







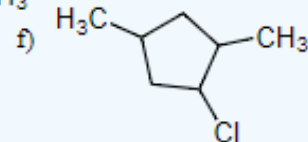
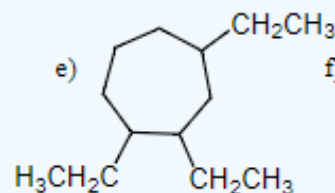
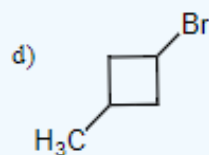
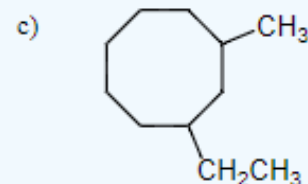
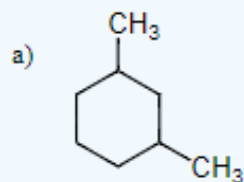


Cycloalkanes

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	$C_{10}H_{20}$	

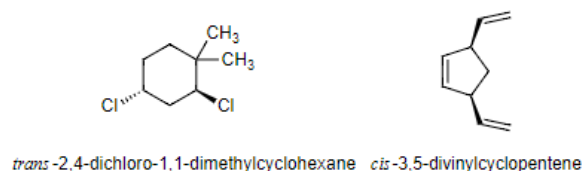
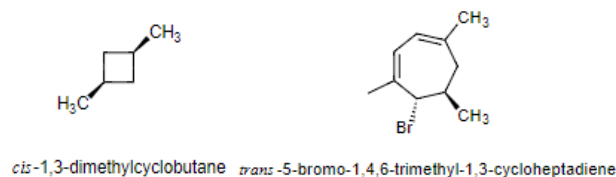
Give the IUPAC names for the following cycloalkane structures.



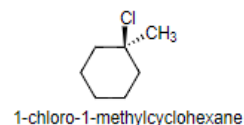
- a) 1,3-Dimethylcyclohexane
- b) 2-Cyclopropylbutane
- c) 1-Ethyl-3-methylcyclooctane
- d) 1-Bromo-3-methylcyclobutane
- e) 1,2,4-Triethylcycloheptane
- f) 1-Chloro-2,4-dimethylcyclopentane

Representing 3D Structures

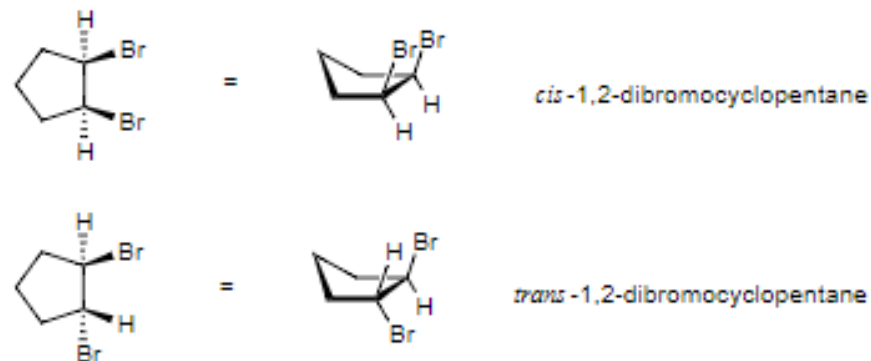
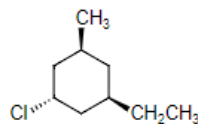
By convention, chemists use heavy, wedge-shaped bonds to indicate a substituent located above the plane of the ring (coming out of the page), a dashed line for bonds to atoms or groups located below the ring (going back into the page), and solid lines for bonds in the plane of the page.



In general, if any two sp^3 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.



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)



Draw the following molecules:

trans-1,3-dimethylcyclohexane

trans-1,2-dibromocyclopentane

cis-1,3-dichlorocyclobutane

Ring Strain

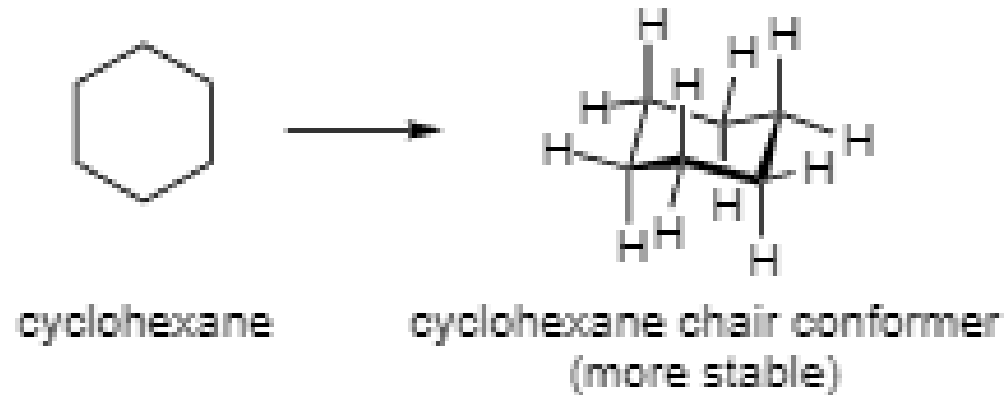
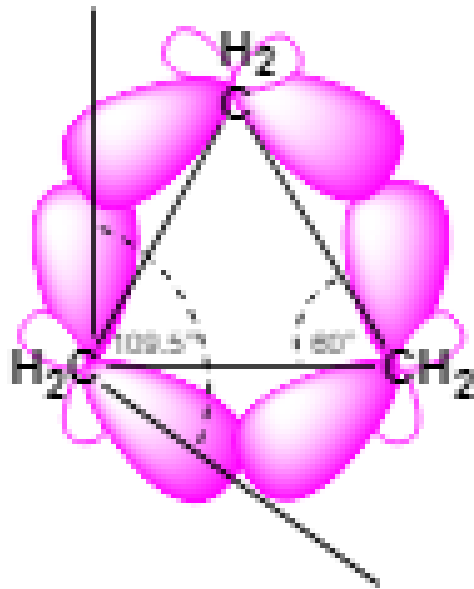
The following table lists the heat of combustion data for some simple cycloalkanes. These cycloalkanes do not have the same molecular formula, so the heat of combustion per each CH₂ unit present in each molecule is calculated (the fourth column) to provide a useful comparison. From the data, cyclopropane and cyclobutane have significantly higher heats of combustion per CH₂, 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.

