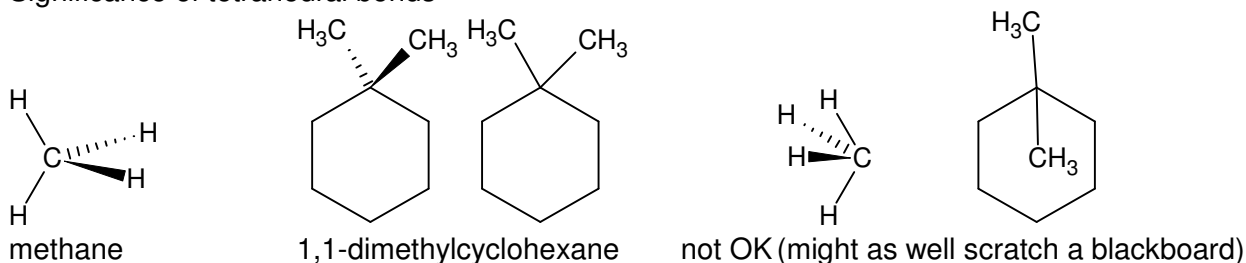


## Chapter 4: Stereoisomers of Alkanes and Cycloalkanes

## Stereochemistry

Significance of tetrahedral bonds



## Conformation versus Configuration versus Constitutional Isomers

## 3 types of structural isomers

1.

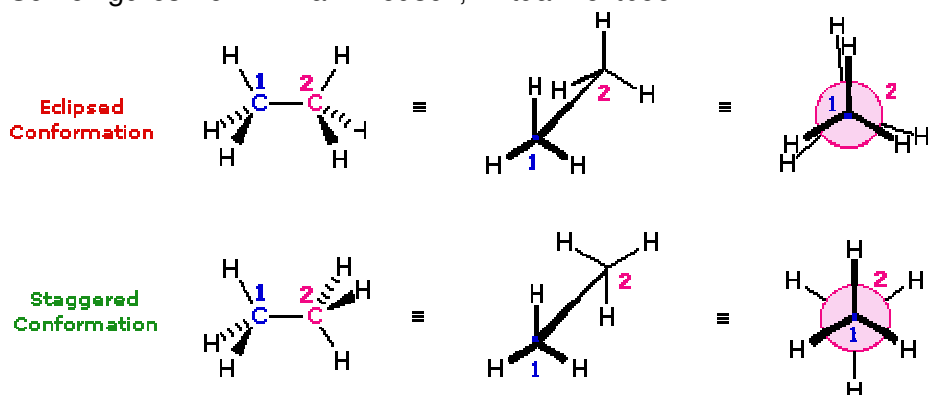
2.

3.

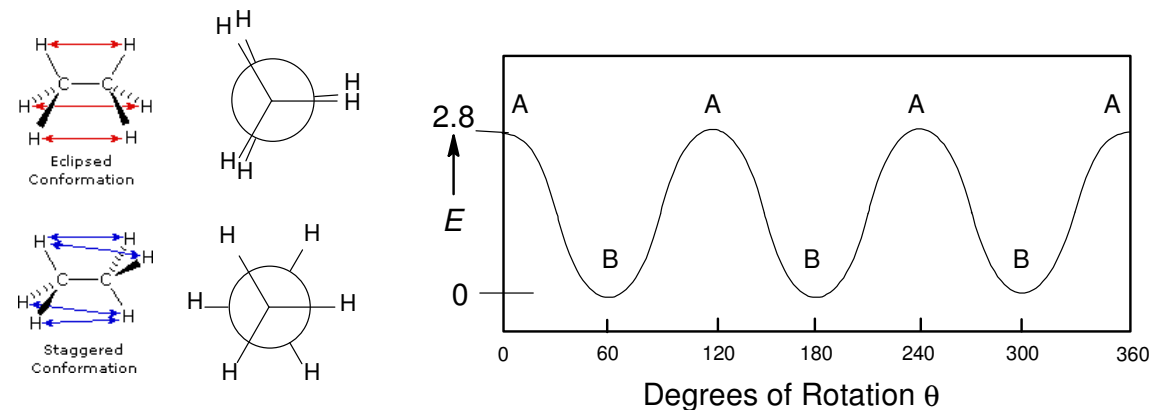
**Conformational isomers:** Same formula: Different structures based on rotation around sigma bonds.**Start with ethane.** Here are 3 different representations of the two unique conformations of ethane.

The last one is called a Newman projection and you need to be able to make these.

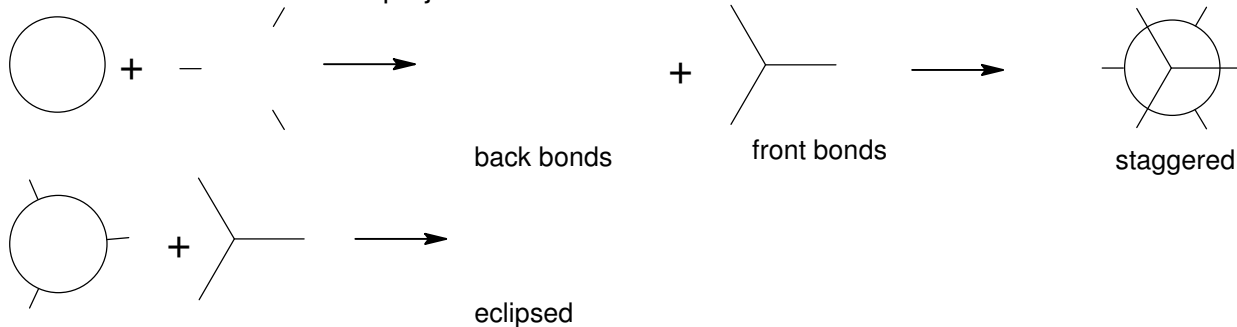
Some figures from William Reusch, Virtual Textbook



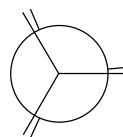
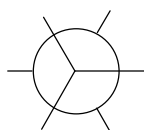
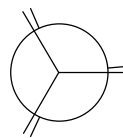
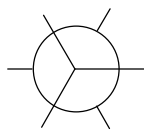
Energetic Consequences of ethane. Each eclipsed bond is about 1 kcal/mole.



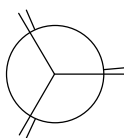
How to construct a Newman projection:



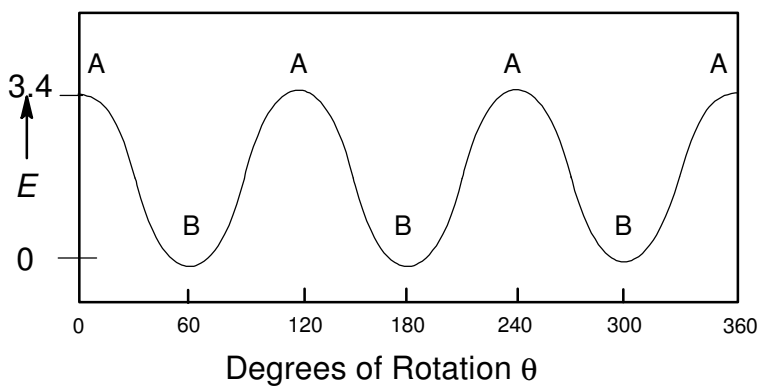
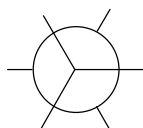
Practice

Draw 2 Newman projection for staggered and eclipsed conformations of  $\text{Cl}_3\text{C}-\text{CH}_3$ Group A  $\text{C}_1 = \text{Cl}_3\text{C}$ Group B  $\text{C}_1 = \text{CH}_3$ Next consider **propane**:  $\text{CH}_3\text{CH}_2\text{CH}_3$  Show the two conformations of propane.

