4: ORGANIC COMPOUNDS - CYCLOALKANES AND THEIR STEREOCHEMISTRY

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> **◖❙ LEARNING OBJECTIVES**
>
> After you have completed Chapter 4, you should be able to
>
> 1. fulfill all of the detailed objectives listed under each individual section.
> 2. draw the *cis-trans* isomers of some simple disubstituted cycloalkanes, and write the IUPAC names of such compounds.
> 3. define, and use in context, the key terms introduced in this chapter.

This chapter deals with the concept of stereochemistry and conformational analysis in cyclic compounds. The causes of various ring strains and their effects on the overall energy level of a cycloalkane are discussed. We shall stress the stereochemistry of alicyclic compounds.

4.0: CHAPTER OBJECTIVES

Cycloalkanes, a fundamental class of organic compounds, possess intriguing structural characteristics that distinguish them within the realm of organic chemistry. Unlike their linear counterparts, cycloalkanes form closed-ring structures composed entirely of carbon atoms, bonded together in a cyclic fashion. This unique geometry gives rise to diverse stereochemical phenomena, influencing the properties and reactivity of these compounds.

In this exploration, we embark on a journey into the world of cycloalkanes and delve into their stereochemistry. Stereochemistry examines the spatial arrangement of atoms within molecules and its impact on their behavior. For cycloalkanes, stereochemistry becomes particularly captivating due to the constraints imposed by the cyclic framework, leading to fascinating structural isomerism and conformational dynamics.

Throughout our investigation, we will uncover the principles underlying cycloalkane stereochemistry, including cis-trans isomerism, ring strain, and conformational analysis. By elucidating these concepts, we aim to unravel the complexity inherent in cycloalkane structures and shed light on their significance in various fields, from organic synthesis to medicinal chemistry.

Join us as we navigate the intricate world of cycloalkanes and explore the nuances of their stereochemistry, unveiling the secrets hidden within these remarkable molecules.

4.1: NAMING CYCLOALKANES

Many organic compounds found in nature contain rings of carbon atoms. These compounds are known as **cycloalkanes**. Cycloalkanes only contain carbon-hydrogen bonds and carbon-carbon single bonds. The simplest examples of this class consist of a single, un-substituted carbon ring, and these form a homologous series similar to the unbranched alkanes.

Like alkanes, cycloalkane molecules are often drawn as skeletal structures in which each intersection between two lines is assumed to have a carbon atom with its corresponding number of hydrogens. Cyclohexane, one of the most common cycloalkanes is shown below as an example.
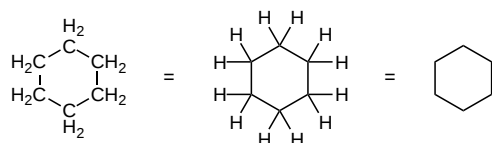
Cyclic hydrocarbons have the prefix "cyclo-". The IUPAC names, molecular formulas, and skeleton structures of the cycloalkanes with 3 to 10 carbons are given in Table 4.1.1. Note that the general formula for a cycloalkane composed of n carbons is C_nH_{2n}, and not $C_nH_{2n_2^+}$ as for alkanes. Although a cycloalkane has two fewer hydrogens than the equivalent alkane, each carbon is bonded to four other atoms so are still considered to be **saturated** with hydrogen.

Table 4.1.1: Examples of Simple Cycloalkanes

Cycloalkane	Molecular Formula	Skeleton Structure
Cyclopropane	C_3H_6	△
Cyclobutane	C_4H_8	□
Cyclopentane	C_5H_{10}	⬠
Cyclohexane	C_6H_{12}	⬡
Cycloheptane	C_7H_{14}	⬡
Cyclooctane	C_8H_{16}	⯂
Cyclononane	C_9H_{18}	⬡
Cyclodecane	$C_{10}H_{20}$	⬡

IUPAC RULES FOR NOMENCLATURE

The naming of substituted cycloalkanes follows the same basic steps used in naming alkanes.

1. Determine the parent chain.
2. Number the substituents of the ring beginning at one substituent so that the nearest substituent is numbered the lowest possible. If there are multiple choices that are still the same, go to the next substituent and give it the lowest number possible.
3. Name the substituents and place them in alphabetical order.

More specific rules for naming substituted cycloalkanes with examples are given below.

1. Determine the cycloalkane to use as the parent. If there is an alkyl straight chain that has a greater number of carbons than the cycloalkane, then the alkyl chain must be used as the primary parent chain. Cycloalkanes substituents have an ending "-yl". If there are two cycloalkanes in the molecule, use the cycloalkane with the higher number of carbons as the parent.
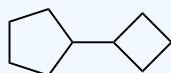

✔ **EXAMPLE 4.1.1**
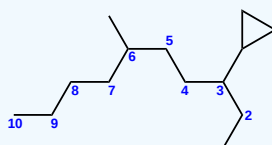
The longest straight chain contains 10 carbons, compared with cyclopropane, which only contains 3 carbons. The parent chain in this molecule is decane and cyclopropane is a substituent. The name of this molecule is 3-cyclopropyl-6-methyldecane.

✔ **EXAMPLE 4.1.2**

Name the cycloalkane structure.

Solution

There are two different cycloalkanes in this molecule. Because it contains more carbons, the cyclopentane ring will be named as the parent chain. The smaller ring, cyclobutane, is named as a substituent on the parent chain. The name of this molecule is cyclobutylcyclopentane.

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2. When there is only one substituent on the ring, the ring carbon attached to the substituent is automatically carbon #1. Indicating the number of the carbon with the substituent in the name is optional.

✔ **EXAMPLE 4.1.3**
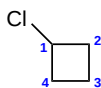
| 1-chlorocyclobutane or cholorocyclobutane | 1-propylcyclohexane or propylcyclohexane |
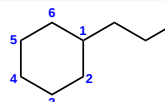
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3. If there are multiple substituents on the ring, number the carbons of the cycloalkane so that the carbons with substituents have the lowest possible number. A carbon with multiple substituents should have a lower number than a carbon with only one substituent or functional group. One way to make sure that the lowest number possible is assigned is to number the carbons so that when the numbers corresponding to the substituents are added, their sum is the lowest possible.
4. When naming the cycloalkane, the substituents must be placed in alphabetical order. Remember the prefixes di-, tri-, etc. , are not used for alphabetization.

✔ **EXAMPLE 4.1.4**
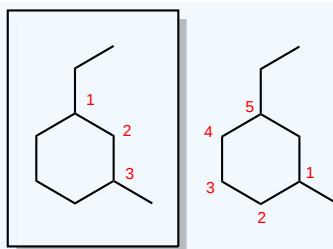
In this example, the ethyl or the methyl subsistent could be attached to carbon one. The ethyl group attachment is assigned carbon 1 because ethyl comes before methyl alphabetically. After assigning carbon 1 the cyclohexane ring can be numbered going clockwise or counterclockwise. When looking at the numbers produced going clockwise produces lower first substituent numbers (1,3) than when numbered counterclockwise (1,5). So the correct name is 1-ethyl-3-methylcyclohexane.

✔ EXAMPLE 4.1.5

Name the following structure using IUPAC rules.

Solution

Remember when dealing with cycloalkanes with more than two substituents, finding the lowest possible 2nd substituent numbering takes precedence. Consider a numbering system with each substituent attachment point as being carbon one. Compare them and whichever produces the lowest first point of difference will be correct.

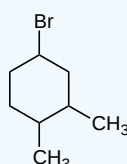The first structure would have 1,4 for the relationship between the first two groups. The next structure would have 1,3. The final 2 structures both have 1,2 so those are preferable to the first two. Now we have to determine which is better between the final 2 structures. The 3rd substituent on structure 3 would be at the 5 position leading to 1,2,5 while in the final structure the 3rd methyl group is on carbon 4 leading to 1,2,4. This follows the rules of giving the lowest numbers at the first point of difference.
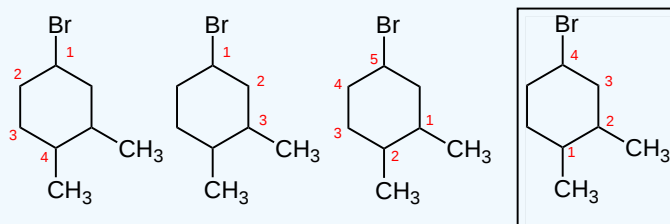
The correct name for the molecule is 4-Bromo-1,2-dimethylcyclohexane.

✔ EXAMPLE 4.1.6
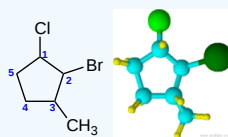
2-bromo-1-chloro-3-methylcyclopentane

Notice that "b" of bromo alphabetically precedes the "m" of methyl. Also, notice that the chlorine attachment point is assigned carbon 1 because it comes first alphabetically and the overall sum of numbers would be the same if the methyl attachment carbon was assigned as 1 and the chlorine attachment as 3.

✔ EXAMPLE 4.1.7

(2-bromo-1,1-dimethylcyclohexane)

Although "di" alphabetically precedes "f", "di" is not used in determining the alphabetical order.

✔ EXAMPLE 4.1.8

2-fluoro-1,1,-dimethylcyclohexane **NOT** 1,1-dimethyl-2-fluorocyclohexane also 2-fluoro-1,1,-dimethylcyclohexane **NOT** 1-fluoro-2,2-dimethylcyclohexane (as that would give a larger number to the first point of difference)

Although "di" alphabetically precedes "f", "di" is not used in determining the alphabetical order of the substituents. Notice that the attachment point of the two methyl g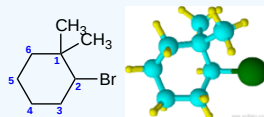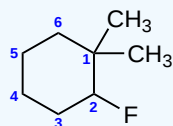roups is assigned carbon 1 despite the fact that fluorine comes first alphabetically. This is because this assignment allows for a lower overall numbering of substituents, so assigning alphabetical priority is not necessary.

POLYCYCLIC COMPOUNDS

Hydrocarbons having more than one ring are common, and are referred to as **bicyclic** (two rings), **tricyclic** (three rings) and in general, **polycyclic compounds**. The molecular formulas of such compounds have H/C ratios that decrease with the number of rings. In general, for a hydrocarbon composed of n carbon atoms associated with m rings the formula is: $C_nH_{2n+2-2m}$. The structural relationship of rings in a polycyclic compound can vary. They may be separate and independent, or they may share one or two common atoms. Some examples of these possible arrangements are shown in the following table.

Table 4.1.2: Examples of Isomeric C_8H_{14} Bicycloalkanes

Isolated Rings	Spiro Rings	Fused Rings	Bridged Rings
No common atoms	One common atom	One common bond	Two common atoms

Polycyclic compounds, like cholesterol shown below, are biologically important and typically have common names accepted by IUPAC. However, the common names do not generally follow the basic IUPAC nomenclature rules, and will not be covered here.
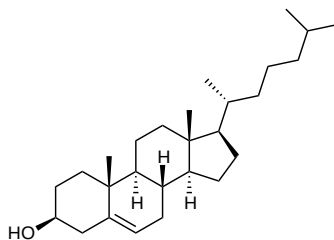
Cholesterol (polycyclic)

? EXERCISE 4.1.1

Give the IUPAC names for the following cycloalkane structures.

a)

CH₃

CH₃

b)

c)

CH₃

CH₂CH₃

d)

Br

H₃C

e)

CH₂CH₃

H₃CH₂C

CH₂CH₃

f)

H₃C

CH₃

Cl
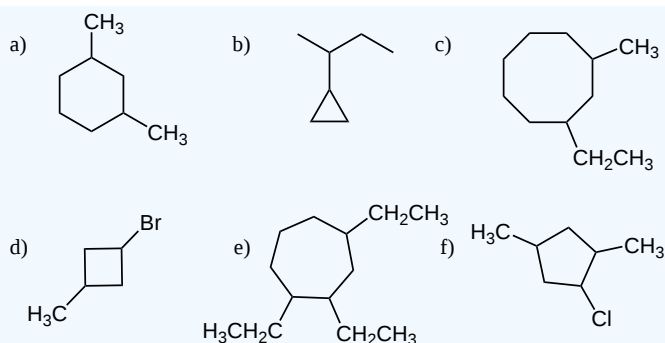
Answer

    a. 1,3-Dimethylcyclohexane

    b. 2-Cyclopropylbutane

    c. 1-Ethyl-3-methylcyclooctane

    d. 1-Bromo-3-methylcyclobutane

    e. 1,2,4-Triethylcycloheptane

    f. 1-Chloro-2,4-dimethylcyclopentane

? EXERCISE 4.1.2

Draw the structures for the IUPAC names below.

  a. 2,3-dicyclopropylpentane

  b. 1,2,3-triethylcyclopentane

  c. 3-cyclobutyl-2-methylhexane

  d. 2-bromo-1-chloro-4-methylcyclohexane

  e. 1-bromo-5-propylcyclododecane

Answer
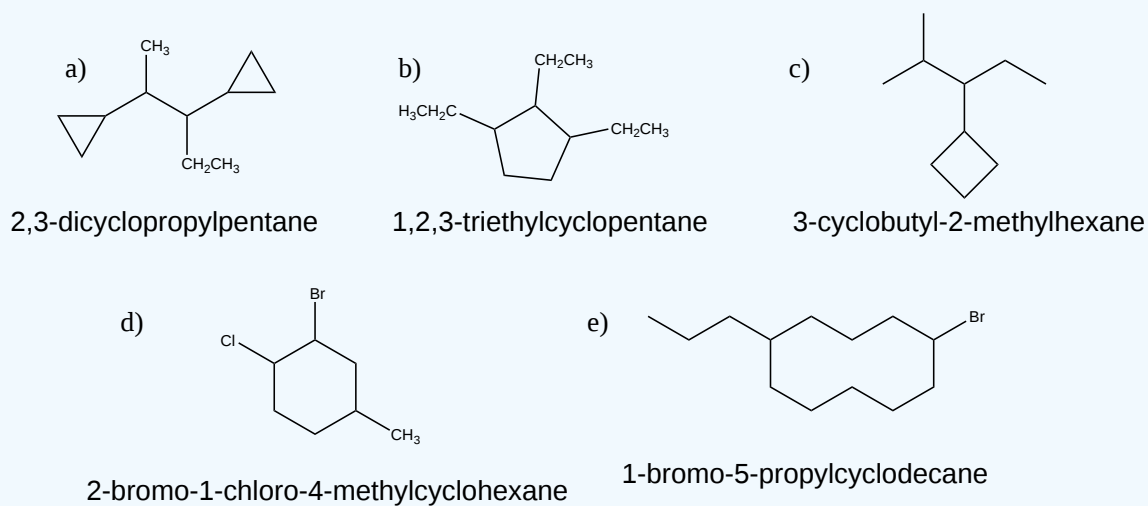
a)

CH₃

CH₂CH₃

2,3-dicyclopropylpentane

b)

CH₂CH₃

H₃CH₂C

CH₂CH₃

1,2,3-triethylcyclopentane

c)

3-cyclobutyl-2-methylhexane

d)

Br

Cl

CH₃

2-bromo-1-chloro-4-methylcyclohexane

e)

Br

1-bromo-5-propylcyclodecane

4.2: CIS-TRANS ISOMERISM IN CYCLOALKANES

◑ OBJECTIVES

After completing this section, you should be able to
- draw structural formulas that distinguish between *cis* and *trans* disubstituted cycloalkanes.
- construct models of *cis* and *trans* disubstituted cycloalkanes using ball-and-stick molecular models.