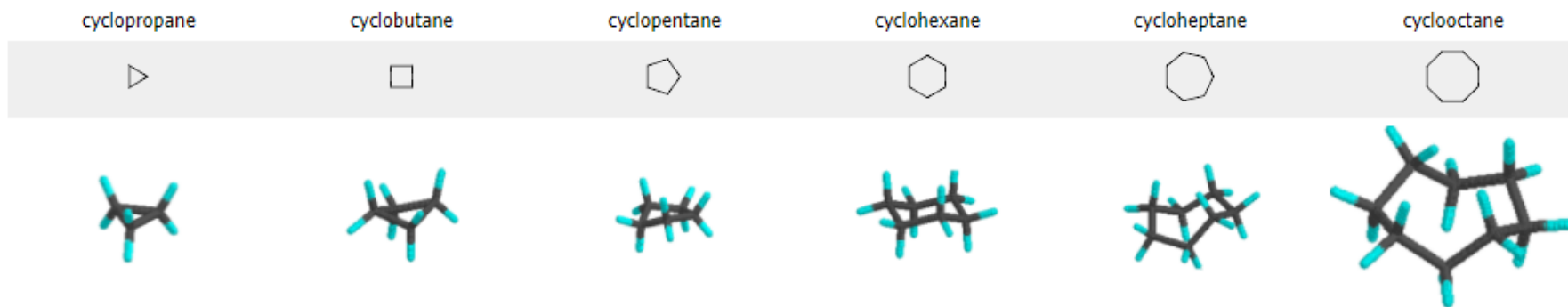
Cycloalkane (CH ₂) _n	CH ₂ Units n	ΔH ^{25°} kcal/mol	ΔH ^{25°} per CH ₂ Unit	Ring Strain kcal/mol
Cyclopropane	n = 3	468.7	156.2	27.6
Cyclobutane	n = 4	614.3	153.6	26.4
Cyclopentane	n = 5	741.5	148.3	6.5
Cyclohexane	n = 6	882.1	147.0	0.0
Cycloheptane	n = 7	1035.4	147.9	6.3
Cyclooctane	n = 8	1186.0	148.2	9.6
Cyclononane	n = 9	1335.0	148.3	11.7
Cyclodecane	n = 10	1481	148.1	11.0
CH ₃ (CH ₂) _m CH ₃	m = large	—	147.0	0.0

The combustion of carbon compounds, especially hydrocarbons, has been the most important source of heat energy for human civilizations throughout recorded history. The practical importance 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.

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 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° , 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.





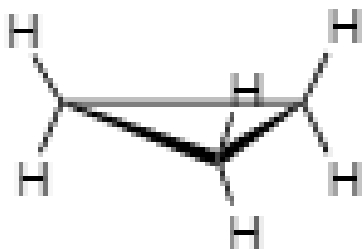
Cyclopropane is necessarily planar (flat), with the carbon atoms at the corners of an equilateral triangle. The 60° bond angles are much smaller than the optimum 109.5° angles of a normal tetrahedral carbon atom, and the resulting angle strain dramatically influences the chemical behavior of this cycloalkane. 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 25°), but the total eclipsing and angle strain remains high. Cyclopentane has very little angle strain (the angles of a pentagon are 108°), 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).

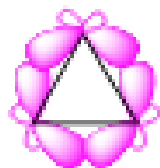
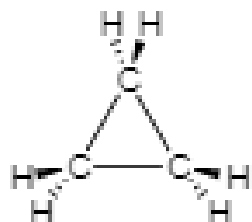
Cyclic systems are a little different from open-chain systems. In an open chain, any bond can be rotated 360° , going through many different conformations. That complete rotation isn't possible in a cyclic system, because the parts that would be trying to twist away from each other would still be connected 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.

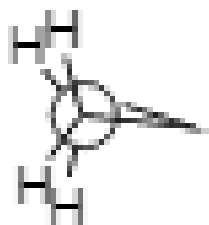
In addition to angle strain, there is also steric (transannular) strain and torsional strain in many cycloalkanes. Transannular strain exists when there is steric repulsion between atoms.



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.



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 109.5° . The angles in an equilateral triangle are actually 60° , 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:

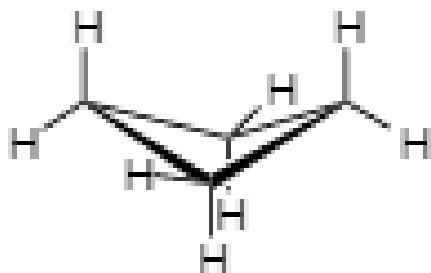


Newman projection



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.



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 relieves some of the torsional strain but increases the angle strain because the ring bond angles decrease to 88 deg.

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

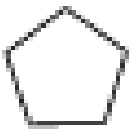


With bond angles of 88 deg rather than 109.5 degrees, cyclobutane has significant amounts of angle strain, but less than in cyclopropane.

Although torsional strain is still present, the neighboring C-H bonds are not exactly eclipsed in the cyclobutane's puckered conformation.

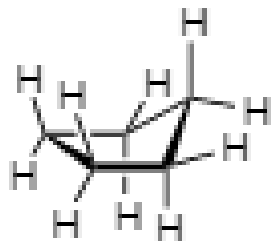
Steric strain is very low. Cyclobutane is still not large enough that substituents can reach around to cause crowding.

Overall the ring strain in cyclobutane (110 kJ/mol) is slightly less than cyclopropane (115 kJ/mol).