A Eclipsed



B Staggered



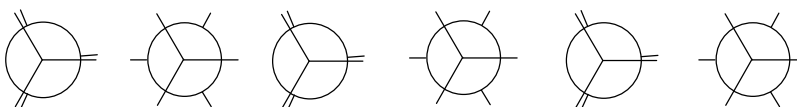
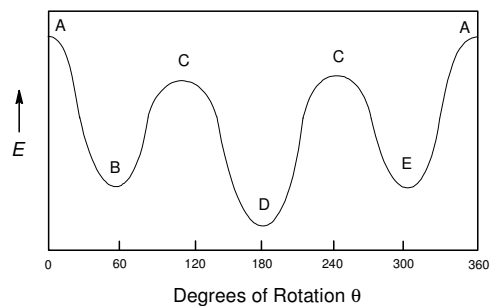
What are the relative energies of the eclipsed bonds?

C-H/C-H eclipsed

C-H/C-H eclipsed

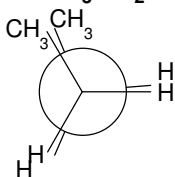
C-H/C- $\text{CH}_3$  eclipsed

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

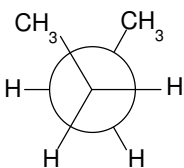


Now consider butane  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$  Show the four conformations of butane:

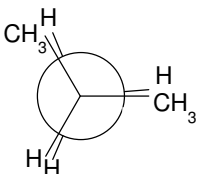
A Eclipsed



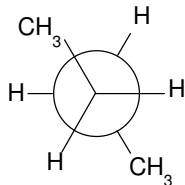
B Gauche



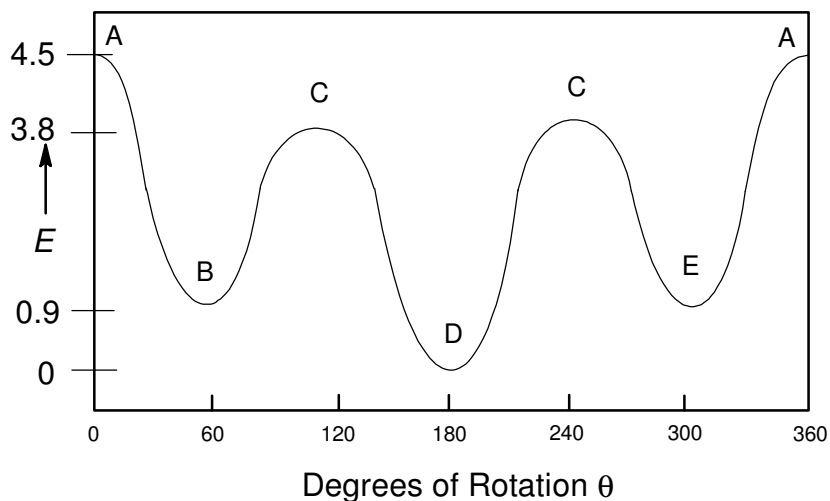
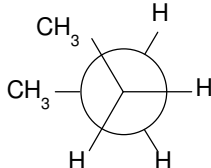
C Eclipsed



D Anti



E Gauche



Formulaic breakdown of strain energies:

Given E (kcal/mole): All eclipsed (C-H/C-H) = 1; (C-CH<sub>3</sub>/C-CH<sub>3</sub>) = 2.6; (C-H/C-CH<sub>3</sub>) = 1.4.

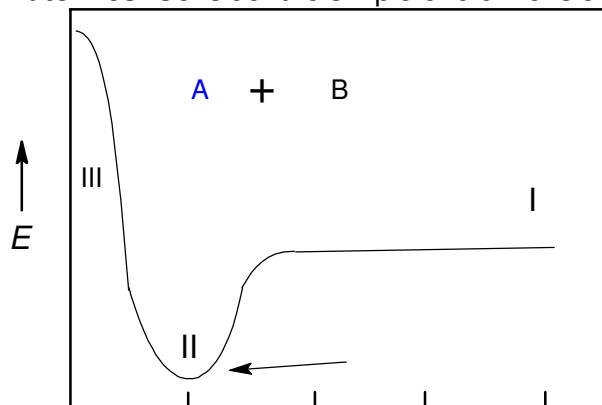
A = 4.5 kcal/mole = \_\_\_\_\_ (C-H/C-H) + \_\_\_\_\_ (C-CH<sub>3</sub>/C-CH<sub>3</sub>) = \_\_\_\_\_

C = 3.8 kcal/mole = \_\_\_\_\_ (C-H/C-H) + \_\_\_\_\_ (C-H/C-CH<sub>3</sub>) = \_\_\_\_\_

**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:

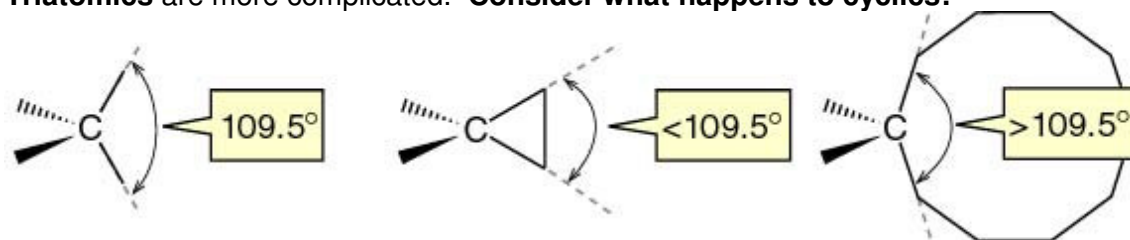


Describe the situations for the 3 main regions:

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!



