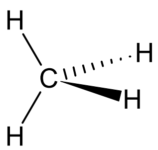
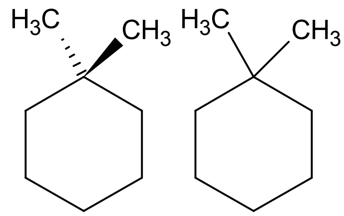
Chapter 4: Stereoisomers of Alkanes and Cycloalkanes

Stereochemistry

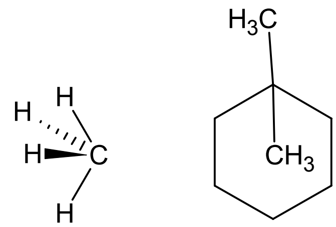
Significance of tetrahedral bonds



methane



1,1-dimethylcyclohexane



not OK (might as well scratch a blackboard)

Conformation versus Configuration versus Constitutional Isomers

3 types of structural isomers

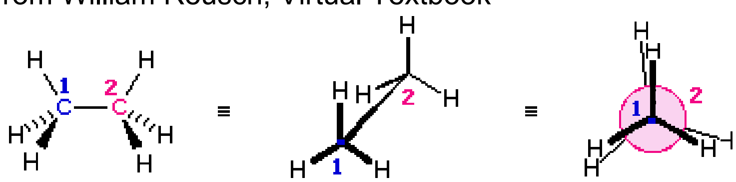
1.

2.

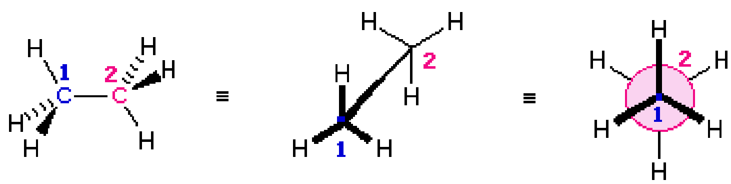
3.

Conformational isomers: Same formula: Different structures based on rotation around sigma bonds.
Start with ethane. Here are 3 different representations of the the two unique conformations of ethane. The last one is called a Newman projection and you need to be able to make these.
Some figures from William Reusch, Virtual Textbook

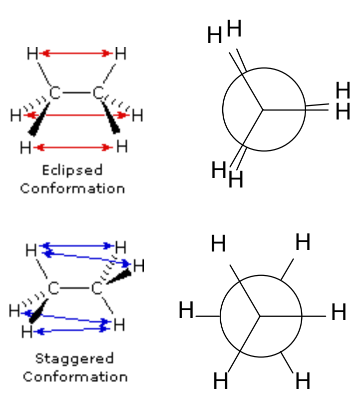
Eclipsed Conformation

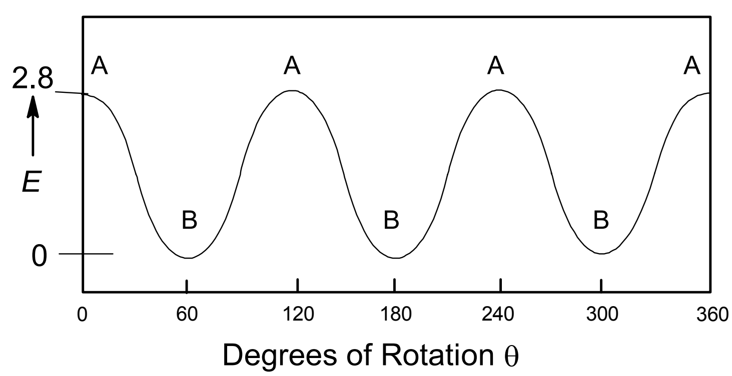


Staggered Conformation

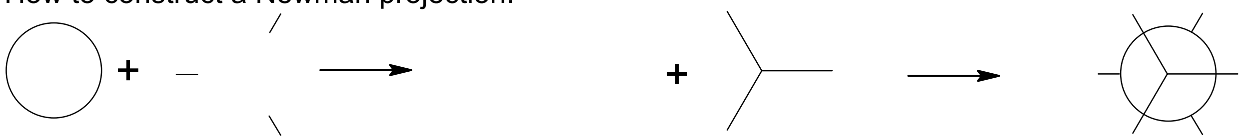


Energetic Consequences of ethane. Each eclipsed bond is about _ kcal/mole.

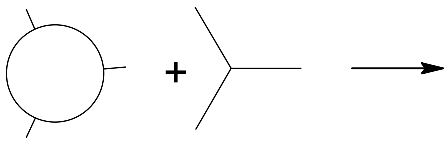




How to construct a Newman projection:



back bonds front bonds staggered



eclipsed

Practice

Draw 2 Newman projection for staggered and eclipsed conformations of $Cl_3C\text{-}CH_3$

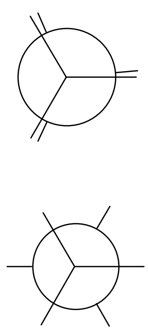
Group A $C_1 = Cl_3C$

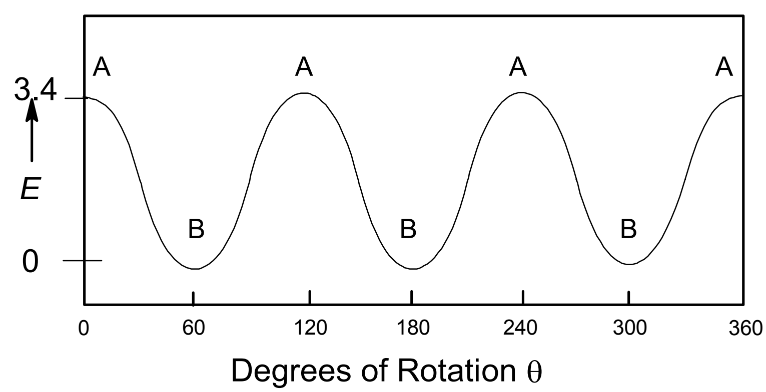
Group B $C_1 = CH_3$

Next consider **propane: $CH_3CH_2CH_3$** Show the two conformations of propane.

A Eclipsed

B Staggered





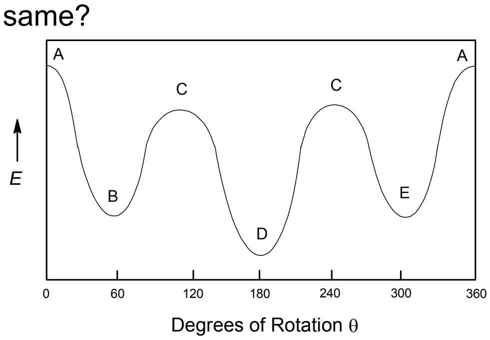
What are the relative energies of the eclipsed bonds?

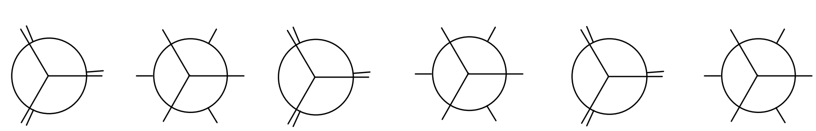
C-H/C-H eclipsed

C-H/C-H eclipsed

C-H/C-CH_3 eclipsed

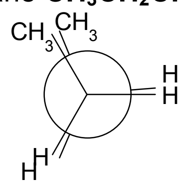
Construct the case for 2 different substituents like 1,2-dichloroethane. Label A-E. Which are the same?