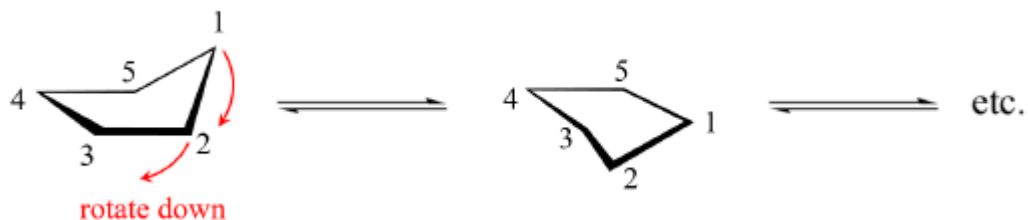


cyclopentane

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 adopts a non-planar conformation even though it slightly increases angle strain.

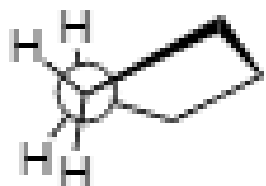


The lowest energy conformation of cyclopentane is known as the 'envelope', with four of the ring atoms in the same plane and one out of plane (notice that this shape resembles an envelope with the flap open). The out-of-plane carbon is said to be in the endo position ('endo' means 'inside'). The envelope 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.



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.



The angle strain in the envelope conformation of cyclopentane is low. The ideal angle in a regular pentagon is about 107 deg, very close to the preferred 109.5 deg tetrahedral bond angle.

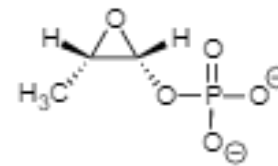
There is some torsional strain in cyclopentane. The envelope conformation reduces torsional strain by placing some bonds in nearly staggered positions. However, other bonds are still almost fully eclipsed.

Cyclopentane is not large enough to allow for steric strain to be created.

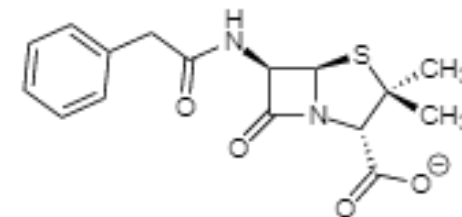
Overall, cyclopentane has very little ring strain (26 kJ/mol) when compared to cyclopropane and cyclobutane.

C3-C5 Cycloalkanes in Nature

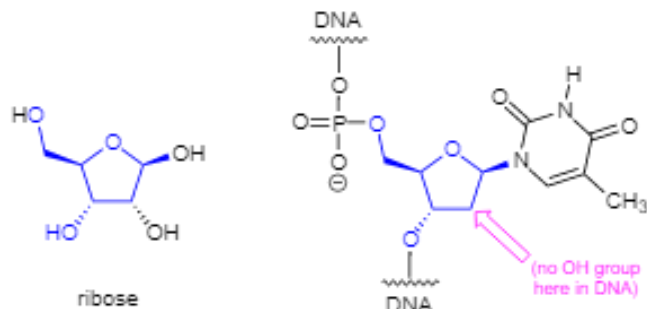
If one of the carbon-carbon bonds is broken in cyclopropane or cyclobutane, the ring will 'spring' open, releasing energy as the bonds reassume their preferred tetrahedral geometry. The effectiveness of two antibiotic drugs, fosfomycin and penicillin, is due in large part to the high reactivity of the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



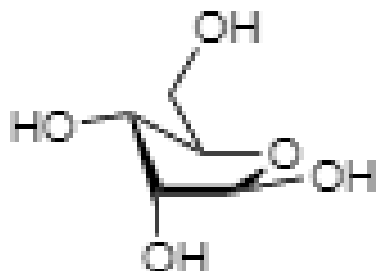
fosfomycin



penicillin G

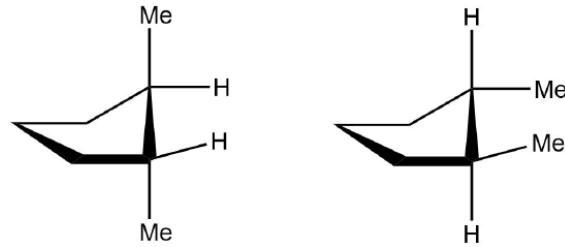


One of the most important five-membered rings in nature is a sugar called ribose – DNA and RNA are both constructed upon 'backbones' derived from ribose. Pictured below is one thymidine (T) deoxy-nucleotide from a stretch of DNA. Since the ribose has lost one of the OH groups (at carbon 2 of the ribose 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 C3 or C2 are endo, on the same side as the C5 substituent.

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



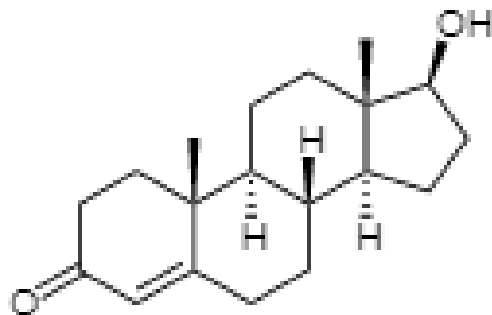
2) In methylcyclopentane, which carbon would most likely be in the endo position?

Answer:

1) 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.

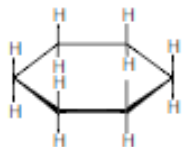
2) The ring carbon attached to the methyl group would most likely be the endo carbon. The large methyl group would create the most torsional strain if eclipsed. Being in the endo position would place the bonds in a more staggered position which would reduce strain.

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.



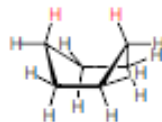
testosterone, which contains three cyclohexane rings and one cyclopentane ring

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.



