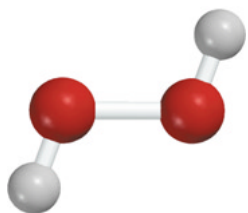


CHAPTER 3

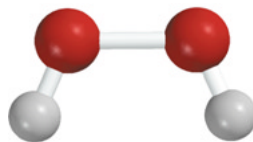
CONFORMATIONS OF ALKANES AND CYCLOALKANES

Hydrogen peroxide is formed in the cells of plants and animals but is toxic to them. Consequently, living systems have developed mechanisms to rid themselves of hydrogen peroxide, usually by enzyme-catalyzed reduction to water. An understanding of how reactions take place, be they reactions in living systems or reactions in test tubes, begins with a thorough knowledge of the structure of the reactants, products, and catalysts. Even a simple molecule such as hydrogen peroxide may be structurally more complicated than you think. Suppose we wanted to write the structural formula for H_2O_2 in enough detail to show the positions of the atoms relative to one another. We could write two different planar geometries A and B that differ by a 180° rotation about the O—O bond. We could also write an infinite number of nonplanar structures, of which C is but one example, that differ from one another by tiny increments of rotation about the O—O bond.

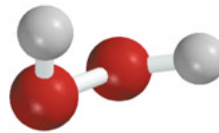
Structures A, B, and C represent different **conformations** of hydrogen peroxide. *Conformations are different spatial arrangements of a molecule that are generated by rotation about single bonds.* Although we can't tell from simply looking at these structures, we now know from experimental studies that C is the most stable conformation.



A



B



C

Learning By Modeling

contains an animation showing the rotation about the O—O bond in hydrogen peroxide.



In this chapter we'll examine the conformations of various alkanes and cycloalkanes, focusing most of our attention on three of them: *ethane*, *butane*, and *cyclohexane*. A detailed study of even these three will take us a long way toward understanding the main ideas of **conformational analysis**.

The conformation of a molecule affects many of its properties. Conformational analysis is a tool used not only by chemists but also by researchers in the life sciences as they attempt to develop a clearer picture of how molecules—as simple as hydrogen peroxide or as complicated as DNA—behave in biological processes.

3.1 CONFORMATIONAL ANALYSIS OF ETHANE

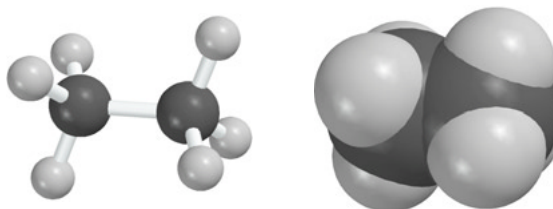
Ethane is the simplest hydrocarbon that can have distinct conformations. Two, the **staggered conformation** and the **eclipsed conformation**, deserve special attention and are illustrated in Figure 3.1. The C—H bonds in the staggered conformation are arranged so that each one bisects the angle made by a pair of C—H bonds on the adjacent carbon. In the eclipsed conformation each C—H bond is aligned with a C—H bond on the adjacent carbon. The staggered and eclipsed conformations interconvert by rotation around the carbon–carbon bond. Different conformations of the same molecule are sometimes called **conformers** or **rotamers**.

Among the various ways in which the staggered and eclipsed forms are portrayed, wedge-and-dash, sawhorse, and Newman projection drawings are especially useful. These are shown for the staggered conformation of ethane in Figure 3.2 and for the eclipsed conformation in Figure 3.3.

We used *wedge-and-dash* drawings in earlier chapters, and so Figures 3.2*a* and 3.3*a* are familiar to us. A *sawhorse* drawing (Figures 3.2*b* and 3.3*b*) shows the conformation of a molecule without having to resort to different styles of bonds. In a *Newman projection* (Figures 3.2*c* and 3.3*c*), we sight down the C—C bond, and represent the front carbon by a point and the back carbon by a circle. Each carbon has three substituents that are placed symmetrically around it.

Newman projections were devised by Professor Melvin S. Newman of Ohio State University in the 1950s.

Staggered conformation of ethane



Eclipsed conformation of ethane

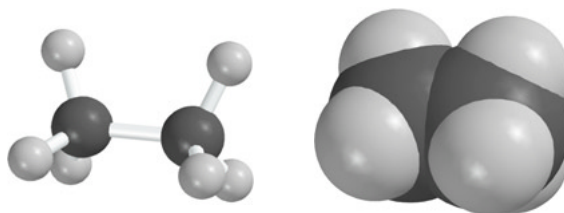


FIGURE 3.1 The staggered and eclipsed conformations of ethane shown as ball-and-spoke models (*left*) and as space-filling models (*right*).



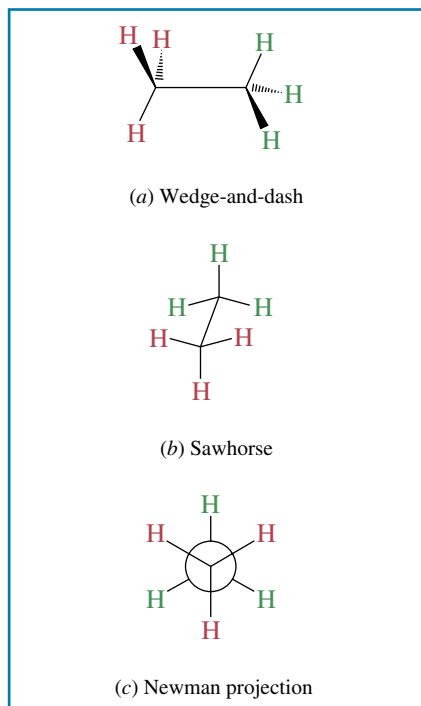


FIGURE 3.2 Some commonly used representations of the staggered conformation of ethane.

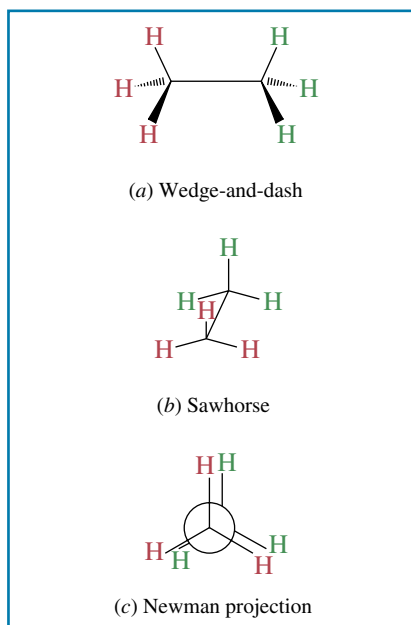
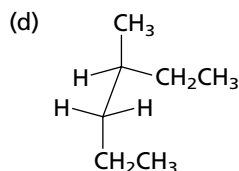
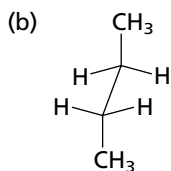
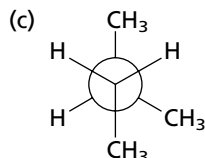
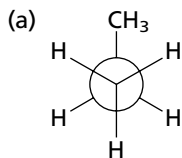


FIGURE 3.3 Some commonly used representations of the eclipsed conformation of ethane.

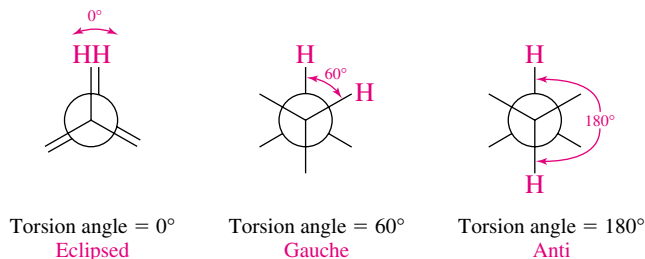
PROBLEM 3.1 Identify the alkanes corresponding to each of the drawings shown.



SAMPLE SOLUTION (a) The Newman projection of this alkane resembles that of ethane except one of the hydrogens has been replaced by a methyl group. The drawing is a Newman projection of propane, $\text{CH}_3\text{CH}_2\text{CH}_3$.

The structural feature that Figures 3.2 and 3.3 illustrate is the spatial relationship between atoms on adjacent carbon atoms. Each $\text{H}-\text{C}-\text{C}-\text{H}$ unit in ethane is characterized by a *torsion angle* or *dihedral angle*, which is the angle between the $\text{H}-\text{C}-\text{C}$

plane and the C—C—H plane. The torsion angle is easily seen in a Newman projection of ethane as the angle between C—H bonds of adjacent carbons.



Eclipsed bonds are characterized by a torsion angle of 0°. When the torsion angle is approximately 60°, we say that the spatial relationship is **gauche**; and when it is 180° we say that it is **anti**. Staggered conformations have only gauche or anti relationships between bonds on adjacent atoms.

Of the two conformations of ethane, the staggered is more stable than the eclipsed. The measured difference in potential energy between them is 12 kJ/mol (2.9 kcal/mol). A simple explanation has echoes of VSEPR (Section 1.10). The staggered conformation allows the electron pairs in the C—H bonds of one carbon to be farther away from the electron pairs in the C—H bonds of the other than the eclipsed conformation allows. Electron-pair repulsions on adjacent carbons govern the relative stability of staggered and eclipsed conformations in much the same way that electron-pair repulsions influence the bond angles at a central atom.

The destabilization that comes from eclipsed bonds on adjacent atoms is called **torsional strain**. Torsional strain is one of several structural features resulting from its three-dimensional makeup that destabilize a molecule. The total strain of all of the spatially dependent features is often called **steric strain**. Because three pairs of eclipsed bonds produce 12 kJ/mol (2.9 kcal/mol) of torsional strain in ethane, it is reasonable to assign an “energy cost” of 4 kJ/mol (1 kcal/mol) to each pair of eclipsed bonds.

In principle there are an infinite number of conformations of ethane, differing by only tiny increments in their torsion angles. Not only is the staggered conformation more stable than the eclipsed, it is the most stable of all of the conformations; the eclipsed is the least stable. Figure 3.4 shows how the potential energy of ethane changes for a 360° rotation about the carbon–carbon bond. Three equivalent eclipsed conformations and three equivalent staggered conformations occur during the 360° rotation; the eclipsed conformations appear at the highest points on the curve (*potential energy maxima*), the staggered ones at the lowest (*potential energy minima*).

PROBLEM 3.2 Find the conformations in Figure 3.4 in which the red circles are (a) gauche and (b) anti.

Diagrams such as Figure 3.4 can be quite helpful for understanding how the potential energy of a system changes during a process. The process can be a simple one such as the one described here—rotation around a carbon–carbon bond. Or it might be more complicated—a chemical reaction, for example. We will see applications of potential energy diagrams to a variety of processes throughout the text.

Let’s focus our attention on a portion of Figure 3.4. The region that lies between a torsion angle of 60° and 180° tracks the conversion of one staggered conformation of

Steric is derived from the Greek word *stereos* for “solid” and refers to the three-dimensional or spatial aspects of chemistry.



The animation on the *Learning By Modeling* CD shows rotation about the C—C bond in ethane.

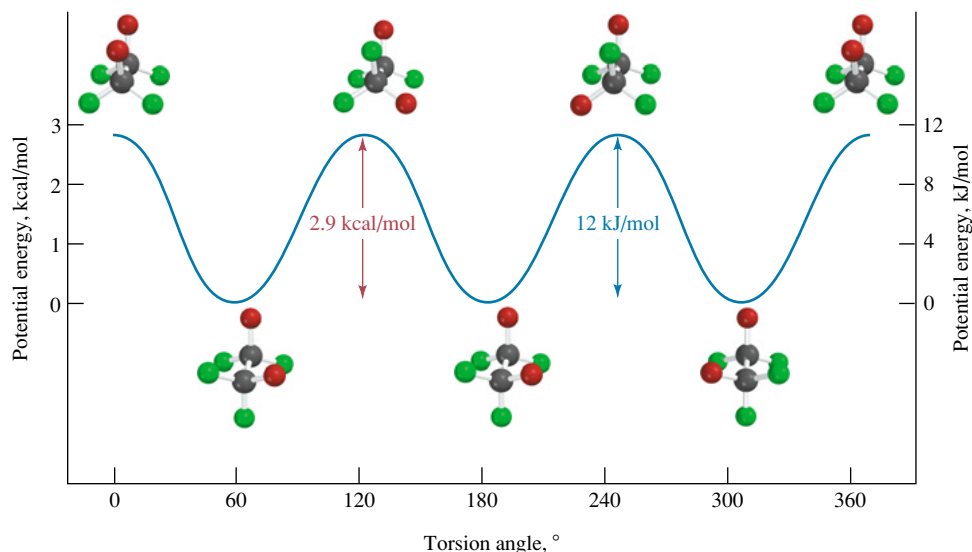


FIGURE 3.4 Potential energy diagram for rotation about the carbon-carbon bond in ethane. Two of the hydrogens are shown in red and four in green so as to indicate more clearly the bond rotation.