A normal tetrahedron  
with a bond angle of  
 $109.5^\circ$

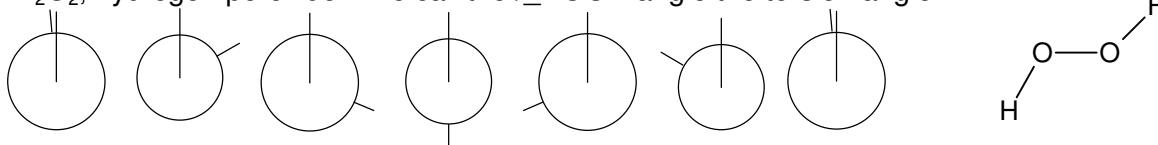
A small ring will  
constrict this angle  
to less than  $109.5^\circ$

A large ring will  
expand this angle  
to more than  $109.5^\circ$

<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>

**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.

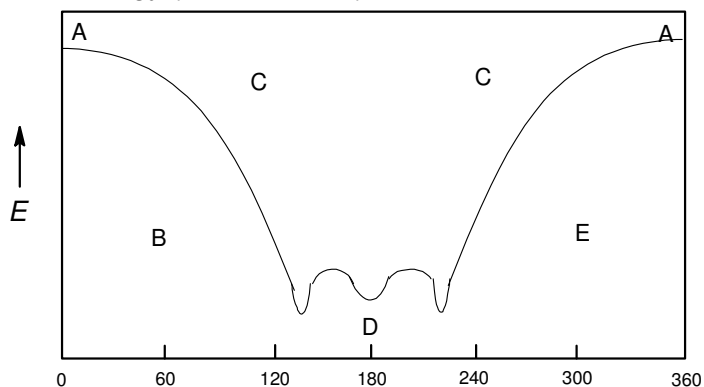
$\text{H}_2\text{O}_2$ , hydrogen peroxide. We call the  $\angle \text{HOOH}$  angle the torsion angle.



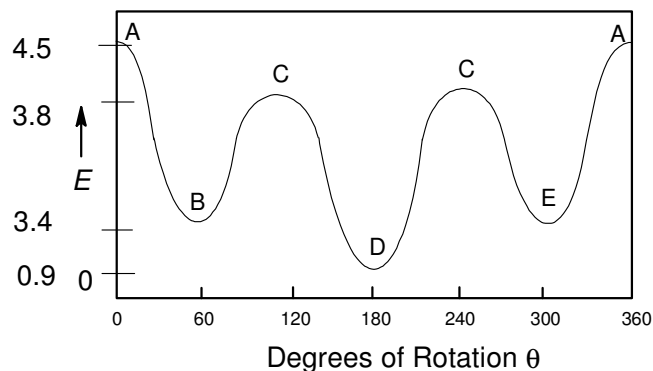
Torsion Angle

Which structure is the highest energy (most strained)?

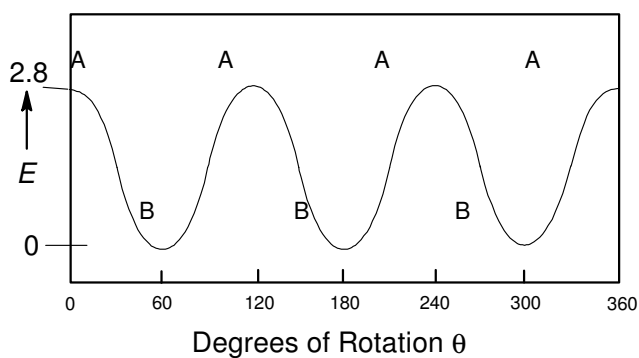
Which structure is the lowest energy (least strained)?



Reconsider butane and ethane in terms of torsional strain:

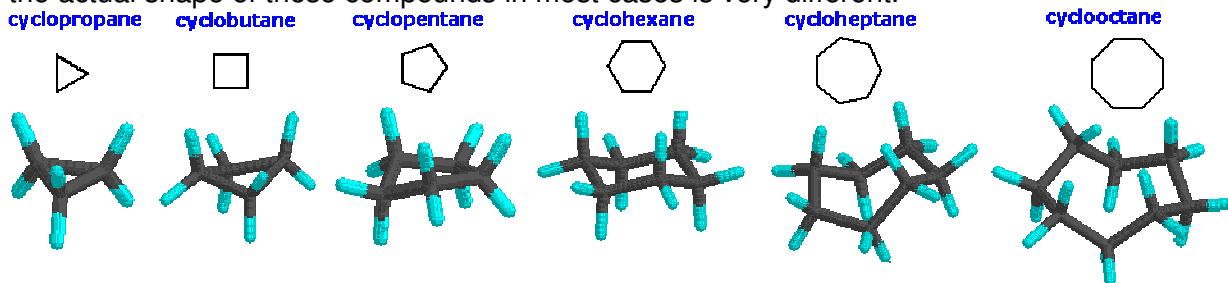


**Torsional Energy diagram of butane**



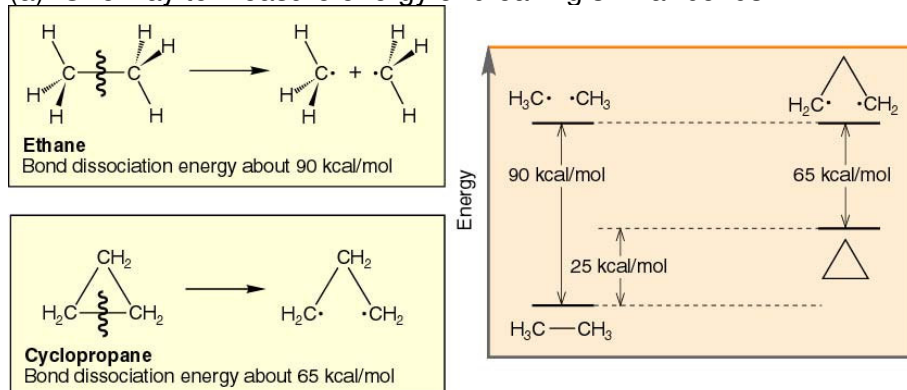
**Torsional Energy diagram of ethane**

**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.

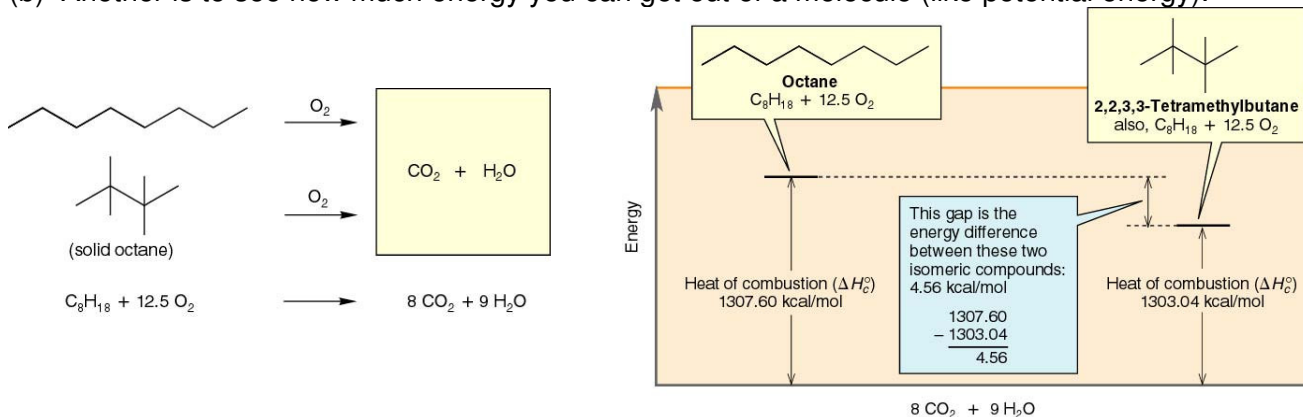
(a) One way to measure energy of breaking similar bonds.



