

Chapter 4 – Organic Compounds: Cycloalkanes and Their Stereochemistry

Chapter Outline

I. Cycloalkanes (Sections 4.1 – 4.2).

A. Cycloalkanes have the general formula C_nH_{2n} , if they have one ring.

B. Naming cycloalkanes (Section 4.1).

1. Find the parent.

- If the number of carbon atoms in the ring is larger than the number in the largest substituent, the compound is named as an alkyl-substituted cycloalkane.
- If the number of carbon atoms in the ring is smaller than the number in the largest substituent, the compound is named as an cycloalkyl-substituted alkane.

2. Number the substituents.

- Start at a point of attachment and number the substituents so that the second substituent has the lowest possible number.
- If necessary, proceed to the next substituent until a point of difference is found.
- If two or more substituents might potentially receive the same number, number them by alphabetical priority.
- Halogens are treated in the same way as alkyl groups.

C. Cis–trans isomerism in cycloalkanes (Section 4.2).

1. Unlike open-chain alkanes, cycloalkanes have much less rotational freedom.

- Very small rings are rigid.
- Large rings have more rotational freedom.

2. Cycloalkanes have a "top" side and a "bottom" side.

- If two substituents are on the same side of a ring, the ring is cis-disubstituted.
- If two substituents are on opposite sides of a ring, the ring is trans-disubstituted.

3. Substituents in the two types of disubstituted cycloalkanes are connected in the same order but differ in spatial orientation.

- These cycloalkanes are stereoisomers that are known as cis–trans isomers.
- Cis–trans isomers are stable compounds that can't be interconverted.

II. Conformations of cycloalkanes (Sections 4.3 – 4.9).

A. General principles (Section 4.3).

1. Ring strain.

- A. von Baeyer suggested that rings other than those of 5 or 6 carbons were too strained to exist.
- This concept of angle strain is true for smaller rings, but larger rings can be easily prepared.

2. Heats of combustion of cycloalkanes.

- To measure strain, it is necessary to measure the total energy of a compound and compare it to a strain-free reference compound.
- Heat of combustion measures the amount of heat released when a compound is burned in oxygen.
 - The more strained the compound, the higher the heat of combustion.
 - Strain per CH_2 unit can be calculated and plotted as a function of ring size.
- Graphs show that only small rings have serious strain.

3. The nature of ring strain.
 - a. Rings tend to adopt puckered conformations.
 - b. Several factors account for ring strain.
 - i. Angle strain occurs when bond angles are distorted from their normal values.
 - ii. Torsional strain is due to eclipsing of bonds.
 - iii. Steric strain results when atoms approach too closely.
- B. Conformations of small rings (Section 4.4).
 1. Cyclopropane.
 - a. Cyclopropane has bent bonds.
 - b. Because of bent bonds, cyclopropane is more reactive than other cycloalkanes.
 2. Cyclobutane.
 - a. Cyclobutane has less angle strain than cyclopropane but has more torsional strain.
 - b. Cyclobutane has almost the same total strain as cyclopropane.
 - c. Cyclobutane is slightly bent to relieve torsional strain, but this increases angle strain.
 3. Cyclopentane
 - a. Cyclopentane has little angle strain but considerable torsional strain.
 - b. To relieve torsional strain, cyclopentane adopts a puckered conformation.

In this conformation, one carbon is bent out of plane; hydrogens are nearly staggered.
- C. Conformations of cyclohexane (Sections 4.5 – 4.8).
 1. Chair cyclohexane (Section 4.5).
 - a. The chair conformation of cyclohexane is strain-free.
 - b. In a standard drawing of cyclohexane, the lower bond is in front.
 - c. The twist-boat conformation of cyclohexane has little angle strain but experiences both steric strain and torsional strain.
 2. Axial and equatorial bonds in cyclohexane (Section 4.6).
 - a. There are two kinds of positions on a cyclohexane ring.
 - i. Six axial hydrogens are perpendicular to the plane of the ring.
 - ii. Six equatorial hydrogens are roughly in the plane of the ring.
 - b. Each carbon has one axial hydrogen and one equatorial hydrogen.
 - c. Each side of the ring has alternating axial and equatorial hydrogens.
 - d. All hydrogens on the same side of the ring are cis.
 3. Conformational mobility of cyclohexanes.
 - a. Different chair conformations of cyclohexanes interconvert by a ring-flip.
 - b. After a ring-flip, an axial bond becomes an equatorial bond, and vice versa.
 - c. The energy barrier to interconversion is 45 kJ/mol, making interconversion rapid at room temperature.
 4. Conformations of monosubstituted cyclohexanes (Section 4.7).
 - a. Both conformations aren't equally stable at room temperature.

In methylcyclohexane, 95% of molecules have the methyl group in the equatorial position.
 - b. The energy difference is due to 1,3-diaxial interactions.
 - i. These interactions are due to steric strain.
 - ii. They are the same interactions as occur in gauche butane.
 - c. Axial methylcyclohexane has two gauche interactions that cause it to be 7.6 kJ/mol less stable than equatorial methylcyclohexane.
 - d. All substituents are more stable in the equatorial position.

The size of the strain depends on the size of the group.

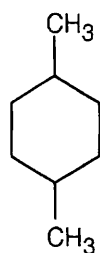
5. Conformations of disubstituted cyclohexanes (Section 4.8).
 - a. In *cis*-1,2-dimethylcyclohexane, one methyl group is axial and one is equatorial in both chair conformations, which are of equal energy.
 - b. In *trans*-1,2-dimethylcyclohexane, both methyl groups are either both axial or both equatorial.
 - i. The conformation with both methyl groups axial is 15.2 kJ/mol less stable than the conformation with both groups equatorial.
 - ii. The *trans* isomer exists almost exclusively in the diequatorial conformation.
 - c. This type of conformational analysis can be carried out for most substituted cyclohexanes.
- D. Conformations of polycyclic molecules (Section 4.9).
 1. Decalin has two rings that can be either *cis*-fused or *trans*-fused. The two decalins are nonconvertible.
 2. Steroids have four fused rings.
 3. Bicyclic ring systems have rings that are connected by bridges. In norbornane, the six-membered ring is locked into a boat conformation.

Solutions to Problems

- 4.1 Strategy:** The steps for naming a cycloalkane are very similar to the steps used for naming an open-chain alkane.
- Step 1:* Name the parent cycloalkane. In (a), the parent is cyclohexane. If the compound has an alkyl substituent with more carbons than the ring size, the compound is named as a cycloalkyl-substituted alkane.
- Step 2:* Identify the substituents. In (a), both substituents are methyl groups.
- Step 3:* Number the substituents so that the second substituent receives the lowest possible number. In (a), the substituents are in the 1- and 4- positions.
- Step 4:* Name the compound. If two different alkyl groups are present, cite them alphabetically. Halogen substituents follow the same rules as alkyl substituents.

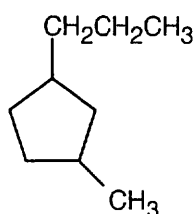
Solution:

(a)



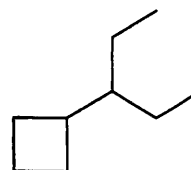
1,4-Dimethylcyclohexane

(b)



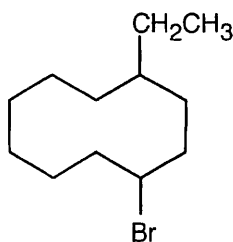
1-Methyl-3-propylcyclopentane

(c)



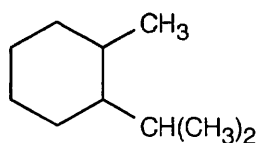
3-Cyclobutylpentane

(d)



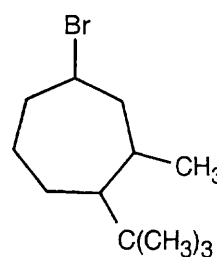
1-Bromo-4-ethylcyclodecane

(e)



1-Isopropyl-2-methylcyclohexane

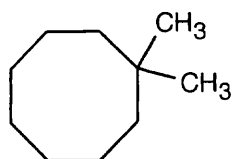
(f)



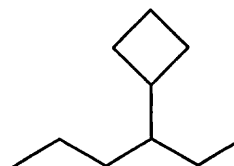
4-Bromo-1-tert-butyl-2-methylcycloheptane

- 4.2** To draw a substituted cycloalkane, simply draw the ring and attach substituents in the specified positions.