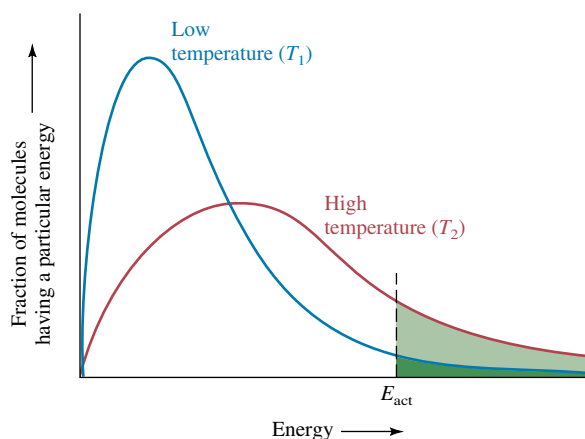
ethane to the next one. Both staggered conformations are equivalent and equal in energy, but for one staggered conformation to get to the next, it must first pass through an eclipsed conformation and needs to gain 12 kJ/mol (2.9 kcal/mol) of energy to reach it. This amount of energy is the **activation energy** (E_{act}) for the process. Molecules must become energized in order to undergo a chemical reaction or, as in this case, to undergo rotation around a carbon-carbon bond. Kinetic (thermal) energy is absorbed by a molecule from collisions with other molecules and is transformed into potential energy. When the potential energy exceeds E_{act} , the unstable arrangement of atoms that exists at that instant can relax to a more stable structure, giving off its excess potential energy in collisions with other molecules or with the walls of a container. The point of maximum potential energy encountered by the reactants as they proceed to products is called the **transition state**. The eclipsed conformation is the transition state for the conversion of one staggered conformation of ethane to another.

Rotation around carbon-carbon bonds is one of the fastest processes in chemistry. Among the ways that we can describe the rate of a process is by its *half-life*, which is the length of time it takes for one half of the molecules to react. It takes less than 10^{-6} seconds for half of the molecules in a sample of ethane to go from one staggered conformation to another at 25°C. At any instant, almost all of the molecules are in staggered conformations; hardly any are in eclipsed conformations.

As with all chemical processes, the rate of rotation about the carbon-carbon bond increases with temperature. The reason for this can be seen by inspecting Figure 3.5, where it can be seen that most of the molecules in a sample have energies that are clustered around some average value; some have less energy, a few have more. Only molecules with a potential energy greater than E_{act} , however, are able to go over the transition state and proceed on to products. The number of these molecules is given by the shaded areas under the curve in Figure 3.5. The energy distribution curve flattens out at higher temperatures, and a greater proportion of molecules have energies in excess of E_{act} at T_2 (higher) than at T_1 (lower). The effect of temperature is quite pronounced; an increase of only 10°C produces a two- to threefold increase in the rate of a typical chemical process.

The structure that exists at the transition state is sometimes referred to as the *transition structure* or the *activated complex*.

FIGURE 3.5 Distribution of molecular energies. (a) The number of molecules with energy greater than E_{act} at temperature T_1 is shown as the darker-green shaded area. (b) At some higher temperature T_2 , the shape of the energy distribution curve is different, and more molecules have energies in excess of E_{act} .



3.2 CONFORMATIONAL ANALYSIS OF BUTANE

The next alkane that we examine is butane. In particular, we consider conformations related by rotation about the bond between the middle two carbons ($\text{CH}_3\text{CH}_2\text{—CH}_2\text{CH}_3$). Unlike ethane, in which the staggered conformations are equivalent, two different staggered conformations occur in butane, shown in Figure 3.6. The methyl groups are gauche to each other in one, anti in the other. Both conformations are staggered, so are free of torsional strain, but two of the methyl hydrogens of the gauche conformation lie within 210 pm of each other. This distance is less than the sum of their van der Waals radii (240 pm), and there is a repulsive force between them. The destabilization of a molecule that results when two of its atoms are too close to each other is

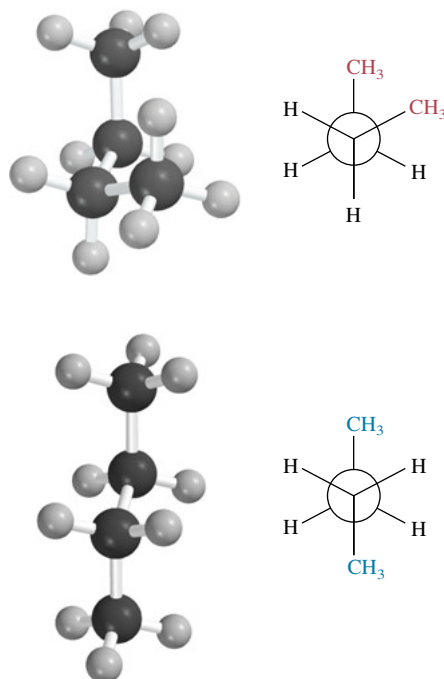


FIGURE 3.6 The gauche and anti conformations of butane shown as ball-and-spoke models (*left*) and as Newman projections (*right*). The gauche conformation is less stable than the anti because of the van der Waals strain between the methyl groups.

called **van der Waals strain**, or **steric hindrance** and contributes to the total steric strain. In the case of butane, van der Waals strain makes the gauche conformation approximately 3.2 kJ/mol (0.8 kcal/mol) less stable than the anti.

Figure 3.7 illustrates the potential energy relationships among the various conformations of butane. The staggered conformations are more stable than the eclipsed. At any instant, almost all the molecules exist in staggered conformations, and more are present in the anti conformation than in the gauche. The point of maximum potential energy lies some 25 kJ/mol (6.1 kcal/mol) above the anti conformation. The total strain in this structure is approximately equally divided between the torsional strain associated with three pairs of eclipsed bonds (12 kJ/mol; 2.9 kcal/mol) and the van der Waals strain between the methyl groups.

PROBLEM 3.3 Sketch a potential energy diagram for rotation around a carbon-carbon bond in propane. Clearly identify each potential energy maximum and minimum with a structural formula that shows the conformation of propane at that point. Does your diagram more closely resemble that of ethane or of butane? Would you expect the activation energy for bond rotation in propane to be more than or less than that of ethane? Of butane?

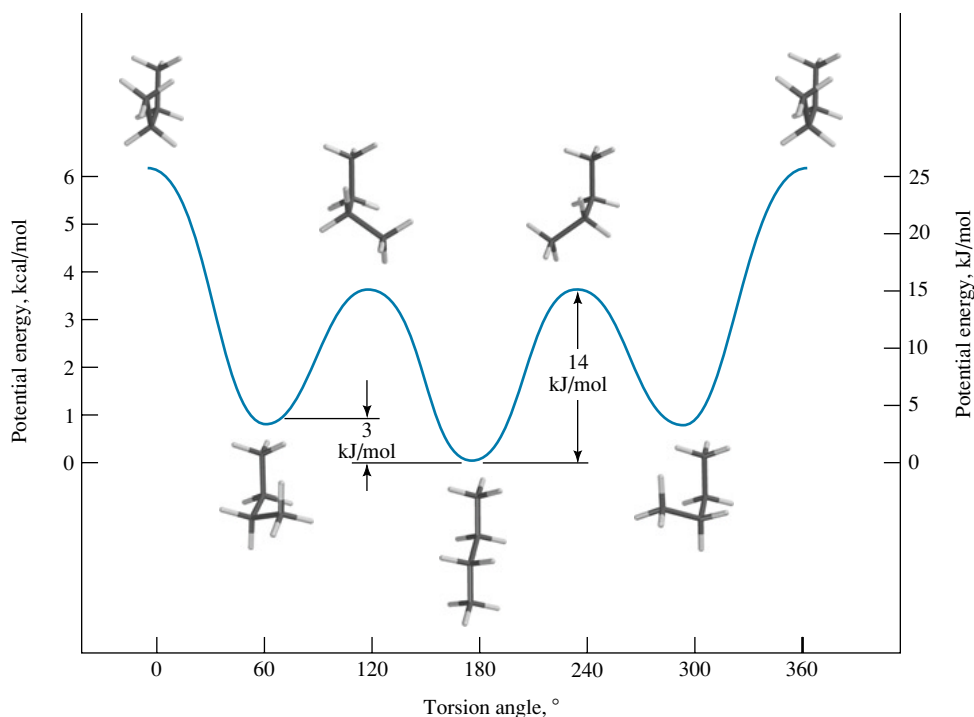


FIGURE 3.7 Potential energy diagram for rotation around the central carbon-carbon bond in butane.

MOLECULAR MECHANICS APPLIED TO ALKANES AND CYCLOALKANES

Of the numerous applications of computer technology to chemistry, one that has been enthusiastically embraced by organic chemists examines molecular structure from a perspective similar to that gained by manipulating molecular models but with an additional quantitative dimension. *Molecular mechanics* is a computational method that allows us to assess the stability of a molecule by comparing selected features of its structure with those of ideal “unstrained” standards. Molecular mechanics makes no attempt to explain why the van der Waals radius of hydrogen is 120 pm, why the bond angles in methane are 109.5°, why the C—C bond distance in ethane is 153 pm, or why the staggered conformation of ethane is 12 kJ/mol more stable than the eclipsed, but instead uses these and other experimental observations as benchmarks to which the corresponding features of other substances are compared.

If we assume that there are certain “ideal” values for bond angles, bond distances, and so on, it follows that deviations from these ideal values will destabilize a particular structure and increase its potential energy. This increase in potential energy is referred to as the **strain energy** of the structure. Other terms include **steric energy** and **steric strain**. Arithmetically, the total strain energy (E_s) of an alkane or cycloalkane can be considered as

$$E_s = E_{\text{bond stretching}} + E_{\text{angle bending}} + E_{\text{torsional}} + E_{\text{van der Waals}}$$

where

$E_{\text{bond stretching}}$ is the strain that results when C—C and C—H bond distances are distorted from their ideal values of 153 pm and 111 pm, respectively.

$E_{\text{angle bending}}$ is the strain that results from the expansion or contraction of bond angles from the normal values of 109.5° for sp^3 hybridized carbon.

$E_{\text{torsional}}$ is the strain that results from deviation of torsion angles from their stable staggered relationship.

$E_{\text{van der Waals}}$ is the strain that results from “nonbonded interactions.”

Nonbonded interactions are the forces between atoms that aren't bonded to one another; they may be either attractive or repulsive. It often happens that the shape of a molecule may cause two atoms to be close in space even though they are separated from each other by many bonds. Induced-dipole/induced-dipole interactions make van der Waals forces in alkanes weakly attractive at most distances, but when two atoms are closer to each other than the sum of their van der Waals radii, nuclear–nuclear and electron–electron repulsive forces between them dominate the $E_{\text{van der Waals}}$ term. The resulting destabilization is called van der Waals strain.

At its most basic level, separating the total strain of a structure into its components is a qualitative exercise. For example, a computer-drawn model of the eclipsed conformation of butane using ideal bond angles and bond distances (Figure 3.8) reveals that two pairs of hydrogens are separated by a distance of only 175 pm, a value considerably smaller than the sum of their van der Waals radii ($2 \times 120 \text{ pm} = 240 \text{ pm}$). Thus, this conformation is destabilized not only by the torsional strain associated with its eclipsed bonds, but also by van der Waals strain.

At a higher level, molecular mechanics is applied quantitatively to strain energy calculations. Each component of strain is separately described by a mathematical expression developed and refined so that it gives solutions that match experimental observations for reference molecules. These empirically derived and tested expressions are then used to calculate the most stable structure of a substance. The various structural features are interdependent; van der Waals strain, for example, might be decreased at the expense of introducing some angle strain, torsional strain, or both. The computer program searches for the combination of bond angles, distances, torsion angles, and nonbonded interactions that gives the molecule the lowest total strain. This procedure is called *strain energy minimization* and is based on the commonsense notion that the most stable structure is the one that has the least strain.

—Cont.

The first widely used molecular mechanics program was developed by Professor N. L. Allinger of the University of Georgia and was known in its various versions as *MM2*, *MM3*, and so on. They have been refined to the extent that many structural features can be calculated more easily and more accurately than they can be measured experimentally.

Once requiring minicomputers and workstations, many molecular mechanics programs are available for personal computers. The information that strain energy calculations can provide is so helpful

that molecular mechanics is no longer considered a novelty but rather as one more tool to be used by the practicing organic chemist. They have been joined by programs that calculate the energies of conformations by molecular orbital methods. The *Learning By Modeling* CD that accompanies this text contains molecular mechanics software that lets you seek out the most stable conformation of the structures you assemble. It also contains the most stable conformations of some molecules as determined by molecular orbital calculations.