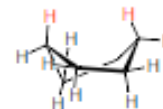
planar structure

severe angle strain (120°)
severe eclipsing strain (all bonds)
small steric strain



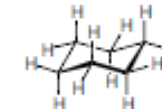
boat conformation

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

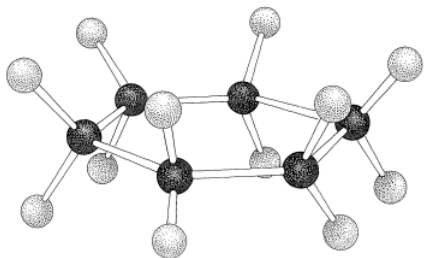


chair conformation

no angle strain
no eclipsing strain
small steric strain

Conformations of Cyclohexane

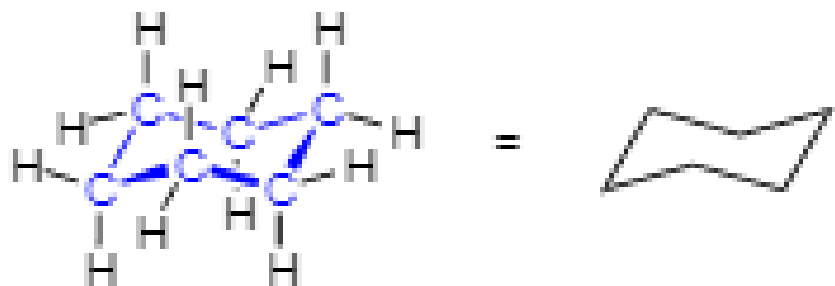
A planar structure for cyclohexane is clearly improbable. The bond angles would necessarily be 120° , 10.5° larger than the ideal tetrahedral angle. Also, every carbon-hydrogen bond in such a structure would be eclipsed. The resulting angle and eclipsing strains would severely destabilize this structure.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



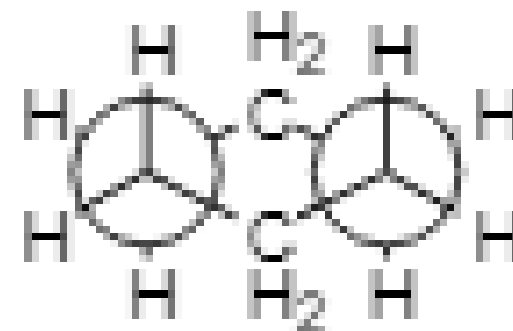
Cyclohexane in the strained planar configuration showing how the hydrogens become eclipsed.

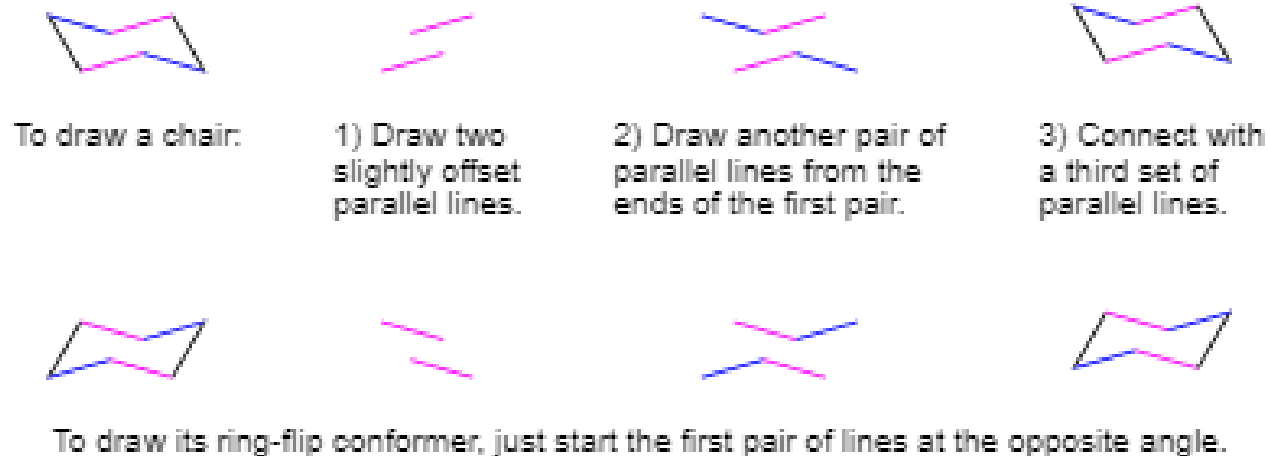
Chair Conformation of Cyclohexane

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 $\sim 111^\circ$ which is very near the optimal tetrahedral 109.5° so angle strain has been eliminated.



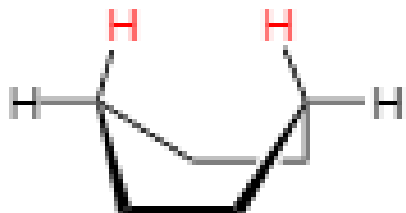
Also, the C-H ring bonds are staggered so torsional strain has also been eliminated. This is clearly seen when looking at a Newman projection of chair cyclohexane sighted down the two central C-C bonds.





Boat Conformation of Cyclohexane

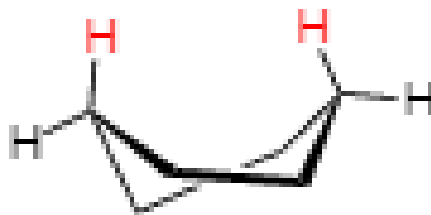
The Boat Conformation of cyclohexane is created when two carbon atoms on opposite sides of the six-membered ring are both lifted up out of the plane of the ring creating a shape which slightly resembles a boat. The boat conformation is less stable than the chair form for two major reasons. The boat conformation has unfavorable steric interactions between a pair of 1,4 hydrogens (the so-called "**flagpole**" hydrogens) that are forced to be very close together (1.83\AA). 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 is 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.