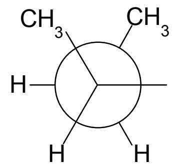


Now consider butane **$CH_3CH_2CH_2CH_3$** Show the four conformations of butane:

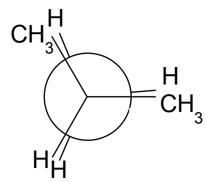
A Eclipsed



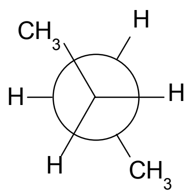
B Gauche



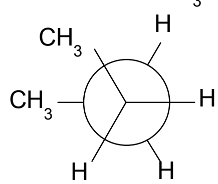
C Eclipsed

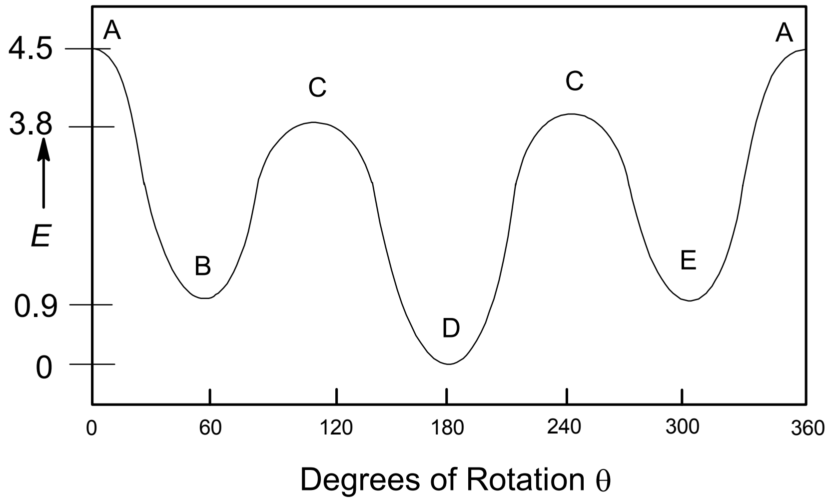


D Anti



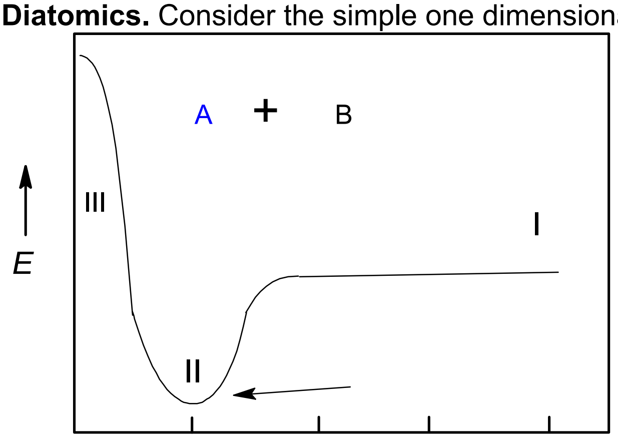
E Gauche





Formulaic breakdown of strain energies:
Given E (kcal/mole): All eclipsed (C-H/C-H) = 1; ($C-CH_3/C-CH_3$) = 2.6; ($C-H/C-CH_3$) = 1.4.
A = 4.5 kcal/mole = ______ (C-H/C-H) + _______ ($C-CH_3/C-CH_3$) = _________
C = 3.8 kcal/mole = ______ (C-H/C-H) + _______ ($C-H/C-CH_3$) = ___________

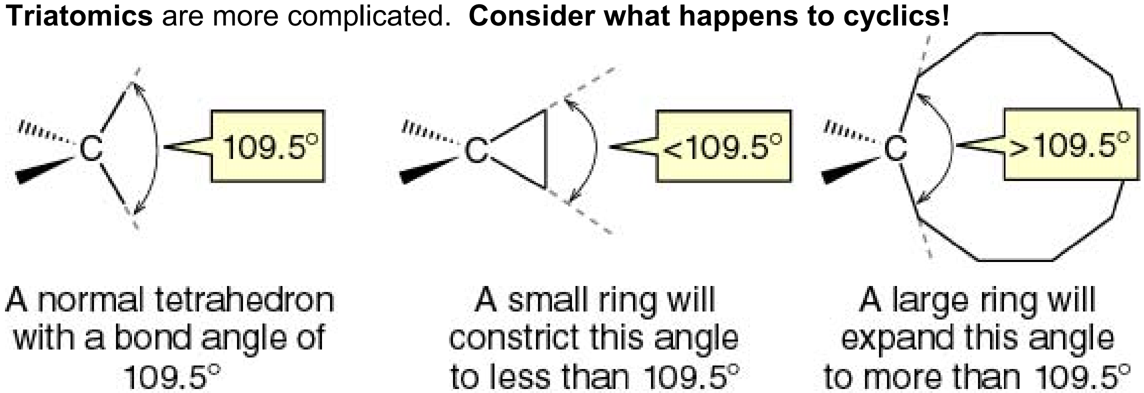
The concept of strain: Molecular interactions are a combination of attraction and repulsion
3 new terms: Steric, Angle, and Torsion.
Diatomics. Consider the simple one dimensional correlation of two objects to form a covalent bond:



Describe the situations for the 3 main regions:
I
II
III

Bringing A-B Distance the atoms too close together is related to what we call **steric** strain.

Triatomics are more complicated. **Consider what happens to cyclics!**



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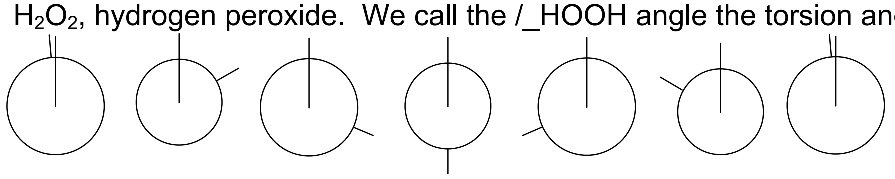
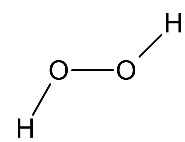
4-tomics: Torsional strain is based on overlapping areas of electron density on a sigma bond.
Let's use a modified Newman projection to describe the molecule.
H_2O_2, hydrogen peroxide. We call the /_HOOH angle the torsion angle.