📌 KEY TERMS

Make certain that you can define, and use in context, the key terms below.
- constitutional isomer
- stereoisomer
- *cis-trans* isomers

Previously, constitutional isomers have been defined as molecules that have the same molecular formula, but different atom connectivity. In this section, a new class of isomers, stereoisomers, will be introduced. **Stereoisomers** are molecules that have the same molecular formula, the same atom connectivity, but they differ in the relative spatial orientation of the atoms.

Cycloalkanes are similar to open-chain alkanes in many respects. They both tend to be nonpolar and relatively inert. One important difference, is that cycloalkanes have much less freedom of movement than open-chain alkanes. As discussed in Sections 3.6 and 3.7, open-chain alkanes are capable of rotation around their carbon-carbon sigma bonds. The ringed structures of cycloalkanes prevent such free rotation, causing them to be more rigid and somewhat planar.

Di-substituted cycloalkanes are one class of molecules that exhibit stereoisomerism. 1,2-dibromocyclopentane can exist as two different stereoisomers: *cis*-1,2-dibromocyclopentane and *trans*-1,2-dibromocyclopentane. The *cis*-1,2-dibromocyclopentane and *trans*-1,2-dibromocyclopentane stereoisomers of 1,2-dibromocyclopentane are shown below. Both molecules have the same molecular formula and the same atom connectivity. They differ only in the relative spatial orientation of the two bromines on the ring. In *cis*-1,2-dibromocyclopentane, both bromine atoms are on the same "face" of the cyclopentane ring, while in *trans*-1,2-dibromocyclopentane, the two bromines are on opposite faces of the ring. Stereoisomers require an additional nomenclature prefix be added to the IUPAC name in order to indicate their spatial orientation. Di-substituted cycloalkane stereoisomers are designated by the nomenclature prefixes ***cis*** (Latin, meaning on this side) and ***trans*** (Latin, meaning across).

cis-1,2-dibromocyclopentane

trans-1,2-dibromocyclopentane
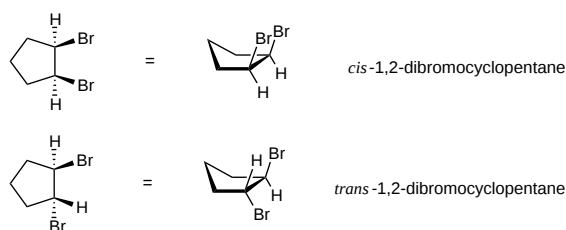
## REPRESENTING 3D STRUCTURES

By convention, chemists use heavy, wedge-shaped bonds to indicate a substituent located above the plane of the ring (coming out of the page), a dashed line for bonds to atoms or groups located below the ring (going back into the page), and solid lines for bonds in the plane of the page.


cis-1,3-dimethylcyclobutane *trans*-5-bromo-1,4,6-trimethyl-1,3-cycloheptadiene
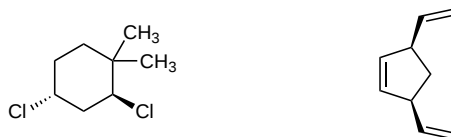
trans-2,4-dichloro-1,1-dimethylcyclohexane   *cis*-3,5-divinylcyclopentene

In general, if any two *sp³* carbons in a ring have two different substituent groups (not counting other ring atoms) cis/trans stereoisomerism is possible. However, the cis/trans designations are not used if both groups are on the same carbon. For example, the chlorine and the methyl group are on the same carbon in 1-chloro-1-methylcyclohexane and the *trans* prefix should not be used.
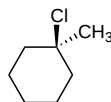

1-chloro-1-methylcyclohexane

If more than two ring carbons have substituents, the stereochemical notation distinguishing the various isomers becomes more complex and the prefixes *cis* and *trans cannot be used to formally name the molecule*. However, the relationship of any two substituents can be informally described using *cis* or *trans*. For example, in the tri-substituted cyclohexane below, the methyl group is *cis* to the ethyl group, and also *trans* to the chlorine. However, the entire molecule cannot be designated as either a *cis* or trans *isomer*. Later sections will describe how to name these more complex molecules (5.5: Sequence Rules for Specifying Configuration)
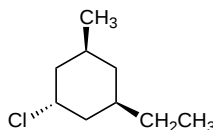
✔ EXAMPLE 4.2.1

Name the following cycloalkanes:
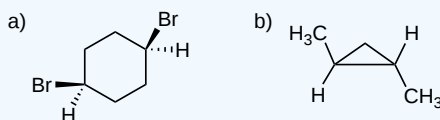
Solution

These two example represent the two main ways of showing spatial orientation in cycloalkanes.

a. In example "a" the cycloalkane is shown as being flat and in the plane of the page. The positioning of the substituents is shown by using dash-wedge bonds. Cis/trans positioning can be determined by looking at the type of bonds attached to the substituents. If the substituents are both on the same side of the ring (Cis) they would both have either dash bonds or wedge bonds. If the the substituents are on opposite side of the ring (Trans) one substituent would have a dash bond and the other a wedge bond. Because both bromo substituents have a wedge bond they are one the same side of the ring and are cis. The name of this molecule is cis-1,4-Dibromocyclohexane.
b. Example "b" shows the cycloalkane ring roughly perpendicular to the plane of the page. When this is done, the upper and lower face of the ring is defined and each carbon in the ring will have a bond one the upper face and a bond on the lower face. Cis substituents will either both be on the upper face or the lower face. Trans substituents will have one on the upper face and one one the lower face. In example "b", one of the methyl substituents is on the upper face of the ring and one is on the lower face which makes them trans to each other. The name of this molecule is *trans*-1,2-Dimethylcyclopropane.

❓ EXERCISE 4.2.2

Draw the following molecules:

1. *trans*-1,3-dimethylcyclohexane
2. *trans*-1,2-dibromocyclopentane
3. *cis*-1,3-dichlorocyclobutane

Answer

 1

 2

 3
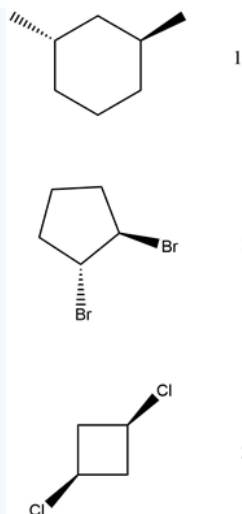
? EXERCISE 4.2.3

Cis/Trans nomenclature can be used to describe the relative positioning of substituents on molecules with more complex ring structures. The molecule below is tesosterone, the primary male sex hormone. Is the OH and the adjacent methyl group cis or trans to each other? What can you deduce about the relative positions of the indicated hydrogens?
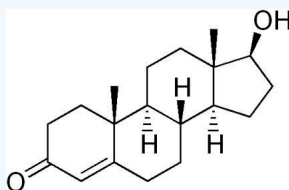
Answer

Both the OH and the methyl group have wedge bonds. This implies that they are both on the same side of the testosterone ring making them cis. Two of the hydrogens have wedge bonds while one has a wedge. This means two of the hydrogens are on one side of the testosterone ring while one is on the other side.

? EXERCISE 4.2.4

Name the following compounds:
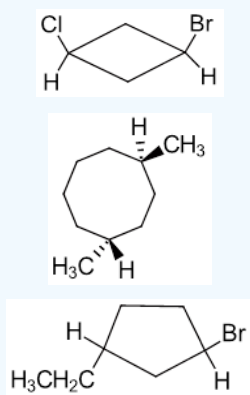
Answer

Cis-1-Bromo-3-Chlorocyclobutane

Trans-1,4-Dimethylcyclooctane

Trans-1-Bromo-3-ethylcyclopentane

> **? EXERCISE 4.2.5**
>
> Draw the following molecules:
>
>   a. *trans*-1,3-dimethylcyclohexane
>   b. *trans*-1,2-dibromocyclopentane
>   c. *cis*-1,3-dichlorocyclobutane
>
> **Answer**
>
>
>
>   1   2   3
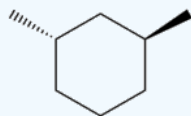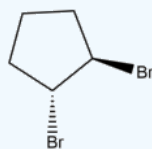
4.2: Cis-Trans Isomerism in Cycloalkanes is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Krista Cunningham, Kelly Matthews, & Kelly Matthews.

4.3: STABILITY OF CYCLOALKANES - RING STRAIN

> ### 🔹 OBJECTIVES
>
> After completing this section, you should be able to:
> - Describe the Baeyer strain theory.
> - Describe how the measurement of heats of combustion provides information about the amount of strain present in a cycloalkane ring.
> - Determine the relative stability of cyclic compounds, by assessing such factors as angle strain, torsional strain and steric strain.

> ### 📌 KEY TERMS
>
> Make certain that you can define, and use in context, the key terms below.
> - angle strain
> - steric strain
> - torsional strain
> - ring strain
> - heat of combustion

HEAT OF COMBUSTION AS A MEASURE OF BOND STRENGTH

The combustion of carbon compounds, especially hydrocarbons, has been the most important source of heat energy for human civilizations throughout recorded history. The practical impo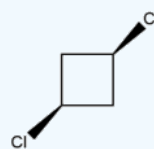rtance of this reaction cannot be denied, but the massive and uncontrolled chemical changes that take place in combustion make it difficult to deduce mechanistic paths. Using the combustion of propane as an example, we see from the following equation that every covalent bond in the reactants has been broken and an entirely new set of covalent bonds have formed in the products. No other common reaction involves such a profound and pervasive change, and the mechanism of combustion is so complex that chemists are just beginning to explore and understand some of its elementary features.

$$CH_3CH_2CH_3 + 5\,O_2 \longrightarrow 3\,CO_2 + 4\,H_2O + heat$$
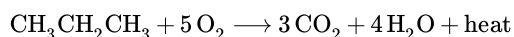
Since all the covalent bonds in the reactant molecules are broken, the quantity of heat evolved in this reaction, and any other combustion reaction, is related to the strength of these bonds (and, of course, the strength of the bonds formed in the products). Precise heat of combustion measurements can provide useful information about the structure of molecules and their relative stability.

For example, heat of combustion is useful in determining the relative stability of isomers. Pentane has a heat of combustion of -782 kcal/mol, while that of its isomer, 2,2-dimethylpropane (neopentane), is –777 kcal/mol. These values indicate that 2,3-dimethylpentane is 5 kcal/mol more stable than pentane, since it has a lower heat of combustion.

RING STRAIN

Table 4.3.1 lists the heat of combustion data for some simple cycloalkanes. These cycloalkanes do not have the same molecular formula, so the heat of combustion per each CH_2 unit present in each molecule is calculated (the fourth column) to provide a useful comparison. From the data, cyclopropane and cyclobutane have significantly higher heats of combustion per CH_2, while cyclohexane has the lowest heat of combustion. This indicates that cyclohexane is more stable than cyclopropane and cyclobutane, and in fact, that cyclohexane has a same relative stability as long chain alkanes that are not cyclic. This difference in stability is seen in nature where six membered rings are by far the most common. What causes the difference in stability or the strain in small cycloalkanes?

Table 4.3.1: Heats of combustion of select hydrocarbons

| Cycloalkane $(CH_2)_n$	CH_2 Units n	$\Delta H^{25°}$ kcal/mol	$\Delta H^{25°}$ per CH_2 Unit	Ring Strain kcal/mol
Cyclopropane	n = 3	468.7	156.2	27.6
Cyclobutane	n = 4	614.3	153.6	26.4
Cyclopentane	n = 5	741.5	148.3	6.5
Cyclohexane	n = 6	882.1	147.0	0.0
Cycloheptane	n = 7	1035.4	147.9	6.3
Cyclooctane	n = 8	1186.0	148.2	9.6
Cyclononane	n = 9	1335.0	148.3	11.7
Cyclodecane	n = 10	1481	148.1	11.0
$CH_3(CH_2)_mCH_3$	m = large	—	147.0	0.0

THE BAEYER THEORY ON THE STRAIN IN CYCLOALKANE RINGS

In 1890, the famous German organic chemist, A. Baeyer, suggested that cyclopropane and cyclobutane are less stable than cyclohexane, because the the smaller rings are more "strained". There are many different types of strain that contribute to the overall ring strain in cycloalkanes, including angle strain, torsional strain, and steric strain. **Torsional strain** and **steric strain** were previously defined in the discussion of conformations of butane. **Angle Strain** occurs when the sp^3 hybridized carbons in cycloalkanes do not have the expected ideal bond angle of 109.5^o, causing an increase in the potential energy. An example of angle strain can be seen in the diagram of cyclopropane below in which the bond angle is 60° between the carbons. The compressed bond angles causes poor overlap of the hybrid orbitals forming the carbon-carbon sigma bonds which in turn creates destabilization.
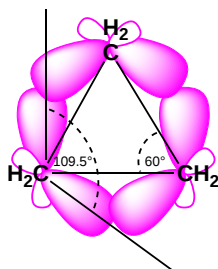

The C-C-C bond angles in cyclopropane (diagram above) (60°) and cyclobutane (90°) are much different than the ideal bond angle of 109.5^o. This bond angle causes cyclopropane and cyclobutane to be less stable than molecules such as cyclohexane and cyclopentane, which have a much lower ring strain because the bond angle between the carbons is much closer to 109.5^o. Changes in chemical reactivity as a consequence of angle strain are dramatic in the case of cyclopropane, and are also evident for cyclobutane.