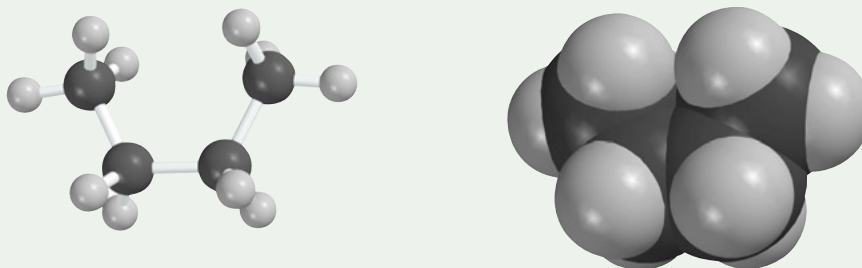


FIGURE 3.8 Ball-and-spoke and space-filling models of methyl-methyl eclipsed conformation of butane.

3.3 CONFORMATIONS OF HIGHER ALKANES

Higher alkanes having unbranched carbon chains are, like butane, most stable in their all-anti conformations. The energy difference between gauche and anti conformations is similar to that of butane, and appreciable quantities of the gauche conformation are present in liquid alkanes at 25°C. In depicting the conformations of higher alkanes it is often more helpful to look at them from the side rather than end-on as in a Newman projection. Viewed from this perspective, the most stable conformations of pentane and hexane have their carbon “backbones” arranged in a zigzag fashion, as shown in Figure 3.9. All the bonds are staggered, and the chains are characterized by anti arrangements of C—C—C—C units.

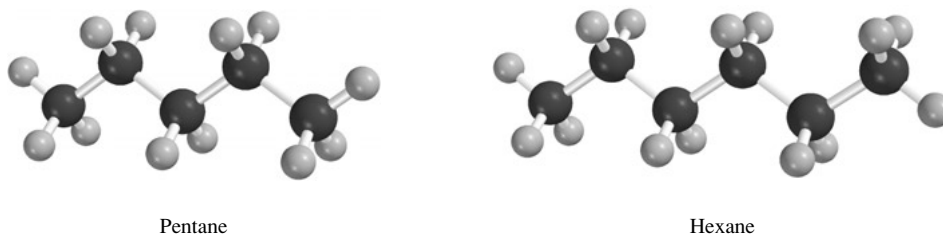


FIGURE 3.9 Ball-and-spoke models of pentane and hexane in their all-anti (zigzag) conformations.

3.4 THE SHAPES OF CYCLOALKANES: PLANAR OR NONPLANAR?

During the nineteenth century it was widely believed—incorrectly, as we'll soon see—that cycloalkane rings are planar. A leading advocate of this view was the German chemist Adolf von Baeyer. He noted that compounds containing rings other than those based on cyclopentane and cyclohexane were rarely encountered naturally and were difficult to synthesize. Baeyer connected both observations with cycloalkane stability, which he suggested was related to how closely the angles of planar rings match the tetrahedral value of 109.5° . For example, the 60° bond angle of cyclopropane and the 90° bond angles of a planar cyclobutane ring are much smaller than the tetrahedral angle of 109.5° . Baeyer suggested that three- and four-membered rings suffer from what we now call **angle strain**. *Angle strain* is the strain a molecule has because one or more of its bond angles deviate from the ideal value; in the case of alkanes the ideal value is 109.5° .

According to Baeyer, cyclopentane should be the most stable of all the cycloalkanes because the ring angles of a planar pentagon, 108° , are closer to the tetrahedral angle than those of any other cycloalkane. A prediction of the *Baeyer strain theory* is that the cycloalkanes beyond cyclopentane should become increasingly strained and correspondingly less stable. The angles of a regular hexagon are 120° , and the angles of larger polygons deviate more and more from the ideal tetrahedral angle.

Some of the inconsistencies in the Baeyer strain theory will become evident as we use heats of combustion (Table 3.1) to probe the relative energies of cycloalkanes. The most important column in the table is the heat of combustion per methylene (CH_2) group. Since all of the cycloalkanes have molecular formulas of the type C_nH_{2n} , dividing the heat of combustion by n allows direct comparison of ring size and potential energy. Cyclopropane has the highest heat of combustion per methylene group, which is consistent with the idea that its potential energy is raised by angle strain. Cyclobutane has less angle strain at each of its carbon atoms and a lower heat of combustion per methylene group. Cyclopentane, as expected, has a lower value still. Notice, however, that contrary to the prediction of the Baeyer strain theory, cyclohexane has a smaller heat of combustion per methylene group than cyclopentane. If bond angle distortion were greater in cyclohexane than in cyclopentane, the opposite would have been observed.

Although better known now for his incorrect theory that cycloalkanes were planar, Baeyer was responsible for notable advances in the chemistry of organic dyes such as indigo and was awarded the 1905 Nobel Prize in chemistry for his work in that area.

TABLE 3.1 Heats of Combustion ($-\Delta H^\circ$) of Cycloalkanes

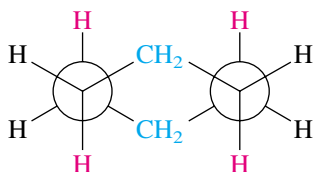
Cycloalkane	Number of CH_2 groups	Heat of combustion		Heat of combustion per CH_2 group	
		kJ/mol	(kcal/mol)	kJ/mol	(kcal/mol)
Cyclopropane	3	2,091	(499.8)	697	(166.6)
Cyclobutane	4	2,721	(650.3)	681	(162.7)
Cyclopentane	5	3,291	(786.6)	658	(157.3)
Cyclohexane	6	3,920	(936.8)	653	(156.0)
Cycloheptane	7	4,599	(1099.2)	657	(157.0)
Cyclooctane	8	5,267	(1258.8)	658	(157.3)
Cyclononane	9	5,933	(1418.0)	659	(157.5)
Cyclodecane	10	6,587	(1574.3)	659	(157.5)
Cycloundecane	11	7,237	(1729.8)	658	(157.3)
Cyclododecane	12	7,845	(1875.1)	654	(156.3)
Cyclotetradecane	14	9,139	(2184.2)	653	(156.0)
Cyclohexadecane	16	10,466	(2501.4)	654	(156.3)

Furthermore, the heats of combustion per methylene group of the very large rings are all about the same and similar to that of cyclohexane. Rather than rising because of increasing angle strain in large rings, the heat of combustion per methylene group remains constant at approximately 653 kJ/mol (156 kcal/mol), the value cited in Section 2.15 as the difference between successive members of a homologous series of alkanes. We conclude, therefore, that the bond angles of large cycloalkanes are not much different from the bond angles of alkanes themselves. The prediction of the Baeyer strain theory that angle strain increases steadily with ring size is contradicted by experimental fact.

The Baeyer strain theory is useful to us in identifying angle strain as a destabilizing effect. Its fundamental flaw is its assumption that the rings of cycloalkanes are planar. *With the exception of cyclopropane, cycloalkanes are nonplanar.* Sections 3.5–3.11 describe the shapes of cycloalkanes. Six-membered rings rank as the most important ring size among organic compounds; thus let us begin with cyclohexane to examine the forces that determine the shapes of cycloalkanes.

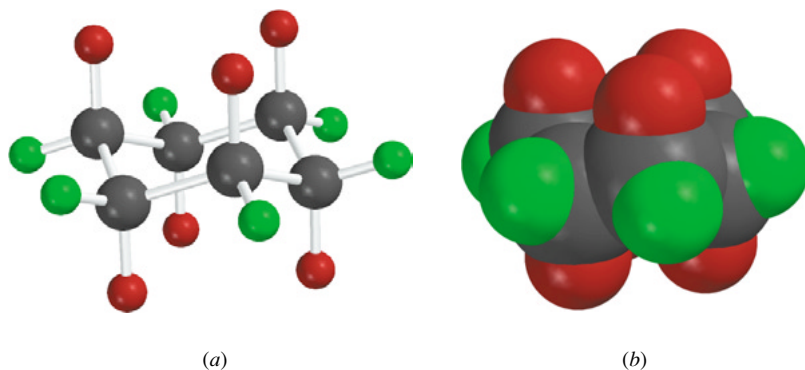
3.5 CONFORMATIONS OF CYCLOHEXANE

Experimental evidence indicating that six-membered rings are nonplanar began to accumulate in the 1920s. Eventually, Odd Hassel of the University of Oslo established that the most stable conformation of cyclohexane has the shape shown in Figure 3.10. This is called the **chair** conformation. With C—C—C bond angles of 111° , the chair conformation is nearly free of angle strain. All its bonds are staggered, making it free of torsional strain as well. The staggered arrangement of bonds in the chair conformation of cyclohexane is apparent in a Newman-style projection.



Staggered arrangement of bonds in chair conformation of cyclohexane

A second, but much less stable, nonplanar conformation called the **boat** is shown in Figure 3.11. Like the chair, the boat conformation has bond angles that are approximately tetrahedral and is relatively free of angle strain. As noted in Figure 3.11, however, the boat is destabilized by van der Waals strain involving its two “flagpole” hydrogens, which are within 180 pm of each other. An even greater contribution to the



(a)

(b)

Hassel shared the 1969 Nobel Prize in chemistry with Sir Derek Barton of Imperial College (London), now at Texas A&M University. Barton demonstrated how Hassel's structural results could be extended to an analysis of conformational effects on chemical reactivity.



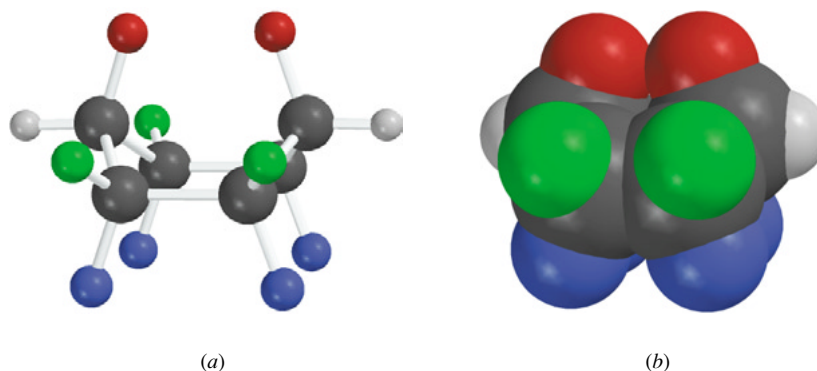
Make a molecular model of the chair conformation of cyclohexane, and turn it so that you can look down one of the C—C bonds.

Recall from Section 3.2 that the sum of the van der Waals radii of two hydrogen atoms is 240 pm.



FIGURE 3.10 (a) A ball-and-spoke model and (b) a space-filling model of the chair conformation of cyclohexane.

FIGURE 3.11 (a) A ball-and-spoke model and (b) a space-filling model of the boat conformation of cyclohexane. The close approach of the two uppermost hydrogen substituents is clearly evident in the space-filling model.



estimated 27 kJ/mol (6.4 kcal/mol) energy difference between the chair and the boat is the torsional strain associated with eclipsed bonds on four of the carbons in the boat. Figure 3.12 depicts the eclipsed bonds and demonstrates how the associated torsional strain may be reduced by rotation about the carbon–carbon bonds to give the slightly more stable **twist boat**, or **skew boat**, conformation. The same bond rotations that reduce the torsional strain also reduce the van der Waals strain by increasing the distance between the two flagpole hydrogens.

The various conformations of cyclohexane are in rapid equilibrium with one another, but at any moment almost all of the molecules exist in the chair conformation. Not more than one or two molecules per thousand are present in the higher energy skew boat and boat conformations. Thus, the discussion of cyclohexane conformational analysis that follows focuses exclusively on the chair conformation.

3.6 AXIAL AND EQUATORIAL BONDS IN CYCLOHEXANE

One of the most important findings to come from conformational studies of cyclohexane is that its 12 hydrogen atoms are not all identical but are divided into two groups, as shown in Figure 3.13. Six of the hydrogens, called **axial** hydrogens, have their bonds parallel to a vertical axis that passes through the ring's center. These axial bonds alter-



FIGURE 3.12 (a) The boat and (b) skew boat conformations of cyclohexane. A portion of the torsional strain in the boat is relieved by rotation about C—C bonds in the skew boat. Bond rotation is accompanied by movement of flagpole hydrogens away from each other, which reduces the van der Waals strain between them.

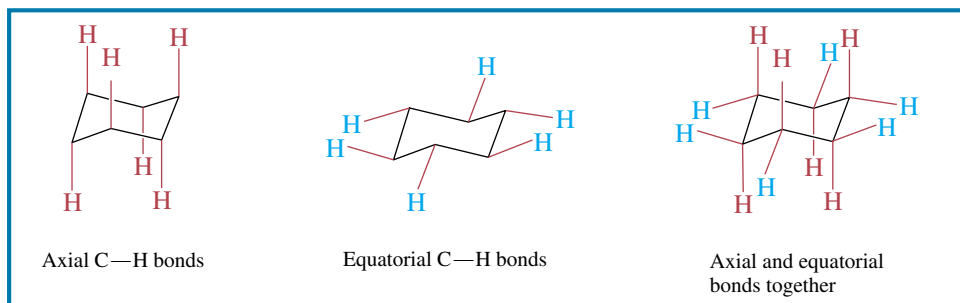
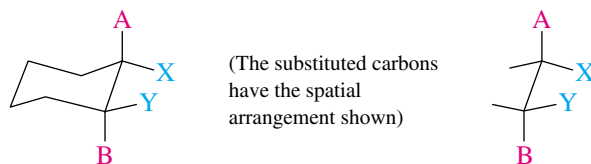


FIGURE 3.13 Axial and equatorial bonds in cyclohexane.

nately are directed up and down on adjacent carbons. The second set of six hydrogens, called **equatorial** hydrogens, are located approximately along the equator of the molecule. Notice that the four bonds to each carbon are arranged tetrahedrally, consistent with an sp^3 hybridization of carbon.