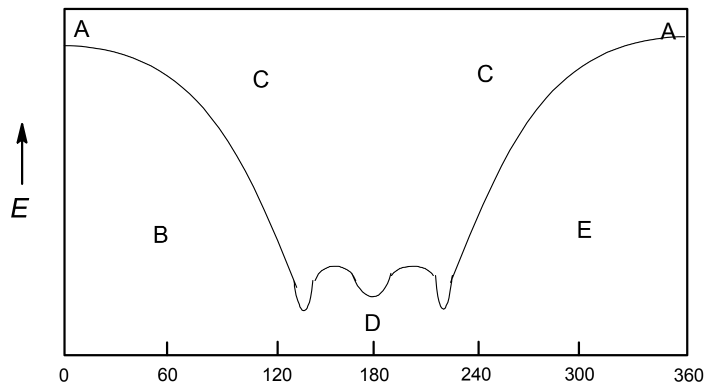




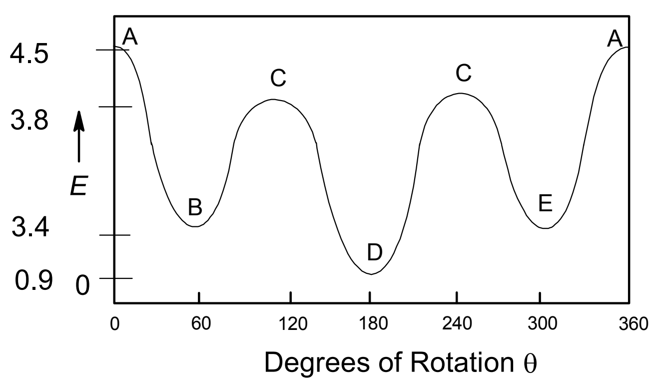
Torsion Angle

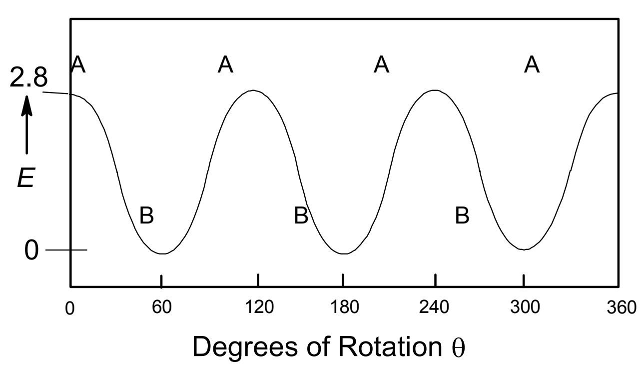
______ ____ ___ ______ ____ ______ _____

Which structure is the highest energy (most strained)?
Which structure is the lowest energy (least strained)?



Reconsider butane and ethane in terms of torsional strain:

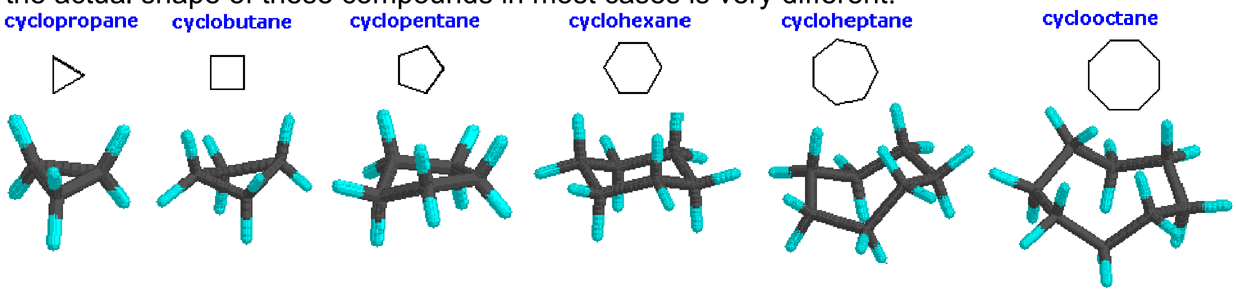




Torsional Energy diagram of butane

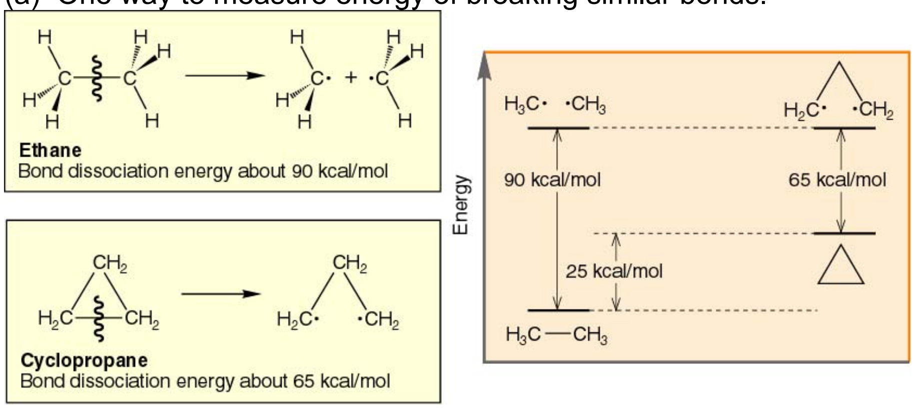
Torsional Energy diagram of ethane

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



Measuring strain.

(a) One way to measure energy of breaking similar bonds.



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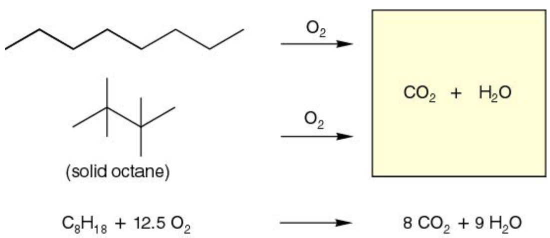
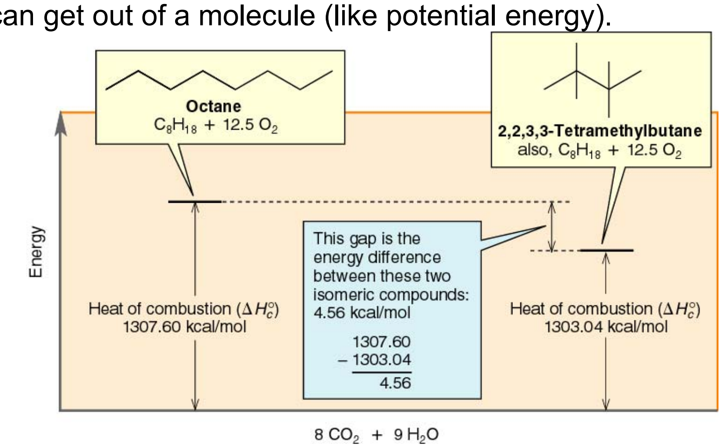
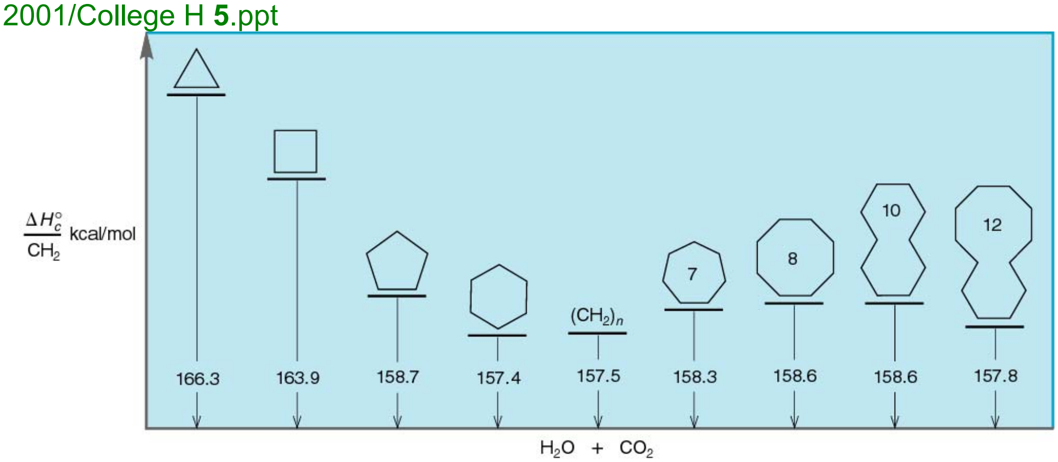
What is the strain in cyclopropane compared to ethane?