In addition to angle strain, there is also steric (transannular) strain and torsional strain in many cycloalkanes. Transannular strain exists when there is steric repulsion between atoms.
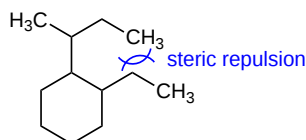

transannular strain

Because cycloalkane lack the ability to freely rotate, torsional (eclipsing) strain exists when a cycloalkane is unable to adopt a staggered conformation around a C-C bond. Torsional strain is especially prevalent in small cycloalkanes, such as cyclopropane, whose structures are nearly planar.
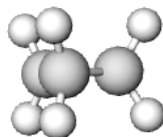
The Eclipsed C-H Bonds in Cyclopropane

Larger rings like cyclohexane, deal with torsional strain by forming conformers in which the rings are not planar. A conformer is a stereoisomer in which molecules of the same connectivity and formula exist as different isomers, in this case, to reduce ring strain. The ring strain is reduced in conformers due to the rotations around the sigma bonds, which decreases the angle and torsional strain in the ring. The non-planar structures of cyclohexane are very stable compared to cyclopropane and cyclobutane, and will be discussed in more detail in the next section.

cyclohexane

cyclohexane chair conformer
(more stable)
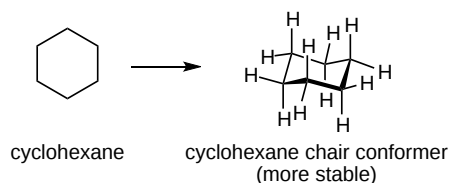
> 📌 **THE TYPES OF STRAIN WHICH CONTRIBUTE TO RING STRAIN IN CYCLOALKANES**
>
> - Angle Strain - The strain caused by the increase or reduction of bond angles
> - Torsional Strain - The strain caused by eclipsing bonds on adjacent atoms
> - Steric Strain - The strain caused by the repulsive interactions of atoms trying to occupy the same space

> ❓ **EXERCISE 4.3.1**
>
> *trans*-1,2-Dimethylcyclobutane is more stable than *cis*-1,2-dimethylcyclobutane. Explain this observation.
>
> **Answer**
>
> The trans form does not have eclipsing methyl groups, therefore lowering the energy within the molecule. It does however have hydrogen-methyl eclipsing interactions which are not as high in energy as methyl-methyl interactions.

> ❓ **EXERCISE 4.3.2**
>
> Cyclobutane has more torsional stain than cyclopropane. Explain this observation.
>
> **Answer**
>
> Cyclobutane has 4 CH_2 groups while cyclopropane only has 3. More CH2 groups means cyclobutane has more eclipsing H-H interactions and therefore has more torsional strain.

EXERCISES

1. *Trans*-1,2-Dimethylcyclobutane is more stable than *cis*-1,2-dimethylcyclobutane. Explain this observation.
2. The trans form does not have eclipsing methyl groups, therefore lowering the energy within the molecule. It does however have hydrogen-methyl interactions, but are not as high in energy than methyl-methyl interactions.

4.4: CONFORMATIONS OF CYCLOALKANES

OBJECTIVES

After completing this section, you should be able to

1. describe, and sketch the conformation of cyclopropane, cyclobutane, and cyclopentane.
2. describe the bonding in cyclopropane, and use this to account for the high reactivity of this compound.
3. analyze the stability of cyclobutane, cyclopentane and their substituted derivatives in terms of angular strain, torsional strain and steric interactions.

STUDY NOTES

Notice that in both cyclobutane and cyclopentane, torsional strain is reduced at the cost of increasing angular (angle) strain.

Although the customary line drawings of simple cycloalkanes are geometrical polygons, the actual shape of these compounds in most cases is very different.

cyclopropane	cyclobutane	cyclopentane	cyclohexane	cycloheptane	cyclooctane
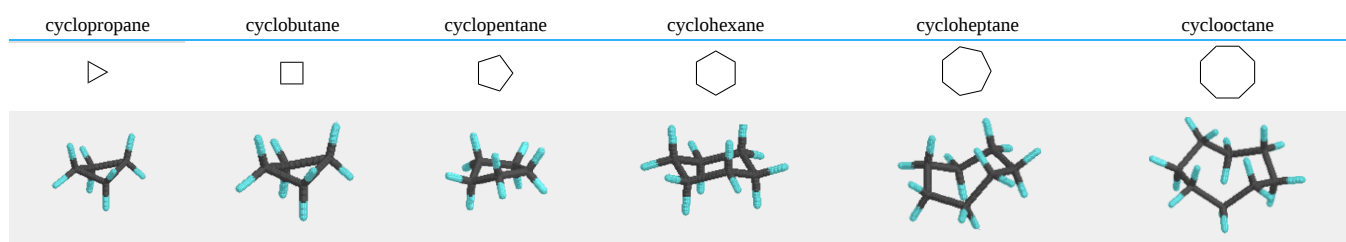
Cyclopropane is necessarily planar (flat), with the carbon atoms at the corners of an equilateral triangle. The 60º bond angles are much smaller than the optimum 109.5º angles of a normal tetrahedral carbon atom, and the resulting angle strain dramatically influences the chemical behavior of this cycloalkane. Cyclopropane also suffers substantial eclipsing strain, since all the carbon-carbon bonds are fully eclipsed. Cyclobutane reduces some bond-eclipsing strain by folding (the out-of-plane dihedral angle is about 25º), but the total eclipsing and angle strain remains high. Cyclopentane has very little angle strain (the angles of a pentagon are 108º), but its eclipsing strain would be large (about 40 kJ/mol) if it remained planar. Consequently, the five-membered ring adopts non-planar puckered conformations whenever possible.

Rings larger than cyclopentane would have angle strain if they were planar. However, this strain, together with the eclipsing strain inherent in a planar structure, can be relieved by puckering the ring. Cyclohexane is a good example of a carbocyclic system that virtually eliminates eclipsing and angle strain by adopting non-planar conformations. Cycloheptane and cyclooctane have greater strain than cyclohexane, in large part due to transannular crowding (steric hindrance by groups on opposite sides of the ring).

Cyclic systems are a little different from open-chain systems. In an open chain, any bond can be rotated 360º, going through many different conformations. That complete rotation isn't possible in a cyclic system, because the parts that would be trying to twist away from each other would still be connected together. Thus cyclic systems have fewer "degrees of freedom" than aliphatic systems; they have "restricted rotation".

Because of the restricted rotation of cyclic systems, most of them have much more well-defined shapes than their aliphatic counterparts. Let's take a look at the basic shapes of some common rings. Many biologically important compounds are built around structures containing rings, so it's important that we become familiar with them. In nature, three- to six-membered rings are frequently encountered, so we'll focus on those.
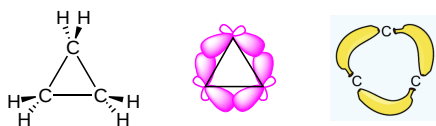
CYCLOPROPANE

A three membered ring has no rotational freedom whatsoever. A plane is defined by three points, so the three carbon atoms in cyclopropane are all constrained to lie in the same plane. This lack of flexibility does not allow cyclopropane to form more stable conformers which are non-planar.
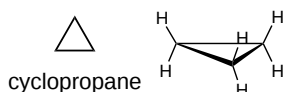
cyclopropane

The main source of ring strain in cyclopropane is angle strain. All of the carbon atoms in cyclopropane are tetrahedral and would prefer to have a bond angle of 109.5º The angles in an equilateral triangle are actually 60º, about half as large as the optimum angle. The large

deviation from the optimal bond angle means that the C-C sigma bonds forming the cyclopropane ring are bent. Maximum bonding occurs when the overlapping orbitals are pointing directly toward each other. The severely strained bond angles in cyclopropane means that the orbitals forming the C-C bonds overlap at a slight angle making them weaker. This strain is partially overcome by using so-called "banana bonds", where the overlap between orbitals is no longer directly in a line between the two nuclei, as shown here in three representations of the bonding in cyclopropane:

The constrained nature of cyclopropane causes neighboring C-H bonds to all be held in eclipsed conformations. Cyclopropane is always at maximum torsional strain. This strain can be illustrated in a Newman projections of cyclopropane as shown from the side.

Newman Projection of cyclopropane

Cyclopropane isn't large enough to introduce any steric strain. Steric strain does not become a factor until we reach six membered rings. Before that point, rings are not flexible enough to allow for two ring substituents to interact with each other.

The combination of torsional and angle strain creates a large amount of ring strain in cyclopropane which weakens the C-C ring bonds (255 kJ/mol) when compared to C-C bonds in open-chain propane (370 kJ/mol).
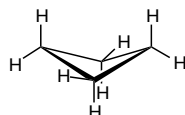
CYCLOBUTANE

Cyclobutane is a four membered ring. The larger number of ring hydrogens would cause a substantial amount of torsional strain if cyclobutane were planar.

cyclobutane

In three dimensions, cyclobutane is flexible enough to buckle into a "puckered" shape which causes the C-H ring hydrogens to slightly deviate away from being completely eclipsed. This conformation relives some of the torsional strain but increases the angle strain because the ring bond angles decreases to 88º.

In a line drawing, this butterfly shape is usually shown from the side, with the near edges drawn using darker lines.

The deviation of cyclobutane's ring C-H bonds away from being fully eclipsed can clearly be seen when viewing a Newman projections signed down one of the C-C bond.

Newman projection of cyclobutane

- With bond angles of 88º rather than 109.5º degrees, cyclobutane has significant amounts of angle strain, but less than in cyclopropane.
- Although torsional strain is still present, the neighboring C-H bonds are not exactly eclipsed in the cyclobutane's puckered conformation.
- Steric strain is very low. Cyclobutane is still not large enough that substituents can reach around to cause crowding.
- Overall the ring strain in cyclobutane (110 kJ/mol) is slightly less than cyclopropane (115 kJ/mol).
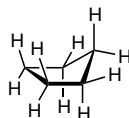
CYCLOPENTANE

Cyclopentanes are even more stable than cyclobutanes, and they are the second-most common cycloalkane ring in nature, after cyclohexanes. Planar cyclopentane has virtually no angle strain but an immense amount of torsional strain. To reduce torsional strain, cyclopentane addops a non-planar conformation even though it slightly increases angle strain.
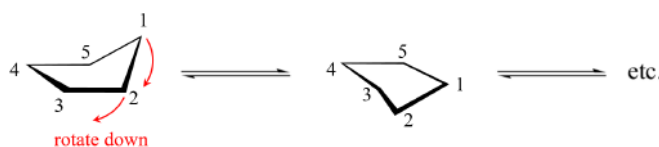
cyclopentane

The lowest energy conformation of cyclopentane is known as the 'envelope', with four of the ring atoms in the same plane and one out of plane (notice that this shape resembles an envelope with the flap open). The out-of-plane carbon is said to be in the **endo** position ('*endo*' means 'inside'). The envelope removes torsional strain along the sides and flap of the envelope. However, the neighboring carbons are eclipsed along the "bottom" of the envelope, away from the flap.


3D structure of cyclopentane (notice that the far top right carbon is the endo position).

At room temperature, cyclopentane undergoes a rapid bond **rotation** process in which each of the five carbons takes turns being in the *endo* position.

Cyclopentane distorts only very slightly into an "envelope" shape in which one corner of the pentagon is lifted up above the plane of the other four. The envelope removes torsional strain along the sides and flap of the envelope by allowing the bonds to be in an almost completely staggered position. However, the neighboring bonds are eclipsed along the "bottom" of the envelope, away from the flap. Viewing a Newman projections of cyclopentane signed down one of the C-C bond show the staggered C-H bonds.
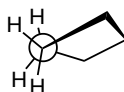

Newman projection of cyclopentane

- The angle strain in the envelope conformation of cyclopentane is low. The ideal angle in a regular pentagon is about 107º, very close to the preferred 109.5º tetrahedral bond angle.
- There is some torsional strain in cyclopentane. The envelope conformation reduces torsional strain by placing some bonds in nearly staggered positions. However, other bonds are still almost fully eclipsed.
- Cyclopentane is not large enough to allow for steric strain to be created.
- Overall, cyclopentane has very little ring strain (26 kJ/mol) when compared to cyclopropane and cyclobutane.