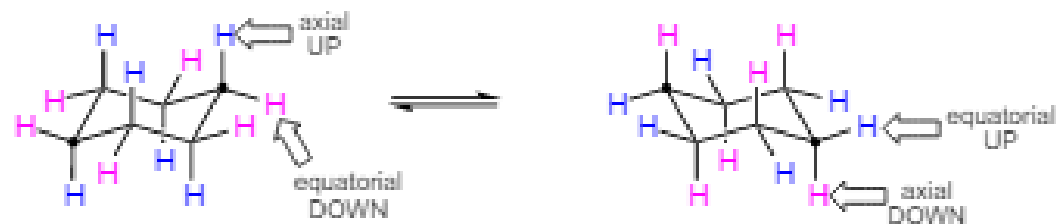
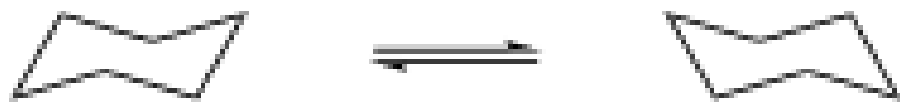


Half Chair Conformation of Cyclohexane

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 120° 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 109.5° 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"

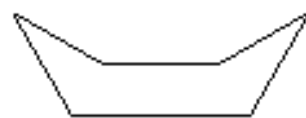
Cyclohexane is rapidly rotating between the two most stable conformations known as the chair conformations in what is called the "ring flip" shown below.



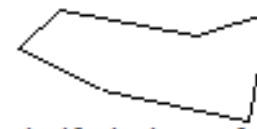
It is important to note that one chair does not immediately become the other chair, rather the ring must travel through the higher energy conformations as transitions. At room temperature the energy barrier created by the half chair conformation is easily overcome allowing for equilibration between the two chair conformations 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 comprise more than 99.9% of the equilibrium mixture at room temperature.



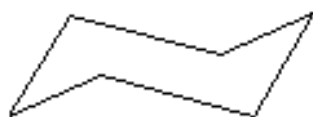
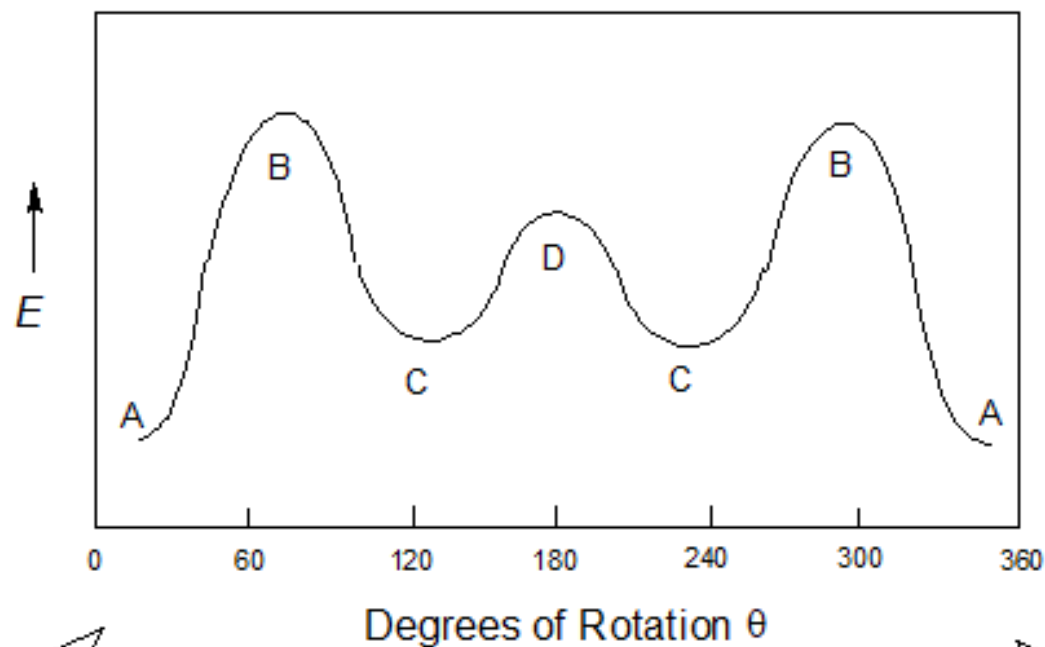
B = half-chair conformation



D = boat conformation



B = half-chair conformation



A = chair conformation



C = Twist conformation



A = chair conformation

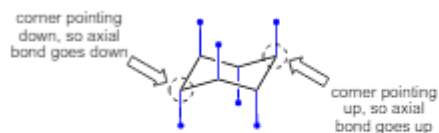
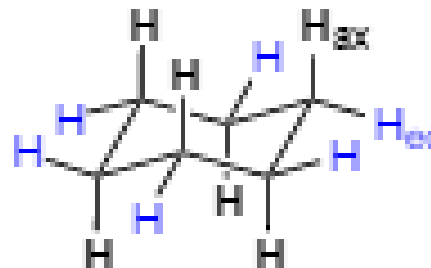
Consider the conformations of cyclohexane: half chair, chair, boat, twist boat. Order them in increasing ring strain in the molecule.

Solutions

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

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.



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



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

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° bond angle.

Each carbon has an axial and an equatorial bond.

Each face of the cyclohexane ring has three axial and three equatorial bonds.

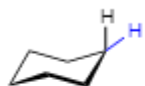
Each face alternates between axial and equatorial bonds. Then looking at the "up" bond on each carbon in the cyclohexane ring they will alternate axial-equatorial-axial etc.

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.

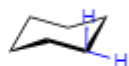
Note! The terms cis and trans in regards to the stereochemistry of a ring are not directly linked to the terms axial and equatorial. It is very common to confuse the two. It typically best not to try and directly inter convert the two naming systems.



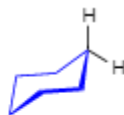
Incorrect.
Equatorial bond should be **down and out**.