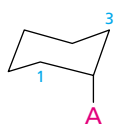
The conformational features of six-membered rings are fundamental to organic chemistry, so it is essential that you have a clear understanding of the directional properties of axial and equatorial bonds and be able to represent them accurately. Figure 3.14 offers some guidance on the drawing of chair cyclohexane rings.

It is no accident that sections of our chair cyclohexane drawings resemble sawhorse projections of staggered conformations of alkanes. The same spatial relationships seen in alkanes carry over to substituents on a six-membered ring. In the structure



substituents A and B are anti to each other, and the other relationships—A and Y, X and Y, and X and B—are gauche.

PROBLEM 3.4 Given the following partial structure, add a substituent X to C-1 so that it satisfies the indicated stereochemical requirement. You may find it helpful to build a molecular model for reference.

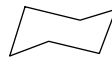


- | | |
|-----------------|-------------------|
| (a) Anti to A | (c) Anti to C-3 |
| (b) Gauche to A | (d) Gauche to C-3 |

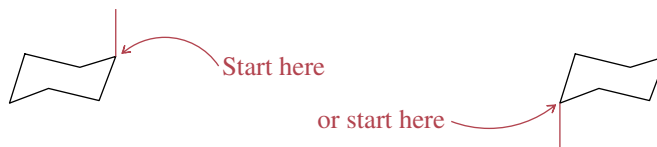
SAMPLE SOLUTION (a) In order to be anti to A, substituent X must be axial. The blue lines in the drawing show the A—C—C—X torsion angle to be 180° .



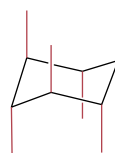
(1) Begin with the chair conformation of cyclohexane.



(2) Draw the axial bonds before the equatorial ones, alternating their direction on adjacent atoms. Always start by placing an axial bond “up” on the uppermost carbon or “down” on the lowest carbon.

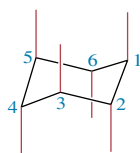


Then alternate to give

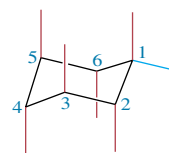


in which all the axial bonds are parallel to one another

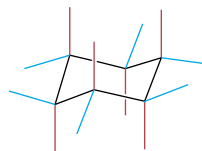
(3) Place the equatorial bonds so as to approximate a tetrahedral arrangement of the bonds to each carbon. The equatorial bond of each carbon should be parallel to the ring bonds of its two nearest neighbor carbons.



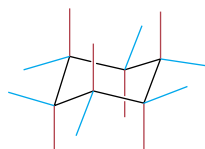
Place equatorial bond at C-1 so that it is parallel to the bonds between C-2 and C-3 and between C-5 and C-6.



Following this pattern gives the complete set of equatorial bonds.



(4) Practice drawing cyclohexane chairs oriented in either direction.



and

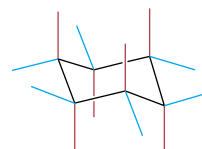
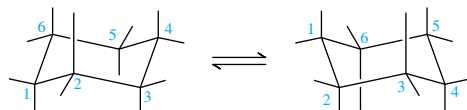


FIGURE 3.14 A guide to representing the orientations of the bonds in the chair conformation of cyclohexane.

3.7 CONFORMATIONAL INVERSION (RING FLIPPING) IN CYCLOHEXANE

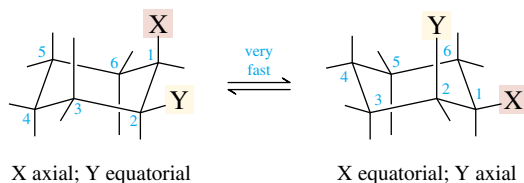
We have seen that alkanes are not locked into a single conformation. Rotation around the central carbon–carbon bond in butane occurs rapidly, interconverting anti and gauche conformations. Cyclohexane, too, is conformationally mobile. Through a process known as **ring inversion**, **chair–chair interconversion**, or, more simply, **ring flipping**, one chair conformation is converted to another chair.



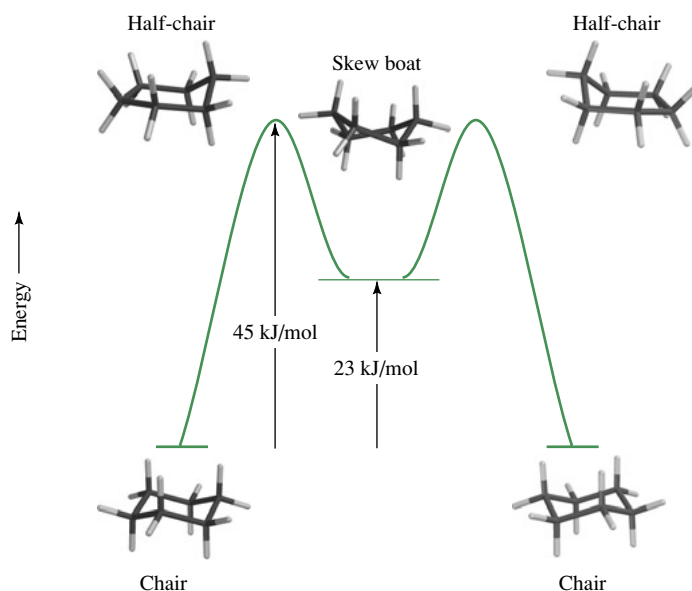
The activation energy for cyclohexane ring inversion is 45 kJ/mol (10.8 kcal/mol). It is a very rapid process with a half-life of about 10^{-5} s at 25°C.

A potential energy diagram for ring inversion in cyclohexane is shown in Figure 3.15. In the first step the chair conformation is converted to a skew boat, which then proceeds to the inverted chair in the second step. The skew boat conformation is an *intermediate* in the process of ring inversion. Unlike a transition state, an **intermediate** is not a potential energy maximum but is a local minimum on the potential energy profile.

The most important result of ring inversion is that any substituent that is axial in the original chair conformation becomes equatorial in the ring-flipped form and vice versa.



The consequences of this point are developed for a number of monosubstituted cyclohexane derivatives in the following section, beginning with methylcyclohexane.



A more detailed discussion of cyclohexane ring inversion can be found in the July 1997 issue of the *Journal of Chemical Education*, pp. 813–814.



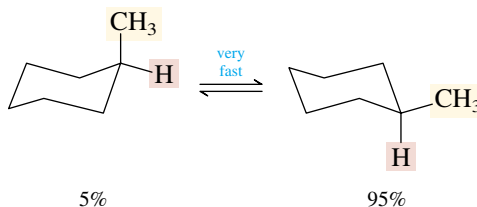
The best way to understand ring flipping in cyclohexane is to view the animation of Figure 3.15 in *Learning By Modeling*.

FIGURE 3.15 Energy diagram showing interconversion of various conformations of cyclohexane. In order to simplify the diagram, the boat conformation has been omitted. The boat is a transition state for the interconversion of skew boat conformations.

3.8 CONFORMATIONAL ANALYSIS OF MONOSUBSTITUTED CYCLOHEXANES

Ring inversion in methylcyclohexane differs from that of cyclohexane in that the two chair conformations are not equivalent. In one chair the methyl group is axial; in the other it is equatorial. At room temperature approximately 95% of the molecules of methylcyclohexane are in the chair conformation that has an equatorial methyl group whereas only 5% of the molecules have an axial methyl group.

See *Learning By Modeling* for an animation of this process.

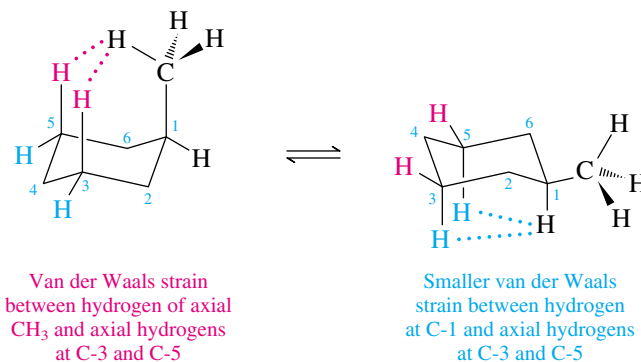


See the box entitled “Enthalpy, Free Energy, and Equilibrium Constant” accompanying this section for a discussion of these relationships.

When two conformations of a molecule are in equilibrium with each other, the one with the lower free energy predominates. Why is equatorial methylcyclohexane more stable than axial methylcyclohexane?

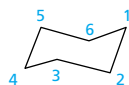
A methyl group is less crowded when it is equatorial than when it is axial. One of the hydrogens of an axial methyl group is within 190–200 pm of the axial hydrogens at C-3 and C-5. This distance is less than the sum of the van der Waals radii of two hydrogens (240 pm) and causes van der Waals strain in the axial conformation. When the methyl group is equatorial, it experiences no significant crowding.

Make a molecular model of each chair conformation of methylcyclohexane, and compare their energies.



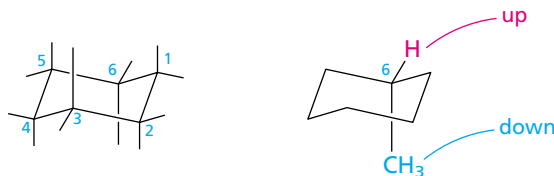
The greater stability of an equatorial methyl group, compared with an axial one, is another example of a *steric effect* (Section 3.2). An axial substituent is said to be crowded because of **1,3-diaxial repulsions** between itself and the other two axial substituents located on the same side of the ring.

PROBLEM 3.5 The following questions relate to a cyclohexane ring depicted in the chair conformation shown.

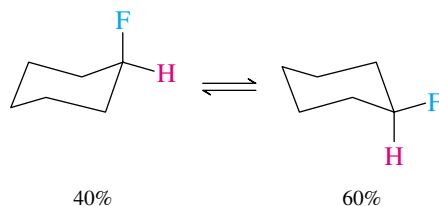


- Is a methyl group at C-6 that is “down” axial or equatorial?
- Is a methyl group that is “up” at C-1 more or less stable than a methyl group that is up at C-4?
- Place a methyl group at C-3 in its most stable orientation. Is it up or down?

SAMPLE SOLUTION (a) First indicate the directional properties of the bonds to the ring carbons. A substituent is down if it is below the other substituent on the same carbon atom. A methyl group that is down at C-6 is therefore axial.

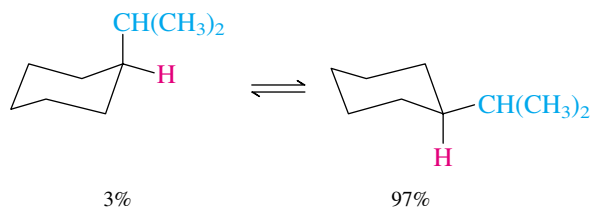


Other substituted cyclohexanes are similar to methylcyclohexane. Two chair conformations exist in rapid equilibrium, and the one in which the substituent is equatorial is more stable. The relative amounts of the two conformations depend on the effective size of the substituent. The size of a substituent, in the context of cyclohexane conformations, is related to the degree of branching at its point of connection to the ring. A single atom, such as a halogen substituent, does not take up much space, and its preference for an equatorial orientation is less pronounced than that of a methyl group.



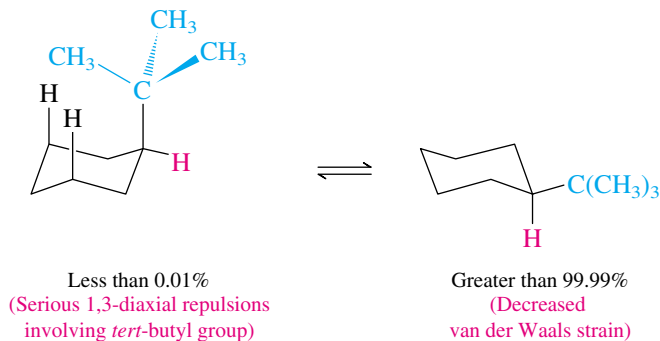
The halogens F, Cl, Br, and I do not differ much in their preference for the equatorial position. As the atomic radius increases in the order $F < Cl < Br < I$, so does the carbon-halogen bond distance, and the two effects tend to cancel.

A branched alkyl group such as isopropyl exhibits a greater preference for the equatorial orientation than does methyl.



A *tert*-butyl group is so large that *tert*-butylcyclohexane exists almost entirely in the conformation in which the *tert*-butyl group is equatorial. The amount of axial *tert*-butylcyclohexane present is too small to measure.

Highly branched groups such as *tert*-butyl are commonly described as "bulky."