## C_3-C_5 CYCLOALKANES IN NATURE

If one of the carbon-carbon bonds is broken in cyclopropane or cyclobutane, the ring will 'spring' open, releasing energy as the bonds reassume their preferred tetrahedral geometry. The effectiveness of two antibiotic drugs, fosfomycin and penicillin, is due in large part to the high reactivity of the three- and four-membered rings in their structures.

fosfomycin   penicillin G
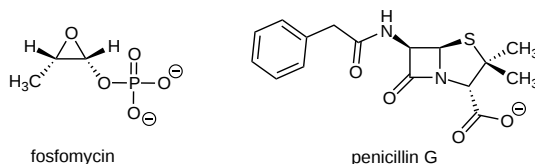
One of the most important five-membered rings in nature is a sugar called ribose – DNA and RNA are both constructed upon 'backbones' derived from ribose. Pictured below is one thymidine (T) deoxy-nucleotide from a stretch of DNA. Since the ribose has lost one of the OH groups (at carbon 2 of the ribose ring), this is part of a deoxyribonucleic acid (DNA). If the OH at carbon 2 of the ribose ring was present, this would be part of a ribonucleic acid (RNA).
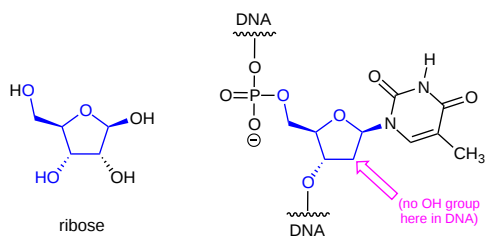
The lowest-energy conformations for ribose are envelope forms in which either C_3 or C_2 are *endo*, on the same side as the C_5 substituent.
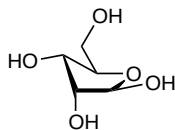

? EXERCISE 4.4.1

If cyclobutane were to be planar, how many H-H eclipsing interactions would there be? Assuming 4 kJ/mol per H-H eclipsing interaction what would the strain be on this "planar" molecule?

Answer

There are eight eclipsing interactions (two per C-C bond). The extra strain on this molecule would be 32 kJ/mol (4 kJ/mol x 8).

? EXERCISE 4.4.1

In the two conformations of *trans*-1,2-Dimethylcyclopentane one is more stable than the other. Explain why this is.
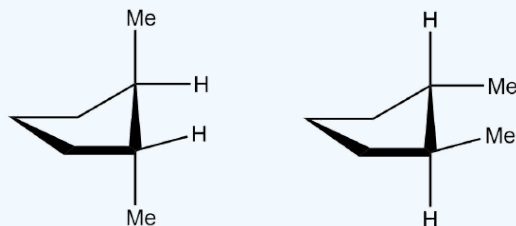
Answer

The first conformation is more stable. Even though the methyl groups are *trans* in both models, they are anti to one another in the first structure (which is lower energy) while they are gauche in the second structure increasing strain within the molecule.

? EXERCISE 4.4.3

In methylcyclopentane, which carbon would most likely be in the *endo* position?

Answer

The ring carbon attached to the methyl group would most likely be the endo carbon. The large methyl group would create the most torsional strain if eclipsed. Being in the *endo* position would place the bonds is a more staggered position which would reduce strain.


? EXERCISE 4.4.4

If cyclobutane were to be planar how many H-H eclipsing interactions would there be, and assuming 4 kJ/mol per H-H eclipsing interaction what is the strain on this "planar" molecule?

Answer

There are eight eclipsing interactions (two per C-C bond). The extra strain on this molecule would be 32 kJ/mol (4 kJ/mol x 8).

? EXERCISE 4.4.5

In the two conformations of *trans*-cyclopentane one is more stable than the other. Explain why this is.
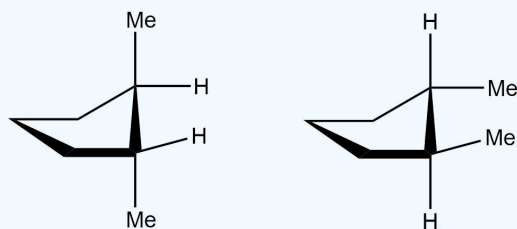
Answer

The first conformation is more stable. Even though the methyl groups are *trans* in both models, in the second structure they are eclipsing one another, therefore increasing the strain within the molecule compared to the first structure where the larger methyl groups are anti to one another.

4.4: Conformations of Cycloalkanes is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Chris Schaller, Steven Farmer, Dietmar Kennepohl, Layne Morsch, Krista Cunningham, William Reusch, & William Reusch.

4.5: CONFORMATIONS OF CYCLOHEXANE

> **◐ OBJECTIVES**
>
> After completing this section, you should be able to
>
> 1. explain why cyclohexane rings are free of angular strain.
> 2. draw the structure of a cyclohexane ring in the chair conformation.

> **📌 KEY TERMS**
>
> Make certain that you can define, and use in context, the key terms below.
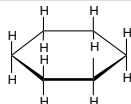> - chair conformation
> - twist-boat conformation

We will find that cyclohexanes tend to have the least angle strain and consequently are the most common cycloalkanes found in nature. A wide variety of compounds including, hormones, pharmaceuticals, and flavoring agents have substituted cyclohexane rings.
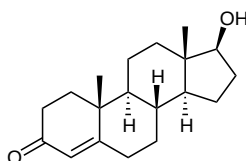

testosterone, which contains three cyclohexane rings and one cyclopentane ring

Rings larger than cyclopentane would have angle strain if they were planar. However, this strain, together with the eclipsing strain inherent in a planar structure, can be relieved by puckering the ring. Cyclohexane is a good example of a carbocyclic system that virtually eliminates eclipsing and angle strain by adopting non-planar conformations. Cycloheptane and cyclooctane have greater strain than cyclohexane, in large part due to transannular crowding (steric hindrance by groups on opposite sides of the ring). Cyclohexane has the possibility of forming multiple conformations each of which have structural differences which lead to different amounts of ring strain.
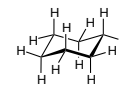

planar structure
severe angle strain (120°)
severe eclipsing strain (all bonds)
small steric strain
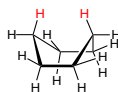
boat conformation
slight angle strain
eclipsing strain at two bonds
steric crowding of two hydrogens
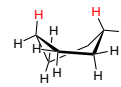
twist boat conformation
slight angle strain
small eclipsing strain
small steric strain

chair conformation
no angle strain
no eclipsing strain
small steric strain

CONFORMATIONS OF CYCLOHEXANE

A planar structure for cyclohexane is clearly improbable. The bond angles would necessarily be 120º, 10.5º larger than the ideal tetrahedral angle. Also, every carbon-hydrogen bond in such a structure would be eclipsed. The resulting angle and eclipsing strains would severely destabilize this structure. The ring strain of planar cyclohexane is in excess of 84 kJ/mol so it rarely discussed other than in theory.
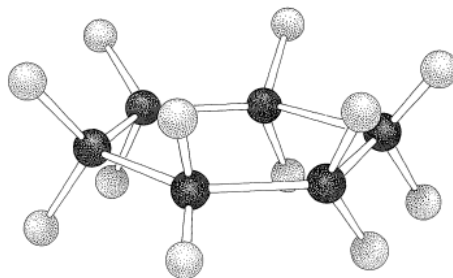

Cyclohexane in the strained planar configuration showing how the hydrogens become eclipsed.

CHAIR CONFORMATION OF CYCLOHEXANE

The flexibility of cyclohexane allows for a conformation which is almost free of ring strain. If two carbon atoms on opposite sides of the six-membered ring are bent out of the plane of the ring, a shape is formed that resembles a reclining beach chair. This **chair conformation** is the lowest energy conformation for cyclohexane with an overall ring strain of 0 kJ/mol. In this conformation, the carbon-carbon ring bonds are able to assume bonding angles of ~111º which is very near the optimal tetrahedral 109.5º so angle strain has been eliminated.
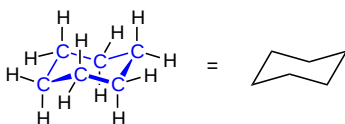
Also, the C-H ring bonds are staggered so torsional strain has also been eliminated. This is clearly seen when looking at a Newman projection of chair cyclohexane sighted down the two central C-C bonds.
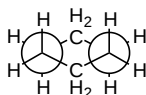
Newman projection of cyclohexane

HOW TO DRAW THE CHAIR CONFORMATION

To draw a chair:

1) Draw two slightly offset parallel lines.

2) Draw another pair of parallel lines from the ends of the first pair.

3) Connect with a third set of parallel lines.

To draw its ring-flip conformer, just start the first pair of lines at the opposite angle.

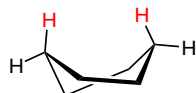### BOAT CONFORMATION OF CYCLOHEXANE

The **Boat Conformation** of cyclohexane is created when two carbon atoms on opposite sides of the six-membered ring are both lifted up out of the plane of the ring creating a shape which slightly resembles a boat. The boat conformation is less stable than the chair form for two major reasons. The boat conformation has unfavorable steric interactions between a pair of 1,4 hydrogens (the so-called "flagpole" hydrogens) that are forced to be very close together (1.83Å). This steric hindrance creates a repulsion energy of about 12 kJ/mol. An additional cause of the higher energy of the boat conformation is that adjacent hydrogen atoms on the 'bottom of the boat' are forced into eclipsed positions. For these reasons, the boat conformation about 30 kJ/mol less stable than the chair conformation.
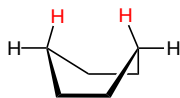
A boat structure of cyclohexane (the interfering "flagpole" hydrogens are shown in red)

TWIST-BOAT CONFORMATION OF CYCLOHEXANE

The boat form is quite flexible and by twisting it at the bottom created the **twist-boat conformer**. This conformation reduces the strain which characterized the boat conformer. The flagpole hydrogens move farther apart (the carbons they are attached to are shifted in opposite directions, one forward and one back) and the eight hydrogens along the sides become largely but not completely staggered. Though more stable than the boat conformation, the twist-boat (sometimes skew-boat) conformation is roughly 23 kJ/mol less stable than the chair conformation.


A twist-boat structure of cyclohexane

HALF CHAIR CONFORMATION OF CYCLOHEXANE

Cyclohexane can obtain a partially plane conformation called "half chair" but with only with excessive amounts of ring strain. The half chair conformation is formed by taking planar cyclohexane and lifting one carbon out of the plane of the ring. The half chair conformation has much of the same strain effects predicted by the fully planar cyclohexane. In the planar portion of half chair cyclohexane the C-C bond

angles are forced to 120º which creates significant amounts of angle strain. Also, the corresponding C-H bonds are fully eclipsed which create torsional strain. The out-of-plane carbon allows for some of the ring's bond angles to reach 109.5º and for some of C-H bonds to not be fully eclipsed. Overall, the half chair conformation is roughly 45 kJ/mol less stable than the chair conformation.

CONFORMATION CHANGES IN CYCLOHEXANE - "RING FLIPS"

Cyclohexane is rapidly rotating between the two most stable conformations known as the chair conformations in what is called the "ring flip" shown below. The importance of the ring flip will be discussed in the next section.

"Ring flip" describes the rapid equilibrium of cyclohexane rings between the two chair conformations
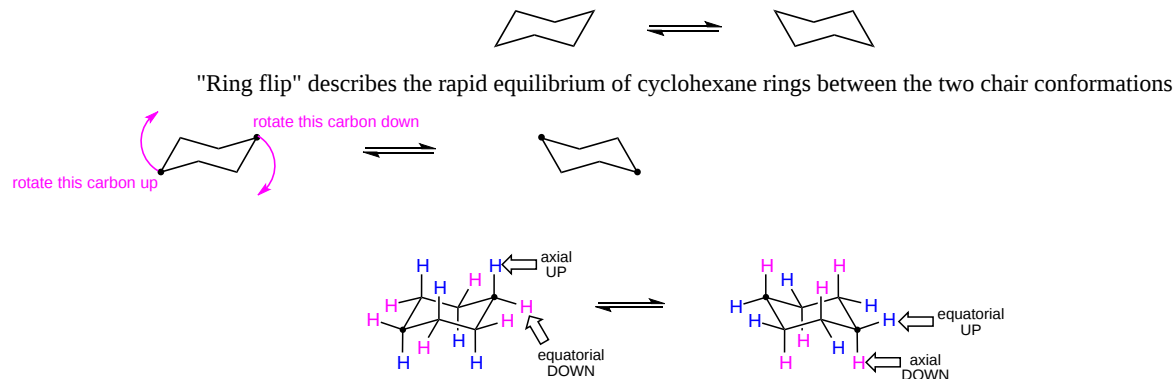
It is important to note that one chair does not immediately become the other chair, rather the ring must travel through the higher energy conformations as transitions. At room temperature the energy barrier created by the half chair conformation is easily overcome allowing for equilibration between the two chair conformation on the order of 80,000 times per second. Although cyclohexane is continually converting between these different conformations, the stability of the chair conformation causes it to comprises more than 99.9% of the equilibrium mixture at room temperature.
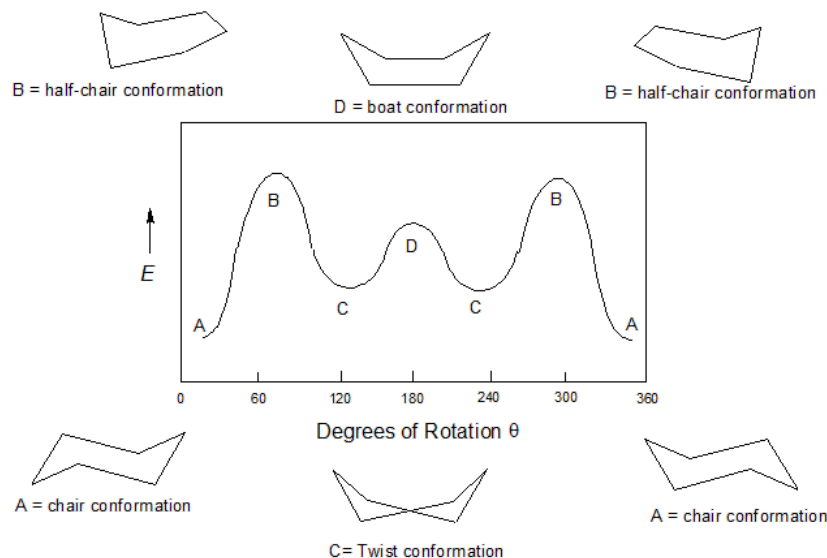
1" id="MathJax-Element-12-Frame" role="presentation" style="position:relative;" tabindex="0">Image of energy diagram of cyclohexane conformations

1" role="presentation" style="position:relative;" tabindex="0">

EXERCISES

1) Consider the conformations of cyclohexane: half chair, chair, boat, twist boat. Order them in increasing ring strain in the molecule.