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



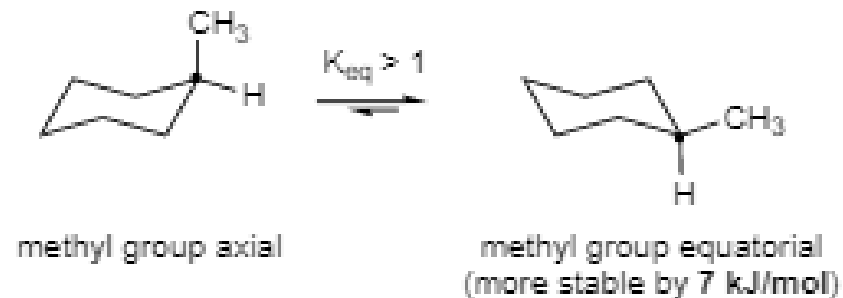
Incorrect.
Axial bond should be **straight down**, equatorial bond should be **up and out**.



Incorrect.
Ring should be **tilted slightly**.

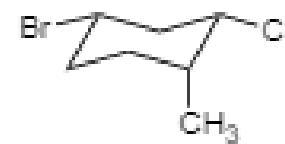
Axial vs. Equatorial Substituents

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.



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

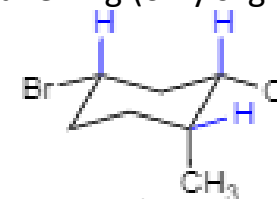
Chair conformation of 4-bromo-2-chloro-1-methylcyclohexane.



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.

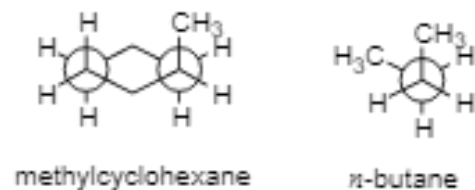
Hydrogens are placed at carbon 1, carbon 2, and carbon 4.



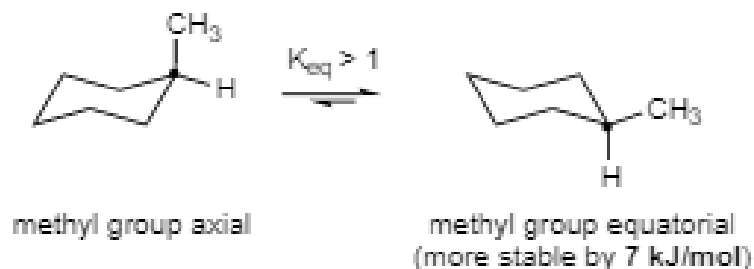
With this it can be concluded that the bromine and chlorine substituents are attached in equatorial positions and the CH₃ substituent is attached in an axial position.

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.

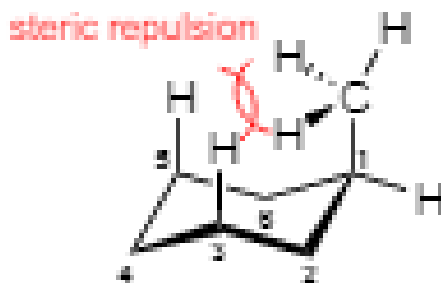
Be prepared to draw Newman-type projections for cyclohexane derivatives as the one shown for methylcyclohexane. Note that this is similar to the Newman projections from chapter 3 such as n-butane.



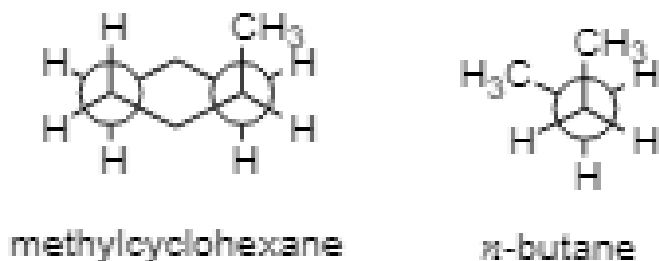
When a substituent is added to a cyclohexane ring, the two possible chair conformations created during a ring flip are not equally stable. In the example of methylcyclohexane the conformation where the methyl group is in the equatorial position is more stable than the axial conformation by 7.6 kJ/mol 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.



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. When butane is in the gauche conformation 3.8 kJ/mol of strain was created due to the steric crowding of two methyl groups with a 60° dihedral angle. When looking at the Newman projection of axial methylcyclohexane the methyl group is at a 60° dihedral angle with the ring carbons in the rear. This creates roughly the same amount of steric strain as the gauche conformer of butane. Given that there are actually two such interactions in axial methylcyclohexane, it makes sense that there is $2(3.8 \text{ kJ/mol}) = 7.6 \text{ kJ/mol}$ of steric strain in this conformation. The Newman projection of equatorial methylcyclohexane shows no such interactions and is therefore more stable.



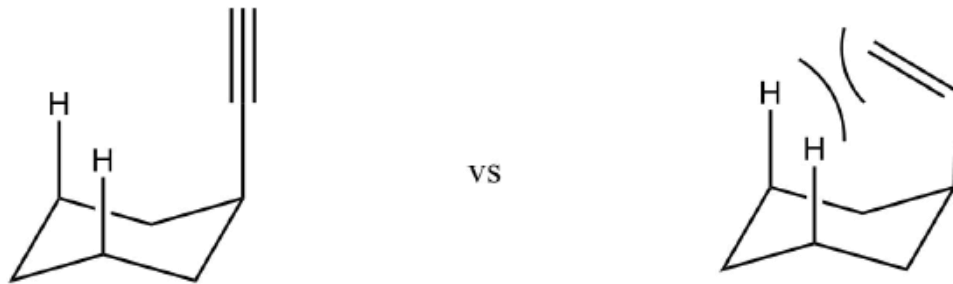
Strain values for other cyclohexane substituents can also be considered. The relative steric hindrance experienced by different substituent groups oriented in an axial versus equatorial location on cyclohexane determined the amount of strain generated. The strain generated can be used to evaluate the 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	$-\Delta G^\circ$ (kcal/mol)	Substituent	$-\Delta G^\circ$ (kcal/mol)
CH ₃ –	1.7	O ₂ N–	1.1
CH ₂ H ₅ –	1.8	N≡C–	0.2
(CH ₃) ₂ CH–	2.2	CH ₃ O–	0.5
(CH ₃) ₃ C–	≥ 5.0	HO ₂ C–	0.7
F–	0.3	H ₂ C=CH–	1.3
Cl–	0.5	C ₆ H ₅ –	3.0
Br–	0.5		
I–	0.5		

1. In the molecule, cyclohexyl ethyne there is little steric strain and also less than cyclohexyl ethene. why?
2. Calculate the energy difference between the axial and equatorial conformations of bromocyclohexane?
Estimate the percentages of axial and equatorial conformations of bromocyclohexane at 25 deg C.
3. 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?

