (Figure 2.13). The six **axial positions** are perpendicular to the ring, parallel to the ring axis, and the six **equatorial positions** are in the rough plane of the ring, around the ring equator. Each carbon atom has one axial and one equatorial position, and each side of the ring has three axial and three equatorial positions in an alternating arrangement.

Figure 2.13 Axial (red) and equatorial (blue) positions in chair cyclohexane. The six axial hydrogens are parallel to the ring axis, and the six equatorial hydrogens are in a band around the ring equator.

Ring axis
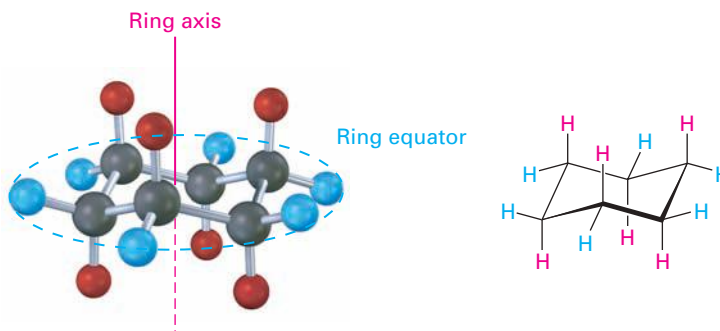
Ring equator

Note that we haven't used the words *cis* and *trans* in this discussion of cyclohexane conformation. Two hydrogens on the same side of a ring are always cis, regardless of whether they're axial or equatorial and regardless of

whether they're adjacent. Similarly, two hydrogens on opposite sides of the ring are always trans.

Axial and equatorial bonds can be drawn by following the procedure in Figure 2.14.

Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up–down.

Equatorial bonds: The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alternate between sides around the ring.

Completed cyclohexane
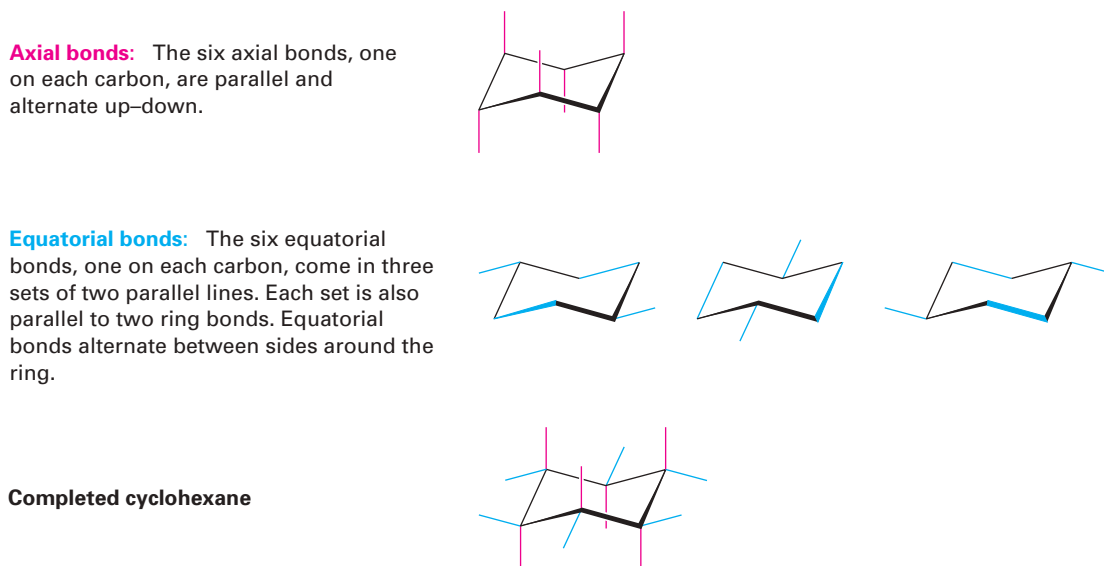
Figure 2.14 A procedure for drawing axial and equatorial bonds in cyclohexane.

Problem 2.24   Draw two chair structures for methylcyclohexane, one with the methyl group axial and one with the methyl group equatorial.

2.11 Conformational Mobility of Cyclohexane

Because chair cyclohexane has two kinds of positions, axial and equatorial, we might expect to find two isomeric forms of a monosubstituted cyclohexane. In fact, we don't. There is only *one* methylcyclohexane, *one* bromocyclohexane, *one* cyclohexanol (hydroxycyclohexane), and so on, because cyclohexane rings are *conformationally mobile* at room temperature. Different chair conformations readily interconvert by a process called a **ring-flip**.