SOLUTIONS

1) Chair < Twist Boat < Boat < half chair (most ring strain)

QUESTIONS

Q4.5.1

Consider the conformations of cyclohexane, chair, boat, twist boat. Order them in increasing strain in the molecule.

S4.5.1

Chair < Twist Boat < Boat (most strain)

4.6: AXIAL AND EQUATORIAL BONDS IN CYCLOHEXANE

◑ OBJECTIVES

After completing this section, you should be able to

1. Draw the chair conformation of cyclohexane, with axial and equatorial hydrogen atoms clearly shown and identified.
2. identify the axial and equatorial hydrogens in a given sketch of the cyclohexane molecule.
3. explain how chair conformations of cyclohexane and its derivatives can interconvert through the process of ring flip.

⚓ KEY TERMS

Make certain that you can define, and use in context, the key terms below.

- axial position
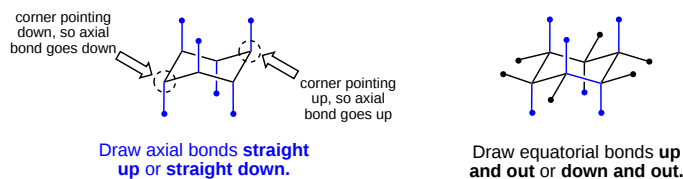- equatorial position
- ring flip

AXIAL AND EQUATORIAL POSITIONS IN CYCLOHEXANE

Careful examination of the chair conformation of cyclohexane, shows that the twelve hydrogens are not structurally equivalent. Six of them are located about the periphery of the carbon ring, and are termed **equatorial**. The other six are oriented above and below the approximate plane of the ring (three in each location), and are termed **axial** because they are aligned parallel to the symmetry axis of the ring.
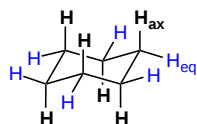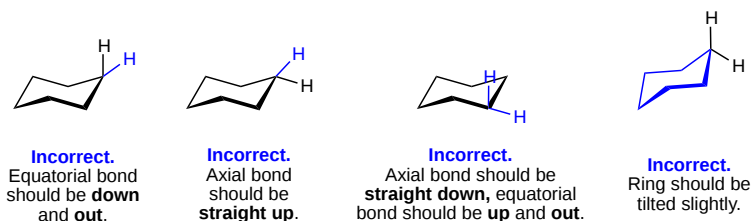

In the figure above, the equatorial hydrogens are colored blue, and the axial hydrogens are black. Since there are two equivalent chair conformations of cyclohexane in rapid equilibrium, all twelve hydrogens have 50% equatorial and 50% axial character.

HOW TO DRAW AXIAL AND EQUATORIAL BONDS

corner pointing down, so axial bond goes down

corner pointing up, so axial bond goes up

Draw axial bonds **straight up** or **straight down.**

Draw equatorial bonds **up and out** or **down and out.**

How **not** to draw the chair:

Incorrect. Equatorial bond should be **down and out**.

Incorrect. Axial bond should be **straight up**.

Incorrect. Axial bond should be **straight down,** equatorial bond should be **up** and **out**.

Incorrect. Ring should be tilted slightly.

Aside from drawing the basic chair, the key points are:

- Axial bonds alternate up and down, and are shown "vertical".
- Equatorial groups are approximately horizontal, but actually somewhat distorted from that (slightly up or slightly down), so that the angle from the axial group is a bit more than a right angle -- reflecting the common 109.5^o bond angle.
- Each carbon has an axial and an equatorial bond.
- Each face of the cyclohexane ring has three axial and three equatorial bonds.
- Each face alternates between axial and equatorial bonds. Then looking at the "up" bond on each carbon in the cyclohexane ring they will alternate axial-equatorial-axial ect.
- When looking down at a cyclohexane ring:
 - the equatorial bonds will form an "equator" around the ring.

- The axial bonds will either face towards you or away. These will alternate with each axial bond. The first axial bond will be coming towards with the next going away. There will be three of each type.
- Note! The terms cis and trans in regards to the stereochemistry of a ring are not directly linked to the terms axial and equatorial. It is very common to confuse the two. It typically best not to try and directly inter convert the two naming systems.

AXIAL VS. EQUATORIAL SUBSTITUENTS

When a substituent is added to cyclohexane, the ring flip allows for two distinctly different conformations. One will have the substituent in the axial position while the other will have the substituent in the equatorial position. In the next section will discuss the energy differences between these two possible conformations. Below are the two possible chair conformations of methylcyclohexane created by a ring-flip. Although the conformation which places the methyl group in the equatorial position is more stable by 7 kJ/mol, the energy provided by ambient temperature allows the two conformations to rapidly interconvert.

methyl group axial   methyl group equatorial
   (more stable by **7 kJ/mol**)
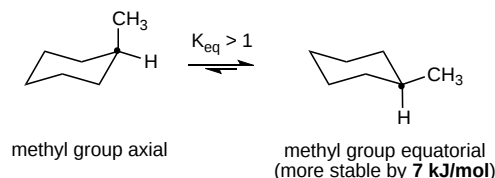
The figure below illustrates how to convert a molecular model of cyclohexane between two different chair conformations - this is something that you should practice with models. Notice that a 'ring flip' causes equatorial groups to become axial, and vice-versa.
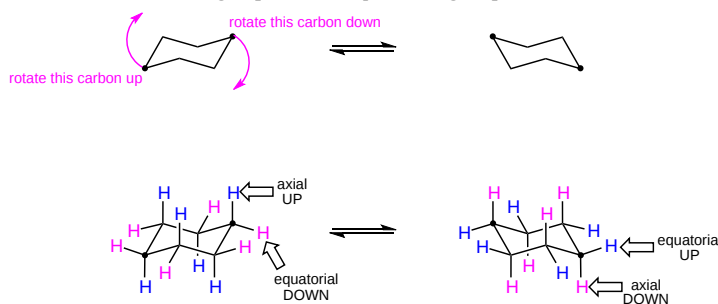

✔ EXAMPLE 4.6.1

For the following please indicate if the substituents are in the axial or equatorial positions.
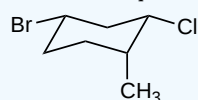
Solution

Due to the large number of bonds in cyclohexane it is common to only draw in the relevant ones (leaving off the hydrogens unless they are involved in a reaction or are important for analysis). It is still possible to determine axial and equatorial positioning with some thought. With problems such as this it is important to remember that each carbon in a cyclohexane ring has one axial and one equatorial bond. Also, remember that axial bonds are perpendicular with the ring and appear to be going either straight up or straight down. Equatorial bonds will be roughly in the plane of the cyclohexane ring (only slightly up or down). Sometimes it is valuable to draw in the additional bonds on the carbons of interest.
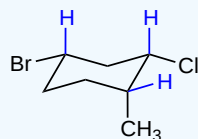

With this it can be concluded that the bromine and chlorine substituents are attached in equatorial positions and the CH_3 substituent is attached in an axial position.
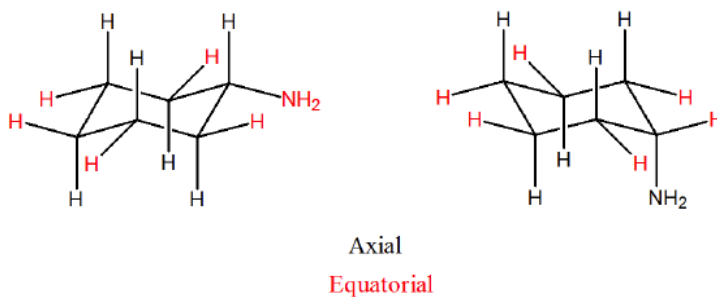
EXERCISES

1) Draw two conformations of cyclohexyl amine ($C_6H_{11}NH_2$). Indicate axial and equatorial positions.

2) Draw the two isomers of 1,4-dihydroxylcyclohexane, identify which are equatorial and axial.

3) In the following molecule, label which are equatorial and which are axial, then draw the chair flip (showing labels 1,2,3).
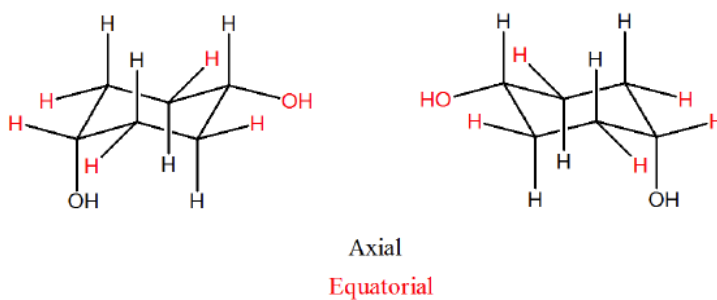

SOLUTIONS

1)

Axial
Equatorial
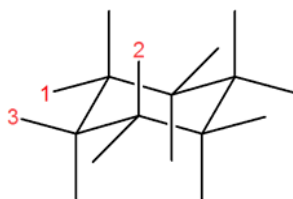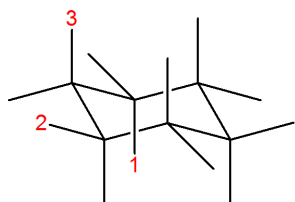
2)
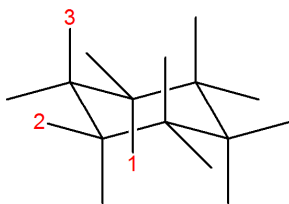
Axial
Equatorial

3) Original conformation: 1 = axial, 2 = equatorial, 3 = axial

Flipped chair now looks like this.

QUESTIONS

Q4.6.1

Draw two conformations of cyclohexyl amine ($C_6H_{11}NH_2$). Indicate axial and equatorial positions.

Q4.6.2

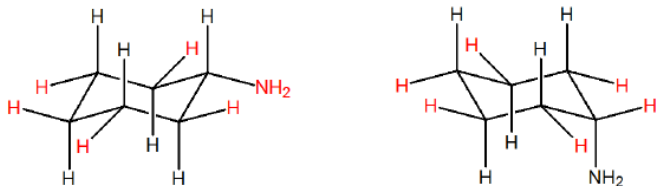Draw the two isomers of 1,4-dihydroxylcyclohexane, identify which are equatorial and axial.

Q4.6.3

In the following molecule, label which are equatorial and which are axial, then draw the chair flip (showing labels 1,2,3).
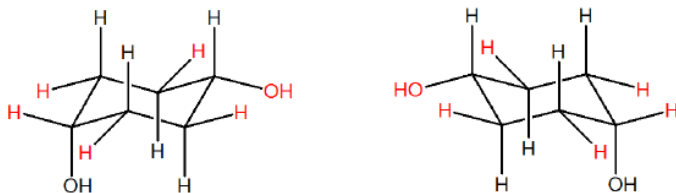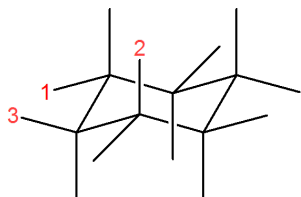
SOLUTIONS

S4.6.1

Axial

Equatorial

S4.6.2

Axial

Equatorial

S4.6.3

Original conformation: 1 = axial, 2 = equatorial, 3 = axial

Flipped chair now looks like this.

4.6: Axial and Equatorial Bonds in Cyclohexane is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Layne Morsch, Krista Cunningham, Tim Soderberg, Kelly Matthews, & Kelly Matthews.

4.7: CONFORMATIONS OF MONOSUBSTITUTED CYCLOHEXANES

OBJECTIVES

After completing this section, you should be able to

1. account for the greater stability of the equatorial conformers of monosubstituted cyclohexanes compared to their axial counterparts, using the concept of 1,3-diaxial interaction.
2. compare the gauche interactions in butane with the 1,3-diaxial interactions in the axial conformer of methylcyclohexane.
3. arrange a given list of substituents in increasing or decreasing order of 1,3-diaxial interactions.

KEY TERMS

Make certain that you can define, and use in context, the key term below.
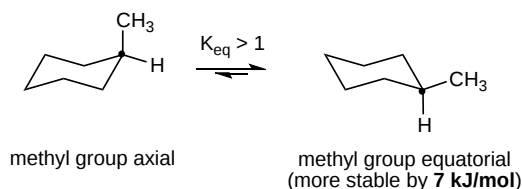
- 1,3-diaxial interaction

STUDY NOTES

1,3-Diaxial interactions are steric interactions between an axial substituent located on carbon atom 1 of a cyclohexane ring and the hydrogen atoms (or other substituents) located on carbon atoms 3 and 5.

Be prepared to draw Newman-type projections for cyclohexane derivatives as the one shown for methylcyclohexane. Note that this is similar to the Newman projections from chapter 3 such as *n*-butane.


methylcyclohexane   *n*-butane
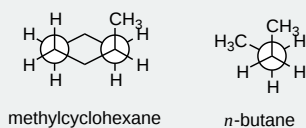
Newman projections of methylcyclohexane and *n*-butane

When a substituent is added to a cyclohexane ring, the two possible chair conformations created during a ring flip are not equally stable. In the example of methylcyclohexane the conformation where the methyl group is in the equatorial position is more stable than the axial conformation by 7.6 kJ/mol at 25° C. The percentages of the two different conformations at equilibrium can be determined by solving the following equation for K (the equilibrium constant): $\Delta E = -RT\ln K$. In this equation ΔE is the energy difference between the two conformations, R is the gas constant (8.314 J/mol•K), T is the temperature in Kelvin, and K is the equilibrium constant for the ring flip conversion. Using this equation, we can calculate a K value of 21 which means about 95% methylcyclohexane molecules have the methyl group in the equatorial position at 25° C.

methyl group axial

methyl group equatorial
(more stable by **7 kJ/mol**)

The energy difference between the two conformations comes from strain, called 1,3-diaxial interactions, created when the axial methyl group experiences steric crowding with the two axial hydrogens located on the same side of the cyclohexane ring. Because axial bonds are parallel to each other, substituents larger than hydrogen experience greater steric crowding when they are oriented axial rather than equatorial. Consequently, **substituted cyclohexanes will preferentially adopt conformations in which the larger substituents are in the equatorial orientation**. When the methyl group is in the equatorial position this strain is not present which makes the equatorial conformer more stable and favored in the ring flip equilibrium.
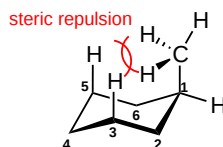
Actually, 1,3-diaxial steric strain is directly related to the steric strain created in the gauche conformer of butane discussed in Section: 3-7. When butane is in the gauche conformation 3.8 kJ/mol of strain was created due the steric crowding of two methyl group with a 60°

dihedral angle. When looking at the a Newman projection of axial methylcyclohexane the methyl group is at a 60° dihedral angle with the ring carbon in the rear. This creates roughly the same amount of steric strain as the gauche conformer of butante. Given that there is actually two such interactions in axial methylcyclohexane, it makes sense that there is 2(3.8 kJ/mol) = 7.6 kJ/mol of steric strain in this conformation. The Newman projection of equatorial methylcyclohexane shows no such interactions and is therefore more stable.

methylcyclohexane   *n*-butane
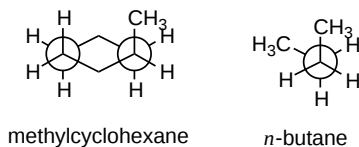
Newman projections of methyl cyclohexane and butane showing similarity of 1,3-diaxial and gauche interactions.