PROBLEM 3.6 Draw or construct a molecular model of the most stable conformation of 1-*tert*-butyl-1-methylcyclohexane.



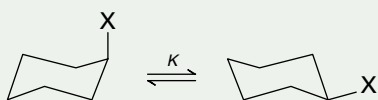
ENTHALPY, FREE ENERGY, AND EQUILIBRIUM CONSTANT

One of the fundamental equations of thermodynamics concerns systems at equilibrium and relates the equilibrium constant K to the difference in **free energy** (ΔG°) between the products and the reactants.

$$\Delta G^\circ = G^\circ_{\text{products}} - G^\circ_{\text{reactants}} = -RT \ln K$$

where T is the absolute temperature in kelvins and the constant R equals $8.314 \text{ J/mol} \cdot \text{K}$ ($1.99 \text{ cal/mol} \cdot \text{K}$).

For the equilibrium between the axial and equatorial conformations of a monosubstituted cyclohexane,



the equilibrium constant is given by the expression

$$K = \frac{[\text{products}]}{[\text{reactants}]}$$

Inserting the appropriate values for R , T (298 K), and K gives the values of ΔG° listed in the table (page 107) for the various substituents discussed in Section 3.8.

The relationship between ΔG° and K is plotted in Figure 3.17. A larger value of K is associated with a more negative ΔG° .

Free energy and enthalpy are related by the expression

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

where ΔS° is the difference in *entropy* between the products and reactants. A positive ΔS° is accompanied by an increase in the disorder of a system. A positive $T\Delta S^\circ$ term leads to a ΔG° that is more negative than ΔH° and a larger K than expected on the basis of enthalpy considerations alone. Conversely, a negative ΔS° gives a smaller K than expected. In the case of conformational equilibration between the chair forms of a substituted cyclohexane, ΔS° is close to zero and ΔG° and ΔH° are approximately equal.

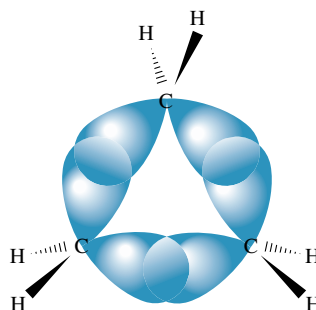
—Cont.

3.9 SMALL RINGS: CYCLOPROPANE AND CYCLOBUTANE

Conformational analysis is far simpler in cyclopropane than in any other cycloalkane. Cyclopropane's three carbon atoms are, of geometric necessity, coplanar, and rotation about its carbon-carbon bonds is impossible. You saw in Section 3.4 how angle strain in cyclopropane leads to an abnormally large heat of combustion. Let's now look at cyclopropane in more detail to see how our orbital hybridization bonding model may be adapted to molecules of unusual geometry.

Strong sp^3 - sp^3 σ bonds are not possible for cyclopropane, because the 60° bond angles of the ring do not permit the orbitals to be properly aligned for effective overlap (Figure 3.16). The less effective overlap that does occur leads to what chemists refer to

FIGURE 3.16 "Bent bonds" in cyclopropane. The orbitals involved in carbon-carbon bond formation overlap in a region that is displaced from the internuclear axis. Orbital overlap is less effective than in a normal carbon-carbon σ bond, and the carbon-carbon bond is weaker.



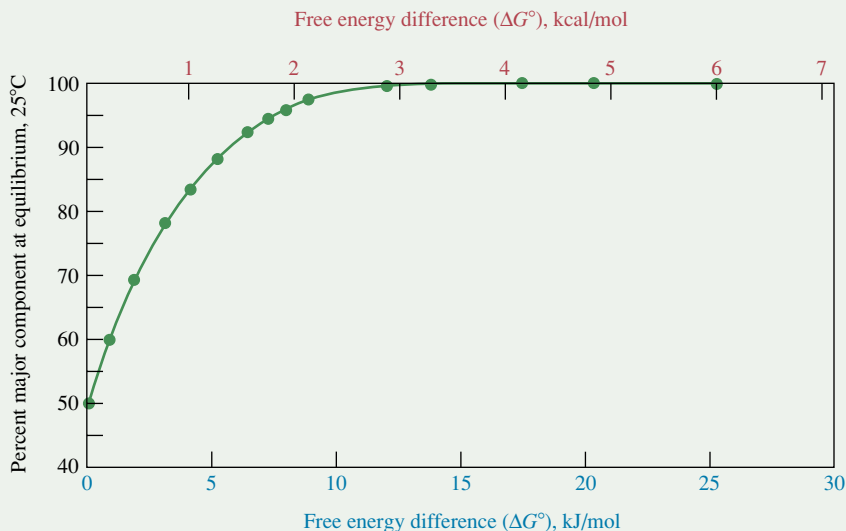


FIGURE 3.17 Distribution of two products at equilibrium plotted as a function of the difference in free energy (ΔG°) at 25°C between them.

Substituent X	Percent axial	Percent equatorial	K	$\Delta G_{298\text{ K}}^\circ$	
				kJ/mol	(kcal/mol)
—F	40	60	1.5	−1.0	(−0.24)
—CH ₃	5	95	19	−7.3	(−1.7)
—CH(CH ₃) ₂	3	97	32.3	−8.6	(−2.1)
—C(CH ₃) ₃	<0.01	>99.99	>9999	−22.8	(−5.5)

as “bent” bonds. The electron density in the carbon–carbon bonds of cyclopropane does not lie along the internuclear axis but is distributed along an arc between the two carbon atoms. The ring bonds of cyclopropane are weaker than other carbon–carbon σ bonds.

In addition to angle strain, cyclopropane is destabilized by torsional strain. Each C—H bond of cyclopropane is eclipsed with two others.



All adjacent pairs of bonds are eclipsed



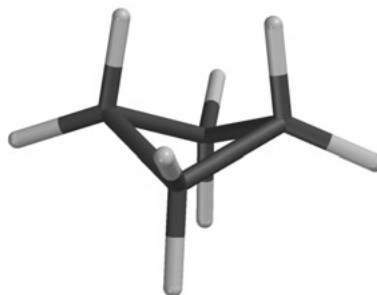
In keeping with the “bent-bond” description of Figure 3.16, the carbon–carbon bond distance in cyclopropane (151 pm) is slightly shorter than that of ethane (153 pm) and cyclohexane (154 pm). The calculated values from molecular models (see *Learning By Modeling*) reproduce these experimental values.

Cyclobutane has less angle strain than cyclopropane and can reduce the torsional strain that goes with a planar geometry by adopting the nonplanar “puckered” conformation shown in Figure 3.18.

PROBLEM 3.7 The heats of combustion of ethylcyclopropane and methylcyclobutane have been measured as 3352 and 3384 kJ/mol (801.2 and 808.8 kcal/mol), respectively. Assign the correct heat of combustion to each isomer.



FIGURE 3.18 Nonplanar (“puckered”) conformation of cyclobutane. The nonplanar conformation is more stable because it avoids the eclipsing of bonds on adjacent carbons that characterizes the planar conformation.



Neighboring C—H bonds are eclipsed in any planar cycloalkane. Thus all planar conformations are destabilized by torsional strain.

3.10 CYCLOPENTANE

Angle strain in the planar conformation of cyclopentane is relatively small because the 108° angles of a regular pentagon are not much different from the normal 109.5° bond angles of sp^3 hybridized carbon. The torsional strain, however, is substantial, since five bonds are eclipsed on the top face of the ring, and another set of five are eclipsed on the bottom face (Figure 3.19a). Some, but not all, of this torsional strain is relieved in nonplanar conformations. Two nonplanar conformations of cyclopentane, the **envelope** (Figure 3.19b) and the **half-chair** (Figure 3.19c) are of similar energy.

In the envelope conformation four of the carbon atoms are coplanar. The fifth carbon is out of the plane of the other four. There are three coplanar carbons in the half-chair conformation, with one carbon atom displaced above that plane and another below it. In both the envelope and the half-chair conformations, in-plane and out-of-plane carbons exchange positions rapidly. Equilibration between conformations of cyclopentane occurs at rates that are comparable with the rate of rotation about the carbon–carbon bond of ethane.

3.11 MEDIUM AND LARGE RINGS

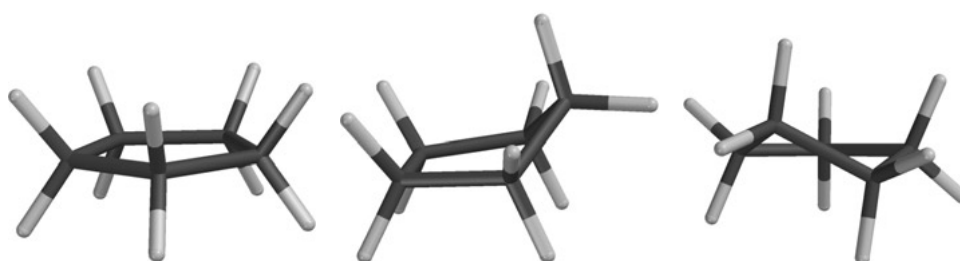
Beginning with cycloheptane, which has four conformations of similar energy, conformational analysis of cycloalkanes becomes more complicated. The same fundamental principles apply to medium and large rings as apply to smaller ones—there are simply more atoms and more bonds to consider and more conformational possibilities.

3.12 DISUBSTITUTED CYCLOALKANES: STEREOISOMERS

When a cycloalkane bears two substituents on different carbons—methyl groups, for example—these substituents may be on the same or on opposite sides of the ring. When substituents are on the same side, we say they are *cis* to each other; if they are on oppo-

In 1978, a German-Swiss team of organic chemists reported the synthesis of a cycloalkane with 96 carbons in its ring (cyclo- $C_{96}H_{192}$).

FIGURE 3.19 The (a) planar, (b) envelope, and (c) half-chair conformations of cyclopentane.

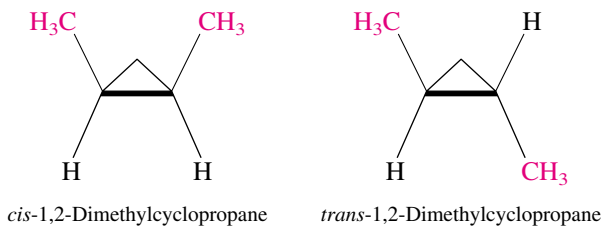


(a) Planar

(b) Envelope

(c) Half-Chair

site sides, they are *trans* to each other. Both terms come from the Latin, in which *cis* means “on this side” and *trans* means “across.”



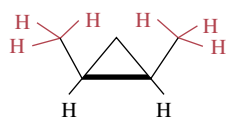
PROBLEM 3.8 Exclusive of compounds with double bonds, four hydrocarbons are *constitutional* isomers of *cis*- and *trans*-1,2-dimethylcyclopropane. Identify these compounds.

The *cis* and *trans* forms of 1,2-dimethylcyclopropane are *stereoisomers*. **Stereoisomers** are isomers that have their atoms bonded in the same order—that is, they have the same constitution, but they differ in the arrangement of atoms in space. Stereoisomers of the *cis*–*trans* type are sometimes referred to as *geometric isomers*. You learned in Section 2.15 that constitutional isomers could differ in stability. What about stereoisomers?

We can measure the energy difference between *cis*- and *trans*-1,2-dimethylcyclopropane by comparing their heats of combustion. As illustrated in Figure 3.20, the two compounds are isomers, and so the difference in their heats of combustion is a direct measure of the difference in their energies. Because the heat of combustion of *trans*-1,2-dimethylcyclopropane is 5 kJ/mol (1.2 kcal/mol) less than that of its *cis* stereoisomer, it follows that *trans*-1,2-dimethylcyclopropane is 5 kJ/mol (1.2 kcal/mol) more stable than *cis*-1,2-dimethylcyclopropane.

The prefix *stereo-* is derived from the Greek word *stereos*, meaning “solid.” *Stereochemistry* is the term applied to the three-dimensional aspects of molecular structure and reactivity.

cis-1,2-Dimethylcyclopropane



trans-1,2-Dimethylcyclopropane

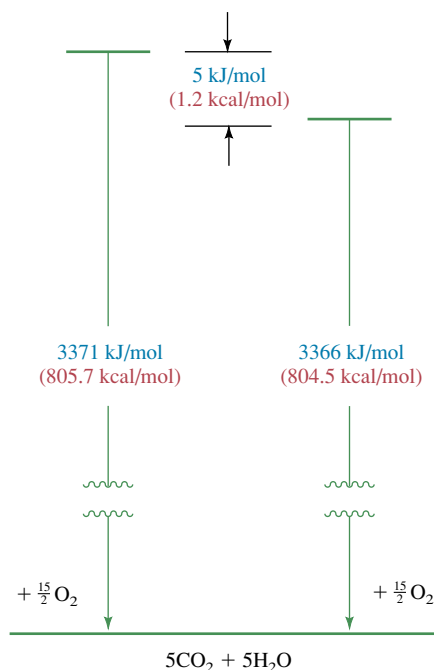
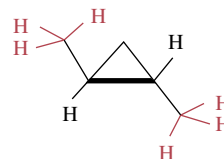


FIGURE 3.20 The enthalpy difference between *cis*- and *trans*-1,2-dimethylcyclopropane can be determined from their heats of combustion. Van der Waals strain between methyl groups on the same side of the ring makes the *cis* isomer less stable than the *trans*.