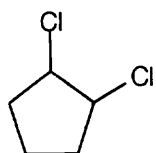
(a)

**1,1-Dimethylcyclooctane**

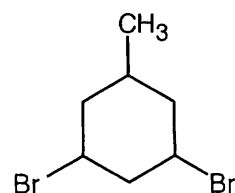
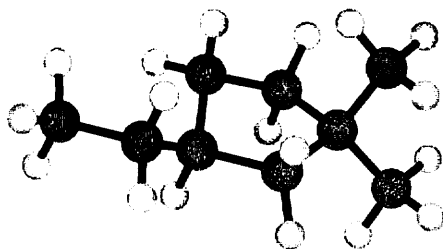
(b)

**3-Cyclobutylhexane**

(c)

**1,2-Dichlorocyclopentane**

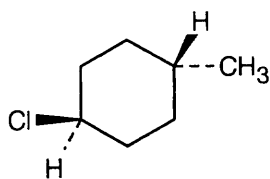
(d)

**1,3-Dibromo-5-methylcyclohexane****4.3****3-Ethyl-1,1-dimethylcyclopentane**

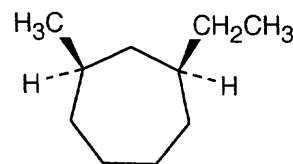
- 4.4 Strategy:** Two substituents are *cis* if they both have either dashed or wedged bonds. The substituents are *trans* if one has a wedged bond and the other has a dashed bond.

Solution:

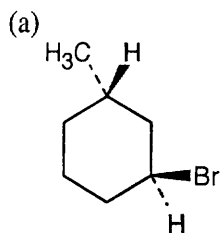
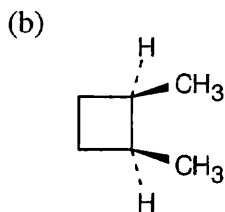
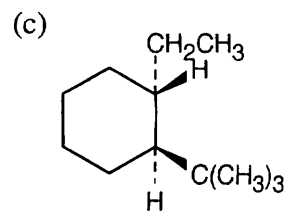
(a)

***trans*-1-Chloro-4-methylcyclohexane**

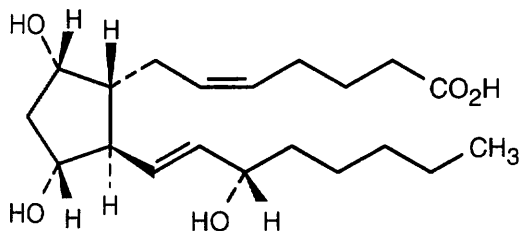
(b)

***cis*-1-Ethyl-3-methylcycloheptane**

4.5

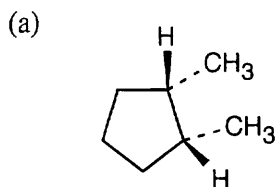
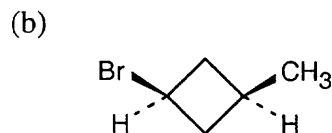
***trans*-1-Bromo-3-methylcyclohexane*****cis*-1,2-Dimethylcyclobutane*****trans*-1-*tert*-Butyl-2-ethylcyclohexane**

4.6

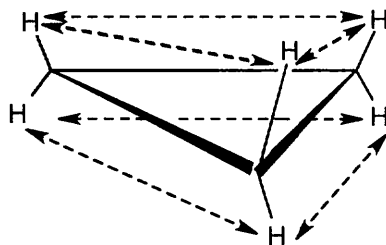
**Prostaglandin $F_{2\alpha}$**

The two hydroxyl groups are *cis* because they both point behind the plane of the page. The carbon chains have a *trans* relationship (one is dashed and the other is wedged).

4.7

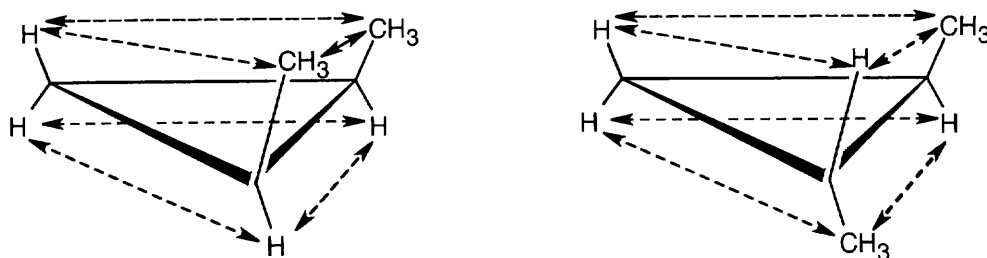
***cis*-1,2-Dimethylcyclopentane*****cis*-1-Bromo-3-methylcyclobutane**

4.8



All hydrogen atoms on the same side of the cyclopropane ring are eclipsed by neighboring hydrogens. If we draw each hydrogen-hydrogen interaction, we count six eclipsing interactions. Since each of these interactions costs 4.0 kJ/mol, all six cost 24.0 kJ/mol. $24 \text{ kJ/mol} \div 115 \text{ kJ/mol} = 0.21$; thus, 21% of the total strain energy of cyclopropane is due to torsional strain.

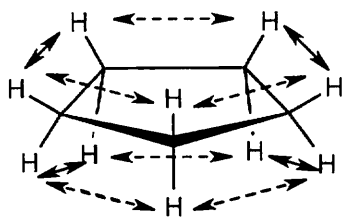
4.9



Eclipsing interaction	Energy cost (kJ/mol)	<i>cis isomer</i>		<i>trans isomer</i>	
		# of interactions	Total energy cost (kJ/mol)	# of interactions	Total energy cost (kJ/mol)
H-H	4.0	3	12.0	2	8.0
H-CH ₃	6.0	2	12.0	4	24.0
CH ₃ -CH ₃	11	1	11	0	0
			<u>35</u>		<u>32</u>

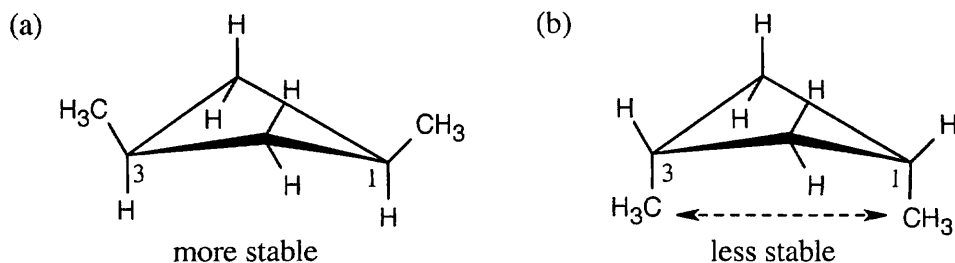
The added energy cost of eclipsing interactions causes *cis*-1,2-dimethylcyclopropane to be of higher energy and to be less stable than the *trans* isomer.

4.10



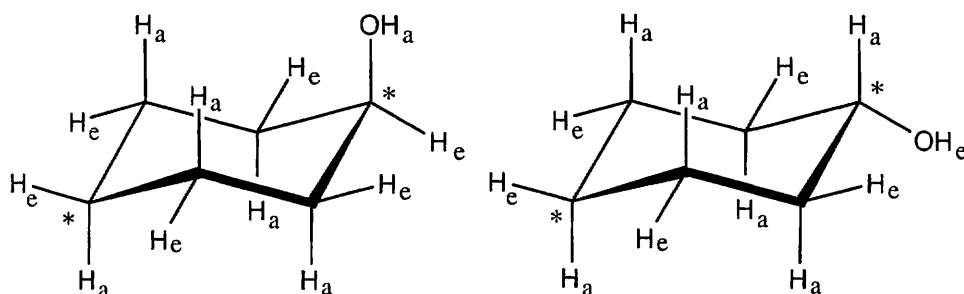
If cyclopentane were planar, it would have ten hydrogen-hydrogen interactions with a total energy cost of 40 kJ/mol. The measured total strain energy of 26 kJ/mol indicates that 14 kJ/mol of eclipsing strain in cyclopentane (35%) has been relieved by puckering.