Strain values for other cyclohexane substituents can also be considered. The relative steric hindrance experienced by different substituent groups oriented in an axial versus equatorial location on cyclohexane determined the amount of strain generated. The strain generated can be used to evaluate the relative tendency of substituents to exist in an equatorial or axial location. Looking at the energy values in this table, it is clear that as the size of the substituent increases, the 1,3-diaxial energy tends to increase, also. Note that it is the size and not the molecular weight of the group that is important. Table 4.7.1 summarizes some of these strain values values.

Table 4.7.1: A Selection of ΔG° *Values for the Change from Axial to Equatorial Orientation of Substituents for Monosubstituted Cyclohexanes*

Substituent	-ΔG° (kcal/mol)	Substituent	-ΔG° (kcal/mol)
CH_3-	1.7	O_2N-	1.1
CH_2H_5-	1.8	$N\equiv C-$	0.2
$(CH_3)_2CH-$	2.2	CH_3O-	0.5
$(CH_3)_3C-$	≥ 5.0	HO_2C-	0.7
$F-$	0.3	$H_2C=CH-$	1.3
$Cl-$	0.5	C_6H_5-	3.0
$Br-$	0.5		
$I-$	0.5		

EXERCISES

1) In the molecule, cyclohexyl ethyne there is little steric strain, why?
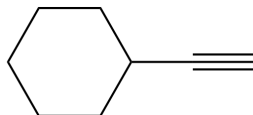
2) Calculate the energy difference between the axial and equatorial conformations of bromocyclohexane?

3) Using your answer from Question 2) estimate the percentages of axial and equatorial conformations of bromocyclohexane at 25° C.

Bromo group axial   **Bromo** group equitorial

4) There very little in 1,3-diaxial strain when going from a methyl substituent (3.8 kJ/mol) to an ethyl substituent (4.0 kJ/mol), why? It may help to use molecular model to answer this question.

SOLUTIONS

1) The ethyne group is linear and therefore does not affect the hydrogens in the 1,3 positions to say to the extent as a bulkier or a bent group (e.g. ethene group) would. This leads to less of a strain on the molecule.

2) The equatorial conformation of bromocyclohexane will have two 1,3 diaxial interactions. The table above states that each interaction accounts for 1.2 kJ/mol of strain. The total strain in equatorial bromocyclohexane will be 2(1.2 kJ/mol) = 2.4 kJ/mol.

3) Remembering that the axial conformation is higher in energy, the energy difference between the two conformations is ΔE = (E equatorial - E axial) = (0 - 2.4 kJ/mol) = -2.4 kJ/mol. After converting °C to Kelvin and kJ/mol to J/mol we can use the equation ΔE = -RT lnK to find that $-\Delta E/RT$ = lnK or (2.4 x 10^3 J/mol) / (8.313 kJ/mol K • 298 K) = lnK. From this we calculate that K = 2.6. Because the ring flip reaction is an equilibrium we can say that K = [Equatorial] / [Axial]. If assumption is made that [Equatorial] = X then [Axial] must be 1-X. Plugging these values into the equilibrium expression produces K = [X] / [1-X]. After plugging in the calculated value for K, X can be solved algebraically. 2.6 = [X] / [1-X] → 2.6 - 2.6X = X → 2.6 = 3.6X → 2.6/3.6 = X = 0.72. This means that bromocyclohexane is in the equatorial position 72% of the time and in the axial position 28% of the time.

Bromo group axial   **Bromo** group equitorial

4) The fact that C-C sigma bonds can freely rotate allows the ethyl subsistent to obtain a conformation which places the bulky CH_3 group away from the cyclohexane ring. This forces the ethyl substituent to have only have 1,3- diaxial interactions between hydrogens, which only provides a slight difference to a methyl group.

Methylcyclohexane   **Ethylcyclohexane**
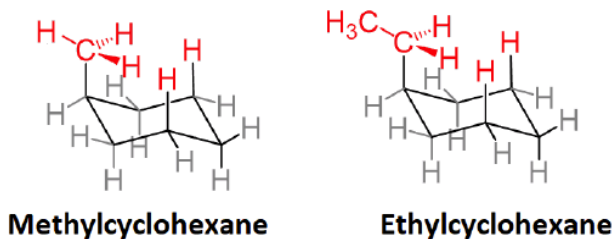
EXERCISES
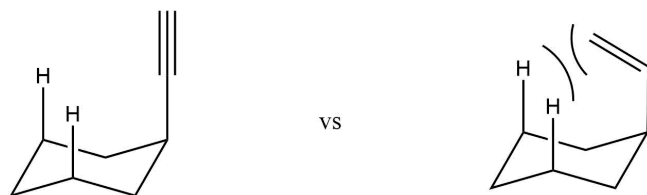
QUESTIONS

Q4.7.1

In the molecule, cyclohexyl ethyne there is little steric strain, why?

SOLUTIONS

S4.7.1

The ethyne group is linear and therefore does not affect the hydrogens in the 1,3 positions to say to the extent as a bulkier or a bent group (e.g. ethene group) would. This leads to less of a strain on the molecule.

4.8: CONFORMATIONS OF DISUBSTITUTED CYCLOHEXANES

> **◗ OBJECTIVE**
>
> After completing this section, you should be able to use conformational analysis to determine the most stable conformation of a given disubstituted cyclohexane.

> **⚲ KEY TERMS**
>
> Make certain that you can define, and use in context, the key term below.
> - conformational analysis

> **⚲ STUDY NOTES**
>
> When faced with the problem of trying to decide which of two conformers of a given disubstituted cyclohexane is the more stable, you may find the following generalizations helpful.
>
> 1. A conformation in which both substituents are equatorial will always be more stable than a conformation with both groups axial.
> 2. When one substituent is axial and the other is equatorial, the most stable conformation will be the one with the bulkiest substituent in the equatorial position. Steric bulk decreases in the order
>
>   tert-butyl > isopropyl > ethyl > methyl > hydroxyl > halogens

MONOSUBSTITUTED CYCLOHEXANES

In the previous section, it was stated that the chair conformation in which the methyl group is equatorial is more stable because it minimizes steric repulsion, and thus the equilibrium favors the more stable conformer. This is true for all monosubstituted cyclohexanes. The chair conformation which places the substituent in the equatorial position will be the most stable and be favored in the ring flip equilibrium.

methyl group axial

methyl group equatorial
(more stable by **7 kJ/mol**)
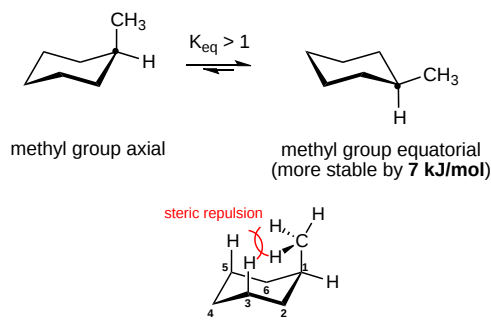
DISUBSTITUTED CYCLOHEXANES

Determining the more stable chair conformation becomes more complex when there are two or more substituents attached to the cyclohexane ring. To determine the stable chair conformation, the steric effects of each substituent, along with any additional steric interactions, must be taken into account for both chair conformations.

In this section, the effect of conformations on the relative stability of disubstituted cyclohexanes is examined using the two principles:

i. Substituents prefer equatorial rather than axial positions in order to minimize the steric strain created of 1,3-diaxial interactions.
ii. The more stable conformation will place the larger substituent in the equatorial position.

### 1,1-DISUBSTITUTED CYCLOHEXANES

The more stable chair conformation can often be determined empirically or by using the energy values of steric interactions previously discussed in this chapter. Note, in some cases there is no discernable energy difference between the two chair conformations which means they are equally stable.

1,1-dimethylcyclohexane does not have *cis* or *trans* isomers, because both methyl groups are on the same ring carbon. Both chair conformers have one methyl group in an axial position and one methyl group in an equatorial position giving both the same relative stability. The steric strain created by the 1,3-diaxial interactions of a methyl group in an axial position (versus equatorial) is 7.6 kJ/mol (from Table 4.7.1), so both conformers will have equal amounts of steric strain. Thus, the equilibrium between the two conformers does not

favor one or the other. Note, that both methyl groups cannot be equatorial at the same time without breaking bonds and creating a different molecule.
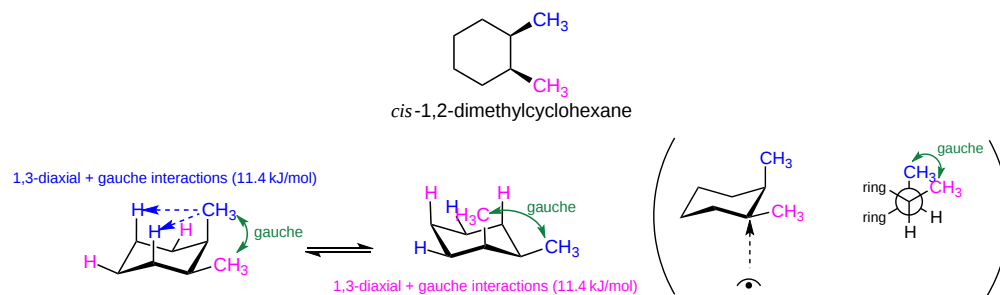

1,1-dimethylcyclohexane
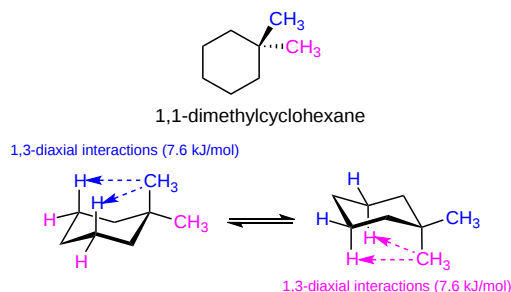
However, if the two groups are different, as in 1-*tert*-butyl-1-methylcyclohexane, then the equilibrium favors the conformer in which the larger group (*tert*-butyl in this case) is in the more stable equatorial position. The energy cost of having one tert-butyl group axial (versus equatorial) can be calculated from the values in table 4.7.1 and is approximately 22.8 kJ/mol. The conformer with the *tert*-butyl group axial is approximately 15.2 kJ/mol (22.8 kJ/mol - 7.6 kJ/mol) less stable then the conformer with the *tert*-butyl group equatorial. Solving for the equilibrium constant K shows that the equatorial is preferred about 460:1 over axial. This means that 1-*tert*-butyl-1-methylcyclohexane will spend the majority of its time in the more stable conformation, with the *tert*-butyl group in the equatorial position.