The ring-flip of a chair cyclohexane can be visualized as shown in Figure 2.15 by keeping the middle four carbon atoms in place while folding the two ends in opposite directions. An axial substituent in one chair form becomes an equatorial substituent in the ring-flipped chair form and vice versa. For example, axial methylcyclohexane becomes equatorial methylcyclohexane after ring-flip. Because this interconversion occurs rapidly at room temperature, the individual axial and equatorial isomers can't be isolated.
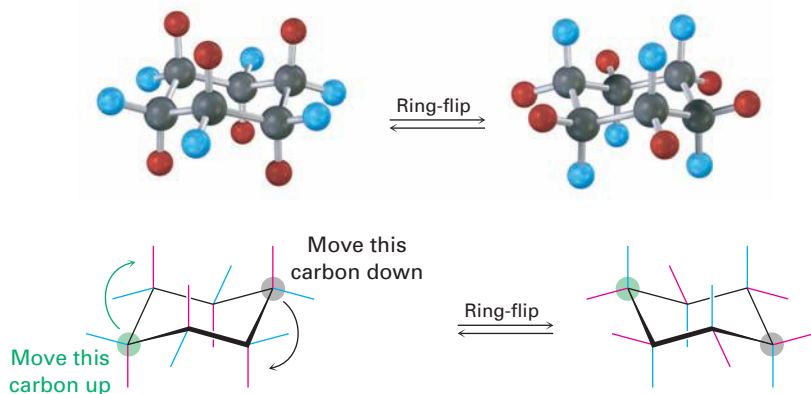
Figure 2.15 A ring-flip in chair cyclohexane interconverts axial and equatorial positions. What is axial (red) in the starting structure becomes equatorial in the ring-flipped structure, and what is equatorial (blue) in the starting structure is axial after ring-flip.

Although axial and equatorial methylcyclohexanes interconvert rapidly, they aren't equally stable. The equatorial conformation is more stable than the axial conformation by 7.6 kJ/mol (1.8 kcal/mol), meaning that about 95% of methylcyclohexane molecules have their methyl group equatorial at any given instant. The energy difference is due to an unfavorable spatial, or *steric,* interaction that occurs in the axial conformation between the methyl group on carbon 1 and the axial hydrogen atoms on carbons 3 and 5. This so-called 1,3-diaxial interaction introduces 7.6 kJ/mol of **steric strain** into the molecule because the axial methyl group and the nearby axial hydrogen are too close together (Figure 2.16).
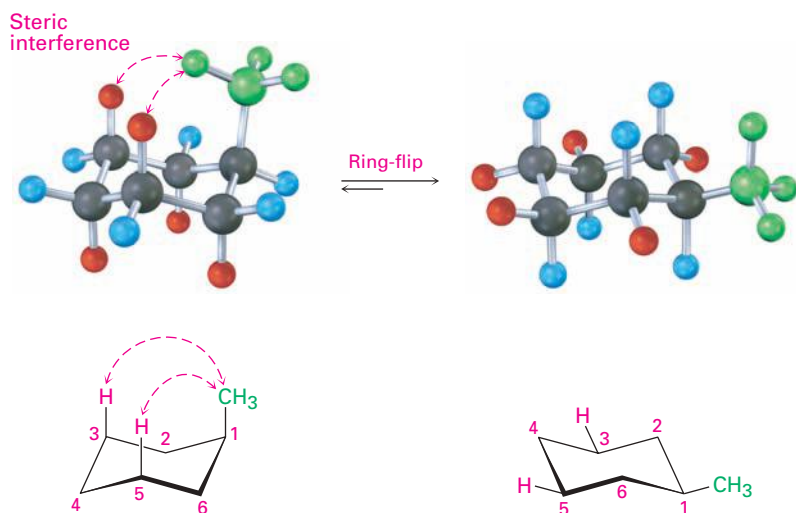
Figure 2.16 Axial versus equatorial methylcyclohexane. The 1,3-diaxial steric interactions in axial methylcyclohexane (easier to see in space-filling models) make the equatorial conformation more stable by 7.6 kJ/mol.

What is true for methylcyclohexane is also true for other monosubstituted cyclohexanes: a substituent is always more stable in an equatorial position than in an axial position. As you might expect, the amount of steric strain increases as the size of the axial substituent group increases.

Worked Example 2.7

Drawing Conformations of Substituted Cyclohexanes

Draw 1,1-dimethylcyclohexane in a chair conformation, indicating which methyl group in your drawing is axial and which is equatorial.

Strategy   Draw a chair cyclohexane ring, and then put two methyl groups on the same carbon. The methyl group in the rough plane of the ring is equatorial, and the one directly above or below the ring is axial.

Solution

Axial methyl group

CH₃

CH₃

Equatorial methyl group
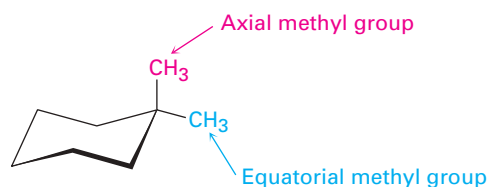
Problem 2.25   Draw two different chair conformations of bromocyclohexane showing all hydrogen atoms. Label all positions as axial or equatorial. Which of the two conformations do you think is more stable?

Problem 2.26   Draw *cis*-1,2-dichlorocyclohexane in a chair conformation, and explain why one chlorine must be axial and one equatorial.