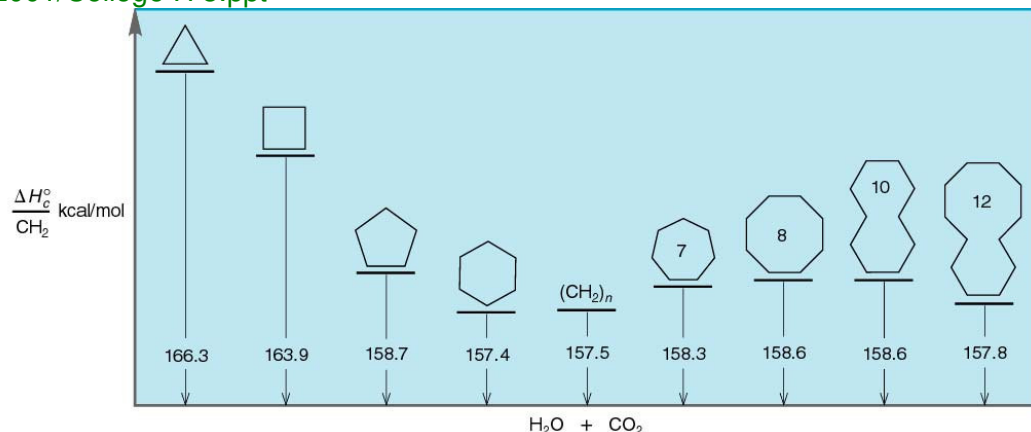
<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>

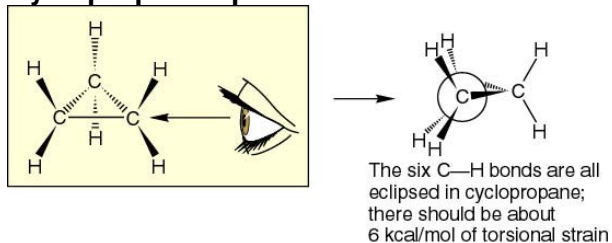
What is the strain in cyclopropane compared to ethane?

(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>



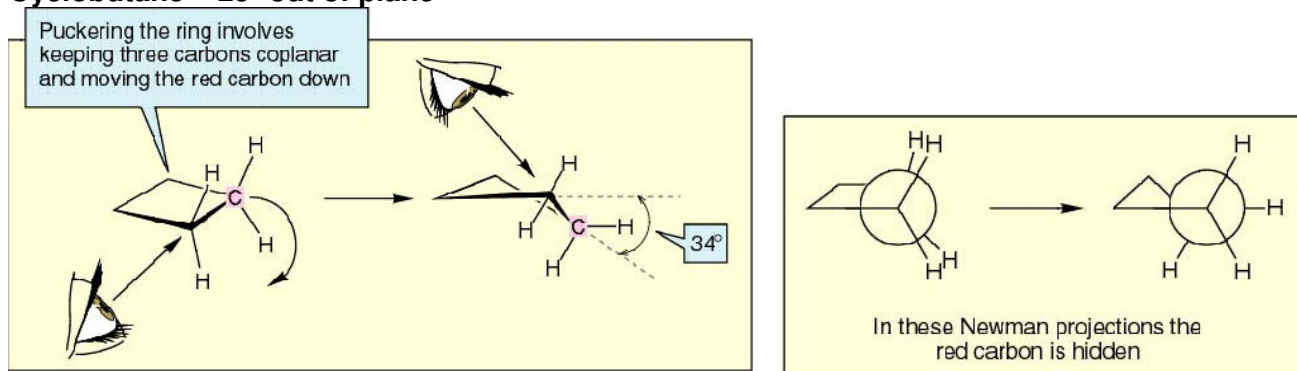
**Cyclopropane --planar**

<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>

Steric Strain

Torsional Strain

Angle strain

**Cyclobutane – 25° out of plane**

<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>

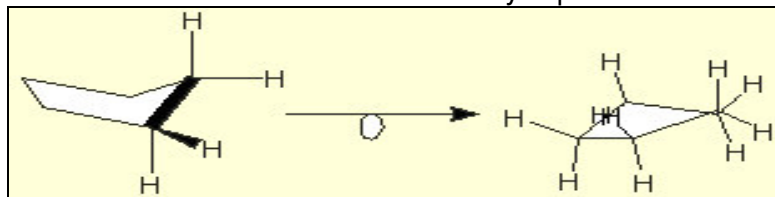
Steric Strain

Torsional Strain

Angle strain

**Cyclopentane -- puckered**

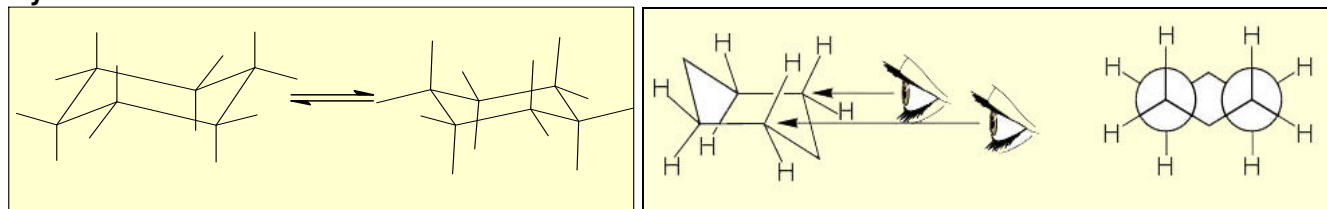
Look down the C-C bond to see how cyclopentane avoids C-H eclipsed.



Angle strain

Steric Strain

Torsional Strain

**Cyclohexane -- chair**

<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>

Steric Strain

Torsional Strain

Angle strain

## Analysis of the conformations of cyclohexane

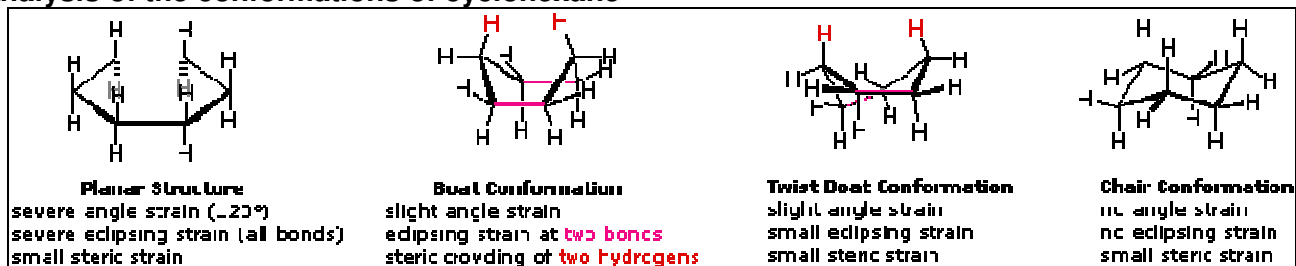


Figure William Reusch, Virtual Textbook

The chair cyclohexane – no strain all tetrahedral angles.