1-(*tert*-butyl)-1-methylcyclohexane
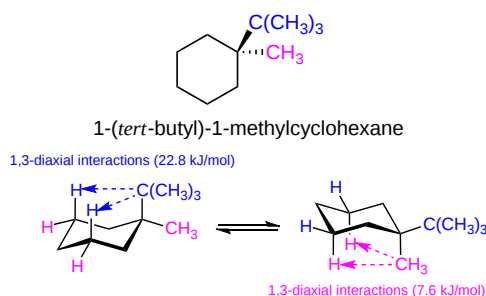
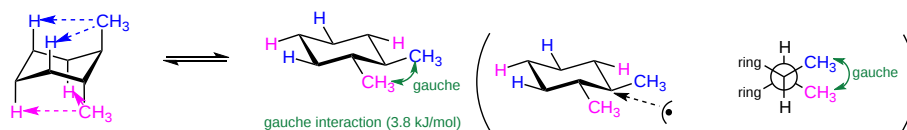## CIS AND *TRANS* STEREOISOMERS OF 1,2-DIMETHYLCYCLOHEXANE

In *cis*-1,2-dimethylcyclohexane, both chair conformations have one methyl group equatorial and one methyl group axial. As previously discussed, the axial methyl group creates 7.6 kJ/mol of steric strain due to 1,3-diaxial interactions. It is important to note, that both chair conformations also have an additional 3.8 kJ/mol of steric strain created by a gauche interaction between the two methyl groups. Overall, both chair conformations have 11.4 kJ/mol of steric strain and are of equal stability.

cis-1,2-dimethylcyclohexane

In *trans*-1,2-dimethylcyclohexane, one chair conformer has both methyl groups axial and the other conformer has both methyl groups equatorial. The conformer with both methyl groups equatorial has no 1,3-diaxial interactions however there is till 3.8 kJ/mol of strain created by a gauche interaction. The conformer with both methyl groups axial has four 1,3-Diaxial interactions which creates 2 x 7.6 kJ/mol (15.2 kJ/mol) of steric strain. This conformer is (15.2 kJ/mol -3.8 kJ/mol) 11.4 kJ/mol less stable than the other conformer. The equilibrium will therefore favor the conformer with both methyl groups in the equatorial position.
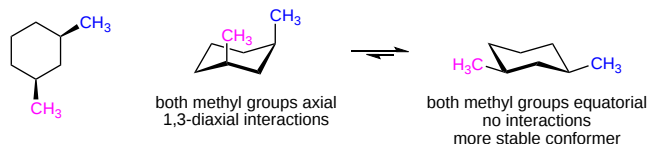

trans-1,2-dimethylcyclohexane
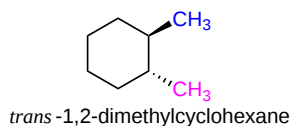
two 1,3-diaxial interactions (15.2 kJ/mol)


gauche interaction (3.8 kJ/mol)

CIS AND *TRANS* STEREOISOMERS OF 1,3-DIMETHYLCYCLOHEXANE

A similar conformational analysis can be made for the *cis* and *trans* stereoisomers of 1,3-dimethylcyclohexane. For *cis*-1,3-dimethylcyclohexane one chair conformation has both methyl groups in axial positions creating 1,3-diaxial interactions. The other conformer has both methyl groups in equatorial positions thus creating no 1,3-diaxial interaction. Because the methyl groups are not on adjacent carbons in the cyclohexane rings gauche interactions are not possible. Even without energy calculations it is simple to determine that the conformer with both methyl groups in the equatorial position will be the more stable conformer.

both methyl groups axial
1,3-diaxial interactions

both methyl groups equatorial
no interactions
more stable conformer

For *trans*-1,3-dimethylcyclohexane both conformations have one methyl axial and one methyl group equatorial. Each conformer has one methyl group creating a 1,3-diaxial interaction so both are of equal stability.

one methyl group axial
and one equatorial

one methyl group axial
and one equatorial

both conformers have equal stability
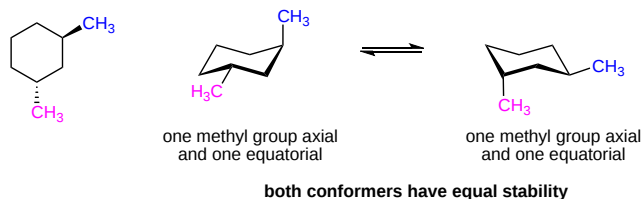
SUMMARY OF DISUBSTITUED CYCLOHEXANE CHAIR CONFORMATIONS

When considering the conformational analyses discussed above a pattern begins to form. There are only two possible relationships which can occur between ring-flip chair conformations:

1) AA/EE: One chair conformation places both substituents in axial positions creating 1,3-diaxial interactions. The other conformer places both substituents in equatorial positions creating no 1,3-diaxial interactions. This diequatorial conformer is the more stable regardless of the substituents.

2) AE/EA: Each chair conformation places one substituent in the axial position and one substituent in the equatorial position. If the substituents are the same, there will be equal 1,3-diaxial interactions in both conformers making them equal in stability. However, if the substituents are different then different 1,3-diaxial interactions will occur. The chair conformation which places the larger substituent in the equatorial position will be favored.

Substitution type	Chair Conformation Relationship
cs-1,2-disubstituted cyclohexanes	AE/EA
trans-1,2-disubstituted cyclohexanes	AA/EE
cis-1,3-disubstituted cyclohexanes	AA/EE
trans-1,3-disubstituted cyclohexanes	AE/EA
cis-1,4-disubstituted cyclohexanes	AE/EA
trans-1,4-disubstituted cyclohexanes	AA/EE

> ✔ EXAMPLE 4.8.1
>
> For *cis*-1-chloro-4-methylcyclohexane, draw the most stable chair conformation and determine the energy difference between the two chair conformers.
>
> **Solution**
> Based on the table above, *cis*-1,4-disubstitued cyclohexanes should have two chair conformations each with one substituent axial and one equatorial. Based on this, we can surmise that the energy difference of the two chair conformations will be based on the difference in the 1,3-diaxial interactions created by the methyl and chloro substituents.

1,3-diaxial interactions (7.6 kJ/mol)

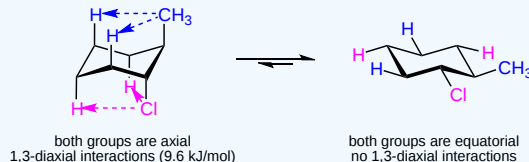1,3-diaxial interactions (2.0 kJ/mol)

As predicted, each chair conformer places one of the substituents in the axial position. Because the methyl group is larger and has a greater 1,3-diaxial interaction than the chloro, the most stable conformer will place it the equatorial position, as shown in the structure on the right. Using the 1,3-diaxial energy values given in the previous sections we can calculate that the conformer on the right is (7.6 kJ/mol - 2.0 kJ/mol) 5.6 kJ/mol more stable than the other.

> ✔ EXAMPLE 4.8.2
>
> For *trans*-1-chloro-2-methylcyclohexane, draw the most stable chair conformation and determine the energy difference between the two chair conformers.
>
> **Solution**
>
> Based on the table above, *trans*-1,2-disubstitued cyclohexanes should have one chair conformation with both substituents axial and one conformation with both substituents equatorial. Based on this, we can predict that the conformer which places both substituents equatorial will be the more stable conformer. The energy difference of the two chair conformations will be based on the 1,3-diaxial interactions created by both the methyl and chloro substituents.
>
>
>
> both groups are axial
> 1,3-diaxial interactions (9.6 kJ/mol)
>
> both groups are equatorial
> no 1,3-diaxial interactions
>
> As predicted, one chair conformer places both substituents in the axial position and other places both substituents equatorial. The more stable conformer will place both substituents in the equatorial position, as shown in the structure on the right. Using the 1,3-diaxial energy values given in the previous sections we can calculate that the conformer on the right is (7.6 kJ/mol + 2.0 kJ/mol) 9.6 kJ/mol more stable than the other.

CONFORMATIONAL ANALYSIS OF COMPLEX SIX MEMBERED RING STRUCTURES

Cyclohexane can have more than two substituents. Also, there are multiple six membered rings which contain atoms other than carbon. All of these systems usually form chair conformations and follow the same steric constraints discussed in this section. Because the most commonly found rings in nature are six membered, conformational analysis can often help in understanding the usual shapes of some biologically important molecules. In complex six membered ring structures a direct calculation of 1,3-diaxial energy values may be difficult. In these cases a determination of the more stable chair conformer can be made by empirically applying the principles of steric interactions.

A later chapter will discuss how many sugars can exist in cyclic forms which are often six remembered rings. When in an aqueous solution the six carbon sugar, glucose, is usually a six membered ring adopting a chair conformation. When looking at the two possible ring-clip chair conformations, one has all of the substituents axial and the other has all the substutents equatorial. Even without a calculation, it is clear that the conformation with all equatorial substituents is the most stable and glucose will most commonly be found in this conformation.
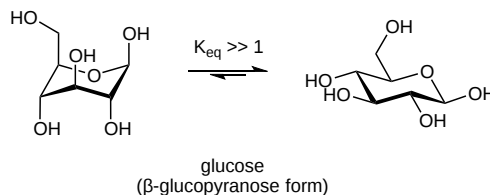
glucose
(β-glucopyranose form)

> ✔ EXAMPLE 4.8.3
>
> The six carbon sugar, fructose, in aqueous solution is also a six-membered ring in a chair conformation. Which of the two possible chair conformations would be expected to be the most stable?
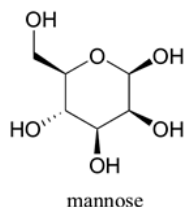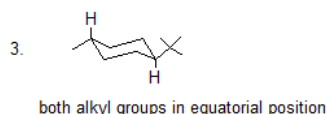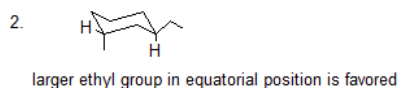
fructose
(β-fructopyranose form)
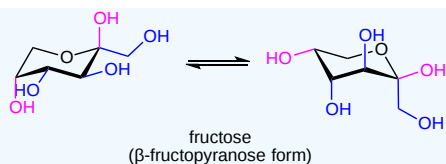
Solution
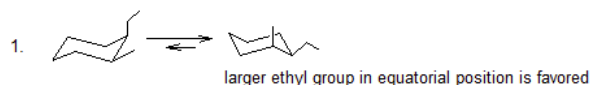
The lower energy chair conformation is the one with three of the five substituents (including the bulky $-CH_2OH$ group) in the equatorial position (pictured on the right). The left structure has 3 equatorial substituents while the structure on the right only has two equatorial substituents.
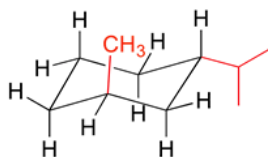
EXERCISES

1. Draw the two chair conformations for *cis*-1-ethyl-2-methylcyclohexane using bond-line structures and indicate the more energetically favored conformation.

2. Draw the most stable conformation for *trans*-1-ethyl-3-methylcyclohexane using bond-line structures.

3. Draw the most stable conformation for trans-1-*t*-butyl-4-methylcyclohexane using bond-line structures.

4. Draw the most stable conformation fo *trans*-1-isopropyl-3-methylcyclohexane.

5. Can a 'ring flip' change a *cis*-disubstituted cyclohexane to *trans*? Explain.

6. Draw the two chair conformations of the six-carbon sugar mannose, being sure to clearly show each non-hydrogen substituent as axial or equatorial. Predict which conformation is likely to be more stable, and explain why.

mannose

SOLUTIONS

1.

larger ethyl group in equatorial position is favored

2.

larger ethyl group in equatorial position is favored

3.

both alkyl groups in equatorial position

4.

The bulkier isopropyl groups is in the equatorial position.

5. No. In order to change the relationship of two substituents on a ring from *cis* to *trans*, you would need to break and reform two covalent bonds. Ring flips involve only *rotation* of single bonds.

6.
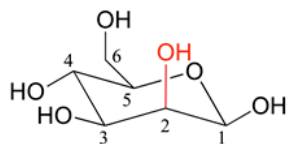
major chair form of mannose
(only one substituent axial)
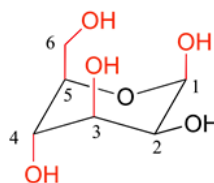
minor chair form of mannose
(four substituents axial)

EXERCISES

QUESTIONS

Q4.8.1

For the following molecules draw the most stable chair conformation and explain why you chose this as an answer

1 = *trans*-1,2-dimethylcyclohexane

2 = *cis*-1,3-dimethylcyclohexane

SOLUTIONS

S4.8.1

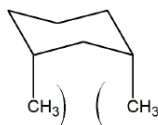1 – The most stable conformation would be to have the methyl groups equatorial reducing steric interaction

2 – The most stable conformation would be to have the groups equatorial this would reduce the strain if they were axial

---

4.9: CONFORMATIONS OF POLYCYCLIC MOLECULES

> **◑ OBJECTIVE**
>
> After completing this section, you should be able to draw the structures and construct molecular models of simple polycyclic molecules.

> **⚲ KEY TERMS**
>
> Make certain that you can define, and use in context, the key terms below.
> - bridgehead carbon atom
> - polycyclic molecule

> **⚲ STUDY NOTES**
>
> A *bridgehead carbon atom* is a carbon atom which is shared by at least two rings. The hydrogen atom which is attached to a bridgehead carbon may be referred to as a bridgehead hydrogen.
>
> Note that bicyclo[2.2.1]heptane is the systematic name of norborane. You need not be concerned over the IUPAC name of norbornane. The nomenclature of compounds of this type is beyond the scope of this course.

NOMENCLATURE OF BICYCLIC RING SYSTEMS

There are many hydrocarbons and hydrocarbon derivatives with two rings having common carbon atoms. There are three main ways that the two rings can be connected. The first is called a **fused bicyclic** ring structure where the two rings share a covalent bond and a have two **bridgehead** carbons (marked in red on the structures below). A bridgehead is defined as a carbon that is part of two or more rings. Hydrogens attached to bridge head carbons are often referred to as bridge head hydrogens. The two rings can also be connected by a bridge containing one or more carbons to form a **bridged bicyclic** molecule. Lastly, the two rings can be joined with a singe bridge head carbon to form **spiro bicyclic** molecules.


fused   bridged   spiro
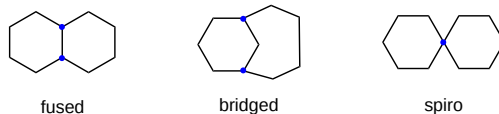
• = bridgehead carbons

**Bicyclic Isomers of $C_{10}H_{18}$**

NAMING FUSED AND BRIDGED COMPOUNDS

Fused and bridged bicyclic compounds are follow similar naming conventions:

1. Count the total number of carbons in both rings. This is the parent name. (eg. ten carbons in the system would be decane)
2. Count the number of carbons between the bridgeheads, then place the numbers in square brackets in descending order separated by periods. Fused and bridged bycyclic compounds should have three numbers such as [2.2.0]. For fused compounds one of the numbers should be zero.
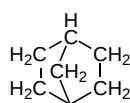3. Place the word **bicyclo** at the beginning of the name.
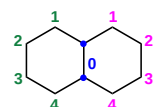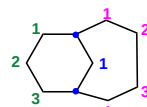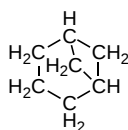

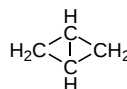bicyclo[4.4.0]decane   bicyclo[4.3.1]decane

Examples with carbons and hydrogens explicitly shown:

bicyclo[2.2.1]heptane   bicyclo[3.1.1]heptane   bicyclo[1.1.0]butane

![LibreTexts logo]
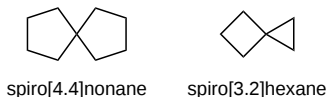
NAMING SPIRO COMPOUNDS

Spiro bicyclics are named using the same basic rules. Because there is only one bridgehead carbon only two numbers will be required in the brackets. Also, the word **spiro** is placed at the beginning.
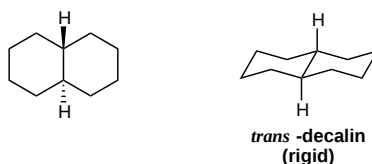

spiro[5.4]decane

EXAMPLES

spiro[4.4]nonane   spiro[3.2]hexane
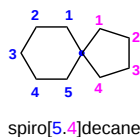
CONFORMATIONS IN BICYCLIC RING SYSTEMS

As expected, the connection of two rings has defined effects on the possible conformations. However, the ideas previously discussed in this chapter can be used for conformational analysis. Fused rings have the possibility of two isomers where the bridgehead hydrogens are either *cis* or *trans* along the shared bond. These two isomers have significant differences in flexibility and stability as seen in bicyclo[4,4,0]decane more commonly known as decalin. If the positioning of the bridgehead hydrogens are shown in a fused ring the prefix cis or trans should be included in the name.