Problem 2.27   Draw *trans*-1,2-dichlorocyclohexane in chair conformation, and explain why both chlorines must be axial or both equatorial.

Problem 2.28   Identify each substituent as axial or equatorial, and tell whether the conformation shown is the more stable or less stable chair form (gray = C, yellow-green = Cl, ivory = H).
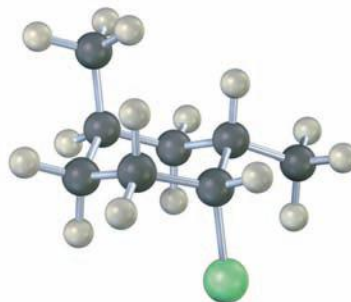
Where Do Drugs Come From?

Approved for sale in March 1998 to treat male impotency, Viagra has been used by more than 16 million men. It is also used to treat pulmonary hypertension and is currently undergoing study as a treatment for preeclampsia, a complication of pregnancy that is responsible for as many as 70,000 deaths each year. Where do new drugs like this come from?

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It has been estimated that major pharmaceutical companies in the United States spend some $33 billion per year on drug research and development, while government agencies and private foundations spend another $28 billion. What does this money buy? For the period 1981 to 2004, the money resulted in a total of 912 new molecular entities (NMEs)—new biologically active chemical substances approved for sale as drugs by the U.S. Food and Drug Administration (FDA). That's an average of only 38 new drugs each year spread over all diseases and conditions, and the number has been steadily falling: in 2004, only 23 NMEs were approved.

Where do the new drugs come from? According to a study carried out at the U.S. National Cancer Institute, only 33% of new drugs are entirely synthetic and completely unrelated to any naturally occurring substance. The remaining 67% take their lead, to a greater or lesser extent, from nature. Vaccines and genetically engineered proteins of biological origin account for 15% of NMEs, but most new drugs come from *natural products,* a catchall term generally taken to mean small molecules found in bacteria, plants, and other living organisms. Unmodified natural products isolated directly from the producing organism account for 28% of NMEs, while natural products that have been chemically modified in the laboratory account for the remaining 24%.

Origin of New Drugs 1981–2004

Natural products (28%)

Natural product related (24%)

Biological (15%)

Synthetic (33%)
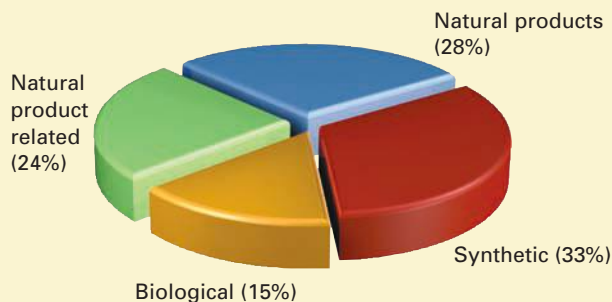
Many years of work go into screening many thousands of substances to identify a single compound that might ultimately gain approval as an NME. But after that single compound has been identified, the work has just begun because it takes an average of 9 to 10 years for a drug to make it through the approval process. First, the safety of the drug in animals must be demonstrated and an economical method of manufacture must be devised. With these preliminaries out of the way, an Investigational New Drug (IND) application is submitted to the FDA for permission to begin testing in humans.

Human testing takes 5 to 7 years and is divided into three phases. Phase I clinical trials are carried out on a small group of healthy volunteers to establish safety and look for side effects. Several months to a year are needed, and only about 70% of drugs pass at this point. Phase

II clinical trials next test the drug for 1 to 2 years in several hundred patients with the target disease or condition, looking both for safety and for efficacy, and only about 33% of the original group pass. Finally, phase III trials are undertaken on a large sample of patients to document definitively the drug's safety, dosage, and efficacy. If the drug is one of the 25% of the original group that make it to the end of phase III, all the data are then gathered into a New Drug Application (NDA) and sent to the FDA for review and approval, which can take another 2 years. Ten years have elapsed and at least $500 million has been spent, with only a 20% success rate for the drugs that began testing. Finally, though, the drug will begin to appear in medicine cabinets. The following timeline shows the process.
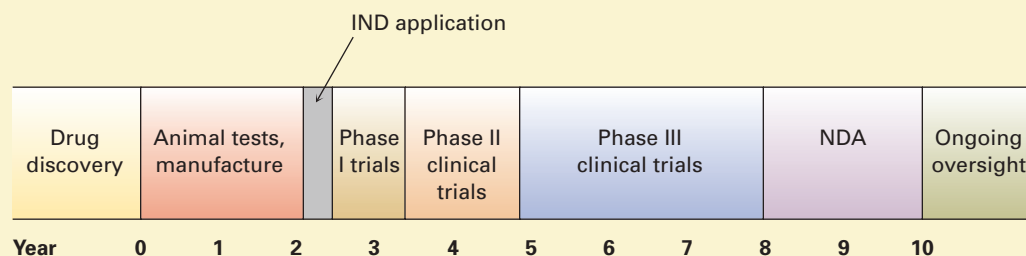
IND application

Drug discovery	Animal tests, manufacture	Phase I trials	Phase II clinical trials	Phase III clinical trials	NDA	Ongoing oversight

Year	0	1	2	3	4	5	6	7	8	9	10

Summary and Key Words

Even though alkanes are relatively unreactive and rarely involved in chemical reactions, they nevertheless provide a useful vehicle for introducing some important general ideas. In this chapter, we've used alkanes to introduce the basic approach to naming organic compounds and to take an initial look at some of the three-dimensional aspects of molecules.