4.11



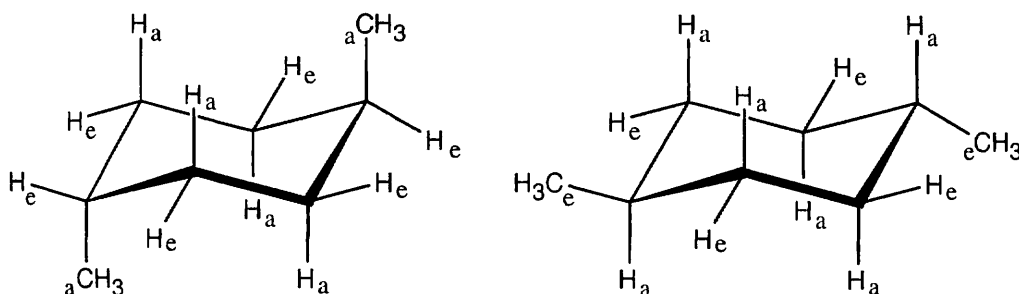
The methyl groups are farther apart in the more stable conformation of *cis*-1,3-dimethylcyclobutane.

- 4.12** Use the technique in Section 4.5 to draw the cyclohexane ring. Figure 4.10 shows how to attach axial and equatorial bonds.



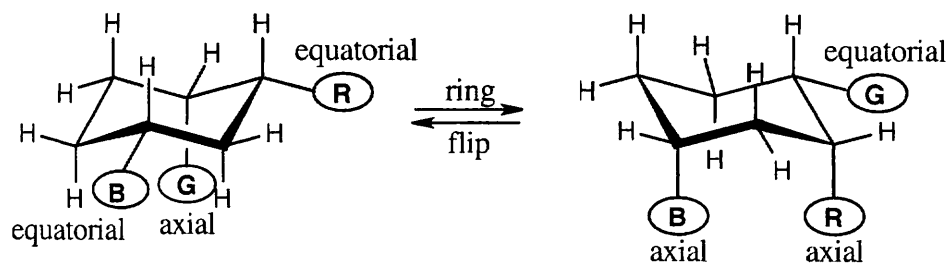
The conformation with -OH in the equatorial position is more stable.
Note: The starred ring carbons lie in the plane of the paper.

- 4.13** In *trans*-1,4-disubstituted cyclohexanes, the methyl substituents are either both axial or both equatorial.

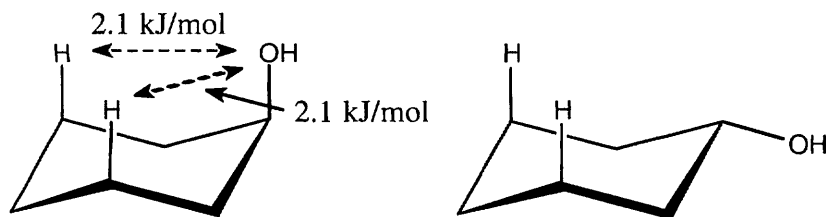


***trans*-1,4-Dimethylcyclohexane**

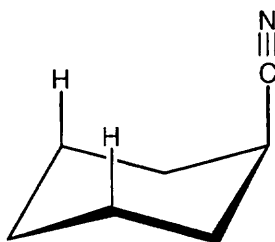
4.14



- 4.15** Table 4.1 shows that an axial hydroxyl group causes 2×2.1 kJ/mol of steric strain. Thus, the energy difference between axial and equatorial cyclohexanol is 4.2 kJ/mol.



- 4.16 There is very little energy difference between an axial and an equatorial cyano group because the small cyano group produces practically no 1,3-diaxial interactions.

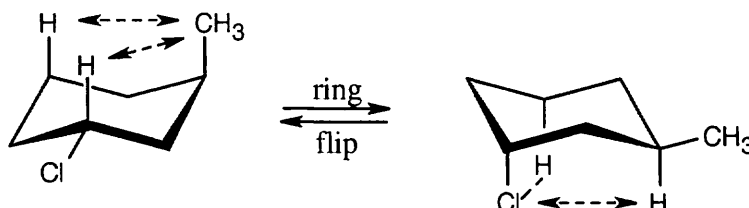


Cyclohexanecarbonitrile

- 4.17 Table 4.1 shows that an axial bromine causes 2×1.0 kJ/mol of steric strain. Thus, the energy difference between axial and equatorial bromocyclohexane is 2.0 kJ/mol. According to Figure 4.12, this energy difference corresponds approximately to a 75:25 ratio of more stable : less stable conformer. Thus, 75% of bromocyclohexane molecules are in the equatorial conformation, and 25% are in the axial conformation at any given moment.
- 4.18 **Strategy:** Draw the two chair conformations of each molecule, and look for gauche and 1,3-diaxial interactions. Use Table 4.1 to estimate the values of the interactions. Calculate the total strain; the conformation with the smaller value for strain energy is more stable.

Solution:

(a)



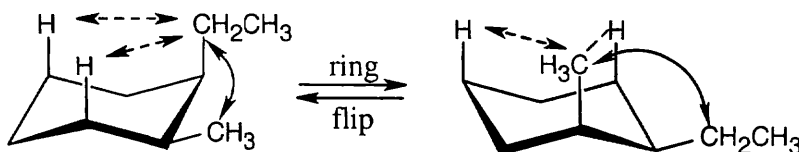
***trans*-1-Chloro-3-methylcyclohexane**

$$2 (\text{H}-\text{CH}_3) = 7.6 \text{ kJ/mol}$$

$$2 (\text{H}-\text{Cl}) = 2.0 \text{ kJ/mol}$$

The second conformation is more stable than the first.

(b)



***cis*-1-Ethyl-2-methylcyclohexane**

$$\begin{array}{l} \text{one } \text{CH}_3-\text{CH}_2\text{CH}_3 \text{ gauche} \\ \text{interaction} = 3.8 \text{ kJ/mol} \\ 2 (\text{H}-\text{CH}_2\text{CH}_3) = 8.0 \text{ kJ/mol} \end{array}$$

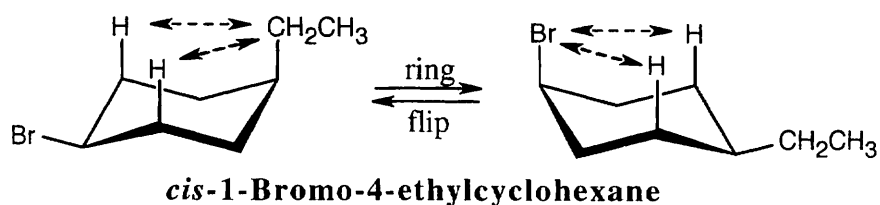
$$\text{Total} = 11.8 \text{ kJ/mol}$$

$$\begin{array}{l} \text{one } \text{CH}_3-\text{CH}_2\text{CH}_3 \text{ gauche} \\ \text{interaction} = 3.8 \text{ kJ/mol} \\ 2 (\text{H}-\text{CH}_3) = 7.6 \text{ kJ/mol} \end{array}$$

$$\text{Total} = 11.4 \text{ kJ/mol}$$

The second conformation is more stable than the first.

(c)

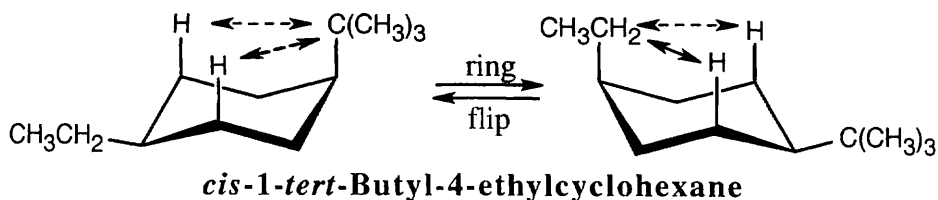


$$2 (\text{H}-\text{CH}_2\text{CH}_3) = 8.0 \text{ kJ/mol}$$

$$2 (\text{H}-\text{Br}) = 2.0 \text{ kJ/mol}$$

The second conformation is more stable than the first.