The trans-isomer is the easiest to describe because the fusion of the two rings creates a rigid, roughly planar, structure made up of two chair conformations. Unlike cyclohexane, the two rings cannot flip from one chair form to another. Accordingly, the orientation of the any substituents is fixed in either an axial or equatorial position in *trans*-decalin. This means that the C-C bonds coming away from the fused edge are held in equatorial positions relative to each ring thus preventing the possibility of any 1,3-diaxial interactions occurring between ring atoms.


***trans*-decalin**
(rigid)

2kcal mol−1" id="MathJax-Element-1-Frame" role="presentation" style="position:relative;" tabindex="0">

The two rings in *cis*-decalin are also both held in a chair conformations. In comparison, the chair-chair forms of *cis*-decalin are relatively flexible, and inversion of both rings at once occurs fairly easily.


***cis*-decalin**
(more flexible)
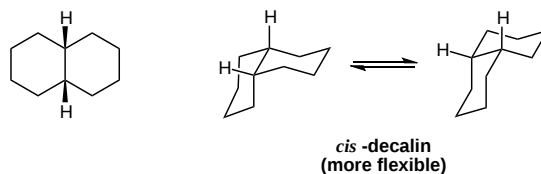
The flexibility of *cis*-decalin allows for a substituent to interconvert between axial and equatorial conformations. In much the same fashion as cyclohexane, equatorial substituents tend to create less steric strain and create a more stable conformer.
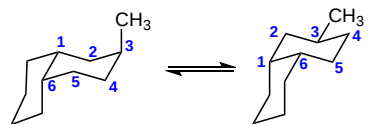
(Note: atoms are mapped in blue for clarity.)

A major difference in *cis*-decalin is the fact that one of C-C bonds coming away from the fused edge is held an an axial position. This is true in both ring-flip conformations. This axial C-C bond causes 1,3-diaxial interactions to occur in *cis*-decalin making it roughly 8.4 kJ/mol less stable than *trans*-decalin. This amount of 1,3-diaxial steric strain is roughly equivalent to that of an ethyl substituent attached to a cyclohexane ring (8.0 kJ/mol)
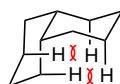
✗ = steric strain

Bicyclic compounds with a bridge typically have very little flexibility and are often held in a ridged conformation. The molecule norbornane represent a cyclohexane ring connected by a single carbon bridge.

norbornane, or
bicyclo[2.2.1]heptane

Norbornane is estimated to have 72 kJ/mol of ring strain which can be understood when viewing the contained rings. The carbon bridge in norbornane holds the cyclohexane ring at the bottom in a boat conformation creating torsional strain from eclipsing bonds along the edge.

(green arrows used to illustrate eclipsing hydrogens)
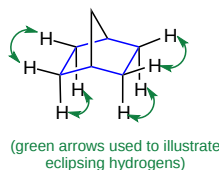
Also, the carbon bridge forms a cyclopentane ring (shown in red below making up the right side of the structure) with increased angle strain throughout the whole molecule.


POLYCYCLIC SYSTEMS IN NATURE

Fused ring systems like decalin are very common in natural products. In fact, similar ring systems are found in steroids, which are an important class of lipids. Steroids generally have structures that include three six-membered rings and a five-membered ring connected by three fused bonds. Most natural steroids have a *trans* configuration at all three fusion points. This tends to give steroids a rigid and semi-flat structure.
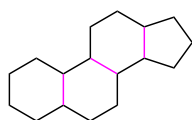

basic steroid ring confguration
(fused bonds highlighted in purple)
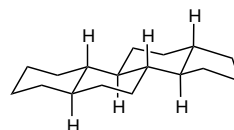
trans-trans-trans

Sex hormones are an example of steroids. The primary male hormone, testosterone, is responsible for the development of secondary sex characteristics. Two female sex hormones, progesterone and estrogen (or estradiol) control the ovulation cycle. Notice that the male and female hormones have only slight differences in structures, but yet have very different physiological effects. Testosterone promotes the normal development of male genital organs and is synthesized from cholesterol in the testes. It also promotes secondary male sexual characteristics such as deep voice, facial and body hair.
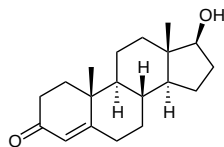

testosterone
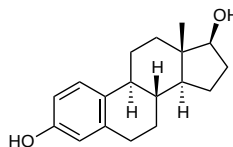
estradiol

The best known and most abundant steroid in the body is cholesterol. Cholesterol is formed in brain tissue, nerve tissue, and the blood stream. It is the major compound found in gallstones and bile salts. Cholesterol also contributes to the formation of deposits on the inner walls of blood vessels. These deposits harden and obstruct the flow of blood. This condition, known as atherosclerosis, results in various heart diseases, strokes, and high blood pressure.
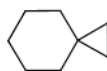
cholesterol

EXERCISES

1)

a)   b)   c)

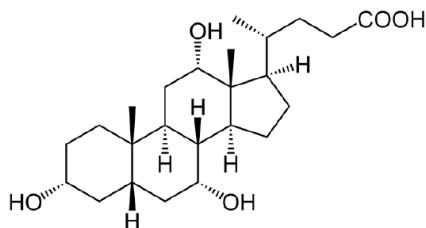d)   e)   =

f)   g)   h)
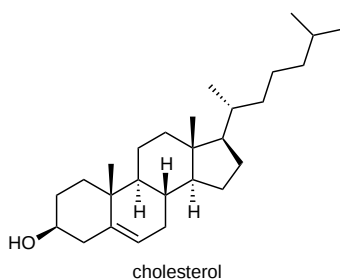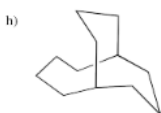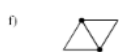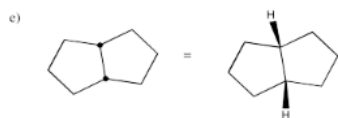
i)

j)

3) The following molecule is cholic acid. Determine if the three fused bonds have a *cis* or *trans* configuration.

SOLUTIONS

1)

a) Bicyclo[2.1.1]hexane

b) Bicyclo[3.2.1]octane

c) Bicyclo[2.1.0]pentane (more commonly called "housane")
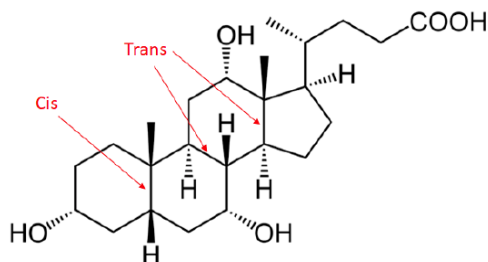
d) Bicyclo[2.2.2]octane

e) cis-Bicyclo[3.3.0]octane

f) cis-Bicyclo[1.1.0]butane

g) Bicyclo[1.1.1]pentane

h) Bicyclo[4.3.3]dodecane

2)

QUESTIONS

Q4.9.1

Someone stated that *trans*-decalin is more stable than *cis*-decalin. Explain why this is incorrect.

SOLUTIONS

S4.9.1

Cis-decalin has fewer steric interactions than *trans*-decalin.

4.S: ORGANIC COMPOUNDS- CYCLOALKANES AND THEIR STEREOCHEMISTRY (SUMMARY)

CONCEPTS & VOCABULARY

4.1: Naming Cycloalkanes

- Cycloalkanes are saturated hydrocarbons that have the generic formula C_nH_{2n} , where **n** is the number of carbons in the ring.
- The IUPAC rules for naming cycloalkanes is very similar to the rules used for naming alkanes.

4.2: Cis-Trans Isomerism in Cycloalkanes

- **Stereoisomers** are molecules that have the same molecular formula, the same atom connectivity, but they differ in the relative spatial orientation of the atoms.
- Di-substituted cycloalkanes exhibit *cis*- / *trans*- stereoisomerism. The *cis*- isomer has both substituents on the same face of the ring, while the **trans**- isomer has groups on opposite faces of the ring.

4.3: Stability of Cycloalkanes - Ring Strain

- **Ring strain** is the total strain in a ring due to **torsional strain**, **steric strain** and **angle strain**.
- Angle strain is when the C-C-C bond angles in rings are different than 109.5º, the optimal bond angle for sp^3 hybridized carbons.
- Ring strain causes small cycloalkanes, like cyclopropane and cyclobutane, to be much less stable than other cycloalkanes.

4.4: Conformations of Cycloalkanes

- Cyclopentane has less ring strain than cyclopropane and cyclobutane, because its ring carbons have more flexibility to rotate away from planarity, resulting in lower angle and torsional strains.

4.5: Conformations of Cyclohexane

- Cyclohexane has significantly lower ring strain than smaller cycloalkanes, because cyclohexane can adopt non-planar structures, which minimize angle strain and torsional strain.
- The common non-planar structures of cyclohexane are the boat, twist-boat, and chair conformations. The most stable, and hence, the most common, is the chair conformation.

4.6: Axial and Equatorial Bonds in Cyclohexane

- The two chair conformations of cyclohexane interconvert rapidly at room temperature in a process called **chair flip** or **ring flip**.
- In the chair conformation of cyclohexane, of the two groups attached to each ring carbon, one of the groups occupies the **axial** position, while the other group occupies the **equatorial** position.
- A group that was axial will switch to the equatorial position during a ring flip, and vice versa.

4.7: Conformations of Monosubstituted Cyclohexanes

- To minimize the steric effects of **1,3-diaxial interactions**, the single group on a monosubstituted cyclohexane ring will prefer to be in the equatorial position over the axial position. The larger the group, the greater is the preference shifts.

### 4.8: Conformations of Disubstituted Cyclohexanes

- The preference for large groups to be in the equatorial position effects the relative stability of the *cis* and *trans* isomers of disubstituted cyclohexanes. **Conformational analysis** is the process used to determine which isomer, *cis* or *trans*, is most stable.

4.9: Conformations of Polycyclic Molecules

SUMMARY PROBLEMS

> **? EXERCISE** $4.S.1$
>
> The following molecule, quinic acid, is a natural product that can be obtained from a variety of sources including the coffee bean. Draw both chair conformations for this molecule, identify each substituent in both structures as axial or equatorial, and clearly indicate which chair conformation is the most stable.
>
>
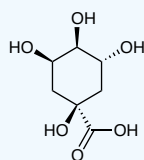
Answer
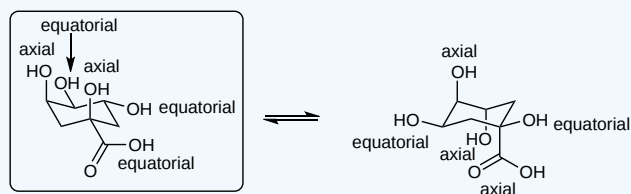
The circled conformation is more stable because it has more equatorial substituents (3 versus 2) and the largest group (the carboxylic acid) is equatorial.

? EXERCISE $4.S.2$

Convert the following name to a skeletal structure: *cis*-1-*t*-butyl-2-ethylcyclohexane. Then, draw this molecule in a chair conformation and perform a ring flip. Circle the most stable of the two conformations.

Answer
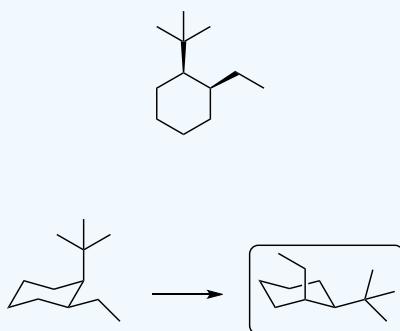
Remember that, due to its large size, the *t*-butyl substituent locks the cyclohexane ring into one conformation with the *t*-butyl in the equatorial position. Thus, this isn't an equilibrium. It exists only as the circled conformation.

? EXERCISE $4.S.3$

Convert the following name to a skeletal structure: *trans*-3-isobutylcyclohexanol. Then, draw the two chair conformations, label substituents as axial or equatorial, and circle the more stable conformation.

Answer
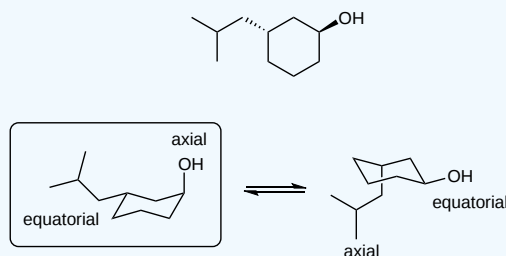
The circled molecule is most stable because the larger substituent is equatorial.

SKILLS TO MASTER

- Skill 4.1 Be able to name and draw cycloalkanes
- Skill 4.2 Identify and draw the *cis*- and *trans*- stereoisomers of disubstituted cycloalkanes.
- Skill 4.3 Determine the effects of torsional strain, steric strain, and angle strain on the overall ring strain of a cycloalkane.
- Skill 4.4 Draw the chair conformers of cyclohexane.
- Skill 4.5 Draw and identify the axial and equatorial positions in a chair conformer of cyclohexane and its ring-flip conformer.
- Skill 4.6 Use conformational analysis to determine the most stable stereoisomer in disubstituted and polysubstituted cyclohexanes.