A **functional group** is an atom or group of atoms within a larger molecule that has a characteristic chemical reactivity. Because functional groups behave approximately the same way in all molecules in which they occur, the reactions of an organic molecule are largely determined by its functional groups.

Alkanes are a class of **saturated hydrocarbons** having the general formula C_nH_{2n+2}. They contain no functional groups, are chemically rather inert, and can be either **straight-chain** or **branched**. Alkanes are named systematically by a series of IUPAC rules of nomenclature. **Isomers**—compounds that have the same chemical formula but different structures—exist for all but the simplest alkanes. Compounds such as butane and isobutane, which have the same formula but differ in the way their atoms are connected, are called **constitutional isomers**.

Because C–C single bonds are formed by head-on orbital overlap, rotation is possible about them. Alkanes can therefore adopt any of a large number of rapidly interconverting **conformations**. A **staggered conformation** is more stable than an **eclipsed conformation**.

Cycloalkanes contain rings of carbon atoms and have the general formula C_nH_{2n}. Because complete rotation around C–C bonds is not possible in cycloalkanes, conformational mobility is reduced and disubstituted cycloalkanes can exist as **cis–trans stereoisomers**. In a cis isomer, both substituents are on the same side of the ring, whereas in a trans isomer, the substituents are on opposite sides of the ring.

Cyclohexanes are the most common of all rings because of their wide occurrence in nature. Cyclohexane exists in a puckered, strain-free **chair conformation** in which all bond angles are near 109° and all neighboring C–H bonds are staggered. Chair cyclohexane has two kinds of bonding positions: axial and equatorial. **Axial bonds** are directed up and down, parallel to the ring axis; **equatorial bonds** lie in a belt around the ring equator. Chair cyclohexanes can undergo a **ring-flip** that interconverts axial and equatorial positions. Substituents on the ring are more stable in the equatorial than in the axial position.

Exercises

Visualizing Chemistry

(Problems 2.1–2.28 appear within the chapter.)

Interactive versions of these problems are assignable in OWL.

2.29 Give IUPAC names for the following substances, and convert each drawing into a skeletal structure.

(a)
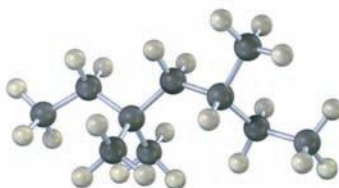
(b)
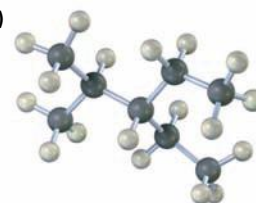
(c)

(d)
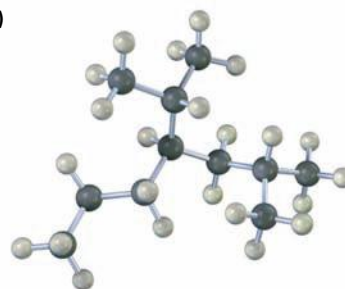
2.30 Identify the functional groups in the following substances, and convert each drawing into a molecular formula (gray = C, red = O, blue = N, ivory = H).