(d)



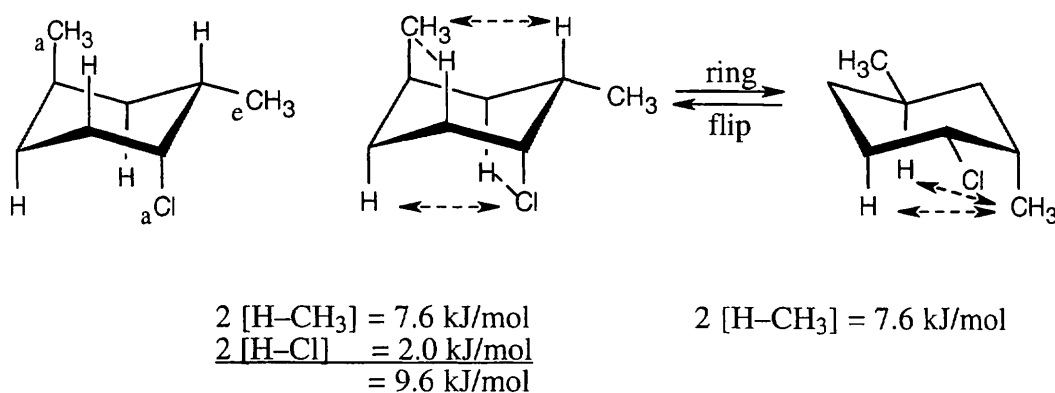
$$2 [\text{H}-\text{C}(\text{CH}_3)_3] = 22.8 \text{ kJ/mol}$$

$$2 (\text{H}-\text{CH}_2\text{CH}_3) = 8.0 \text{ kJ/mol}$$

The second conformation is more stable than the first.

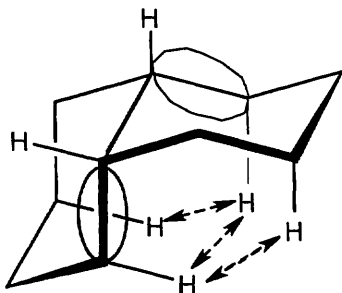
4.19 Strategy: The three substituents have the orientations shown in the first structure. To decide if the conformation shown is the more stable conformation or the less stable conformation, perform a ring-flip on the illustrated conformation and do a calculation like those in the previous problem. Notice that each conformation has a Cl-CH₃ gauche interaction, but we don't need to know its energy cost because it is present in both conformations.

Solution:



The illustrated conformation is the less stable chair form.

4.20



Trans-decalin is more stable than *cis*-decalin because of three 1,3-diaxial interactions present in the *cis* isomer. You may be able to visualize these interactions by thinking of the circled parts of *cis*-decalin as similar to axial methyl groups. The gauche interactions that occur with axial methyl groups also occur in *cis*-decalin.

Visualizing Chemistry

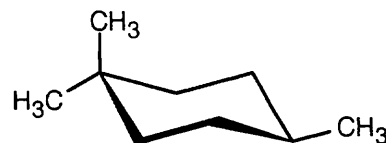
4.21

(a)



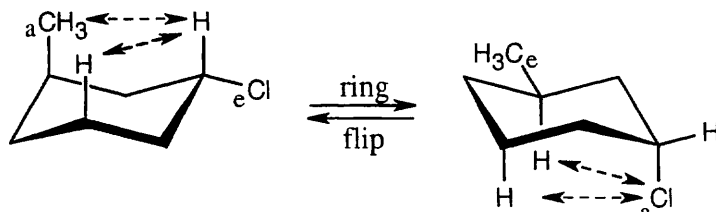
cis-1-Ethyl-3-methyl-
cyclopentane

(b)



1,1,4-Trimethylcyclohexane

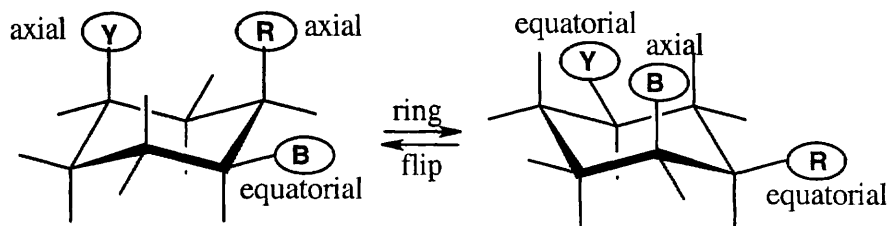
4.22



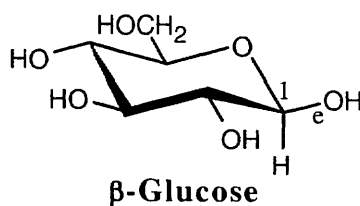
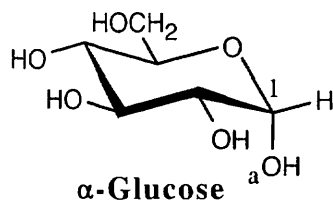
trans-1-Chloro-3-methylcyclohexane

$2 (\text{H}-\text{CH}_3) = 7.6 \text{ kJ/mol}$ $2 (\text{H}-\text{Cl}) = 2.0 \text{ kJ/mol}$
The conformation shown (the left structure) is the less stable conformation.

4.23



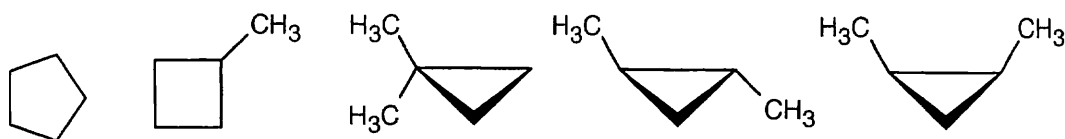
4.24



The only difference between α -glucose and β -glucose is in the orientation of the -OH group at carbon 1; the -OH group is axial in α -glucose, and it is equatorial in β -glucose. You would expect β -glucose to be more stable because it has all substituents in the equatorial position.

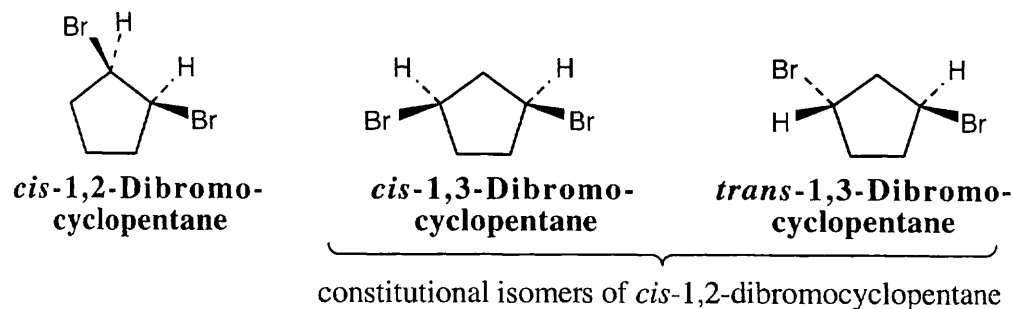
Additional Problems

4.25

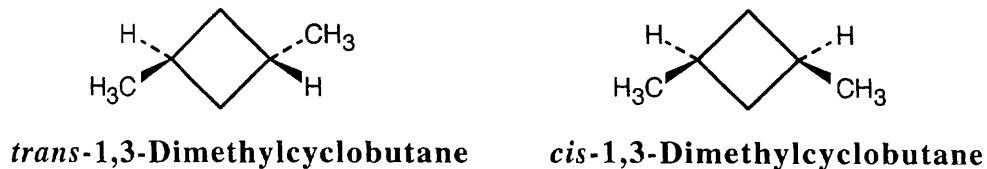


The last two structures are *cis-trans* isomers.