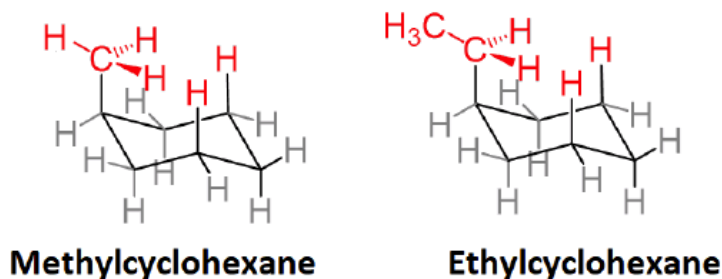
Ans 1. The ethyne group is linear and therefore does not affect the hydrogens in the 1,3 positions to say to the extent as a bulkier or a bent group (e.g. ethene group) would. This leads to less of a strain on the molecule.



Ans 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 $2(1.2 \text{ kJ/mol}) = 2.4 \text{ kJ/mol}$.

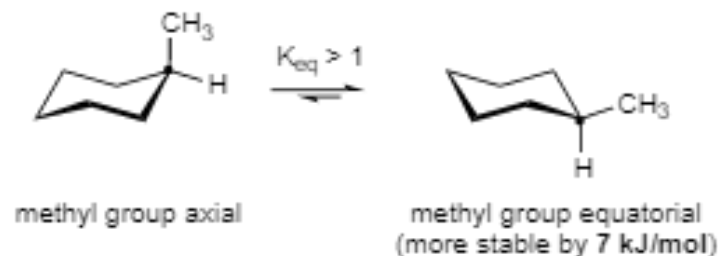
Remembering that the axial conformation is higher in energy, the energy difference between the two conformations is $\Delta E = (E_{\text{equatorial}} - E_{\text{axial}}) = (0 - 2.4 \text{ kJ/mol}) = -2.4 \text{ kJ/mol}$. After converting oC to Kelvin and kJ/mol to J/mol we can use the equation $\Delta E = -RT \ln K$ to find that $-\Delta E/RT = \ln K$ or $(2.4 \times 10^3 \text{ J/mol}) / (8.313 \text{ kJ/mol K} \cdot 298 \text{ K}) = \ln K$. From this we calculate that $K = 2.6$. Because the ring flip reaction is an equilibrium we can say that $K = [\text{Equatorial}] / [\text{Axial}]$. If assumption is made that $[\text{Equatorial}] = X$ then $[\text{Axial}]$ 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. $2.6 = [X] / [1-X] \rightarrow 2.6 - 2.6X = X \rightarrow 2.6 = 3.6X \rightarrow 2.6/3.6 = X = 0.72$. This means that bromocyclohexane is in the equatorial position 72% of the time and in the axial position 28% of the time.

Ans.3. The fact that C-C sigma bonds can freely rotate allows the ethyl substituent to obtain a conformation which places the bulky CH₃ 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.



Monosubstituted Cyclohexanes

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.



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.

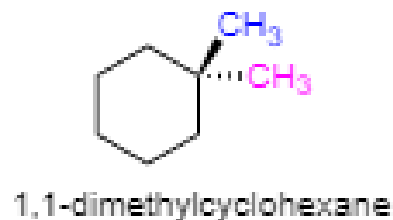
In this section, the effect of conformations on the relative stability of disubstituted cyclohexanes is examined using the two principles:

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

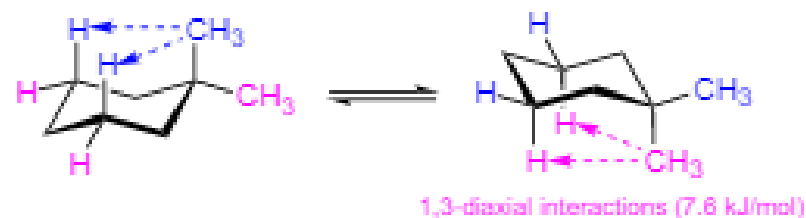
1,1-Disubstituted Cyclohexanes

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.

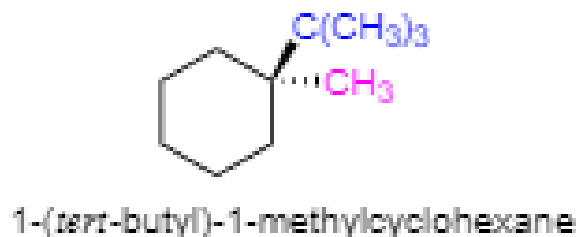
1,1-dimethylcyclohexane does not have cis or trans isomers, because both methyl groups are on the same ring carbon. Both chair conformers have one methyl group in an axial position and one methyl group in an equatorial position giving both the same relative stability. The steric strain created by the 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.



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



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 than 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.

