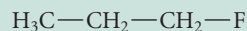




fluorocyclohexane

(b) Estimate the energy difference between the gauche and anti conformations of 1-fluoropropane.



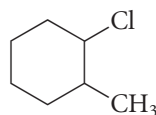
1-fluoropropane

7.5 Suggest a reason why the energy difference between conformations of ethylcyclohexane is about the same as that for methylcyclohexane, even though the ethyl group is larger than a methyl group.

7.4 DISUBSTITUTED CYCLOHEXANES

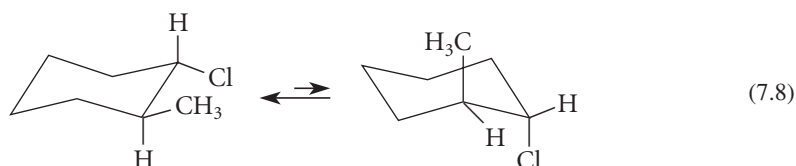
A. Cis-Trans Isomerism in Disubstituted Cyclohexanes

Consider a typical disubstituted cyclohexane, 1-chloro-2-methylcyclohexane.

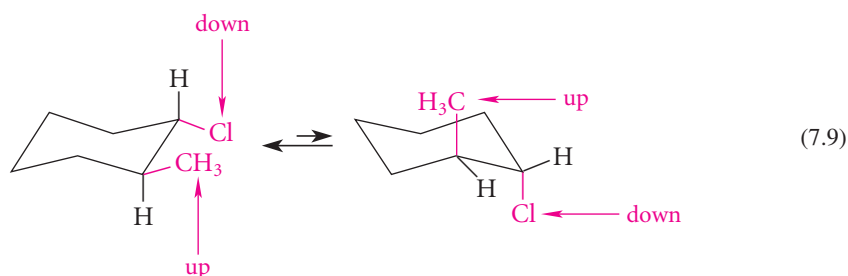


1-chloro-2-methylcyclohexane

In one stereoisomer of this compound, both the chloro and methyl groups are in equatorial positions. This compound is in rapid equilibrium with a conformational diastereomer in which both the chloro and methyl groups assume axial positions.

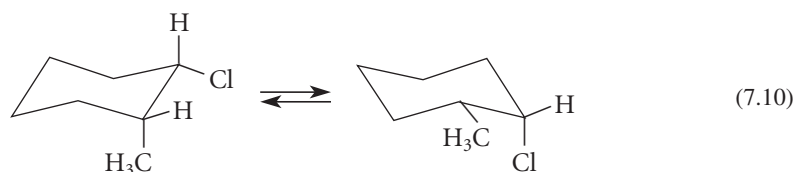
*trans*-1-chloro-2-methylcyclohexane

Either conformation (or the mixture of them) is called *trans*-1-chloro-2-methylcyclohexane. The designation “*trans*” is used with cyclic compounds when two substituents have an up–down relationship.



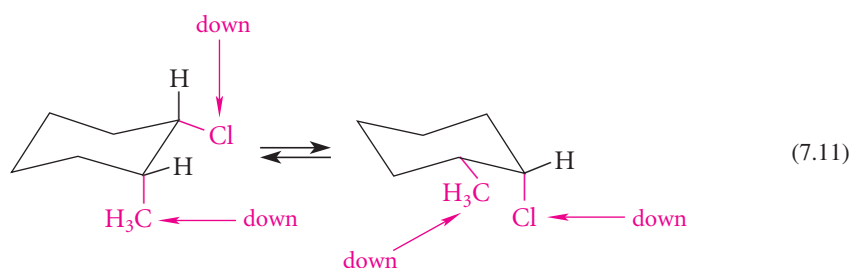
Notice that the up–down relationship is unaffected by the chair interconversion.

In a different stereoisomer of 1-chloro-2-methylcyclohexane, the chloro and methyl groups occupy adjacent equatorial and axial positions.



cis-1-chloro-2-methylcyclohexane

This compound, called *cis*-1-chloro-2-methylcyclohexane, is also a rapidly equilibrating mixture of conformational diastereomers. In a *cis*-disubstituted cycloalkane, the substituents have an up–up or a down–down relationship.