(a)
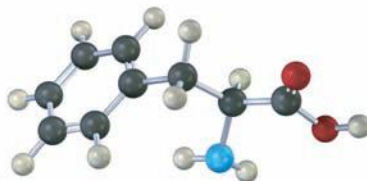
Phenylalanine

(b)
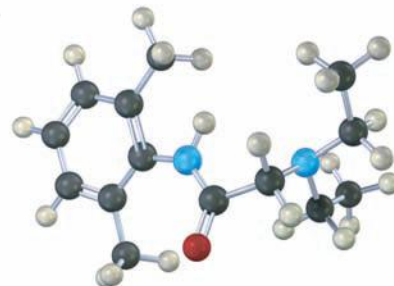
Lidocaine

2.31 The following cyclohexane derivative has three substituents—red, green, and blue. Identify each substituent as axial or equatorial, and identify each pair of relationships (red–blue, red–green, and blue–green) as cis or trans.
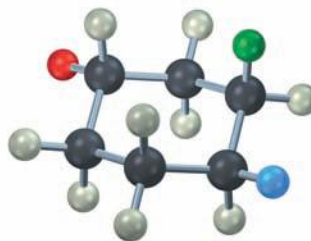
2.32 A trisubstituted cyclohexane with three substituents—red, green, and blue—undergoes a ring-flip to its alternative chair conformation. Identify each substituent as axial or equatorial, and show the positions occupied by the three substituents in the ring-flipped form.
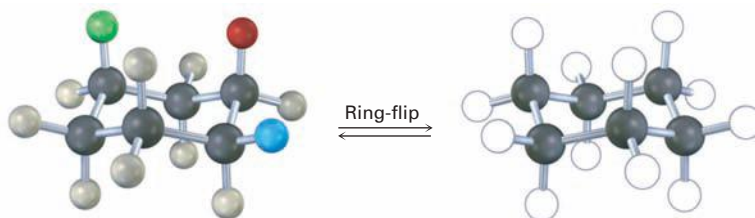
2.33 Glucose exists in two forms having a 36:64 ratio at equilibrium. Draw a skeletal structure of each, describe the difference between them, and tell which of the two you think is more stable (red = O).
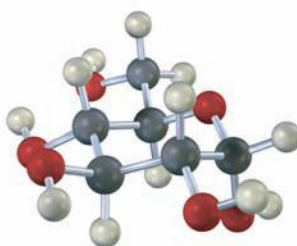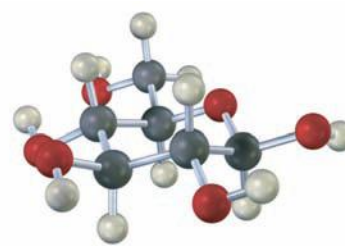
α-Glucose   *β*-Glucose

Additional Problems

FUNCTIONAL GROUPS AND ISOMERISM

2.34 Locate and identify the functional groups in the following molecules. Each intersection of lines and the end of each line represents a carbon atom with the appropriate number of hydrogens attached.
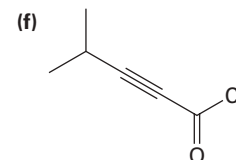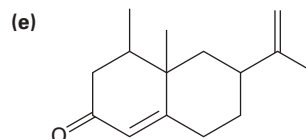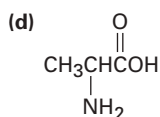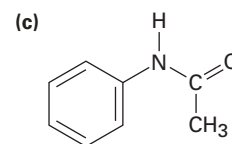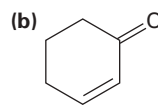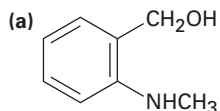
2.35 Propose structures for molecules that fit the following descriptions:
(a) An alkene with six carbons   (b) A cycloalkene with five carbons
(c) A ketone with five carbons   (d) An amide with four carbons
(e) A five-carbon ester   (f) An aromatic alcohol

2.36 Propose suitable structures for the following:
(a) An alkene, C_7H_{14} (b) A cycloalkene, C_3H_4
(c) A ketone, C_4H_8O (d) A nitrile, C_5H_9N
(e) A dialkene, C_5H_8 (f) A dialdehyde, $C_4H_6O_2$

2.37 Write as many structures as you can that fit the following descriptions:
(a) Alcohols with formula $C_4H_{10}O$ (b) Amines with formula $C_5H_{13}N$
(c) Ketones with formula $C_5H_{10}O$ (d) Aldehydes with formula $C_5H_{10}O$
(e) Ethers with formula $C_4H_{10}O$ (f) Esters with formula $C_4H_8O_2$

2.38 Draw all monobromo derivatives of pentane, $C_5H_{11}Br$.

2.39 Draw all monochloro derivatives of 2,5-dimethylhexane.

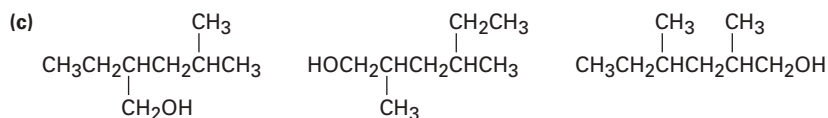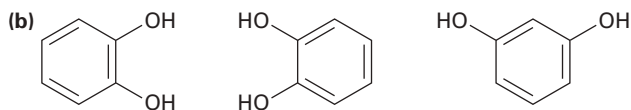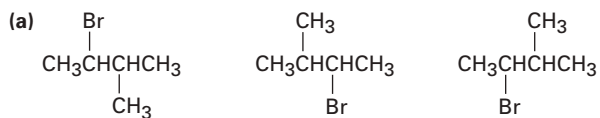**2.40** How many constitutional isomers are there with the formula C_3H_8O? Draw them.