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

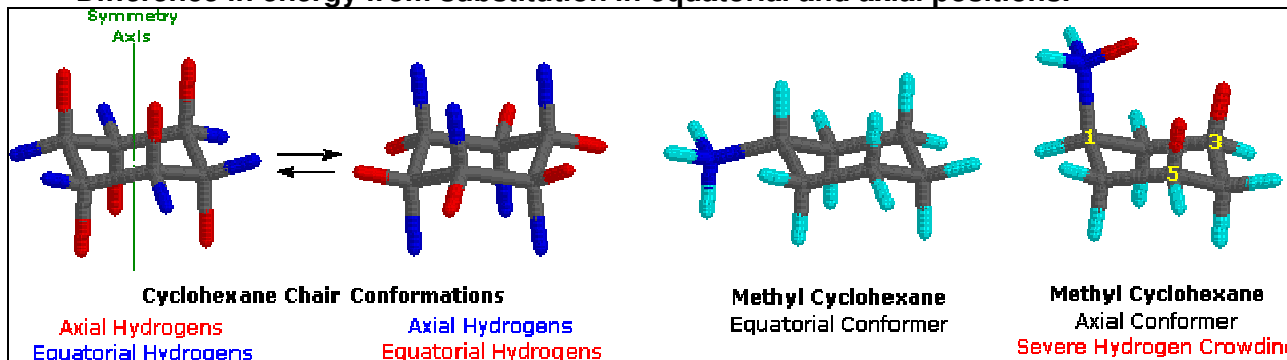
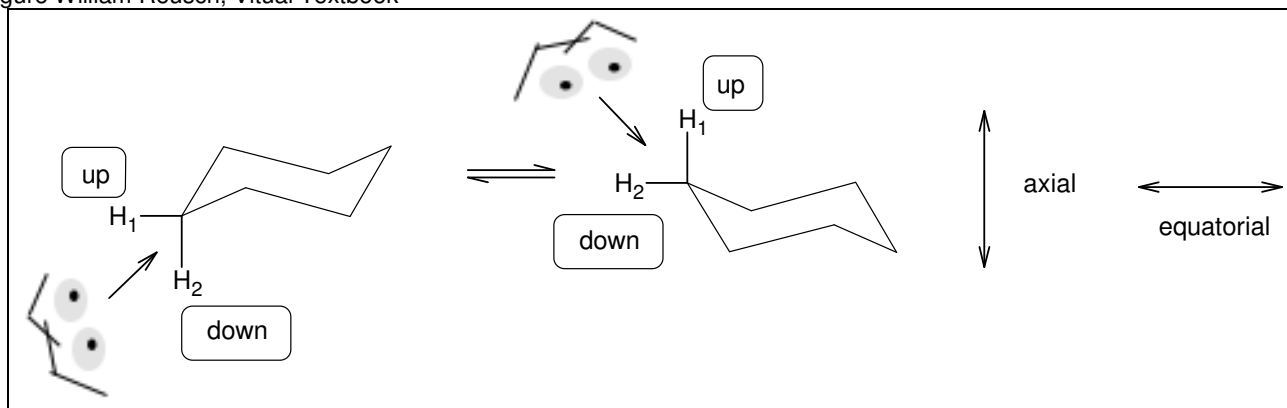
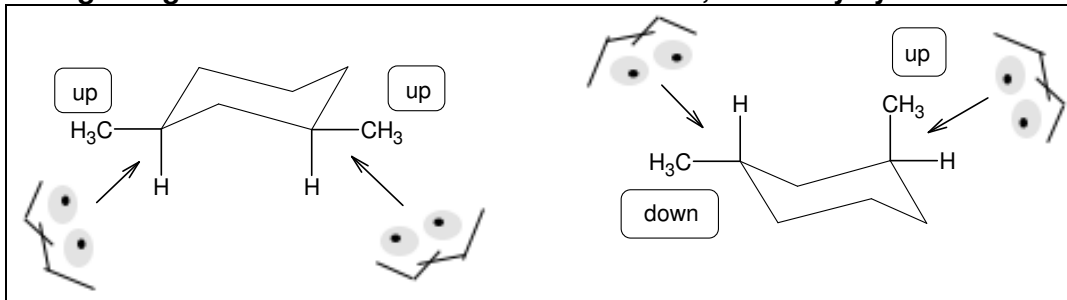


Figure William Reusch, Virtual Textbook



Equatorial substitution is preferred.

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

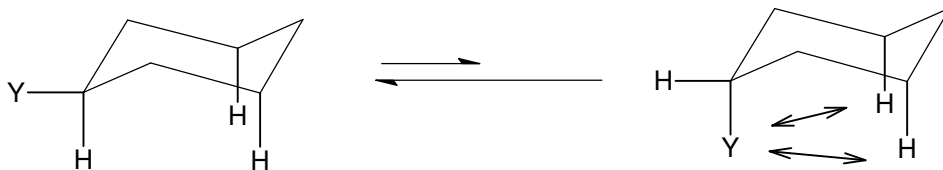


## Practice Drawing Chair-Cyclohexane

				1	2	3	4

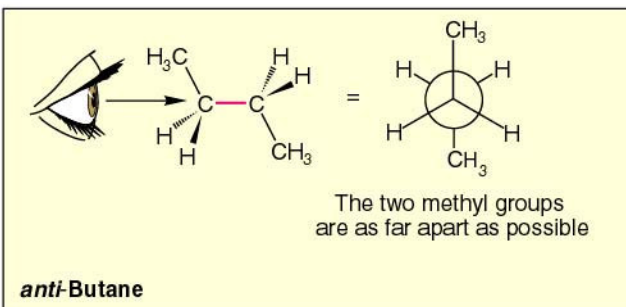
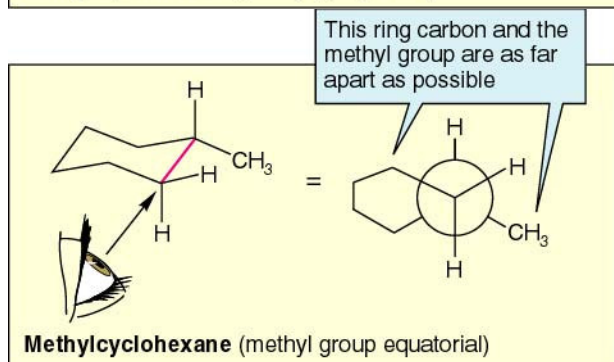
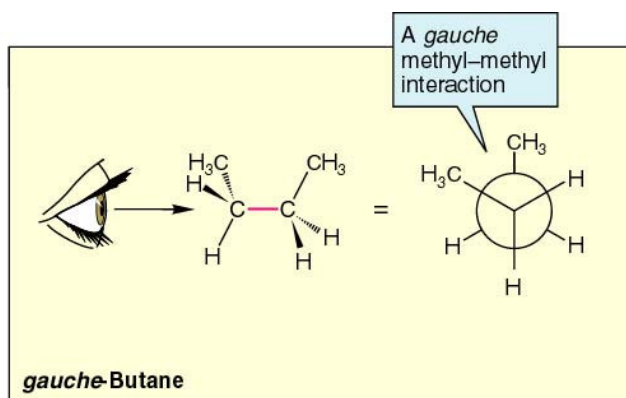
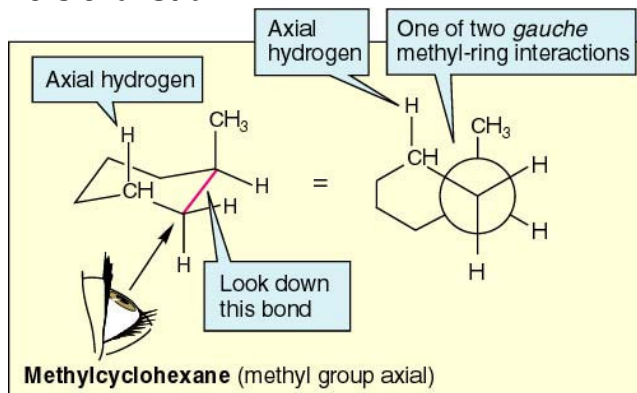
## Energetics of Cyclohexane Conformations