(b) Another is to see how much energy you can get out of a molecule (like potential energy).

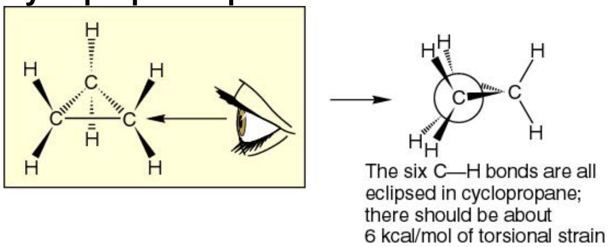




The difference in energy is attributed to the stability of the compound. Now consider rings in relationship to a linear "unstrained" alkane. http://www.sci.kun.nl/chemistry/ onderwijs/oc1-2001/College H **5**.ppt



Cyclopropane --planar



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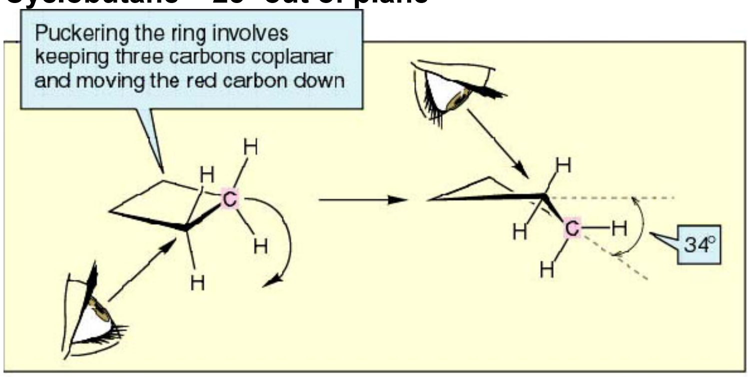
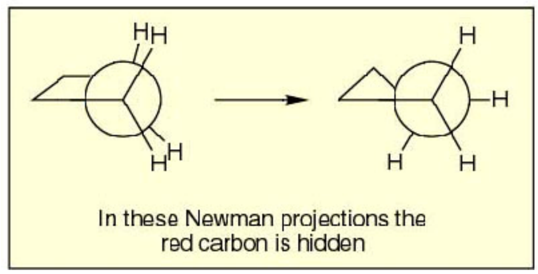
Steric Strain
Torsional Strain
Angle strain

Cyclobutane – 25^0 out of plane





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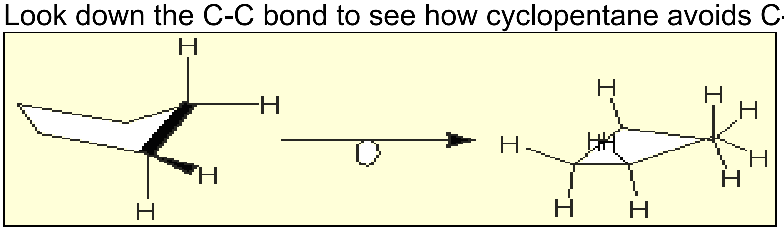
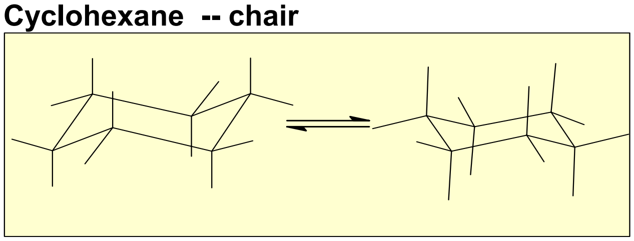
Steric Strain
Torsional Strain
Angle strain

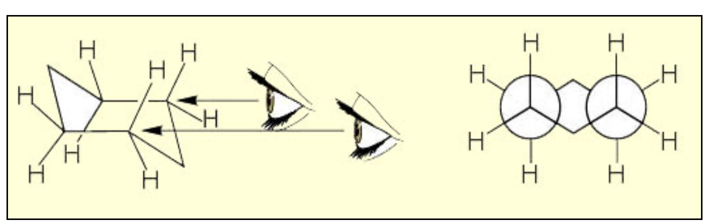
Cyclopentane -- puckered
Look down the C-C bond to see how cyclopentane avoids C-H eclipsed.



Angle strain
Steric Strain
Torsional Strain

Cyclohexane -- chair





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Steric Strain
Torsional Strain
Angle strain

Analysis of the conformations of cyclohexane

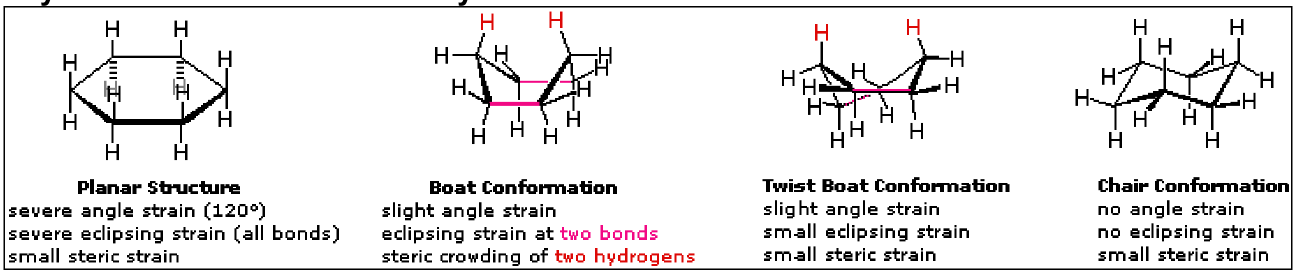


Figure William Reusch, Vitual Textbook

The chair cyclohexane – no strain all tetrahederal angles.

- **Rapid interconversion between 6 axial and 6 equatorial H's.**
- **Difference in energy from substitution in equatorial and axial positions.**