2.41 Propose structures for compounds that contain the following:
(a) A quaternary carbon
(b) Four methyl groups
(c) An isopropyl group
(d) Two tertiary carbons
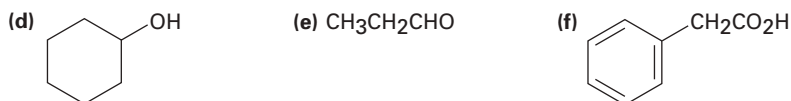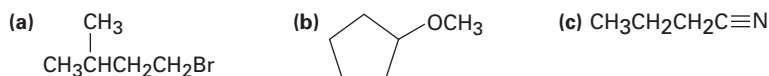(e) An amino group ($-NH_2$) bonded to a secondary carbon

2.42 What hybridization do you expect for the carbon atom in the following functional groups?
(a) Carboxylic acid chloride   (b) Thiol   (c) Imine   (d) Aldehyde

2.43 In each of the following sets, which structures represent the same compound and which represent different compounds?

(a)

$$\underset{\underset{CH_3}{|}}{CH_3CHCHCH_3} \qquad \underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{CH_3CHCHCH_3}} \qquad \underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{CH_3CHCHCH_3}}$$

Br   CH₃   CH₃

(b)

(c)

$$\underset{\underset{CH_2OH}{|}}{\overset{\overset{CH_3}{|}}{CH_3CH_2CHCH_2CHCH_3}} \qquad \underset{\underset{CH_3}{|}}{\overset{\overset{CH_2CH_3}{|}}{HOCH_2CHCH_2CHCH_3}} \qquad \overset{\overset{CH_3 \quad CH_3}{| \quad \ \ |}}{CH_3CH_2CHCH_2CHCH_2OH}$$

2.44 For each of the following compounds, draw a constitutional isomer with the same functional groups:

(a) $\underset{\underset{CH_3}{|}}{CH_3CHCH_2CH_2Br}$ CH₃
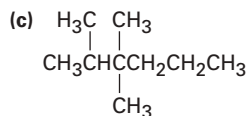
(b) (cyclopentane)—OCH₃

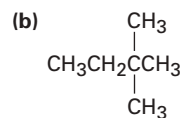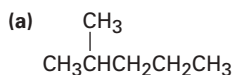(c) $CH_3CH_2CH_2C{\equiv}N$

(d) (cyclohexane)—OH

(e) CH_3CH_2CHO
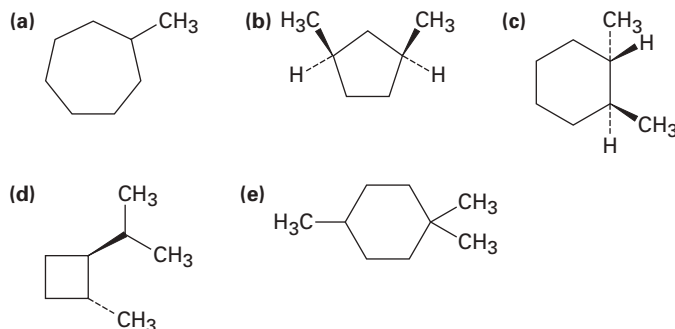
(f) (benzene ring)—CH₂CO₂H

2.45 Draw structures for the following substances:
(a) 2-Methylheptane (b) 4-Ethyl-2-methylhexane
(c) 4-Ethyl-3,4-dimethyloctane (d) 2,4,4-Trimethylheptane
(e) 1,1-Dimethylcyclopentane (f) 4-Isopropyl-3-methylheptane

2.46 Give IUPAC names for the following alkanes:

(a) $\underset{}{\overset{\overset{CH_3}{|}}{CH_3CHCH_2CH_2CH_3}}$

(b) $\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{CH_3CH_2CCH_3}}$

(c) $\underset{\underset{CH_3}{|}}{\overset{\overset{H_3C \ \ CH_3}{| \ \ |}}{CH_3CHCCH_2CH_2CH_3}}$

(d) $\underset{}{\overset{\overset{CH_2CH_3 \quad CH_3}{| \qquad \ \ |}}{CH_3CH_2CHCH_2CH_2CHCH_3}}$

(e) $\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3 \quad CH_2CH_3}{| \qquad \ |}}{CH_3CH_2CH_2CHCH_2CCH_3}}$

(f) $\underset{\underset{H_3C \ \ CH_3}{| \quad \ \ |}}{\overset{\overset{H_3C \ \ CH_3}{| \quad \ \ |}}{CH_3C{-}CCH_2CH_2CH_3}}$
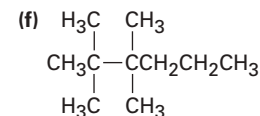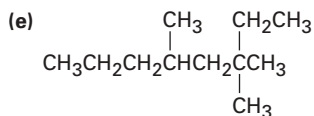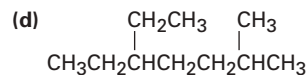
2.47 Give IUPAC names for the following compounds:

(a)   (b)   (c)

(d)   (e)

2.48 Draw and name the five isomers of C_6H_{14}.

2.49 Propose structures and give IUPAC names for the following:
  (a) A dimethyloctane
  (b) A diethyldimethylhexane
  (c) A cycloalkane with three methyl groups

2.50 The following names are incorrect. Draw the structures represented, and give the proper IUPAC names.
  (a) 2,2-Dimethyl-6-ethylheptane   (b) 4-Ethyl-5,5-dimethylpentane
  (c) 3-Ethyl-4,4-dimethylhexane   (d) 5,5,6-Trimethyloctane

**2.51** Draw the structures of the following molecules:
  (a) *Biacetyl,* $C_4H_6O_2$, a substance with the aroma of butter; it contains no rings or carbon–carbon multiple bonds.
  (b) *Ethylenimine,* C_2H_5N, a substance used in the synthesis of melamine polymers; it contains no multiple bonds.
  (c) *Glycerol,* $C_3H_8O_3$, a substance used in cosmetics; it has an –OH group on each carbon.