Make molecular models of *cis*- and *trans*-1,2-dimethylcyclopropane, and compare their strain energies.

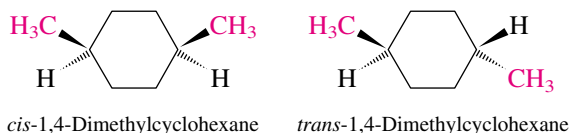


In this case, the relationship between stability and stereochemistry is easily explained on the basis of van der Waals strain. The methyl groups on the same side of the ring in *cis*-1,2-dimethylcyclopropane crowd each other and increase the potential energy of this stereoisomer. Steric hindrance between methyl groups is absent in *trans*-1,2-dimethylcyclopropane.

Disubstituted cyclopropanes exemplify one of the simplest cases involving stability differences between stereoisomers. A three-membered ring has no conformational mobility, and there is no way the ring can adjust to reduce the van der Waals strain between *cis* substituents on adjacent carbons. The situation is different in disubstituted derivatives of cyclohexane.

3.13 CONFORMATIONAL ANALYSIS OF DISUBSTITUTED CYCLOHEXANES

We'll begin with *cis*- and *trans*-1,4-dimethylcyclohexane. A conventional method to represent *cis* and *trans* stereoisomers in cyclic systems uses wedge-and-dash descriptions as shown.



Wedge-and-dash drawings fail to show conformation, and it's important to remember that the rings of *cis*- and *trans*-1,2-dimethylcyclohexane exist in a chair conformation. This fact must be taken into consideration when evaluating the relative stabilities of the stereoisomers.

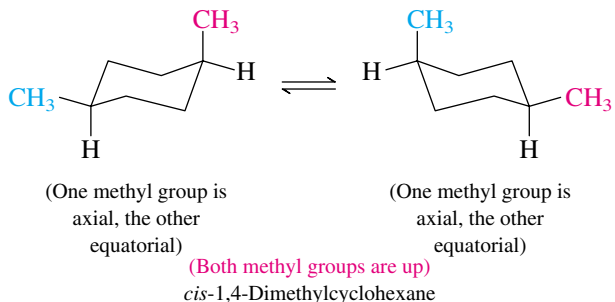
Their heats of combustion (Table 3.2) reveal that *trans*-1,4-dimethylcyclohexane is 7 kJ/mol (1.6 kcal/mol) more stable than the *cis* stereoisomer. It is unrealistic to believe that van der Waals strain between *cis* substituents is responsible, because the methyl groups are too far away from each other. To understand why *trans*-1,4-dimethylcyclohexane is more stable than *cis*-1,4-dimethylcyclohexane, we need to examine each stereoisomer in its most stable conformation.

cis-1,4-Dimethylcyclohexane can adopt either of two equivalent chair conformations, each having one axial methyl group and one equatorial methyl group. The two are

TABLE 3.2 Heats of Combustion of Isomeric Dimethylcyclohexanes

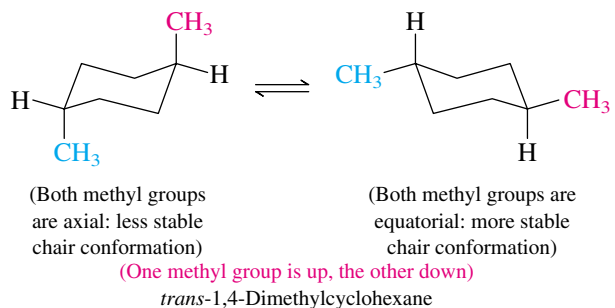
Compound	Orientation of methyl groups in most stable conformation	Heat of combustion		Difference in heat of combustion		More stable stereoisomer
		kJ/mol	(kcal/mol)	kJ/mol	(kcal/mol)	
<i>cis</i> -1,2-Dimethylcyclohexane	Axial–equatorial	5223	(1248.3)	6	(1.5)	<i>trans</i>
<i>trans</i> -1,2-Dimethylcyclohexane	Diequatorial	5217	(1246.8)			
<i>cis</i> -1,3-Dimethylcyclohexane	Diequatorial	5212	(1245.7)	7	(1.7)	<i>cis</i>
<i>trans</i> -1,3-Dimethylcyclohexane	Axial–equatorial	5219	(1247.4)			
<i>cis</i> -1,4-Dimethylcyclohexane	Axial–equatorial	5219	(1247.4)	7	(1.7)	<i>trans</i>
<i>trans</i> -1,4-Dimethylcyclohexane	Diequatorial	5212	(1245.7)			

in rapid equilibrium with each other by ring flipping. The equatorial methyl group becomes axial and the axial methyl group becomes equatorial.



The methyl groups are described as *cis* because both are up relative to the hydrogen present at each carbon. If both methyl groups were down, they would still be *cis* to each other. Notice that ring flipping does not alter the *cis* relationship between the methyl groups. Nor does it alter their up-versus-down quality; substituents that are up in one conformation remain up in the ring-flipped form.

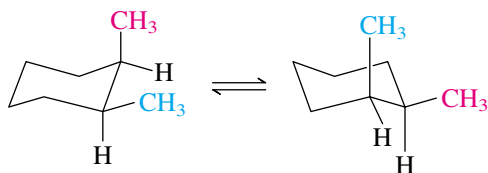
The most stable conformation of *trans*-1,4-dimethylcyclohexane has both methyl groups in equatorial orientations. The two chair conformations of *trans*-1,4-dimethylcyclohexane are not equivalent to each other. One has two equatorial methyl groups; the other, two axial methyl groups.



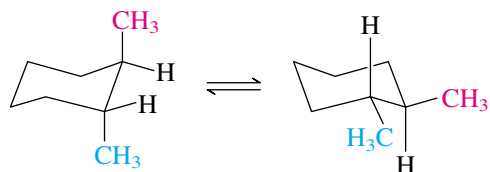
The more stable chair—the one with both methyl groups equatorial—is the conformation adopted by most of the *trans*-1,4-dimethylcyclohexane molecules.

trans-1,4-Dimethylcyclohexane is more stable than *cis*-1,4-dimethylcyclohexane because both methyl groups are equatorial in its most stable conformation. One methyl group must be axial in the *cis* stereoisomer. Remember, it is a general rule that any substituent is more stable in an equatorial orientation than in an axial one. It is worth pointing out that the 7 kJ/mol (1.7 kcal/mol) energy difference between *cis*- and *trans*-1,4-dimethylcyclohexane is the same as the energy difference between the axial and equatorial conformations of methylcyclohexane. There is a simple reason for this: in both instances the less stable structure has one axial methyl group, and the 7 kJ/mol (1.6 kcal/mol) energy difference can be considered the “energy cost” of having a methyl group in an axial rather than an equatorial orientation.

Like the 1,4-dimethyl derivatives, *trans*-1,2-dimethylcyclohexane has a lower heat of combustion (see Table 3.2) and is more stable than *cis*-1,2-dimethylcyclohexane. The *cis* stereoisomer has two chair conformations of equal energy, each containing one axial and one equatorial methyl group.

*cis*-1,2-Dimethylcyclohexane

Both methyl groups are equatorial in the most stable conformation of *trans*-1,2-dimethylcyclohexane.



(Both methyl groups are axial: less stable chair conformation)

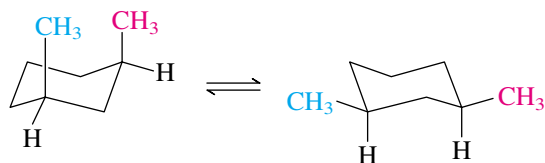
(Both methyl groups are equatorial: more stable chair conformation)

trans-1,2-Dimethylcyclohexane

As in the 1,4-dimethylcyclohexanes, the 6 kJ/mol (1.5 kcal/mol) energy difference between the more stable (*trans*) and the less stable (*cis*) stereoisomer is attributed to the strain associated with the presence of an axial methyl group in the *cis* isomer.

Probably the most interesting observation in Table 3.2 concerns the 1,3-dimethylcyclohexanes. Unlike the 1,2- and 1,4-dimethylcyclohexanes, in which the *trans* stereoisomer is more stable than the *cis*, we find that *cis*-1,3-dimethylcyclohexane is 7 kJ/mol (1.7 kcal/mol) more stable than *trans*-1,3-dimethylcyclohexane. Why?

The most stable conformation of *cis*-1,3-dimethylcyclohexane has both methyl groups equatorial.

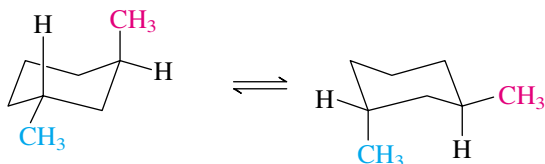


(Both methyl groups are axial: less stable chair conformation)

(Both methyl groups are equatorial: more stable chair conformation)

cis-1,3-Dimethylcyclohexane

The two chair conformations of *trans*-1,3-dimethylcyclohexane are equivalent to each other. Both contain one axial and one equatorial methyl group.



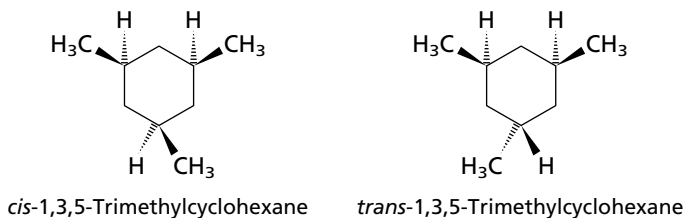
(One methyl group is axial, the other equatorial)

(One methyl group is axial, the other equatorial)

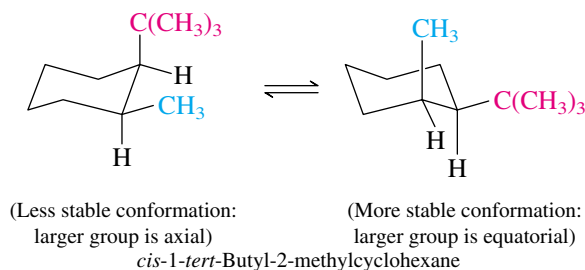
trans-1,3-Dimethylcyclohexane

Thus the *trans* stereoisomer, with one axial methyl group, is less stable than *cis*-1,3-dimethylcyclohexane where both methyl groups are equatorial.

PROBLEM 3.9 Based on what you know about disubstituted cyclohexanes, which of the following two stereoisomeric 1,3,5-trimethylcyclohexanes would you expect to be more stable?



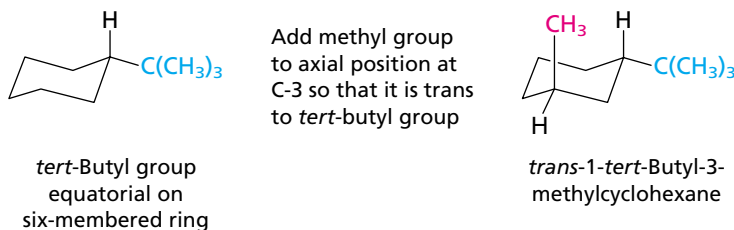
If a disubstituted cyclohexane has two different substituents, then the most stable conformation is the chair that has the larger substituent in an equatorial orientation. This is most apparent when one of the substituents is a bulky group such as *tert*-butyl. Thus, the most stable conformation of *cis*-1-*tert*-butyl-2-methylcyclohexane has an equatorial *tert*-butyl group and an axial methyl group.



PROBLEM 3.10 Write structural formulas or make molecular models for the most stable conformation of each of the following compounds:

- trans*-1-*tert*-Butyl-3-methylcyclohexane
- cis*-1-*tert*-Butyl-3-methylcyclohexane
- trans*-1-*tert*-Butyl-4-methylcyclohexane
- cis*-1-*tert*-Butyl-4-methylcyclohexane

SAMPLE SOLUTION (a) The most stable conformation is the one that has the larger substituent, the *tert*-butyl group, equatorial. Draw a chair conformation of cyclohexane, and place an equatorial *tert*-butyl group at one of its carbons. Add a methyl group at C-3 so that it is *trans* to the *tert*-butyl group.

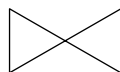


Cyclohexane rings that bear *tert*-butyl substituents are examples of conformationally biased molecules. A *tert*-butyl group has such a pronounced preference for the equatorial orientation that it will strongly bias the equilibrium to favor such conformations. This does not mean that ring inversion does not occur, however. Ring inversion does occur, but at any instant only a tiny fraction of the molecules exist in conformations having axial *tert*-butyl groups. It is not strictly correct to say that *tert*-butylcyclohexane and its derivatives are “locked” into a single conformation; conformations related by ring flipping are in rapid equilibrium with one another, but the distribution between them strongly favors those in which the *tert*-butyl group is equatorial.