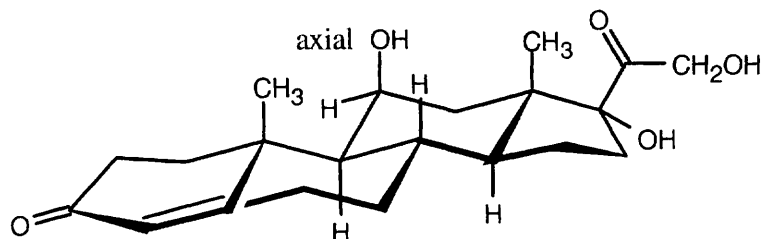
4.26



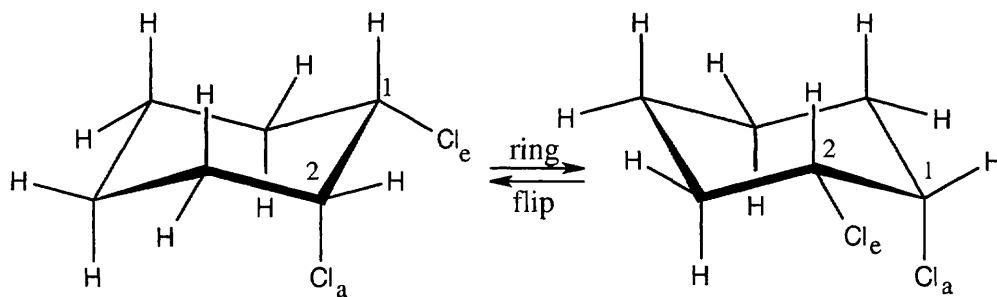
4.27



4.28

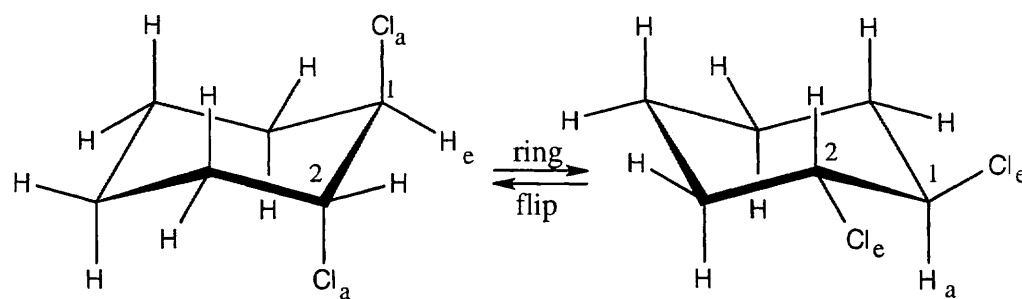


- 4.29** Make a model of *cis*-1,2-dichlorocyclohexane. Notice that all *cis* substituents are on the same side of the ring and that two adjacent *cis* substituents have an axial–equatorial relationship. Now, perform a ring-flip on the cyclohexane.



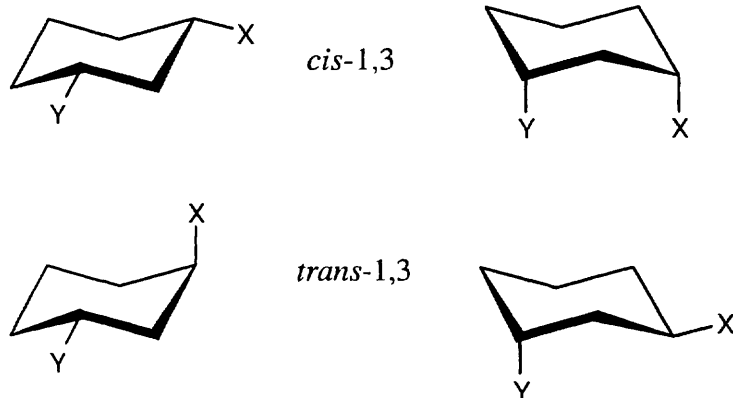
After the ring-flip, the relationship of the two substituents is still axial–equatorial. No two adjacent *cis* substituents can be converted to being both axial or both equatorial. Don't forget that there are only two chair conformations of any given cyclohexane.

- 4.30** For a *trans*-1,2-disubstituted cyclohexane, two adjacent substituents must be either both axial or both equatorial.



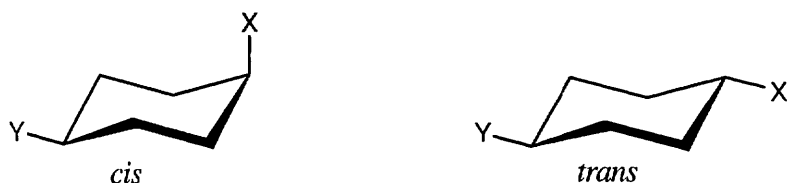
A ring flip converts two adjacent axial substituents to equatorial substituents, and vice versa. As in Problem 4.29, no two adjacent *trans* substituents can have an axial–equatorial relationship.

4.31



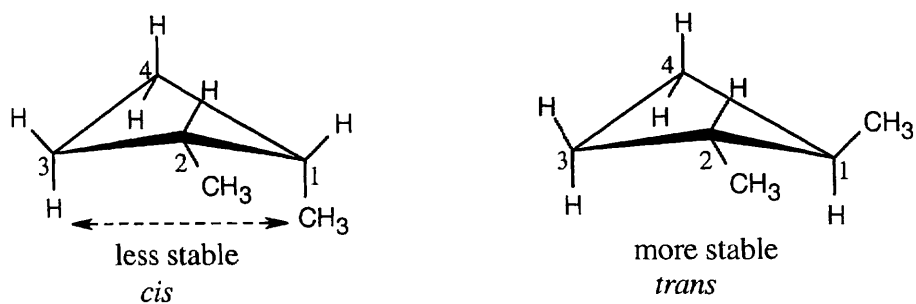
A *cis*-1,3-disubstituted isomer exists almost exclusively in the diequatorial conformation, which has no 1,3-diaxial interactions. The *trans* isomer must have one group axial, leading to 1,3-diaxial interactions. Thus, the *trans* isomer is less stable than the *cis* isomer. When a molecule has two conformations available, the molecule exists mainly in the lower energy conformation.

4.32

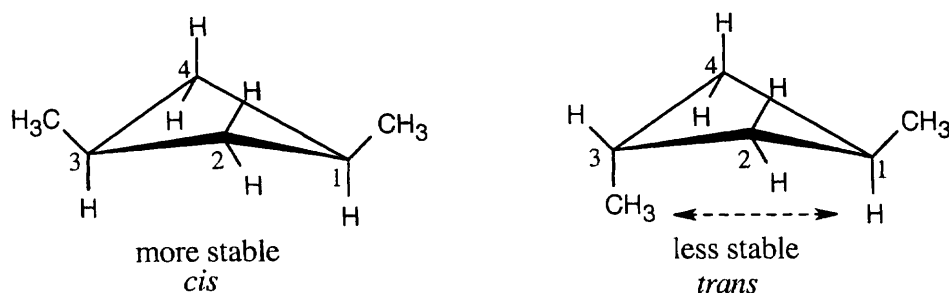


The *trans*-1,4-isomer is more stable.

4.33

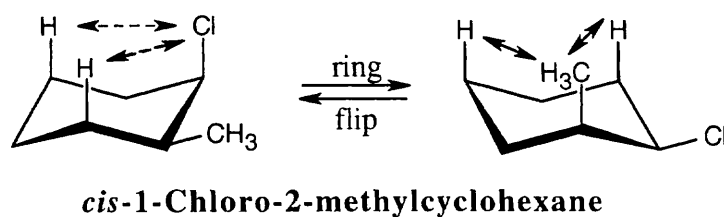


Two types of interaction are present in *cis*-1,2-dimethylcyclobutane. One interaction occurs between the two methyl groups, which are almost eclipsed. The other is an across-the-ring interaction between methyl group at position 1 of the ring and a hydrogen at position 3. Because neither of these interactions are present in *trans* isomer, it is more stable than the *cis* isomer.



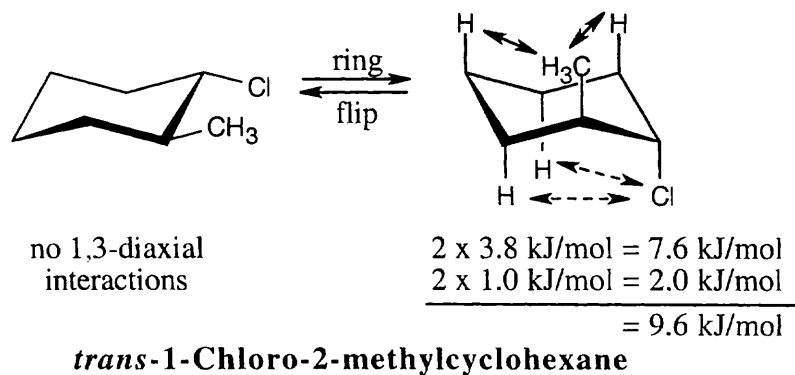
In *trans*-1,3-dimethylcyclobutane, an across-the-ring interaction occurs between the methyl group at position 3 of the ring and a hydrogen at position 1. Because no interactions are present in the *cis* isomer, it is more stable than the *trans* isomer.

4.34



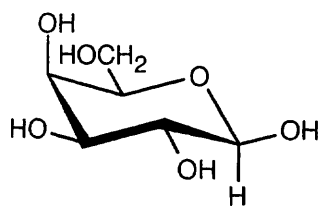
Use Table 4.1 to find the values of 1,3-diaxial interactions. For the first conformation, the steric strain is $2 \times 1.0 \text{ kJ/mol} = 2.0 \text{ kJ/mol}$. The steric strain in the second conformation is $2 \times 3.8 \text{ kJ/mol}$, or 7.6 kJ/mol . The first conformation is more stable than the second conformation by 5.6 kJ/mol .