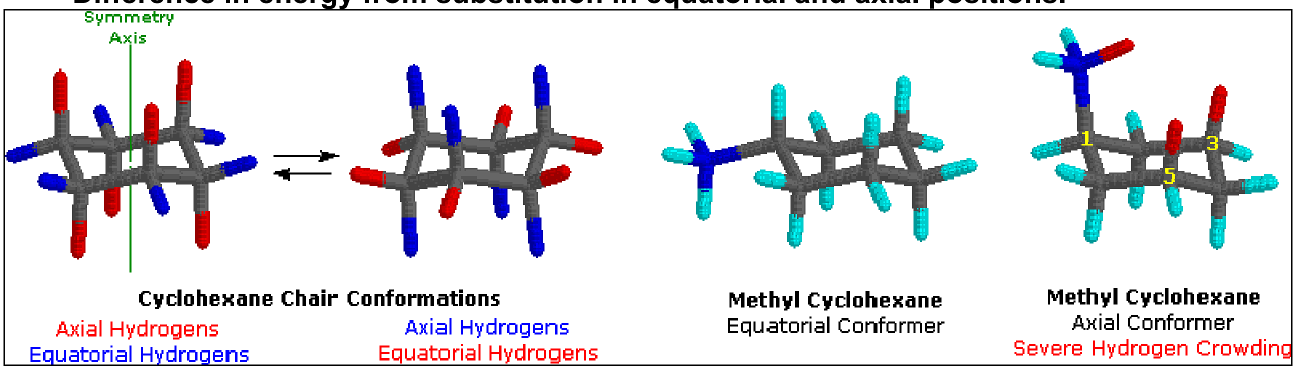
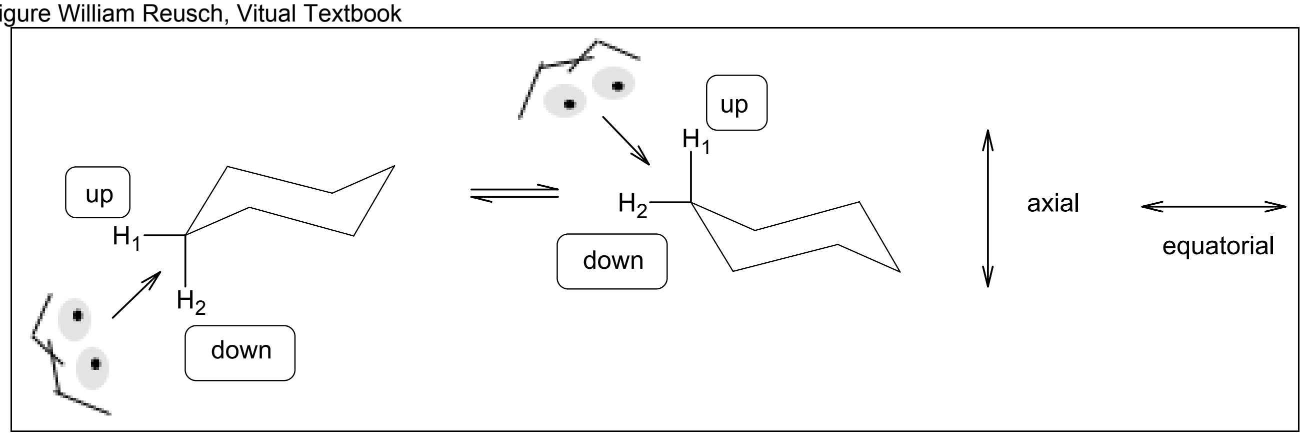
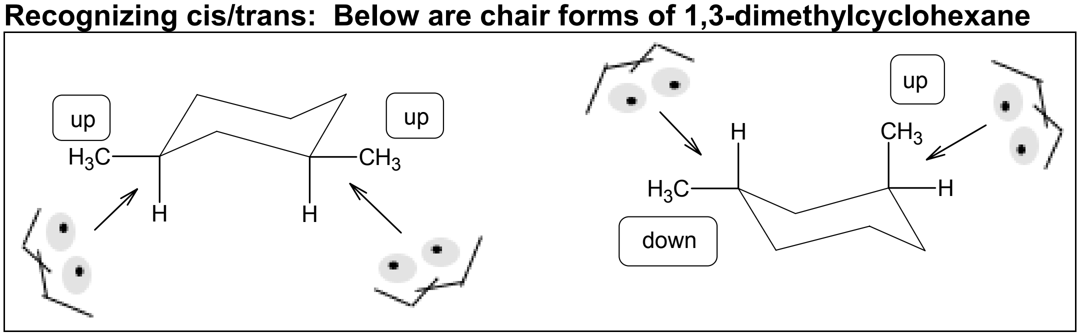


Figure William Reusch, Vitual Textbook

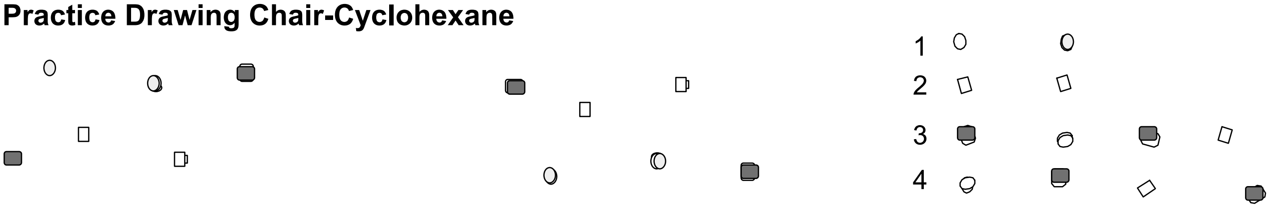


Equatorial substitution is preferred.

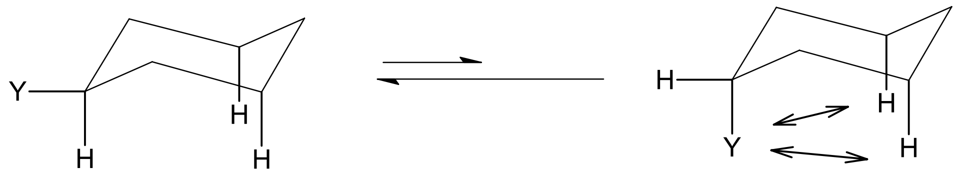
Recognizing cis/trans: Below are chair forms of 1,3-dimethylcyclohexane



Practice Drawing Chair-Cyclohexane



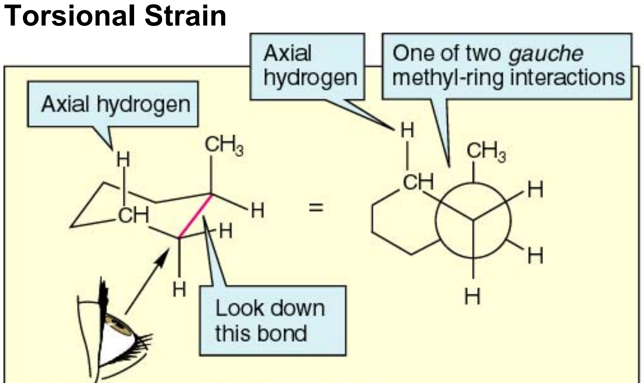
Energetics of Cyclohexane Conformations
Steric and Torsional Strain



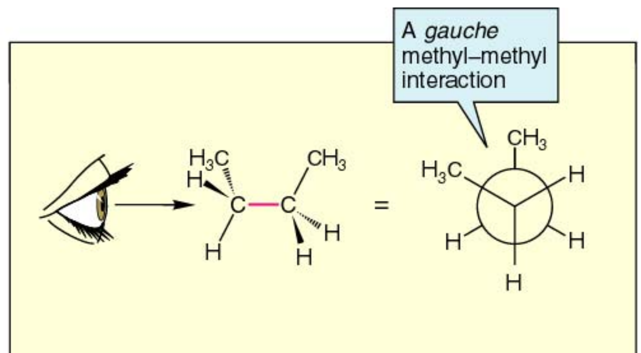
Preference for Y_{eq} =

Y	E (kcal/mol)
Cl	0.5
CH_3	1.7
CH_3CH_2=	1.8
$(CH_3)_2CH$=	2.1
$(CH_3)_3C$=	5.4

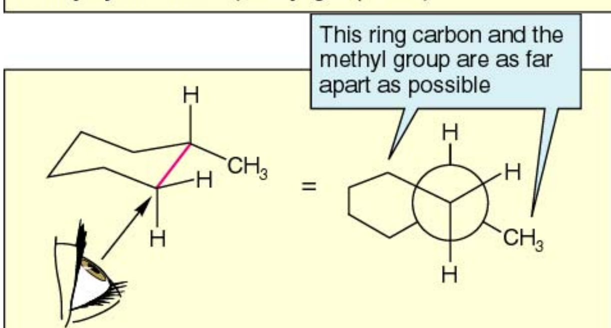
Torsional Strain



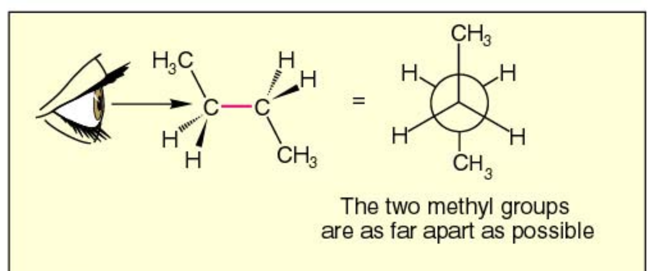
Methylcyclohexane (methyl group axial)