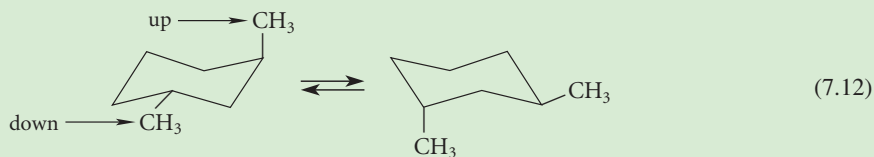
Again, the *cis* relationship is unaltered by the chair interconversion.

The same definition of *cis* and *trans* substitution can be applied to substituent groups in other positions of a cyclohexane ring, as illustrated by Study Problem 7.2.

Study Problem 7.2

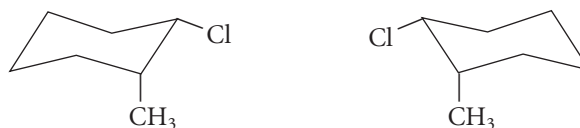
Draw structures of the two chair conformations of *trans*-1,3-dimethylcyclohexane.

Solution In a *trans*-disubstituted cyclohexane, the two substituent groups have an up–down relationship. It doesn't matter which chair conformation is drawn first, because the chair interconversion does not affect the *trans* relationship of the two methyl groups:



trans-1,3-dimethylcyclohexane

Notice that when the substituents in a disubstituted cyclohexane are on asymmetric carbons, the designations *cis* and *trans* specify the *relative* stereochemical configurations of the two asymmetric carbons, but they say nothing about the *absolute* configurations of these carbons. Thus, there are two enantiomers of *cis*-1-chloro-2-methylcyclohexane.



(1*S*,2*R*)-1-chloro-2-methylcyclohexane (1*R*,2*S*)-1-chloro-2-methylcyclohexane
 ————— enantiomers of *cis*-1-chloro-2-methylcyclohexane —————



When a ring contains more than two substituents, cis–trans nomenclature is usually cumbersome. For such cases, other systems have been developed to designate relative configuration. (See Further Exploration 7.1.)

PROBLEMS

- 7.6 For each of the following compounds, draw the two chair conformations that are in equilibrium.
(a) *cis*-1,3-dimethylcyclohexane (b) *trans*-1-ethyl-4-isopropylcyclohexane
- 7.7 For each of the compounds in Problem 7.6, draw a boat conformation.

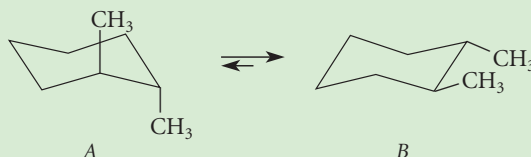
B. Conformational Analysis

Disubstituted cyclohexanes, like monosubstituted cyclohexanes, can be subjected to conformational analysis. The relative stability of the two chair conformations is determined by comparing the 1,3-diaxial interactions (or *gauche*-butane interactions) in each conformation. Such an analysis is illustrated in Study Problem 7.3.

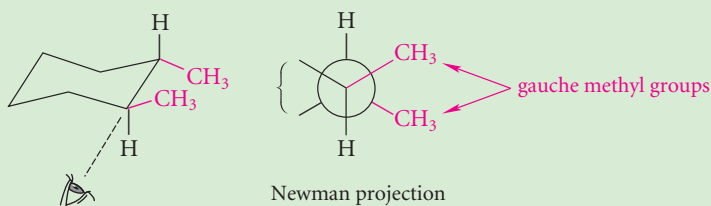
Study Problem 7.3

Determine the relative energies of the two chair conformations of *trans*-1,2-dimethylcyclohexane. Which conformation is more stable?

Solution The first step in solving any problem is to draw the structures of the species involved. The two chair conformations of *trans*-1,2-dimethylcyclohexane are as follows:

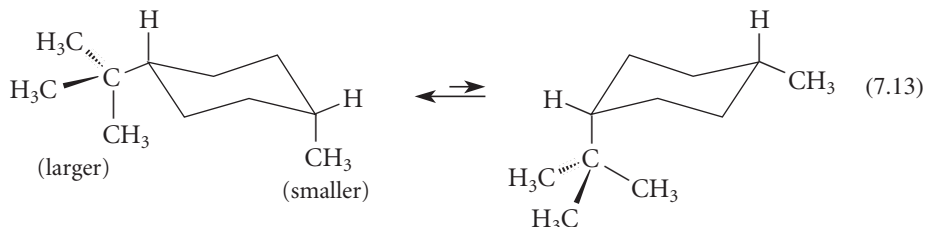


Conformation *A* has the greater number of axial groups and should therefore be the less stable conformation—but by how much? Conformation *A* has four 1,3-diaxial methyl–hydrogen interactions (show these!), which contribute $4 \times 3.7 = 14.8 \text{ kJ mol}^{-1}$ ($4 \times 0.9 = 3.6 \text{ kcal mol}^{-1}$) to its energy. What about *B*? You might be tempted to say that *B* has no unfavorable interactions because it has no axial groups, but in fact *B* does have one *gauche*-butane interaction—the one between the two methyl groups themselves, which have a dihedral angle between them of 60° , just as in *gauche*-butane. This interaction can be seen in a Newman projection of the bond between the carbons bearing the methyl groups:



This *gauche*-butane interaction contributes 2.8 kJ mol^{-1} ($0.7 \text{ kcal mol}^{-1}$) to the energy of conformation *B* (Fig. 2.5, p. 54). The relative energy of the two conformations is the difference between their methyl–hydrogen interactions: $14.8 - 2.8 = 12.0 \text{ kJ mol}^{-1}$ (or $3.6 - 0.7 = 2.9 \text{ kcal mol}^{-1}$). The diaxial conformation *A* is less stable by this amount of energy.

When two groups on a substituted cyclohexane conflict in their preference for the equatorial position, the preferred conformation can usually be predicted from the relative conformational preferences of the two groups. Consider, for example, the chair interconversion of *cis*-1-*tert*-butyl-4-methylcyclohexane.



The *tert*-butyl group is so large that its van der Waals repulsions control the conformational equilibrium (see Eq. 7.7, p. 280). Hence, the chair conformation in which the *tert*-butyl group assumes the equatorial position is overwhelmingly favored. The methyl group is thus forced to take up the axial position.

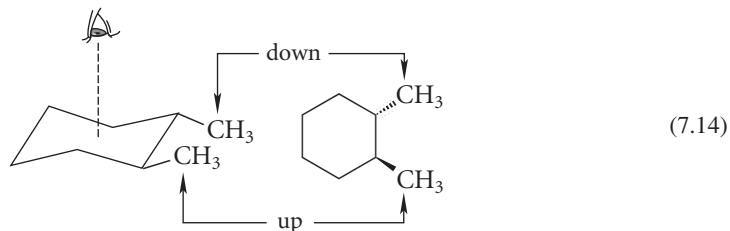
There is so little of the conformation with an axial *tert*-butyl group that chemists say sometimes that the conformational equilibrium is “locked.” This statement is somewhat misleading because it implies that the two conformations are not at equilibrium. The equilibrium indeed occurs rapidly, but simply contains very little of the conformation in which the *tert*-butyl group is axial.

PROBLEMS

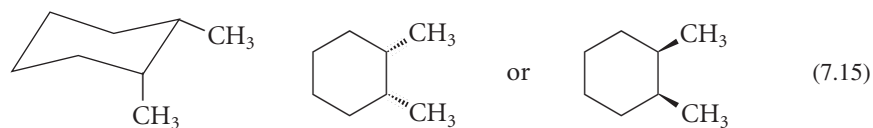
- 7.8 Calculate the energy difference between the two chair conformations of *trans*-1,4-dimethylcyclohexane.
- 7.9 Calculate the energy difference between *cis*-1,4-dimethylcyclohexane and the more stable conformation of *trans*-1,4-dimethylcyclohexane.

C. Use of Planar Structures for Cyclic Compounds

Although many cyclic compounds (such as cyclohexane and its derivatives) have nonplanar conformations, planar structures of these compounds can be used for situations in which conformational issues are not important. In this notation, the structures of cyclic compounds are represented by planar polygons with the stereochemistry of substituents indicated by dashed or solid wedges. In this type of structure, imagine viewing the ring from above. If a substituent is up, the bond to it is represented by a solid wedge; if it is down, the bond to it is represented as a dashed wedge. In this convention, one enantiomer of *trans*-1,2-dimethylcyclohexane can be drawn as follows:

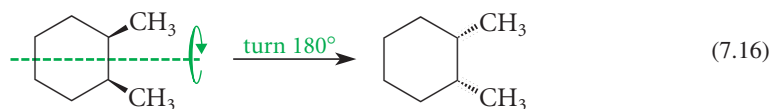


A planar structure for *cis*-1,2-dimethylcyclohexane can be drawn in either of two ways:

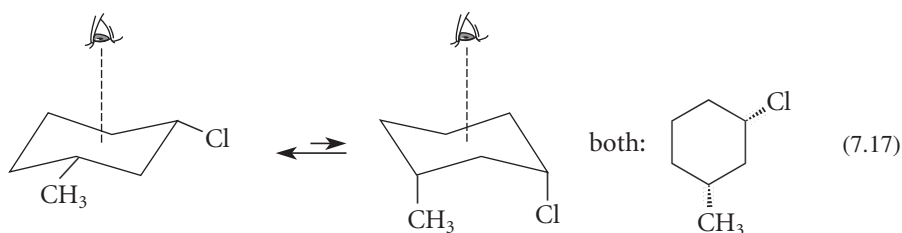


cis-1,2-dimethylcyclohexane

The two planar structures are derived, respectively, by viewing the ring from above or below. That the two structures are equivalent can be further demonstrated by turning either one over:



A planar structure does not convey any conformational information. That is, so long as all conformations are viewed from the same face of the ring, the chair interconversion does not interchange wedges and dashed lines because it does not change the up or down relationship of the ring substituents.

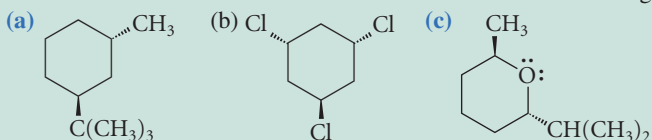


PROBLEMS

7.10 Draw a planar structure for each of the following compounds using dashed or solid wedges to show the stereochemistry of substituent groups.

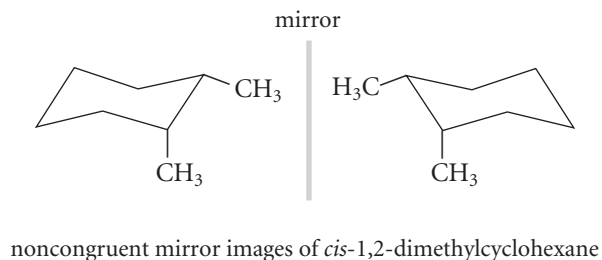
- (a) *cis*-1,3-dimethylcyclohexane
- (b) *trans*-1,3-dimethylcyclohexane
- (c) (1*R*,2*S*,3*R*)-2-chloro-1-ethyl-3-methylcyclohexane
- (d) (1*S*,2*R*)-1-chloro-2-methylcyclopentane

7.11 Draw the more stable chair conformation for each of the following compounds:

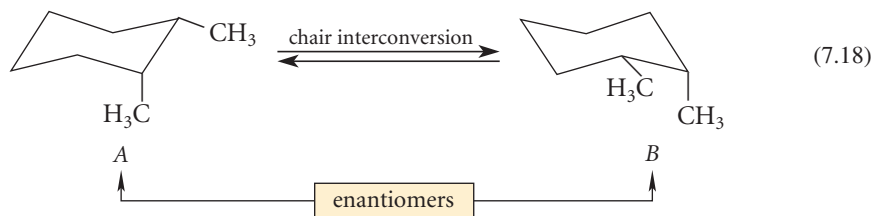


D. Stereochemical Consequences of the Chair Interconversion

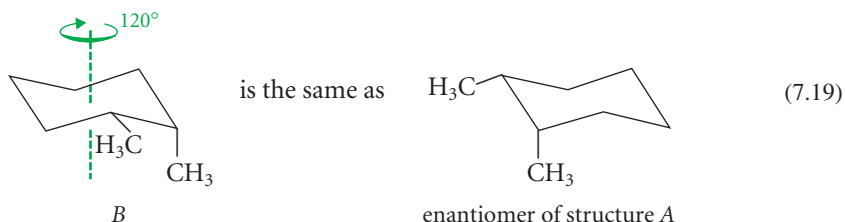
The chair interconversion has some interesting stereochemical consequences that can be illustrated with interconversion dimethylcyclohexanes. First, consider *cis*-1,2-dimethylcyclohexane. The chirality of either conformation can be demonstrated by showing that its mirror image is noncongruent.