4.35



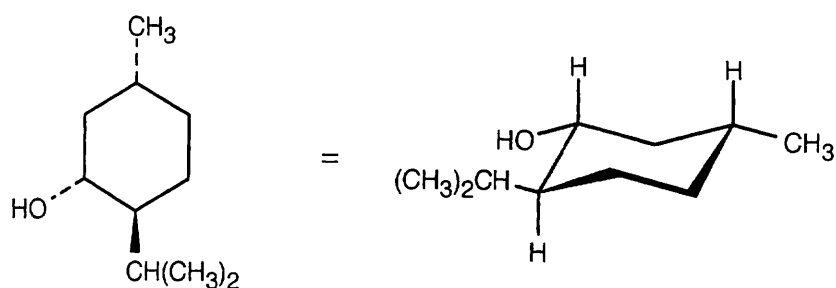
The first conformation is more stable than the second conformation by a maximum of 9.6 kJ/mol . (A gauche interaction between the two substituents in the diequatorial conformation reduces the value of the energy difference.)

4.36

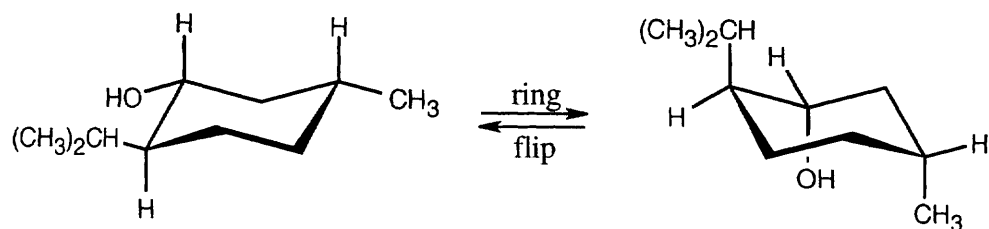
**Galactose**

In this conformation, all substituents, except for one hydroxyl group, are equatorial.

- 4.37** From the flat-ring drawing you can see that the methyl group and the -OH group have a cis relationship, and the isopropyl group has a trans relationship to both of these groups. Draw a chair cyclohexane ring and attach the groups with the correct relationship.

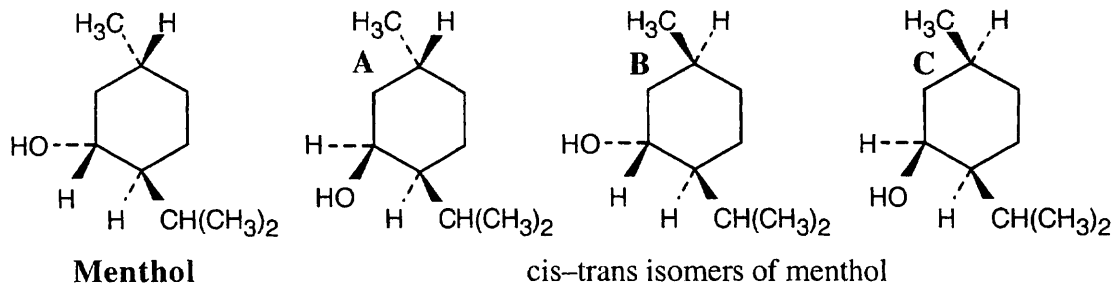


In this conformation, all substituents are equatorial. Now, perform a ring flip.



The second conformation is less stable because all substituents are axial.

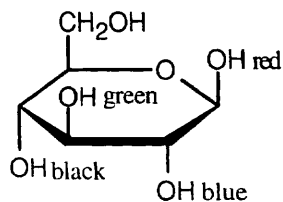
4.38



The substituents on the ring have the following relationships:

	Menthol	Isomer A	Isomer B	Isomer C
$-\text{CH}(\text{CH}_3)_2, -\text{CH}_3$	trans	trans	cis	cis
$-\text{CH}(\text{CH}_3)_2, -\text{OH}$	trans	cis	trans	cis
$-\text{CH}_3, -\text{OH}$	cis	trans	trans	cis

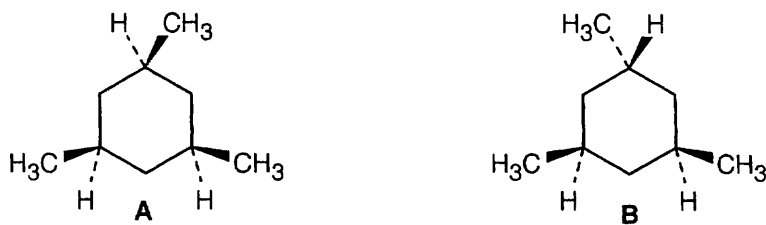
4.39



cis relationship: red–green, blue–black

trans relationship: red–blue, green–blue
red–black, green–black

4.40

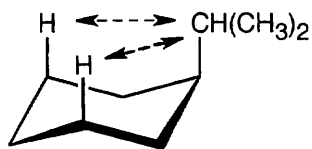


Two cis-trans isomers of 1,3,5-trimethylcyclohexane are possible. In one isomer (**A**), all methyl groups are cis; in **B**, one methyl group is trans to the other two.

4.41 Strategy: To solve this problem: (1) Find the energy cost of a 1,3-diaxial interaction by using Table 4.1. (2) Convert this energy difference into a percent by using Figure 4.12.

Solution:

(a)

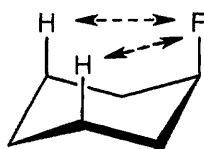


$$2 (\text{H} - \text{CH}(\text{CH}_3)_2) = 9.2 \text{ kJ/mol}$$

$$\% \text{ equatorial} = 97$$

$$\% \text{ axial} = 3$$

(b)

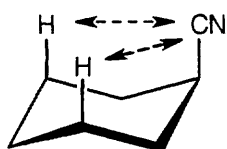


$$2 (\text{H} - \text{F}) = 1.0 \text{ kJ/mol}$$

$$\% \text{ equatorial} = 63$$

$$\% \text{ axial} = 37$$

(c)



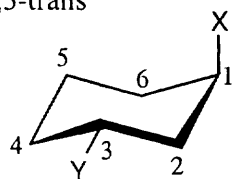
$$2 (\text{H} - \text{CN}) = 0.8 \text{ kJ/mol}$$

$$\% \text{ equatorial} = 60$$

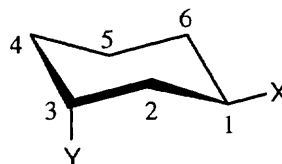
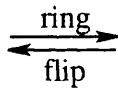
$$\% \text{ axial} = 40$$

4.42 Make sure you know the difference between axial–equatorial and cis–trans. Axial substituents are parallel to the axis of the ring; equatorial substituents lie around the equator of the ring. Cis substituents are on the same side of the ring; trans substituents are on opposite side of the ring.

(a) 1,3-trans

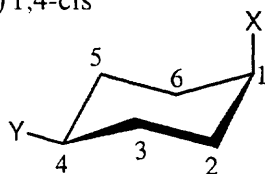


axial, equatorial

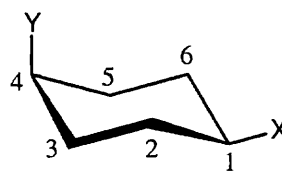
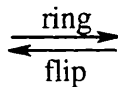


equatorial, axial

(b) 1,4-cis

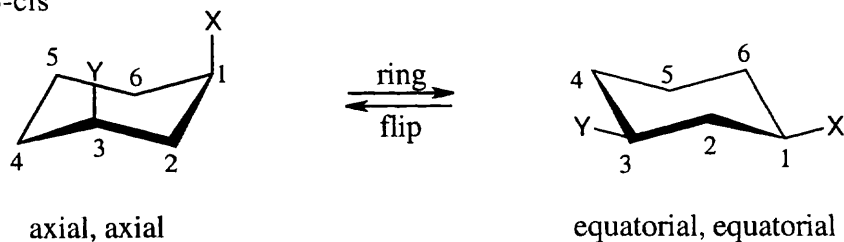


axial, equatorial



equatorial, axial

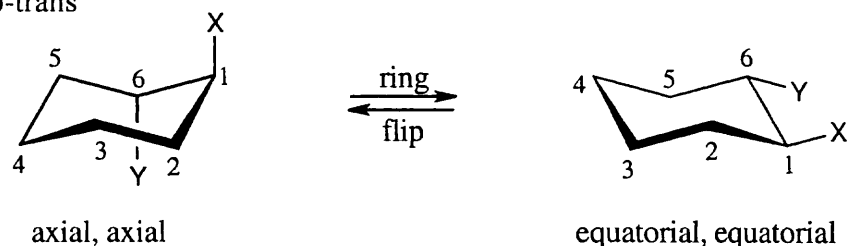
(c) 1,3-cis



(d) 1,5-trans is the same as 1,3-trans

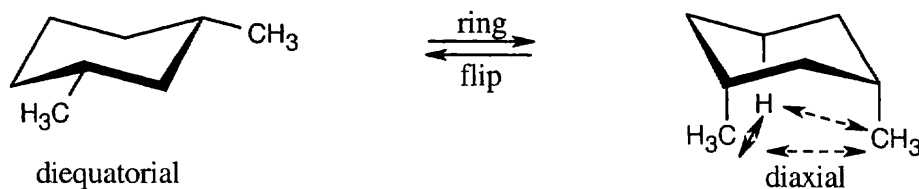
(e) 1,5-cis is the same as 1,3-cis

(f) 1,6-trans



1,6-trans is the same as 1,2-trans.