***gauche*-Butane**



Methylcyclohexane (methyl group equatorial)



***anti*-Butane**

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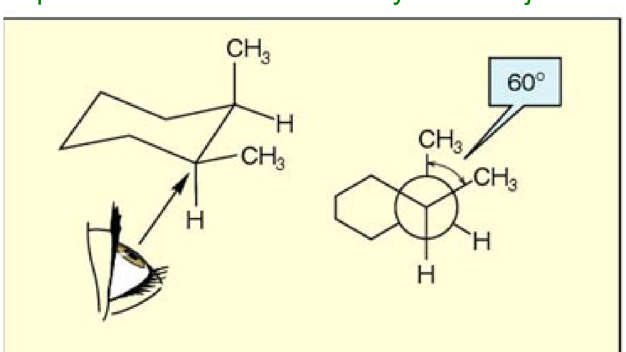
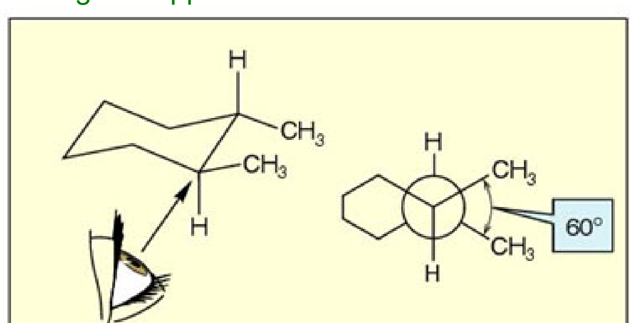


Two views of *cis*-1,2-dimethylcyclohexane; the dihedral angle between the methyl groups is 60°



Two views of *trans*-1,2-dimethylcyclohexane; the dihedral angle between the methyl groups is also 60°

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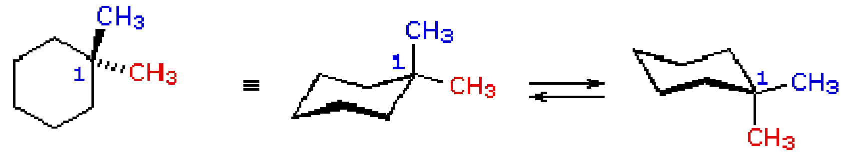
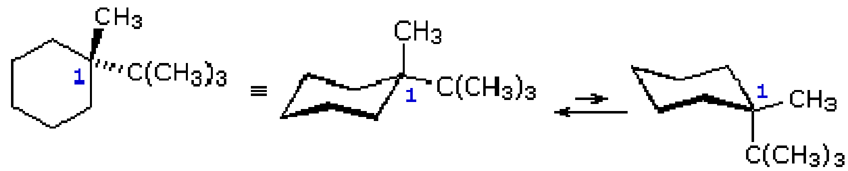
Conformational Structures of Disubstituted Cyclohexanes

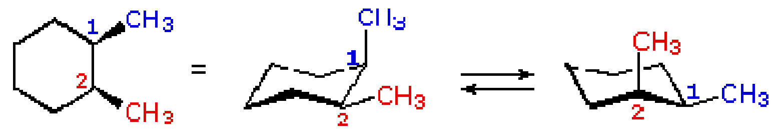
1,1-dimethylcyclohexane



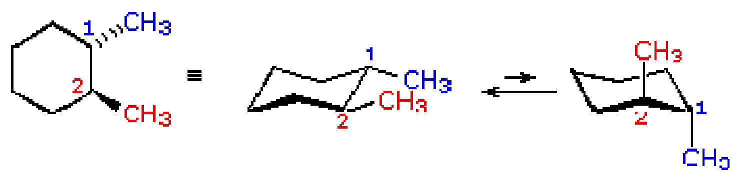
1-t-butyl-1-methylcyclohexane



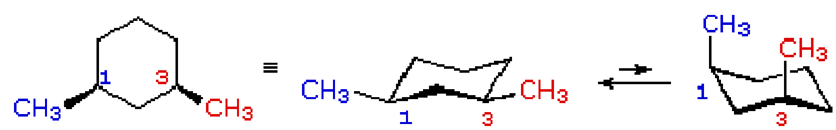
cis-1,2-dimethylcyclohexane



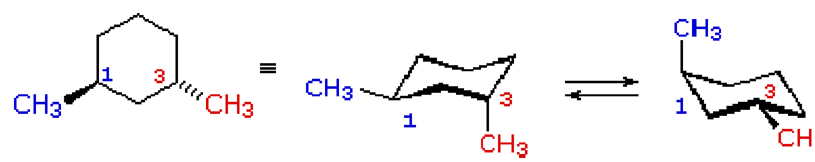
trans-1,2-dimethylcyclohexane



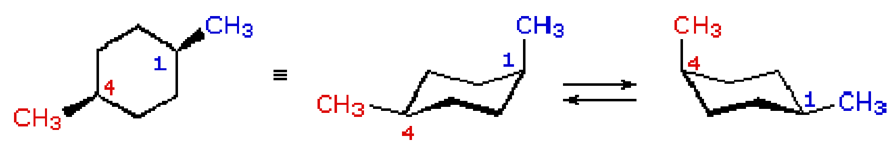
cis-1,3-dimethylcyclohexane



trans-1,3-dimethylcyclohexane



cis-1,4-dimethylcyclohexane



trans-1,4-dimethylcyclohexane

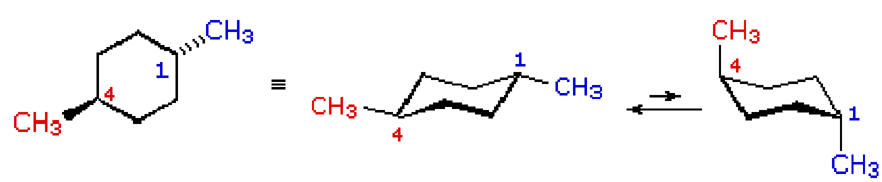
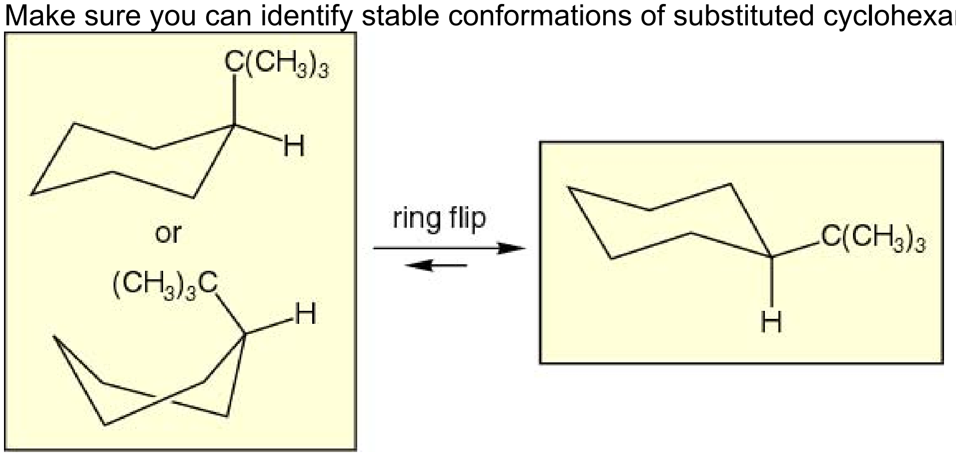


Figure from William Reusch, Virtual Textbook

Make sure you can identify stable conformations of substituted cyclohexanes.