However, the chair interconversion converts one enantiomer into the other:



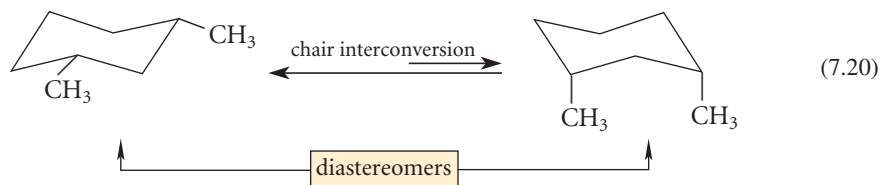
From the way they are drawn, structures A and B may not look like enantiomers, but they are! You can see this by turning structure B 120° about a vertical axis:



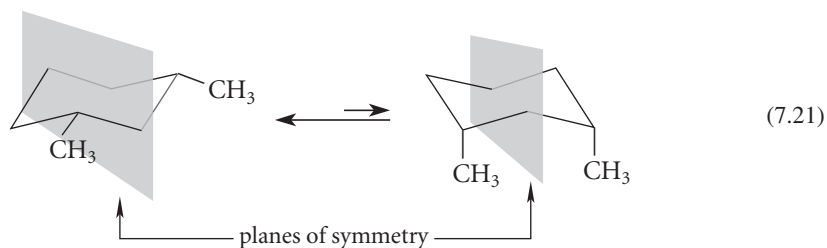
STUDY GUIDE LINK 7.1
Relating
Cyclohexane
Conformations

In other words, *cis*-1,2-dimethylcyclohexane is a mixture of *conformational enantiomers* (Sec. 6.10A). Because these enantiomers are interconverted very rapidly, they cannot be separated at ordinary temperatures. Consequently, *cis*-1,2-dimethylcyclohexane is not optically active at ordinary temperatures.

Cis-1,3-dimethylcyclohexane, another molecule with two asymmetric carbons, is a mixture of conformational diastereomers:

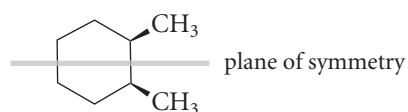
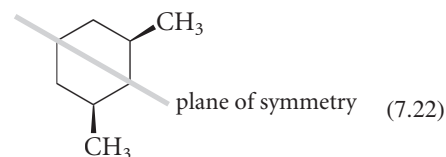


Yet, even though each conformation has two asymmetric carbons, *neither conformation is chiral* because each has an internal plane of symmetry.



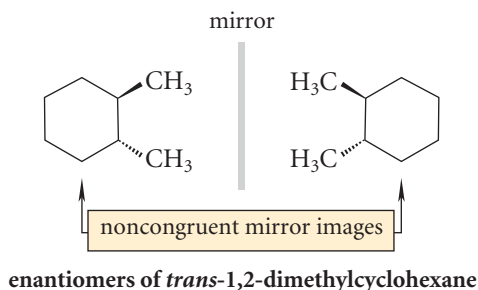
In other words, *both conformations are meso*. *Cis*-1,3-dimethylcyclohexane is thus a rapidly interconverting mixture of two different meso compounds, each a diastereomer of the other. Like any meso compound, *cis*-1,3-dimethylcyclohexane is achiral and optically inactive.

The planar structures of both *cis*-1,2- and *cis*-1,3-dimethylcyclohexane have internal mirror planes (planes of symmetry).

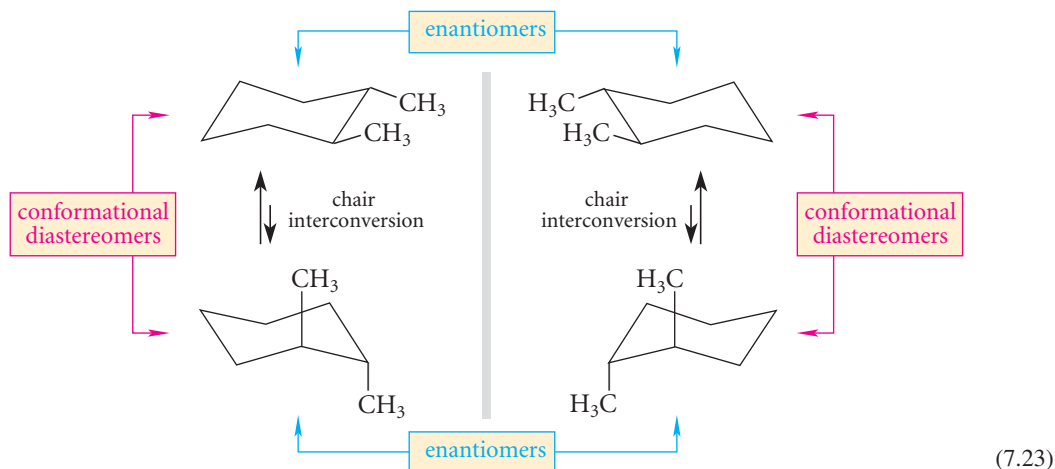
*cis*-1,2-dimethylcyclohexane*cis*-1,3-dimethylcyclohexane