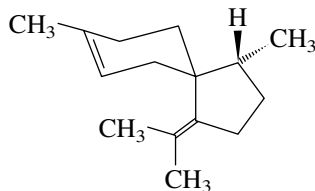
3.14 POLYCYCLIC RING SYSTEMS

Organic molecules in which *one* carbon atom is common to two rings are called **spirocyclic** compounds. The simplest spirocyclic hydrocarbon is *spiropentane*, a product of laboratory synthesis. More complicated spirocyclic hydrocarbons not only have been synthesized but also have been isolated from natural sources. α -*Alaskene*, for example, occurs in the fragrant oil given off by the needles of the Alaskan yellow cedar; one of its carbon atoms is common to both the six-membered ring and the five-membered ring.

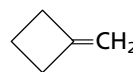
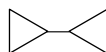
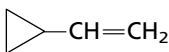
Make a molecular model of spiropentane. What feature of its geometry is more apparent from a model than from its structural formula?



Spiropentane

 α -Alaskene

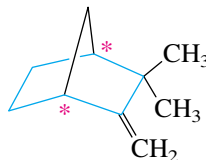
PROBLEM 3.11 Which of the following compounds are isomers of spiropentane?



When *two* or more atoms are common to more than one ring, the compounds are called **polycyclic** ring systems. They are classified as *bicyclic*, *tricyclic*, *tetracyclic* etc., according to the minimum number of bond cleavages required to generate a noncyclic structure. *Bicyclobutane* is the simplest bicyclic hydrocarbon; its four carbons form 2 three-membered rings that share a common side. *Camphene* is a naturally occurring bicyclic hydrocarbon obtained from pine oil. It is best regarded as a six-membered ring (indicated by blue bonds in the structure shown here) in which two of the carbons (designated by asterisks) are bridged by a CH_2 group.



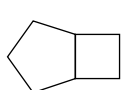
Bicyclobutane



Camphene

PROBLEM 3.12 Use the bond-cleavage criterion to verify that bicyclobutane and camphene are bicyclic.

Bicyclic compounds are named in the IUPAC system by counting the number of carbons in the ring system, assigning to the structure the base name of the unbranched alkane having the same number of carbon atoms, and attaching the prefix “bicyclo-.” The number of atoms in each of the bridges connecting the common atoms is then placed, in descending order, within brackets.



Bicyclo[3.2.0]heptane



Bicyclo[3.2.1]octane

PROBLEM 3.13 Write structural formulas for each of the following bicyclic hydrocarbons:

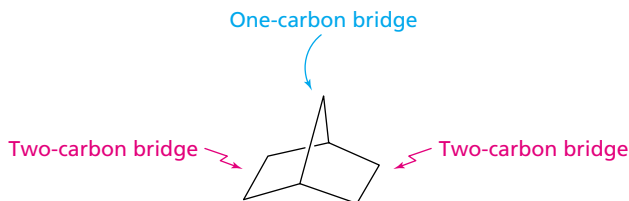
(a) Bicyclo[2.2.1]heptane

(c) Bicyclo[3.1.1]heptane

(b) Bicyclo[5.2.0]nonane

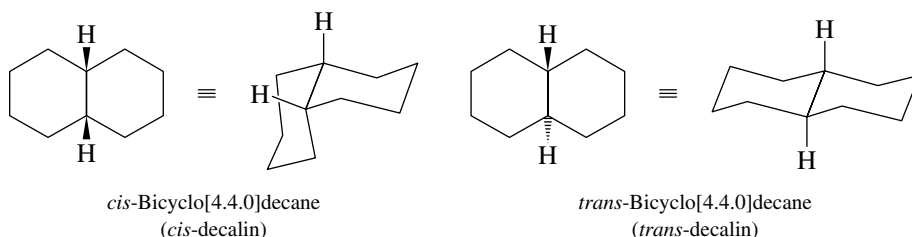
(d) Bicyclo[3.3.0]octane

SAMPLE SOLUTION (a) The bicyclo[2.2.1]heptane ring system is one of the most frequently encountered bicyclic structural types. It contains seven carbon atoms, as indicated by the suffix “-heptane.” The bridging groups contain two, two, and one carbon, respectively.



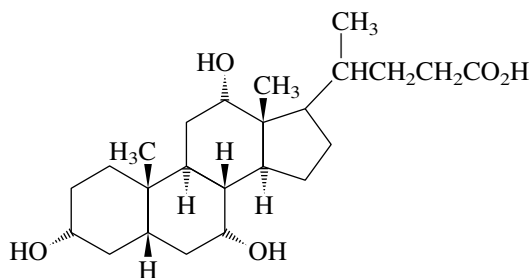
Bicyclo[2.2.1]heptane

Among the most important of the bicyclic hydrocarbons are the two stereoisomeric bicyclo[4.4.0]decanes, called *cis*- and *trans*-decalin. The hydrogen substituents at the ring junction positions are on the same side in *cis*-decalin and on opposite sides in *trans*-decalin. Both rings adopt the chair conformation in each stereoisomer.



Make models of *cis*- and *trans*-decalin. Which is more stable?

Decalin ring systems appear as structural units in a large number of naturally occurring substances, particularly the steroids. Cholic acid, for example, a steroid present in bile that promotes digestion, incorporates *cis*-decalin and *trans*-decalin units into a rather complex *tetracyclic* structure.



Cholic acid

3.15 HETEROCYCLIC COMPOUNDS

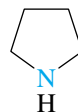
Not all cyclic compounds are hydrocarbons. Many substances include an atom other than carbon, called a *heteroatom* (Section 1.7), as part of a ring. A ring that contains at least one heteroatom is called a **heterocycle**, and a substance based on a heterocyclic ring is a **heterocyclic compound**. Each of the following heterocyclic ring systems will be encountered in this text:



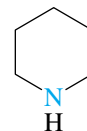
Ethylene oxide



Tetrahydrofuran



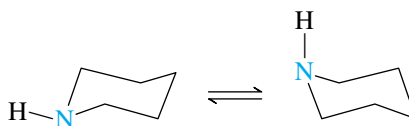
Pyrrolidine



Piperidine

The names cited are common names, which have been in widespread use for a long time and are acceptable in IUPAC nomenclature. We will introduce the systematic nomenclature of these ring systems as needed in later chapters.

The shapes of heterocyclic rings are very much like those of their all-carbon analogs. Thus, six-membered heterocycles such as piperidine exist in a chair conformation analogous to cyclohexane.

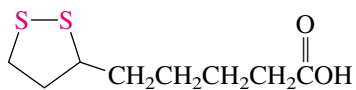


The hydrogen attached to nitrogen can be either axial or equatorial, and both chair conformations are approximately equal in stability.

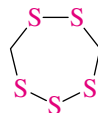


PROBLEM 3.14 Draw or build a molecular model of what you would expect to be the most stable conformation of the piperidine derivative in which the hydrogen bonded to nitrogen has been replaced by methyl.

Sulfur-containing heterocycles are also common. Compounds in which sulfur is the heteroatom in three-, four-, five-, and six-membered rings, as well as larger rings, are all well known. Two interesting heterocyclic compounds that contain sulfur-sulfur bonds are *lipoic acid* and *lenthionine*.



Lipoic acid: a growth factor required by a variety of different organisms



Lenthionine: contributes to the odor of Shiitake mushrooms

Many heterocyclic systems contain double bonds and are related to arenes. The most important representatives of this class are described in Sections 11.21 and 11.22.

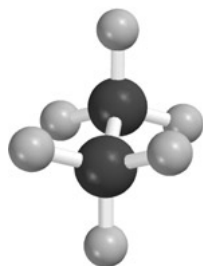
3.16 SUMMARY

In this chapter we explored the three-dimensional shapes of alkanes and cycloalkanes. The most important point to be taken from the chapter is that a molecule adopts the shape that minimizes its total **strain**. The sources of strain in alkanes and cycloalkanes are:

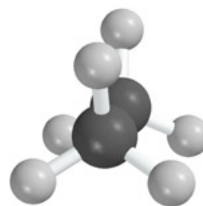
1. *Bond length distortion*: destabilization of a molecule that results when one or more of its bond distances are different from the normal values
2. *Angle strain*: destabilization that results from distortion of bond angles from their normal values
3. *Torsional strain*: destabilization that results from the eclipsing of bonds on adjacent atoms
4. *Van der Waals strain*: destabilization that results when atoms or groups on non-adjacent atoms are too close to one another

The various spatial arrangements available to a molecule by rotation about single bonds are called **conformations**, and **conformational analysis** is the study of the differences in stability and properties of the individual conformations. Rotation around carbon-carbon single bonds is normally very fast, occurring hundreds of thousands of times per second at room temperature. Molecules are rarely frozen into a single conformation but engage in rapid equilibration among the conformations that are energetically accessible.

Section 3.1 The most stable conformation of ethane is the **staggered** conformation. It is approximately 12 kJ/mol (3 kcal/mol) more stable than the **eclipsed**, which is the least stable conformation.



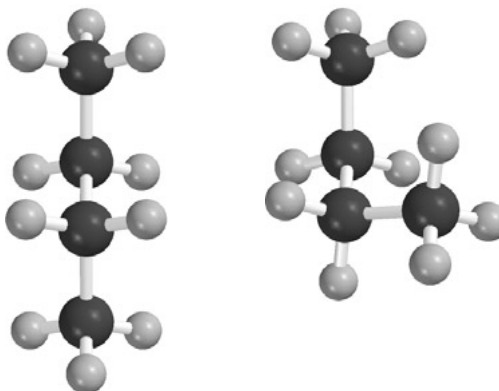
Staggered conformation of ethane (most stable conformation)



Eclipsed conformation of ethane (least stable conformation)

The difference in energy between the staggered and eclipsed forms is due almost entirely to the torsional strain in the eclipsed conformation. At any instant, almost all the molecules of ethane reside in the staggered conformation.

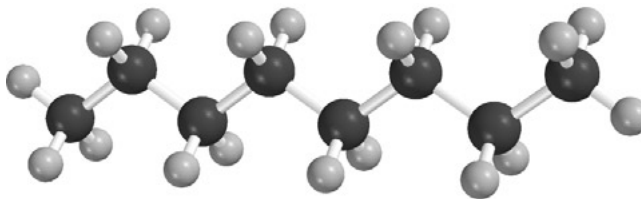
Section 3.2 The two staggered conformations of butane are not equivalent. The **anti** conformation is more stable than the **gauche**.



Anti conformation of butane Gauche conformation of butane

Neither conformation suffers torsional strain, because each has a staggered arrangement of bonds. The gauche conformation is less stable because of van der Waals strain involving the methyl groups.

Section 3.3 Higher alkanes adopt a zigzag conformation of the carbon chain in which all the bonds are staggered.



Octane

Section 3.4 Cyclopropane is the only cycloalkane in which all the ring carbons lie in the same plane. In all other cycloalkanes, the ring is nonplanar. A planar cycloalkane is destabilized by torsional strain and, in most cases, angle strain.



Cyclopropane

Section 3.5 Three conformations of cyclohexane have approximately tetrahedral angles at carbon: the chair, the boat, and the skew boat. The chair is by

far the most stable; it is free of torsional strain, but the boat and skew boat are not. When a cyclohexane ring is present in a compound, it almost always adopts a chair conformation.



Chair

Skew boat

Boat

Section 3.6 The C—H bonds in the chair conformation of cyclohexane are not all equivalent but are divided into two sets of six each, called **axial** and **equatorial**.



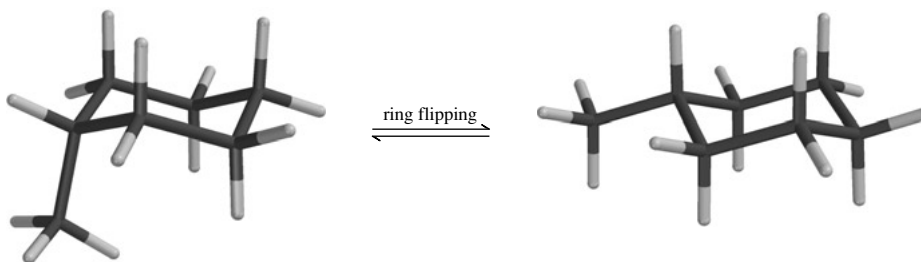
Axial bonds to H in cyclohexane



Equatorial bonds to H in cyclohexane

Section 3.7 Conformational inversion (ring flipping) is rapid in cyclohexane and causes all axial bonds to become equatorial and vice versa. As a result, a monosubstituted derivative of cyclohexane adopts the chair conformation in which the substituent is equatorial (see next section). *No bonds are made or broken in this process.*

Section 3.8 A substituent is less crowded and more stable when it is equatorial than when it is axial on a cyclohexane ring. Ring flipping of a monosubstituted cyclohexane allows the substituent to become equatorial.



Methyl group axial (less stable)

Methyl group equatorial (more stable)

Branched substituents, especially *tert*-butyl, have an increased preference for the equatorial position.

Section 3.9 Cyclopropane is planar and strained (angle strain and torsional strain). Cyclobutane is nonplanar and less strained than cyclopropane.