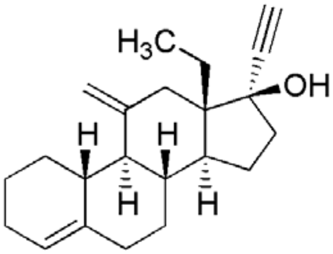


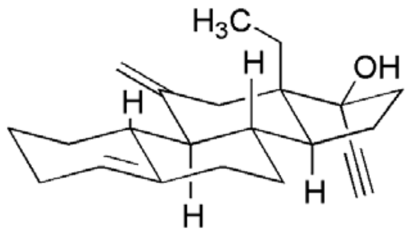
Substituent	E(eq/ax)	K_{eq}
Methyl	1.7	20
Isopropyl	2.6	90
tert-Butyl	5.5	12E3

$\Delta G = -RT\ln K_{eq}$

Naturally occurring chair cyclohexanes – steroids

The majority of naturally occurring steroids contains the 6,6,6,5-trans-fused skeleton

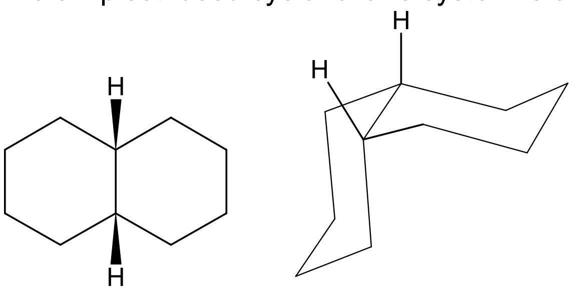




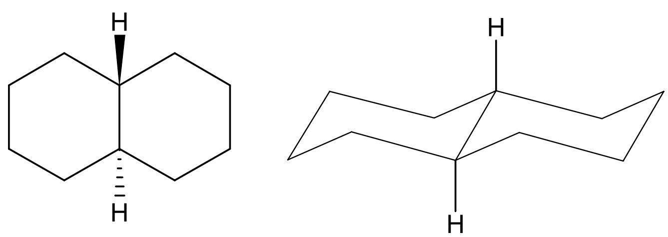
desogestrel

http://www.desogestrel.com/

The simplest fused cyclohexane system is decalin.

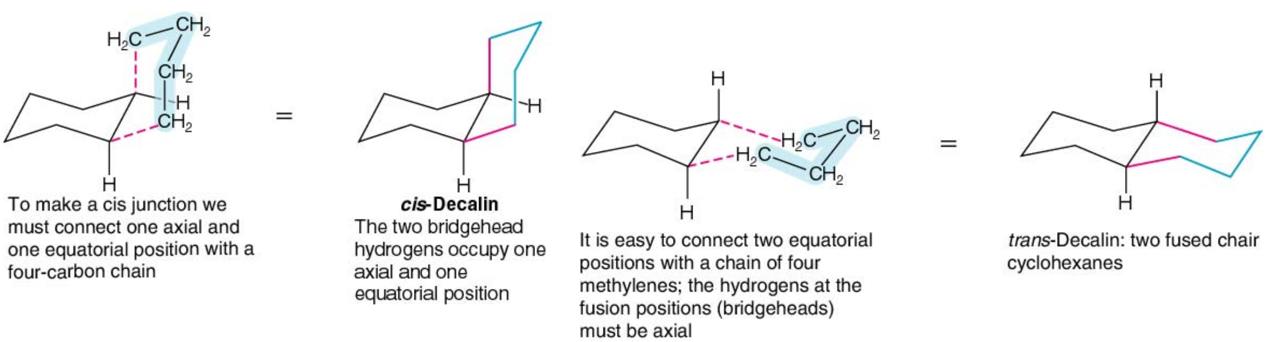


cis-decalin

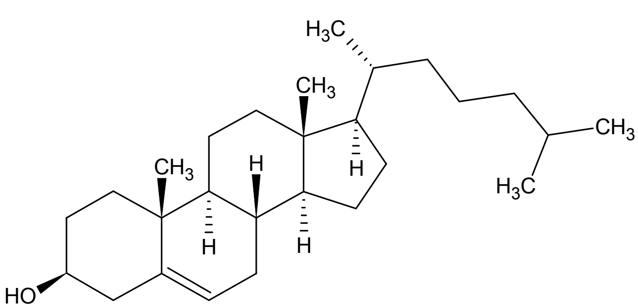


trans-decalin

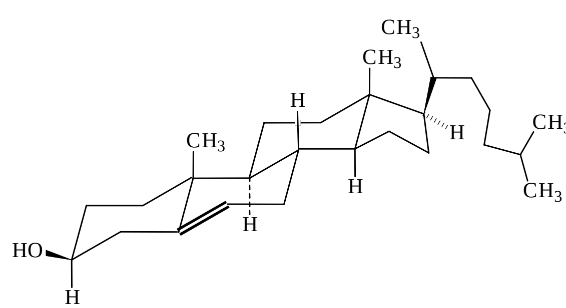
How many gauche interactions are there in cis and trans decalin?



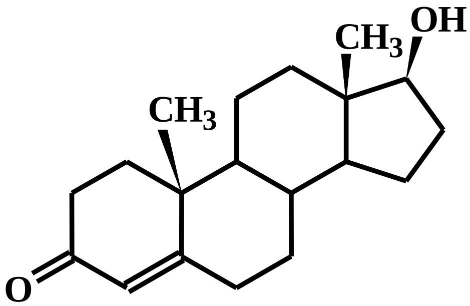
Trans-decalin style fused cyclohexanes are the basis for steroids. Note all the trans-decalins.