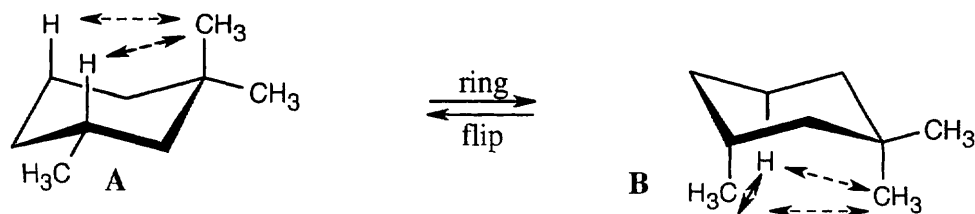
4.43



The large energy difference between conformations is due to the severe 1,3 diaxial interaction between the two methyl groups.

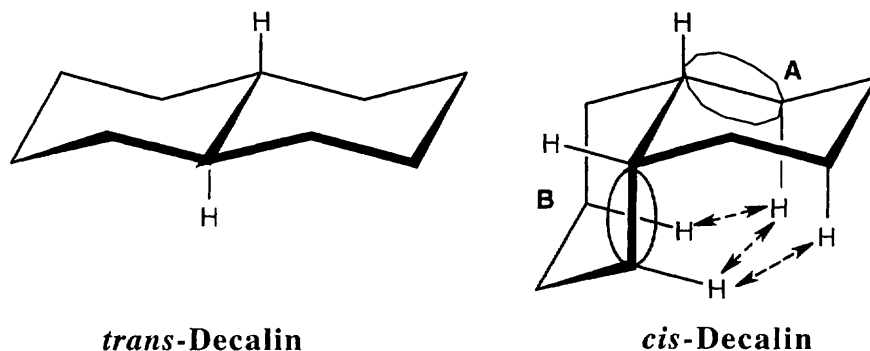
4.44 Diaxial cis-1,3-dimethylcyclohexane contains three 1,3-diaxial interactions -- two H-CH₃ interactions of 3.8 kJ/mol each, and one CH₃-CH₃ interaction. If the diaxial conformation is 23 kJ/mol less stable than the diequatorial, $23 \text{ kJ/mol} - 2(3.8 \text{ kJ/mol}) \approx 15 \text{ kJ/mol}$ of this strain energy must be due to the CH₃-CH₃ interaction.

4.45

2 H - CH₃ interactions = 7.6 kJ/mol
$$\begin{array}{rcl} 2 \text{ H} - \text{CH}_3 \text{ interactions} & = & 7.6 \text{ kJ/mol} \\ 1 \text{ CH}_3 - \text{CH}_3 \text{ interaction} & = & 15 \text{ kJ/mol} \\ & \approx & 23 \text{ kJ/mol} \end{array}$$

Conformation **A** is favored because it is 15 kJ/mol lower in energy than conformation **B**.

- 4.46** Note: In working with decalins, it is essential to use models. Many structural features of decalins that are obvious with models are not easily visualized with drawings.

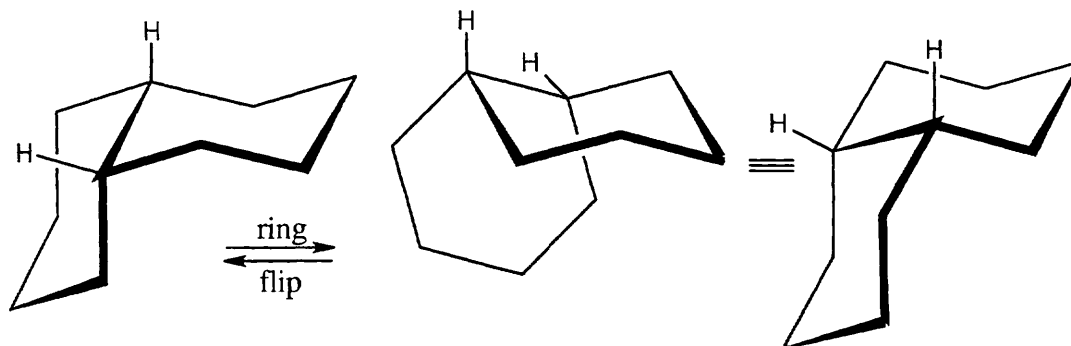


No 1,3-diaxial interactions are present in *trans*-decalin.

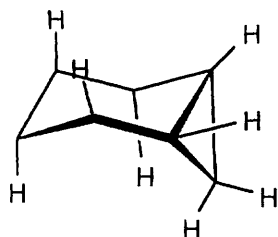
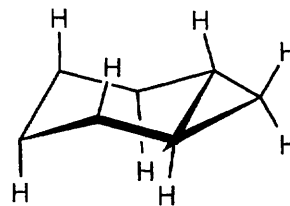
At the ring junction of *cis*-decalin, one ring acts as an axial substituent of the other (see circled bonds). The circled part of ring **B** has two 1,3-diaxial interactions with ring **A** (indicated by arrows). Similarly, the circled part of ring **A** has two 1,3-diaxial interactions with ring **B**; one of these interactions is the same as an interaction of part of the **B** ring with ring **A**. These three 1,3-diaxial interactions have a total energy cost of $3 \times 3.8 \text{ kJ/mol} = 11.4 \text{ kJ/mol}$. *Cis*-decalin is therefore less stable than *trans*-decalin by 11.4 kJ/mol.

- 4.47** A ring-flip converts an axial substituent into an equatorial substituent and vice versa. At the ring junction of *trans*-decalin, each ring is a *trans-trans* diequatorial substituent of the other. If a ring-flip were to occur, the two rings would become axial substituents of each other. You can see with models that a diaxial ring junction is impossibly strained. Consequently, *trans*-decalin does not ring-flip.

The rings of *cis*-decalin are joined by an axial bond and an equatorial bond. After a ring-flip, the rings are still linked by an equatorial and an axial bond. No additional strain or interaction is introduced by a ring-flip of *cis*-decalin.



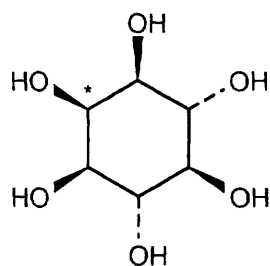
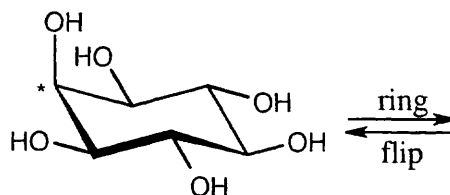
- 4.48 Build models to see the stability difference between the two [4.1.0] ring systems. In both cases, fusing a three-membered ring to a six-membered ring distorts the bond angles of both rings, causing angle strain. This strain is much more severe in the trans isomer than in the cis isomer.

*cis*-Bicyclo[4.1.0]heptane*trans*-Bicyclo[4.1.0]heptane

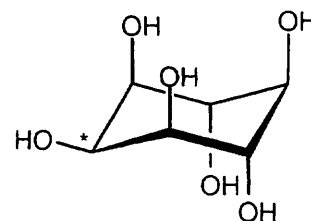
- 4.49 **Strategy:** In the flat-ring structure shown, all -OH groups have a alternating relationship except for the starred group. If all of the groups had a trans relationship, the most stable conformation would have all -OH groups in the equatorial position. We expect that the most stable conformation of this structure has one group in the axial position.