Section 3.10 Cyclopentane has two nonplanar conformations that are of similar stability: the **envelope** and the **half-chair**.

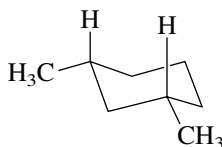


Envelope conformation of cyclopentane

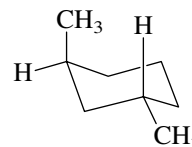
Half-chair conformation of cyclopentane

Section 3.11 Higher cycloalkanes have angles at carbon that are close to tetrahedral and are sufficiently flexible to adopt conformations that are free of torsional strain. They tend to be populated by several different conformations of similar stability.

Sections 3.12–3.13 **Stereoisomers** are isomers that have the same constitution but differ in the arrangement of atoms in space. *Cis*- and *trans*-1,3-dimethylcyclohexane are stereoisomers. The *cis* isomer is more stable than the *trans*.



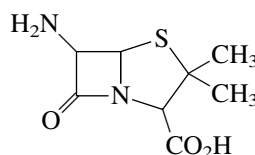
Most stable conformation of *cis*-1,3-dimethylcyclohexane
(no axial methyl groups)



Most stable conformation of *trans*-1,3-dimethylcyclohexane
(one axial methyl group)

Section 3.14 Cyclic hydrocarbons can contain more than one ring. **Spirocyclic** hydrocarbons are characterized by the presence of a single carbon that is common to two rings. **Bicyclic** alkanes contain two rings that share two or more atoms.

Section 3.15 Substances that contain one or more atoms other than carbon as part of a ring are called **heterocyclic** compounds. Rings in which the heteroatom is oxygen, nitrogen, or sulfur rank as both the most common and the most important.



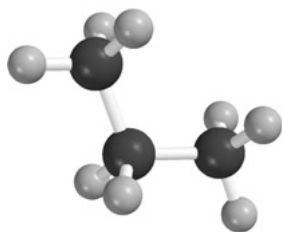
6-Aminopenicillanic acid
(bicyclic and heterocyclic)

PROBLEMS

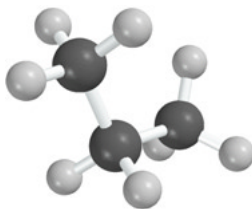


3.15 Like hydrogen peroxide, the inorganic substances hydrazine (H_2NNH_2) and hydroxylamine (H_2NOH) possess conformational mobility. Write structural representations or build molecular models of two different staggered conformations of (a) hydrazine and (b) hydroxylamine.

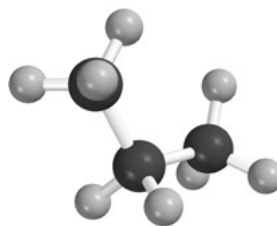
3.16 Of the three conformations of propane shown, which one is the most stable? Which one is the least stable? Why?



(a)



(b)



(c)

3.17 Sight down the C-2—C-3 bond, and draw Newman projection formulas for the

- Most stable conformation of 2,2-dimethylbutane
- Two most stable conformations of 2-methylbutane
- Two most stable conformations of 2,3-dimethylbutane

3.18 One of the staggered conformations of 2-methylbutane in Problem 3.17b is more stable than the other. Which one is more stable? Why?

3.19 Sketch an approximate potential energy diagram similar to that shown in Figures 3.4 and 3.7 for rotation about the carbon-carbon bond in 2,2-dimethylpropane. Does the form of the potential energy curve of 2,2-dimethylpropane more closely resemble that of ethane or that of butane?

3.20 Repeat Problem 3.19 for the case of 2-methylbutane.

3.21 One of the C—C—C angles of 2,2,4,4-tetramethylpentane is very much larger than the others. Which angle? Why?

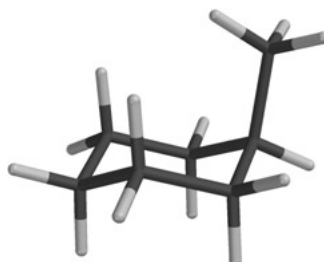
3.22 Even though the methyl group occupies an equatorial site, the conformation shown is not the most stable one for methylcyclohexane. Explain.



3.23 Which of the structures shown for the axial conformation of methylcyclohexane do you think is more stable, A or B? Why?

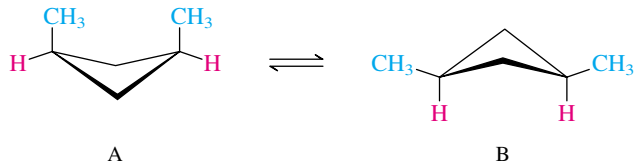


A

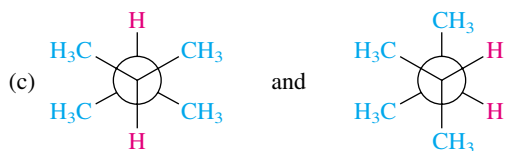
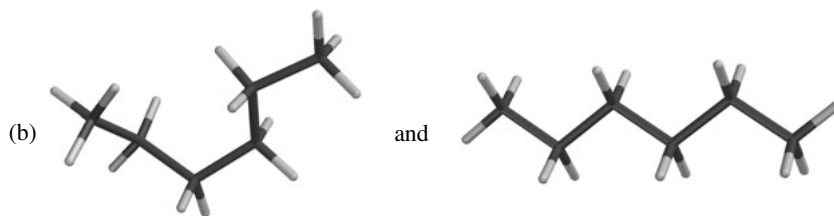
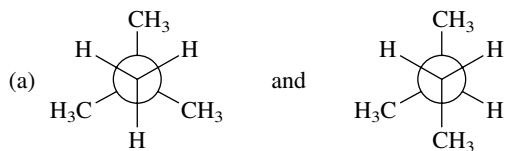


B

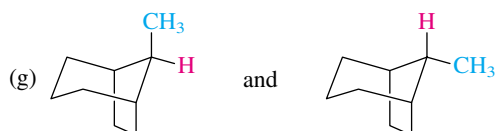
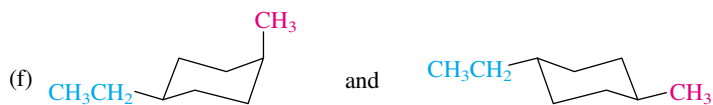
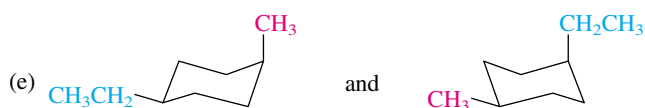
3.24 Which do you expect to be the more stable conformation of *cis*-1,3-dimethylcyclobutane, A or B? Why?



3.25 Determine whether the two structures in each of the following pairs represent *constitutional isomers*, different *conformations* of the same compound, or *stereoisomers* that cannot be interconverted by rotation about single bonds.



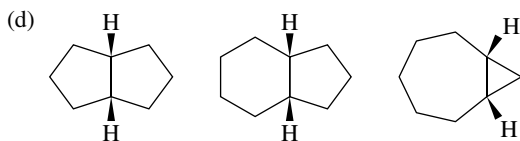
(d) *cis*-1,2-Dimethylcyclopentane and *trans*-1,3-dimethylcyclopentane



3.26 Excluding compounds that contain methyl or ethyl groups, write structural formulas for all the bicyclic isomers of (a) C_5H_8 and (b) C_6H_{10} .

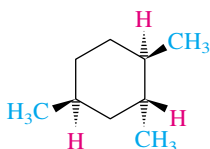
3.27 In each of the following groups of compounds, identify the one with the largest heat of combustion and the one with the smallest. In which cases can a comparison of heats of combustion be used to assess relative stability?

- (a) Cyclopropane, cyclobutane, cyclopentane
 (b) *cis*-1,2-Dimethylcyclopentane, methylcyclohexane, 1,1,2,2-tetramethylcyclopropane



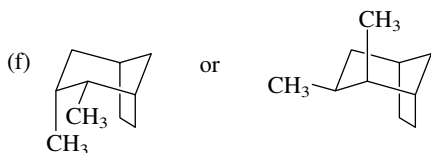
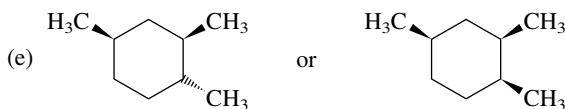
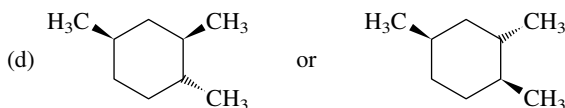
3.28 Write a structural formula for the most stable conformation of each of the following compounds:

- (a) 2,2,5,5-Tetramethylhexane (Newman projection of conformation about C-3—C-4 bond)
 (b) 2,2,5,5-Tetramethylhexane (zigzag conformation of entire molecule)
 (c) *cis*-1-Isopropyl-3-methylcyclohexane
 (d) *trans*-1-Isopropyl-3-methylcyclohexane
 (e) *cis*-1-*tert*-Butyl-4-ethylcyclohexane
 (f) *cis*-1,1,3,4-Tetramethylcyclohexane
 (g)



3.29 Identify the more stable stereoisomer in each of the following pairs, and give the reason for your choice:

- (a) *cis*- or *trans*-1-Isopropyl-2-methylcyclohexane
 (b) *cis*- or *trans*-1-Isopropyl-3-methylcyclohexane
 (c) *cis*- or *trans*-1-Isopropyl-4-methylcyclohexane



3.30 One stereoisomer of 1,1,3,5-tetramethylcyclohexane is 15 kJ/mol (3.7 kcal/mol) less stable than the other. Indicate which isomer is the less stable, and identify the reason for its decreased stability.

3.31 One of the following two stereoisomers is 20 kJ/mol (4.9 kcal/mol) less stable than the other. Indicate which isomer is the less stable, and identify the reason for its decreased stability.



A

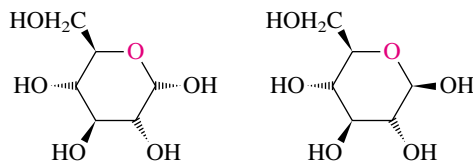
B

3.32 Cubane (C_8H_8) is the common name of a polycyclic hydrocarbon that was first synthesized in the early 1960s. As its name implies, its structure is that of a cube. How many rings are present in cubane?

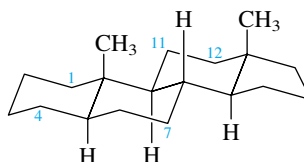


Cubane

3.33 The following are representations of two forms of glucose. The six-membered ring is known to exist in a chair conformation in each form. Draw clear representations of the most stable conformation of each. Are they two different conformations of the same molecule, or are they stereoisomers? Which substituents (if any) occupy axial sites?

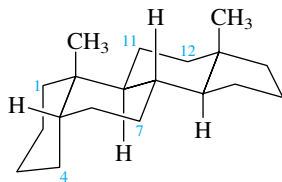


3.34 A typical steroid skeleton is shown along with the numbering scheme used for this class of compounds. Specify in each case whether the designated substituent is axial or equatorial.



- Substituent at C-1 cis to the methyl groups
- Substituent at C-4 cis to the methyl groups
- Substituent at C-7 trans to the methyl groups
- Substituent at C-11 trans to the methyl groups
- Substituent at C-12 cis to the methyl groups

3.35 Repeat Problem 3.34 for the stereoisomeric steroid skeleton having a cis ring fusion between the first two rings.



- 3.36** (a) Write Newman projections for the gauche and anti conformations of 1,2-dichloroethane ($\text{ClCH}_2\text{CH}_2\text{Cl}$).
- (b) The measured dipole moment of $\text{ClCH}_2\text{CH}_2\text{Cl}$ is 1.12 D. Which one of the following statements about 1,2-dichloroethane is false?
- (1) It may exist entirely in the anti conformation.
 - (2) It may exist entirely in the gauche conformation.
 - (3) It may exist as a mixture of anti and gauche conformations.

3.37 Compare the two staggered conformations of 1,1,2,2-tetrafluoroethane on *Learning By Modeling*. Do they differ in respect to their dipole moments? How?



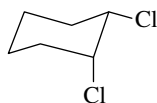
3.38 The compound 2,2,4,4-tetramethylpentane [$(\text{CH}_3)_3\text{CCH}_2\text{C}(\text{CH}_3)_3$] is distinctive because it has an unusually large C—C—C bond angle. What carbons are involved? How large is the angle? What steric factor is responsible for increasing the size of this angle? One of the other bond angles is unusually small. Which one?



3.39 Structural drawings (molecular models, too) can be deceiving. For example, the chlorine atoms in 1,2-dichlorocyclohexane seem much closer to each other in a drawing of the trans stereoisomer than in the cis. Make a molecular model of each, and measure the distance between the chlorines. What do you find?

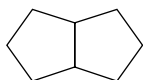


trans-1,2-Dichlorocyclohexane



cis-1,2-Dichlorocyclohexane

3.40 Two stereoisomers of bicyclo[3.3.0]octane are possible. Make molecular models of both, and determine which is more stable.



Bicyclo[3.3.0]octane