### Steric and Torsional Strain

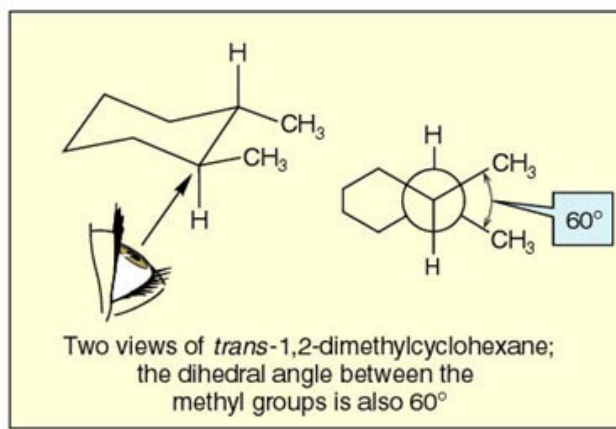
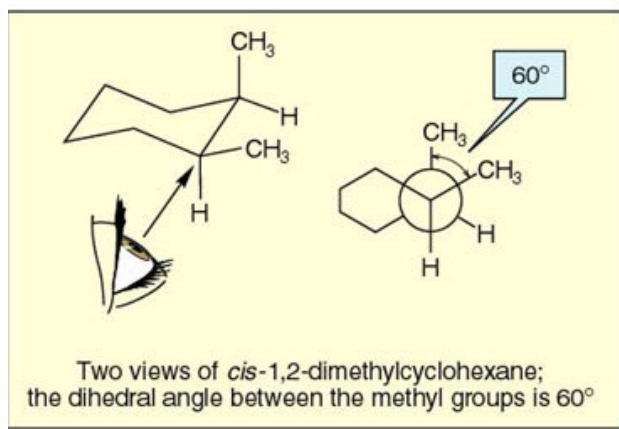
Preference for  $Y_{eq}$  =

Y	E (kcal/mol)
Cl	0.5
CH <sub>3</sub>	1.7
CH <sub>3</sub> CH <sub>2</sub> =	1.8
(CH <sub>3</sub> ) <sub>2</sub> CH=	2.1
(CH <sub>3</sub> ) <sub>3</sub> C=	5.4

### Torsional Strain



<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>



<http://www.sci.kun.nl/chemistry/onderwijs/oc1-2001/College H 5.ppt>



## Conformational Structures of Disubstituted Cyclohexanes

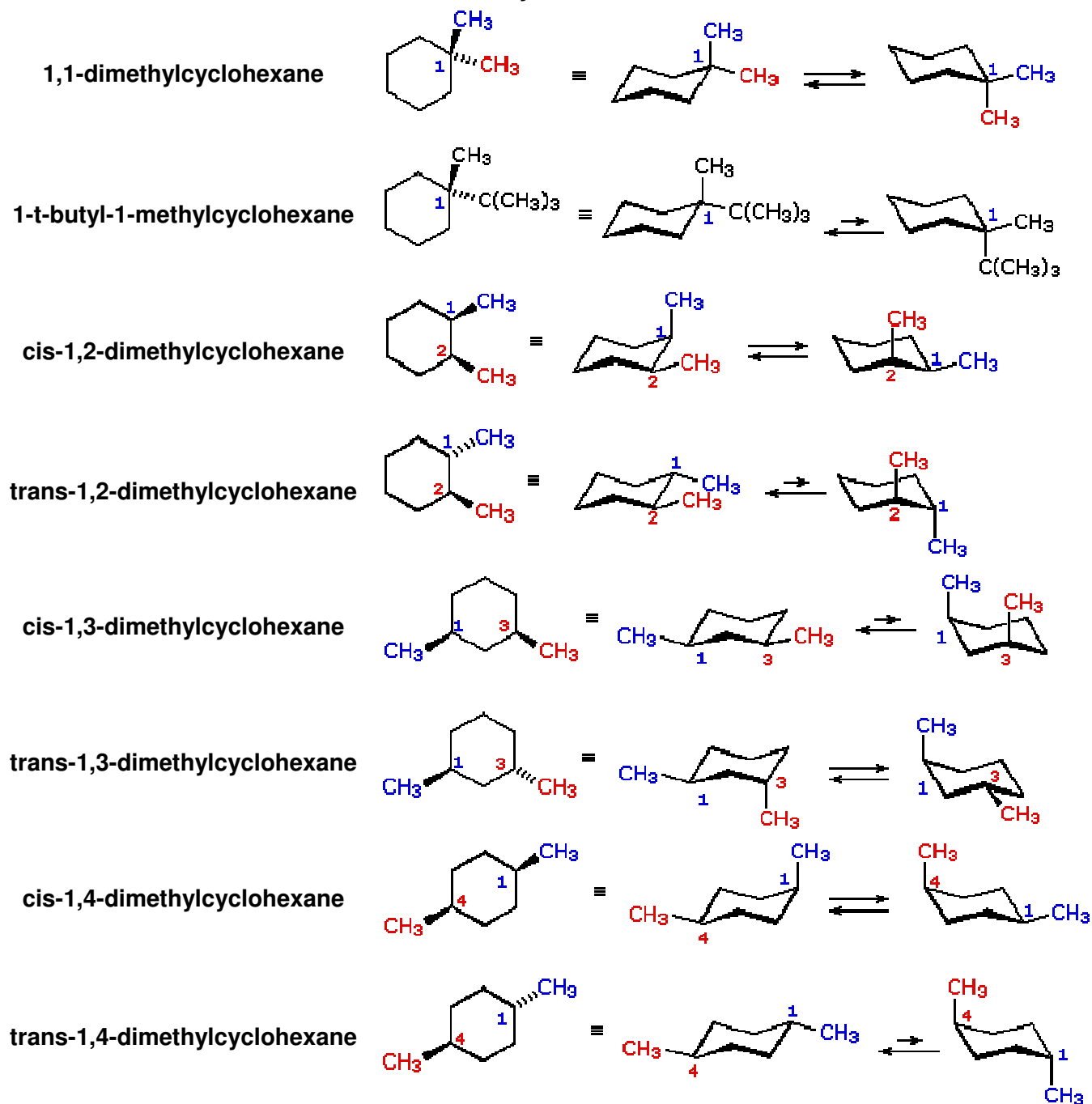
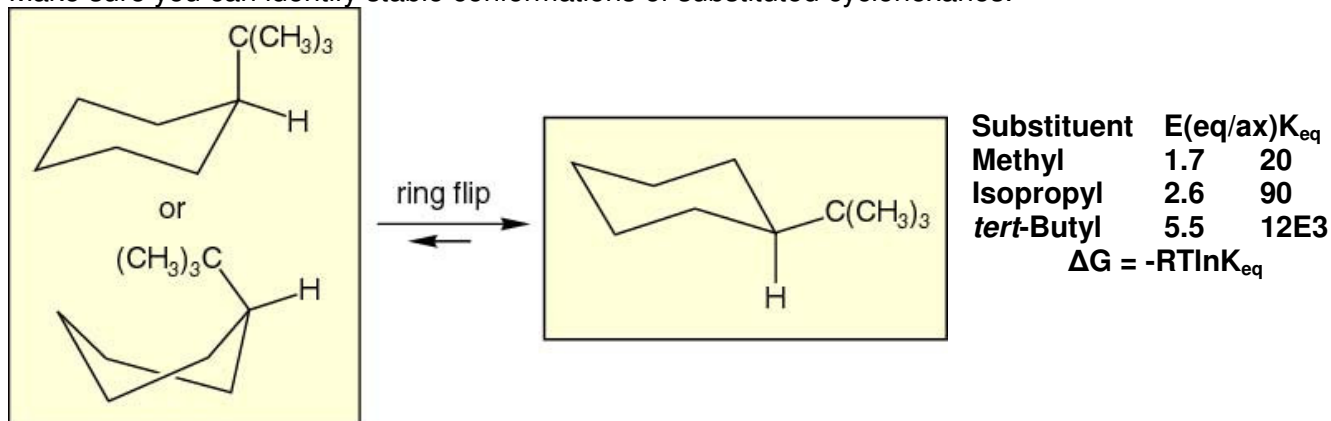