Draw both rings and add -OH groups having the indicated relationships. Perform a ring-flip on the structure you have drawn to arrive at the other conformation.

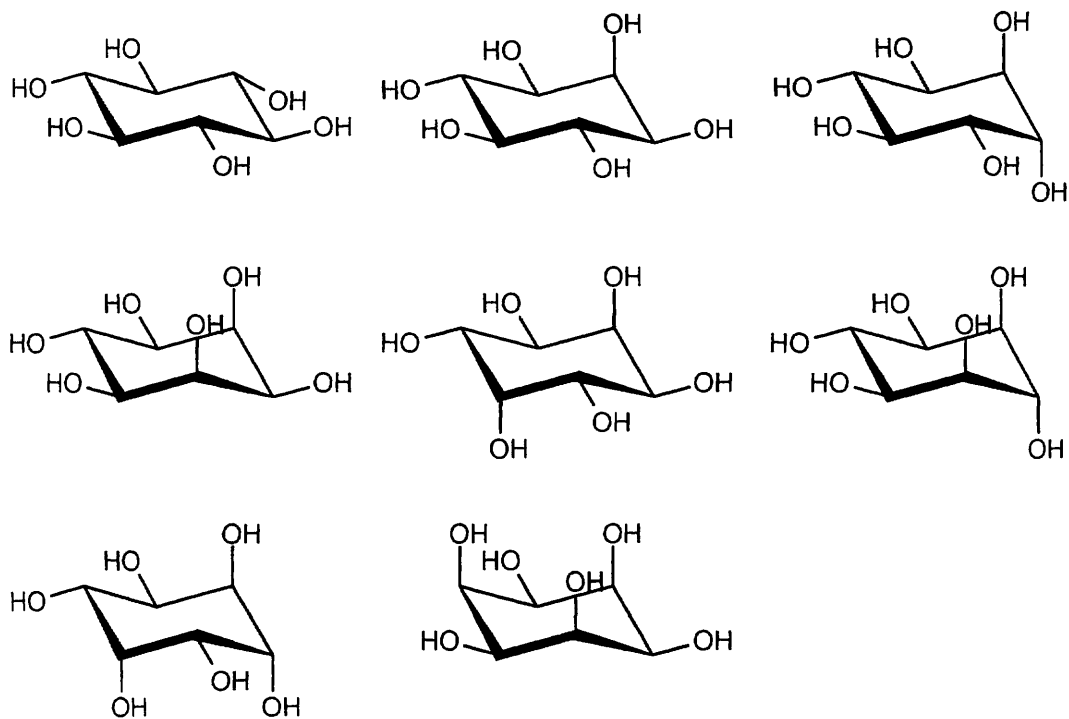
Solution:

*myo*-Inositol

more stable



4.50



There are eight cis–trans stereoisomers of *myo*-inositol. The first isomer is the most stable because all hydroxyl groups can assume an equatorial conformation.

4.51



Conformation **A** of *cis*-1-chloro-3-methylcyclohexane has no 1,3-diaxial interactions and is the more stable conformation. Steric strain in **B** is due to one $\text{CH}_3\text{--H}$ interaction (3.8 kJ/mol), one Cl--H interaction (1.0 kJ/mol) and one $\text{CH}_3\text{--Cl}$ interaction. Since the total-strain energy of **B** is 15.5 kJ/mol, $15.5 \text{ kJ/mol} - 3.8 \text{ kJ/mol} - 1.0 \text{ kJ/mol} = 10.7 \text{ kJ/mol}$ of strain is caused by a $\text{CH}_3\text{--Cl}$ interaction.

4.52

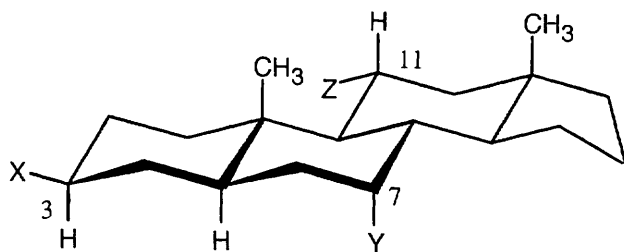


1-Norbornene

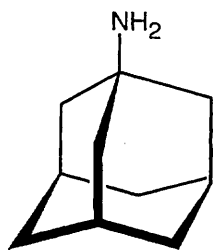
If you build a model of 1-norbornene, you will find that it is almost impossible to form the bridgehead double bond. sp^2 -Hybridization at the double bond requires all carbons bonded to the starred carbons to lie in a common plane in order for the p orbitals to overlap to form the π bond. The bicyclic ring system forces these atoms out of plane, and the bridgehead double bond can't form.

- 4.53 A steroid ring system is fused, and ring-flips don't occur. Thus, substituents such as the methyl groups shown remain axial. Substituents on the same side of the ring system as the methyl groups are in alternating axial and equatorial positions. Thus, an "up" substituent at C3 (a) is equatorial.

Substituents on the bottom side of the ring system also alternate axial and equatorial positions. A substituent at C7 (b) is axial, and one at C11 (c) is equatorial

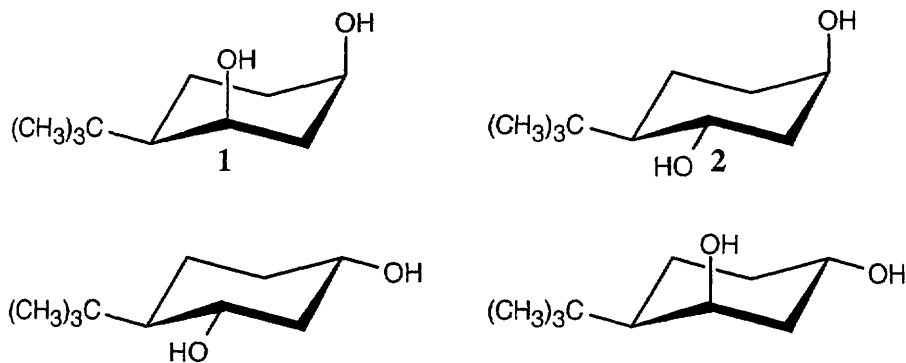


4.54

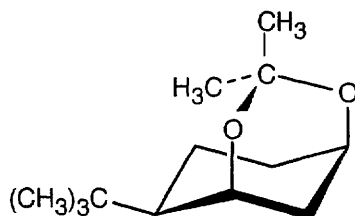


Amantadine

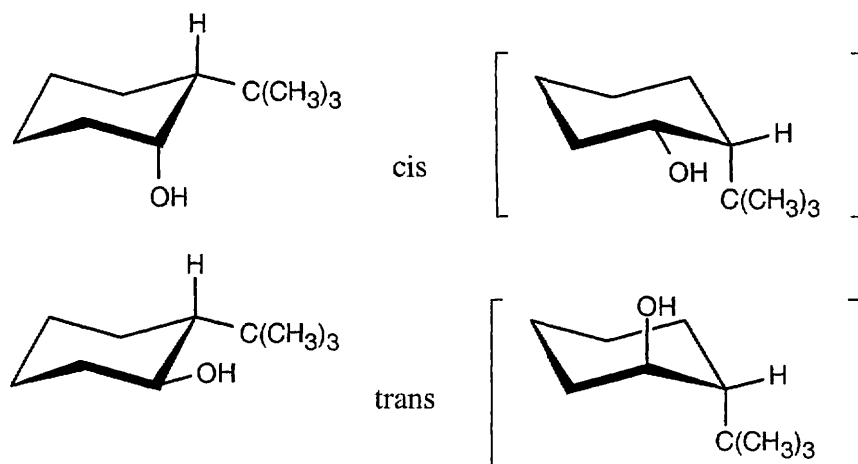
- 4.55** Draw the four possible isomers of 4-*tert*-butylcyclohexane-1,3-diol. Make models of these isomers also. The bulky *tert*-butyl group determines the stable conformation because of its strong preference for the equatorial position.



Only when the two hydroxyl groups are *cis* diaxial (structure 1) can the acetal ring form. In any other conformation, the oxygen atoms are too far apart to be incorporated into a six-membered ring.



4.56



All four conformations of the two isomers are illustrated. The second conformation of each pair has a high degree of steric strain, and thus each isomer adopts the first conformation. Since only the *cis* isomer has the hydroxyl group in the necessary axial position, it oxidizes faster than the *trans* isomer.