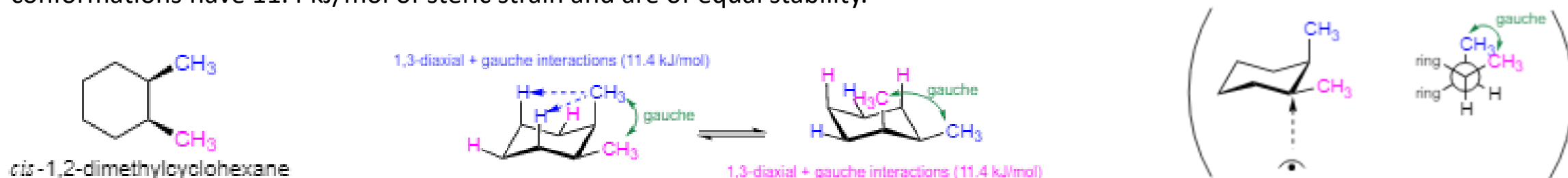


1,3-diaxial interactions (22.8 kJ/mol)

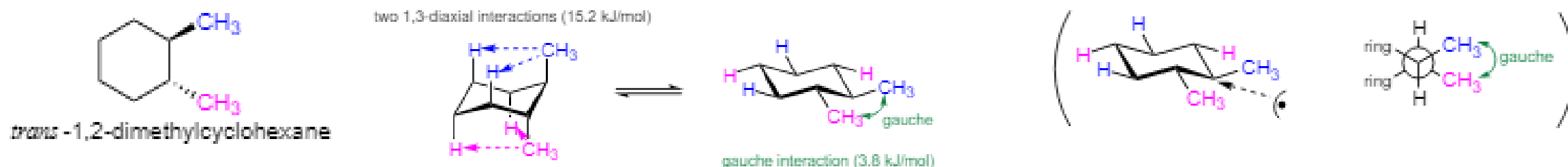


Cis and trans stereoisomers of 1,2-dimethylcyclohexane

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.

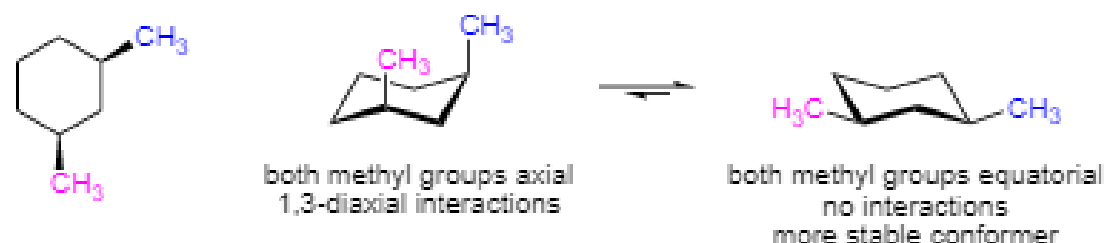


In trans-1,2-dimethylcyclohexane, one chair conformer has both methyl groups axial and the other conformer has both methyl groups equatorial. The conformer with both methyl groups equatorial has no 1,3-diaxial interactions however there is still 3.8 kJ/mol of strain created by a gauche interaction. The conformer with both methyl groups axial has four 1,3-Diaxial interactions which creates 2×7.6 kJ/mol (15.2 kJ/mol) of steric strain. This conformer is $(15.2 \text{ kJ/mol} - 3.8 \text{ kJ/mol})$ 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.

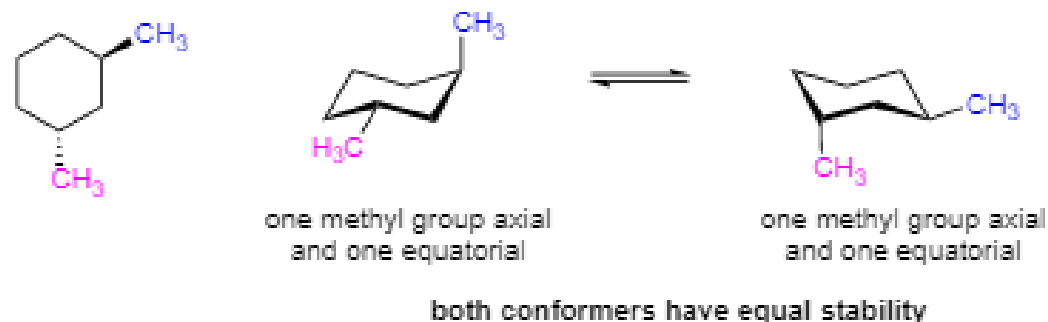


Cis and trans stereoisomers of 1,3-dimethylcyclohexane

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.



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.



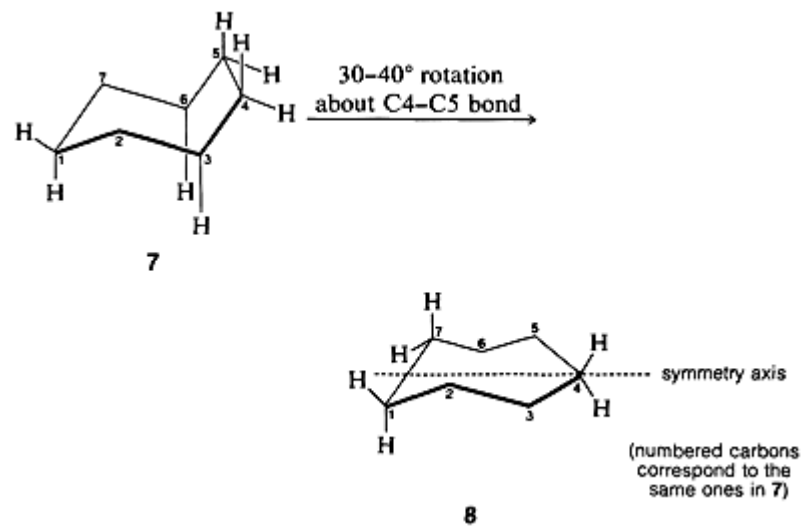
Q. 1. For cis-1-chloro-4-methylcyclohexane, draw the most stable chair conformation and determine the energy difference between the two chair conformers.

Based on the table above, cis-1,4-disubstituted 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.



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 $(7.6 \text{ kJ/mol} - 2.0 \text{ kJ/mol})$ 5.6 kJ/mol more stable than the other.

Cycloheptane



Cyclooctane