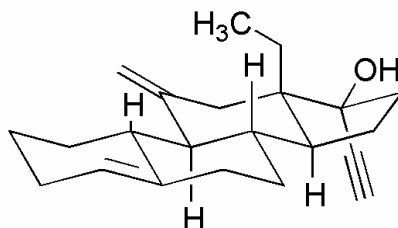
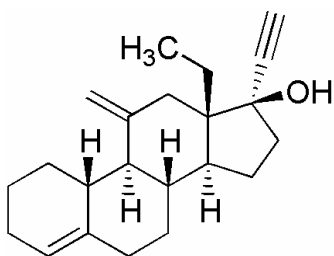
Figure from William Reusch, Virtual Textbook

Make sure you can identify stable conformations of substituted cyclohexanes.



**Naturally occurring chair cyclohexanes – steroids**

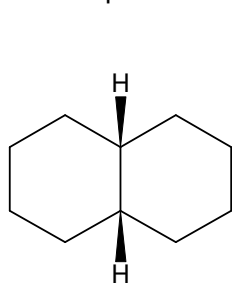
The majority of naturally occurring steroids contains the 6,6,6,5-trans-fused skeleton



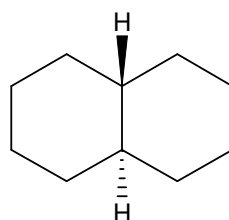
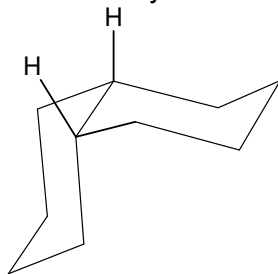
desogestrel

<http://www.desogestrel.com/>

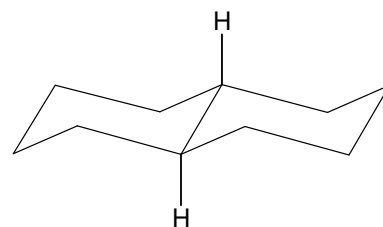
The simplest fused cyclohexane system is decalin.



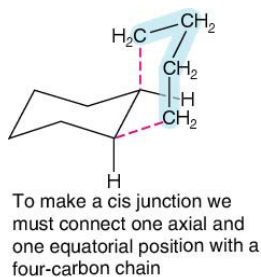
cis-decalin



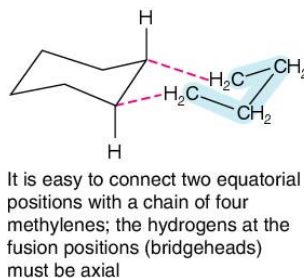
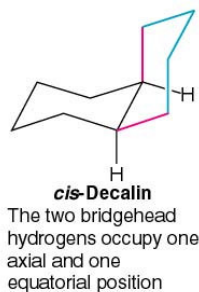
trans-decalin



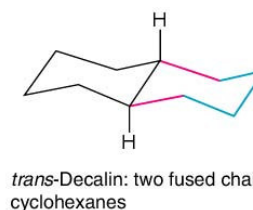
How many gauche interactions are there in cis and trans decalin?



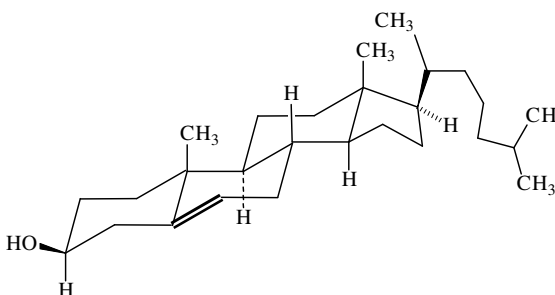
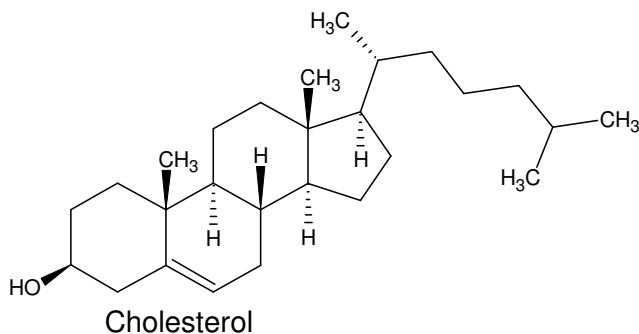
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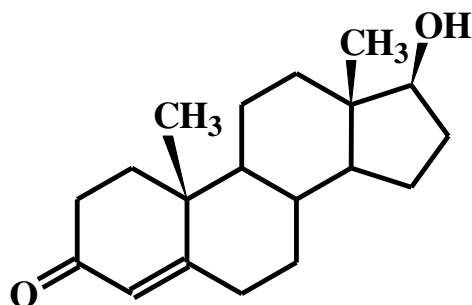
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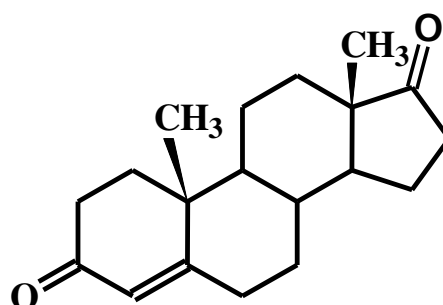
Trans-decalin style fused cyclohexanes are the basis for steroids. Note all the trans-decalins.



