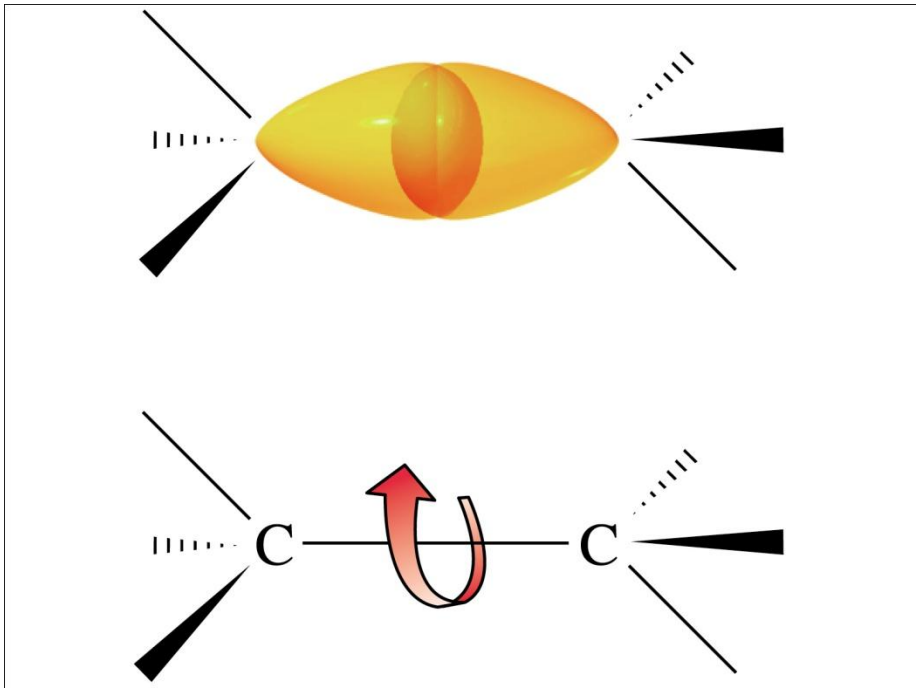
Chapter 2

An Introduction to Organic Compounds

Conformations

Adapted from Profs. Turro & Breslow, Columbia University and Prof. Irene Lee, Case Western Reserve University

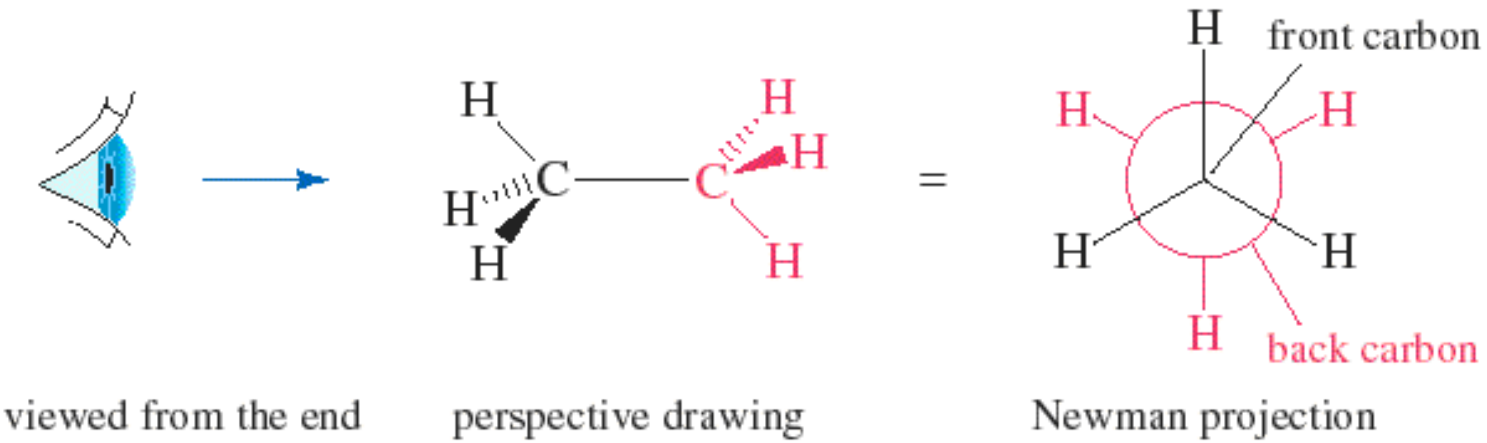
Conformations of Alkanes: Rotation about Carbon–Carbon Bonds