CONFORMATIONS AND CIS-TRANS ISOMERISM

2.52 Sighting along the C2–C3 bond of 2-methylbutane, there are two different staggered conformations. Draw them both in Newman projections, tell which is more stable, and explain your choice.

2.53 Sighting along the C2–C3 bond of 2-methylbutane (see Problem 2.52), there are also two possible eclipsed conformations. Draw them both in Newman projections, tell which you think is lower in energy, and explain.

2.54 *cis*-1-*tert*-Butyl-4-methylcyclohexane exists almost exclusively in the conformation shown. What does this tell you about the relative sizes of a *tert*-butyl substituent and a methyl substituent?


***cis*-1-*tert*-Butyl-4-methylcyclohexane**
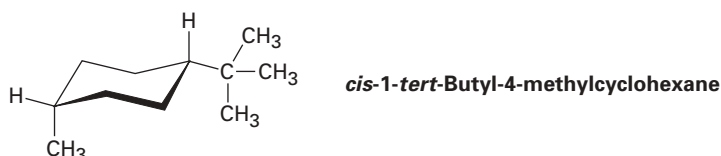
2.55 The barrier to rotation about the C–C bond in bromoethane is 15.0 kJ/mol (3.6 kcal/mol). If each hydrogen–hydrogen interaction in the eclipsed conformation is responsible for 3.8 kJ/mol (0.9 kcal/mol), how much is the hydrogen–bromine eclipsing interaction responsible for?

2.56 Tell whether the following pairs of compounds are identical, constitutional isomers, stereoisomers, or unrelated.

(a) *cis*-1,3-Dibromocyclohexane and *trans*-1,4-dibromocyclohexane

(b) 2,3-Dimethylhexane and 2,3,3-trimethylpentane

(c)
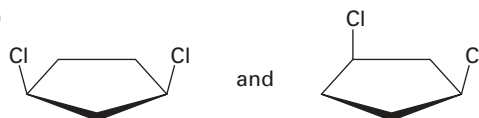
2.57 Draw two constitutional isomers of *cis*-1,2-dibromocyclopentane.

2.58 Draw a stereoisomer of *trans*-1,3-dimethylcyclobutane.

2.59 Draw *trans*-1,2-dimethylcyclohexane in its more stable chair conformation. Are the methyl groups axial or equatorial?

2.60 Draw *cis*-1,2-dimethylcyclohexane in its more stable chair conformation. Are the methyl groups axial or equatorial? Which is more stable, *cis*-1,2-dimethylcyclohexane or *trans*-1,2-dimethylcyclohexane (Problem 2.59)? Explain.

2.61 Which is more stable, *cis*-1,3-dimethylcyclohexane or *trans*-1,3-dimethylcyclohexane? Draw chair conformations of both, and explain your answer.

GENERAL PROBLEMS

2.62 Malic acid, $C_4H_6O_5$, has been isolated from apples. Because malic acid reacts with 2 equivalents of base, it can be formulated as a dicarboxylic acid (that is, it has two $-CO_2H$ groups).
(a) Draw at least five possible structures for malic acid.
(b) If malic acid is also a secondary alcohol (has an $-OH$ group attached to a secondary carbon), what is its structure?

2.63 *N*-Methylpiperidine has the conformation shown. What does this tell you about the relative steric requirements of a methyl group versus an electron lone pair?


N-**Methylpiperidine**
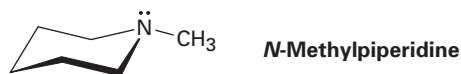
2.64 Identify each pair of relationships among the $-OH$ groups in glucose (red–blue, red–green, red–black, blue–green, blue–black, green–black) as cis or trans.
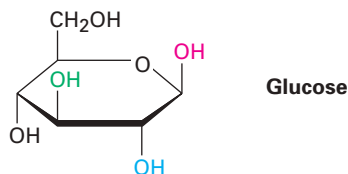

Glucose

2.65 Galactose, a sugar related to glucose, contains a six-membered ring in which all the substituents except the −OH group indicated below in red are equatorial. Draw galactose in its more stable chair conformation.

Galactose
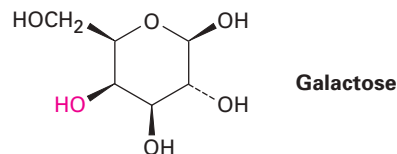
2.66 Draw 1,3,5-trimethylcyclohexane using a hexagon to represent the ring. How many cis–trans stereoisomers are possible?