## Anabolic Steroids

**Testosterone**

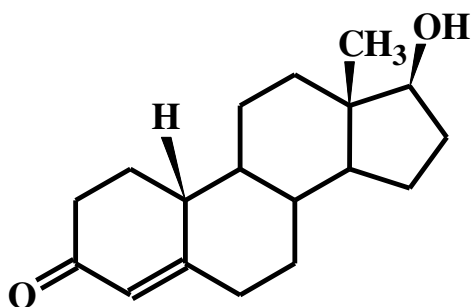
Responsible for many sex-linked behaviors

**Androstenedione**

(4-androstene-3,17-dione)

Popular "stimulant" used in baseball – Mark McGwire

<http://hermes.hhp.ufl.edu/keepingfit/ARTICLE/andro.htm>

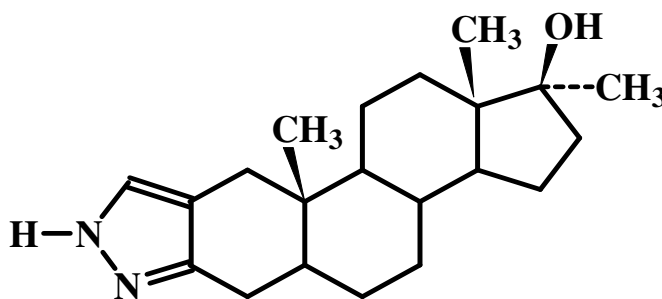
**Nandrolone**

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

"Winning? Formula" for the Sydney Olympics

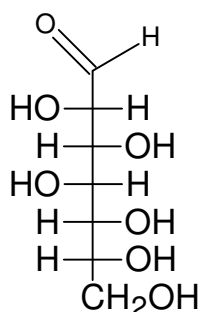
Barcelona Olympic boost

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

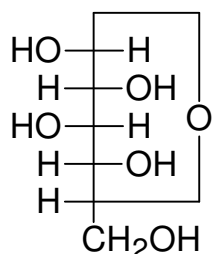
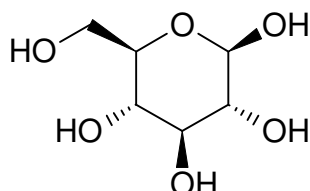
**Stanozolol****Sugars**

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.

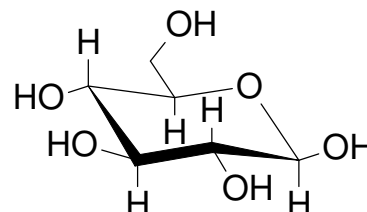
The straight chain form is not particularly stable and tends to cyclize with loss of water to make either an alpha (left side link) or Beta (right side link) as shown below.



Straight chain

 $\beta$  -cyclized form

planar projection

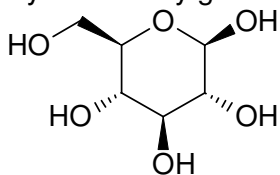
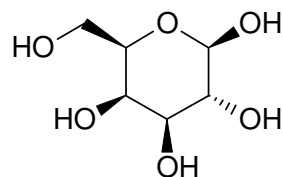
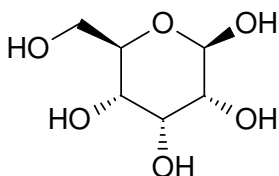
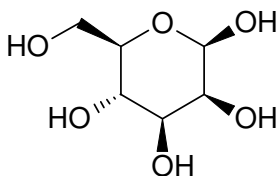
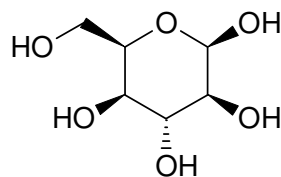
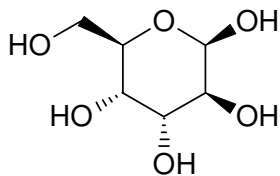
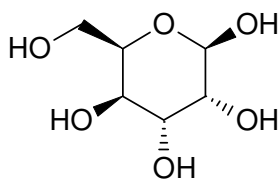
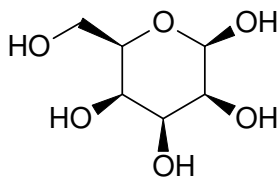
 $\beta$ -chair projection

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

**Sugar Practice**

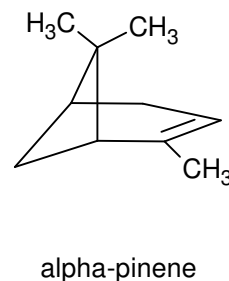
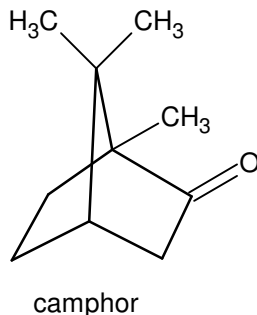
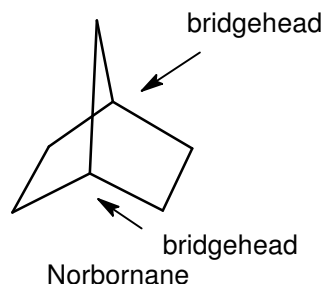
Turn these planar projections into chairs.

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

 **$\beta$ -D-Glucopyranose** **$\beta$ -D-Galactopyranose** **$\beta$ -D-Allopyranose** **$\beta$ -D-Mannopyranose** **$\beta$ -D-Idopyranose** **$\beta$ -D-Altropyranose** **$\beta$ -D-Gulopyranose** **$\beta$ -D-Talopyranose**

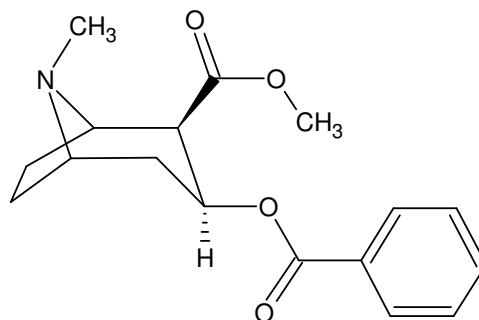
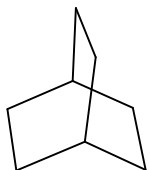
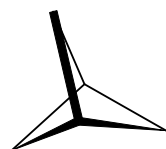
Naturally occurring in our diet order of abundance are glucose > galactose and fructose. Which other 6-carbon sugar would you predict to be important in metabolic cycles?

## Bicyclics



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.