Conformational Analysis

Drawing Acyclic Molecules

- Newman Projections



Conformational Analysis

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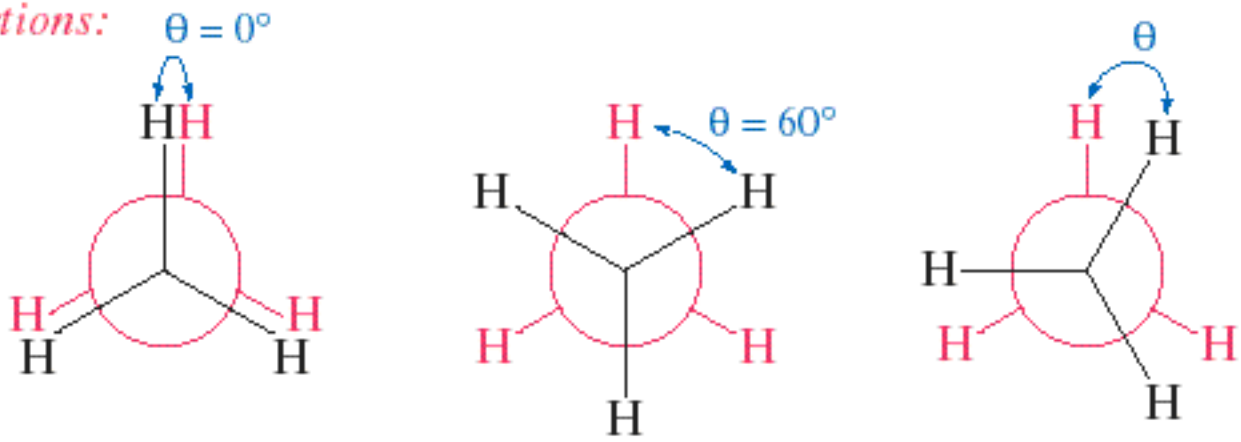
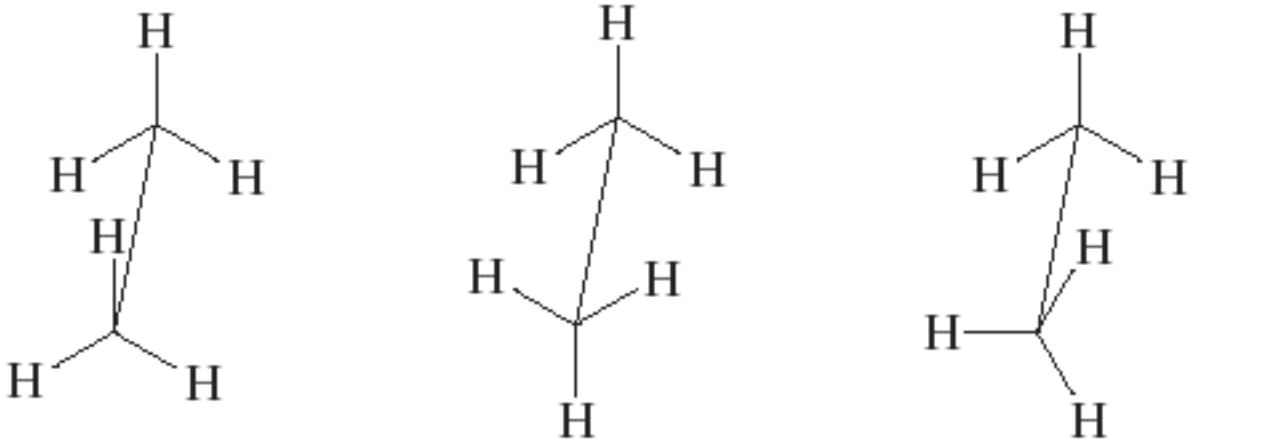