As we've just seen, this plane corresponds to an actual plane of symmetry in either conformation of *cis*-1,3-dimethylcyclohexane (Eq. 7.21). However, this is *not* a plane of symmetry in the case of *cis*-1,2-dimethylcyclohexane, because each conformation is chiral and has no symmetry plane. The symmetry of the planar structures of *cis*-1,2- and *cis*-1,3-dimethylcyclohexane thus conceals a subtle difference between the two isomers. *Cis*-1,2-dimethylcyclohexane is a *mixture of chiral (and enantiomeric) conformations in rapid equilibrium*. Although it does not exhibit optical activity at ordinary temperatures, at a temperature so low that the rate of the chair interconversion would be negligible, it could in principle be separated into enantiomers, each of which would be optically active. *Cis*-1,3-dimethylcyclohexane, on the other hand, is a mixture of meso conformations. Although these, too, might be separated at a very low temperature, neither conformation would be optically active because neither is chiral. Generally speaking, then, if a cyclic compound has asymmetric carbons, and if its planar structure has an internal mirror plane, one of two things must be true: either the compound is a rapidly equilibrating mixture of conformational enantiomers, or the compound is meso. In either case, though, the compound cannot be isolated in optically active form at room temperature.

The enantiomers of *trans*-1,2-dimethylcyclohexane represent a different situation. We can see from its planar structures that *trans*-1,2-dimethylcyclohexane is chiral.



The chair interconversion converts each enantiomer into a conformational diastereomer:



Thus, each of the two enantiomers of *trans*-1,2-dimethylcyclohexane is a rapidly interconverting mixture of conformational diastereomers. Because *trans*-1,2-dimethylcyclohexane is chiral, each enantiomer is capable of independent existence and can be isolated in optically active form.

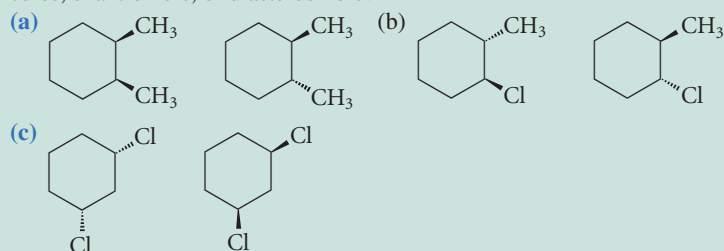
PROBLEMS

7.12 Determine whether each of the following compounds can in principle be isolated in optically active form under ordinary conditions.

- (a) *trans*-1,3-dimethylcyclohexane
 (b) 1,1-dimethylcyclohexane
 (c) *cis*-1,4-dimethylcyclohexane
 (d) *cis*-1-ethyl-3-methylcyclohexane

7.13 (a) Does *trans*-1,4-dimethylcyclohexane contain asymmetric carbons? If so, identify them.
 (b) Does *trans*-1,4-dimethylcyclohexane have any stereocenters? If so, identify them.
 (c) What is the stereochemical relationship of the two chair conformations of *trans*-1,4-dimethylcyclohexane?
 (d) Is *trans*-1,4-dimethylcyclohexane chiral?

7.14 What is the relationship of the two structures in each set? That is, are they identical molecules, enantiomers, or diastereomers?



7.5 CYCLOPENTANE, CYCLOBUTANE, AND CYCLOPROPANE

A. Cyclopentane

Cyclopentane, like cyclohexane, exists in a puckered conformation, called the **envelope conformation** (Fig. 7.10). This conformation undergoes very rapid conformational changes in which each carbon alternates as the “point” of the envelope.

The heats of formation in Table 7.1 (p. 269) show that cyclopentane has somewhat higher energy than cyclohexane. The higher energy of cyclopentane is due mostly to eclipsing between hydrogen atoms, which is also shown in Fig. 7.10.

Substituted cyclopentanes also exist in envelope conformations, but the substituents adopt positions that minimize van der Waals repulsions with neighboring groups. For example, in methylcyclopentane, the methyl group assumes an equatorial position at the point of the envelope.