Cholesterol

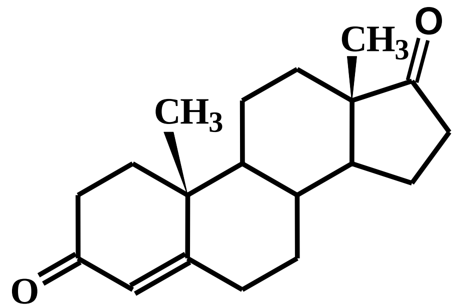


Anabolic Steroids



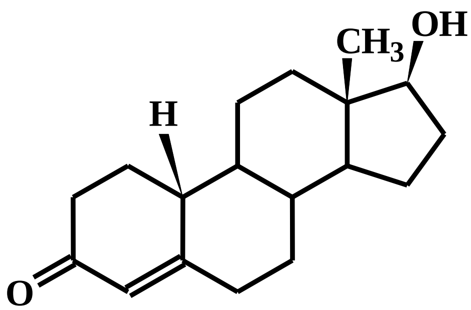
Testosterone

Responsible for many sex-linked behaviors

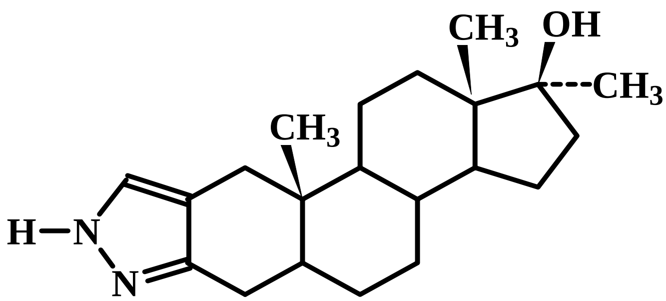


Androstenedione

(4-androstene-3,17-dione)
Popular "stimulant" used in baseball – Mark McGwire
http://hermes.hhp.ufl.edu/keepingfit/ARTICLE/andro.htm



Nandrolone



Stanozolol

http://www.wada-ama.org/en/ Olympic anti-doping site

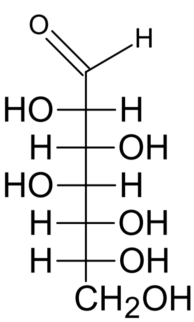
"Winning? Formula" for the Sydney Olympics Barcelona Olympic boost

Information from D. Pavia, http://www.chem.wwu.edu/dept/facstaff/pavia/chap4g.ppt

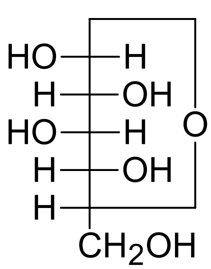
Sugars

Glucose is one of the forms of energy storage in plants and animals and the building blocks of plant tissue and structure. Glucose is a 6-carbon molecule with corresponding OH groups.

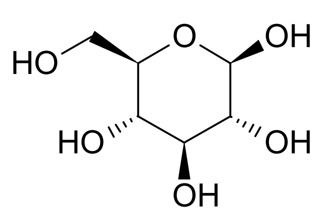
The straight chain form is not particularly stable and tends to cyclize with loss of water to make either an alpha (left side link) or Beta (right side link) as shown below.



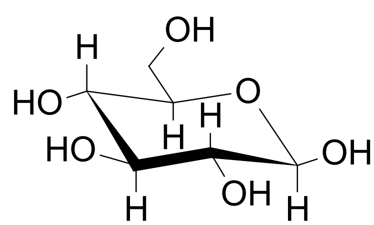
Straight chain



β -cyclized form



planar projection



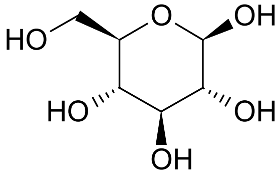
β-chair projection

Practice turning the planar projection into the chair.
Can you make sense out of the cis and trans linkages?

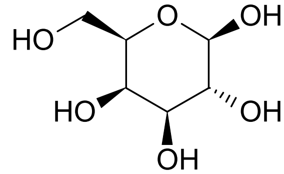
Sugar Practice

Turn these planar projections into chairs.

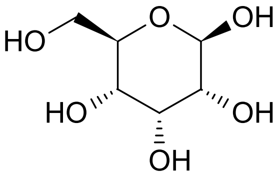
Can you see why glucose is the most abundant sugar in nature?



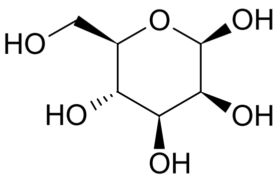
β-D-Glucopyranose



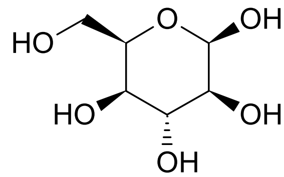
β-D-Galactopyranose



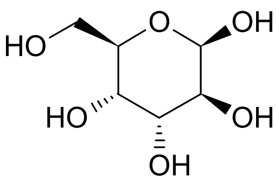
β-D-Allopyranose



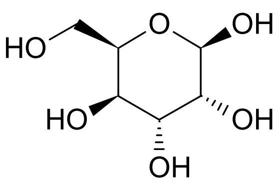
β-D-Mannopyranose



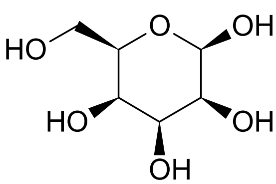
β-D-Idopyranose



β-D-Altropyranose



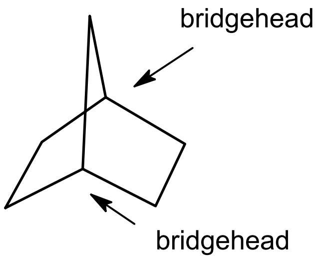
β-D-Gulopyranose



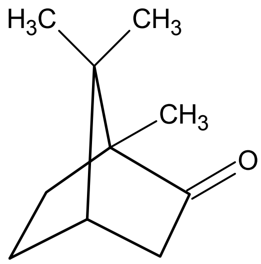
β-D-Talopyranose

Naturally occurring in our diet order of abundance are glucose > galactose and fructose. Which other 6-carbon sugar would you predict to be important in metabolic cycles?

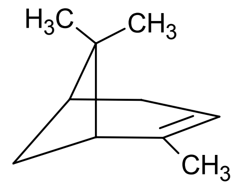
Bicyclics



Norbornane



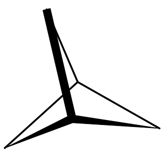
camphor

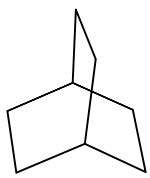


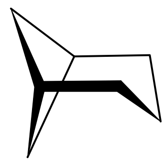
alpha-pinene

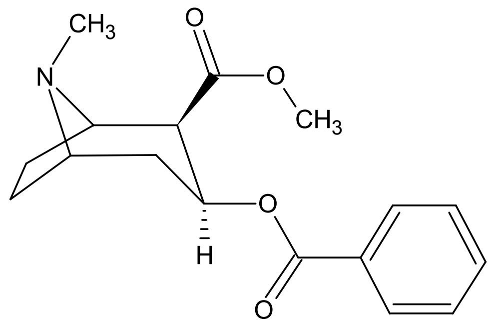
Bicyclo[2.2.1]heptane

Name these bicyclics:









Summaries

1. Make sure that you can draw tetrahedral molecules with dashed and wedged lines in the proper proportion and position.
2. What are the three types of isomers?
3. Be able to draw and interpret a Newman projection.
4. Recognize and draw staggered and eclipsed conformations.
5. Recognize and draw gauche and anti conformations.
6. What are the 3 types of ring strain?
7. How can you measure strain? Write a common reaction that will demonstrate the ring strain of comparable molecules.
8. Understand why cyclohexane is the most stable hydrocarbon cyclic.
9. Draw a chair form of cyclohexane.
10. Draw substituents on chair cyclohexane in the equatorial and axial positions.
11. Draw substituents on chair cyclohexane cis/trans.
12. Be able to predict torsional strain in chair cyclohexanes based on 1,3-diaxial interactions and gauche relationships.
13. Be able to count the number of gauche relationships in a substituted cyclohexane.
14. Understand the high and low energy conformations of chair cyclohexanes.
15. Understand the energy differences between equatorial and axial substitution.
16. See how the cyclohexane chair influences the type of bio-molecules that exist in nature.