2.67 One of the two chair structures of *cis*-1-chloro-3-methylcyclohexane is more stable than the other by 15.5 kJ/mol (3.7 kcal/mol). Which is it?

**2.68** Draw the two chair conformations of menthol, and tell which is more stable.
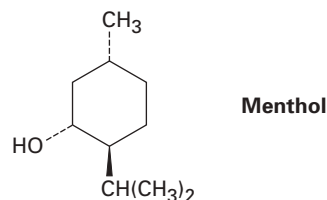
Menthol

2.69 There are four cis–trans isomers of menthol (Problem 2.68), including the one shown. Draw the other three.

2.70 Here's a tough one. There are two different substances named *trans*-1,2-dimethylcyclopentane. What is the relationship between them? (We'll explore this kind of isomerism in Chapter 6.)


and
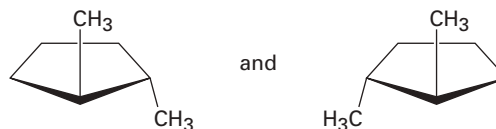
2.71 Hydrocortisone, a naturally occurring hormone produced in the adrenal glands, is often used to treat inflammation, severe allergies, and numerous other conditions. Is the indicated −OH group in the molecule axial or equatorial?

Hydrocortisone
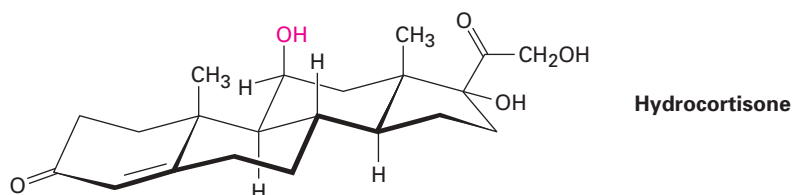
2.72 Amantadine is an antiviral agent that is active against influenza A infection. Draw a three-dimensional representation of amantadine showing the chair cyclohexane rings.

Amantadine
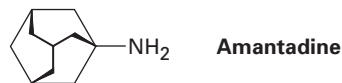
2.73 The so-called statin drugs, such as simvastatin (Zocor), pravastatin (Pravachol), and atorvastatin (Lipitor) are the most widely prescribed drugs in the world, with annual sales estimated at approximately $15 billion.

Zocor (Merck)   **Pravachol (Bristol-Myers Squibb)**   **Lipitor (Pfizer)**
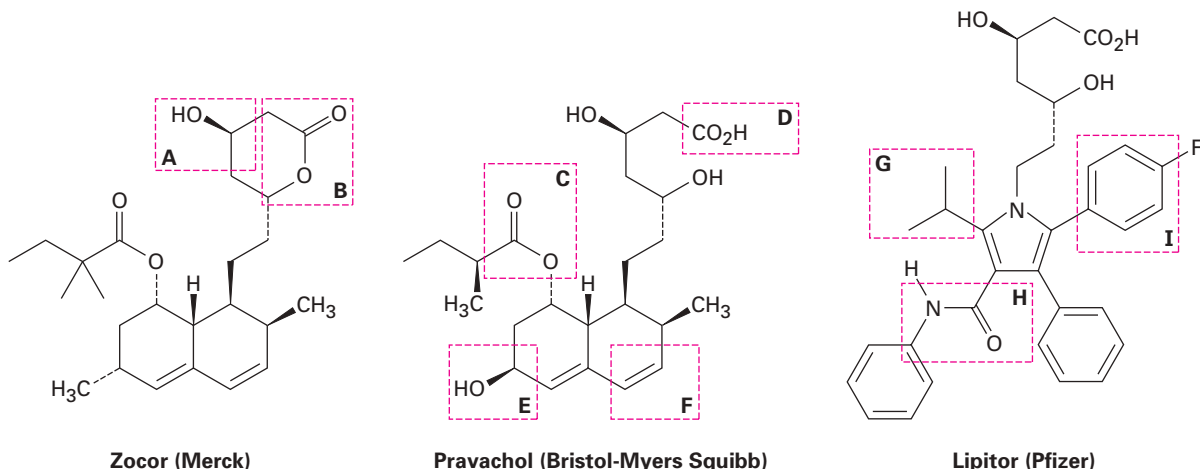
(a) Identify the functional groups (or alkyl groups) labeled **A–I**.
(b) Are the groups **C** and **E** on Pravachol cis or trans?
(c) Why can't groups **G**, **H**, and **I** be identified as cis or trans?

IN THE FIELD **2.74** Metolachlor, a herbicide marketed under the names Bicep, CGA-24705, Dual, Pennant, and Pimagram, is used to control weeds and grasses in fields of plants such as corn, soybeans, cotton, and peanuts. Metolachlor is degraded through oxidation in the environment to produce the water-soluble derivative shown. Identify the three functional groups in metolachlor and the new functional group in the derivative.

Metolachlor   **Metolachlor oxanilic acid**