Sawhorse structures:

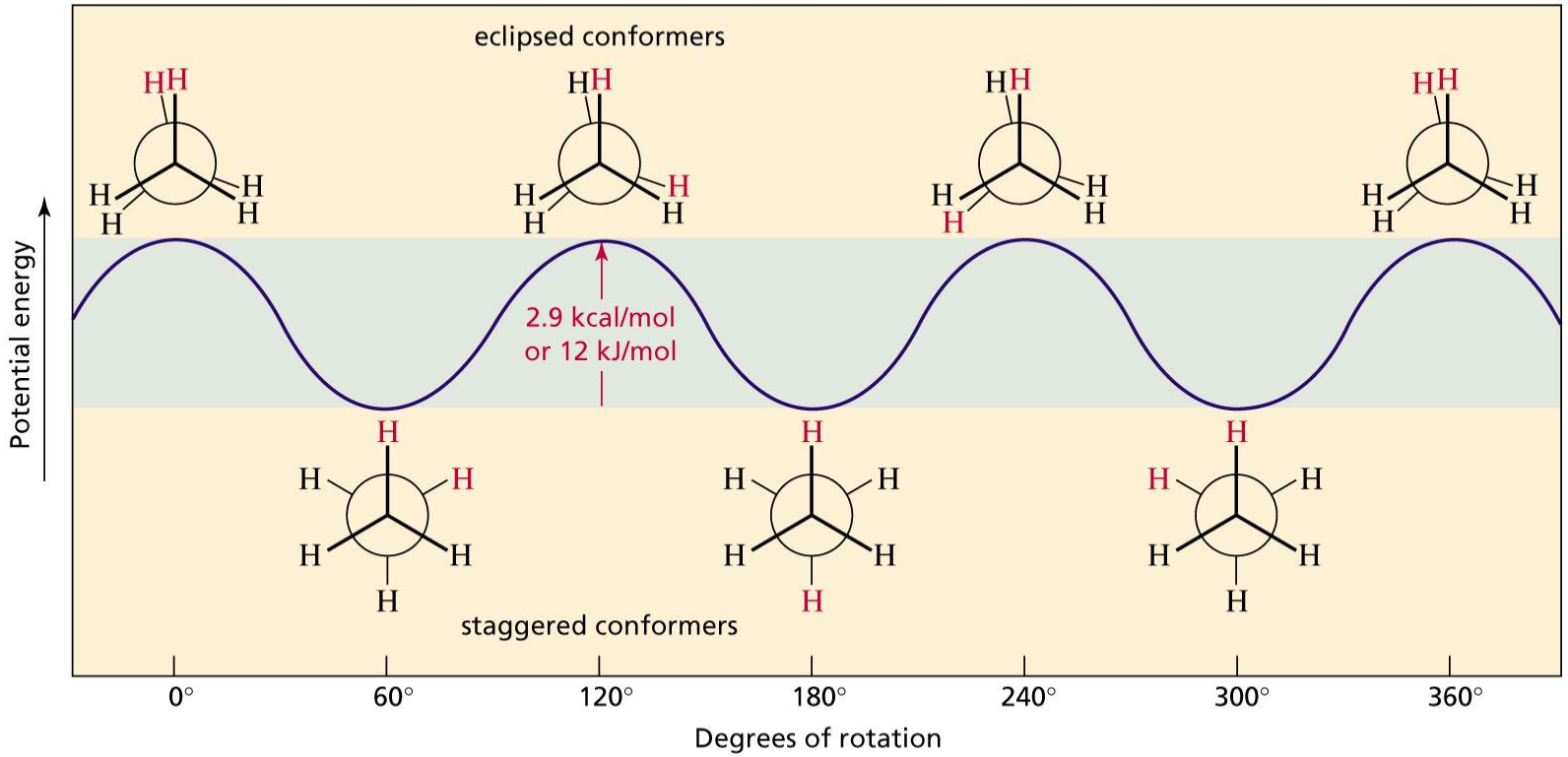


eclipsed, θ = 0°

staggered, θ = 60°

skew, θ = anything else

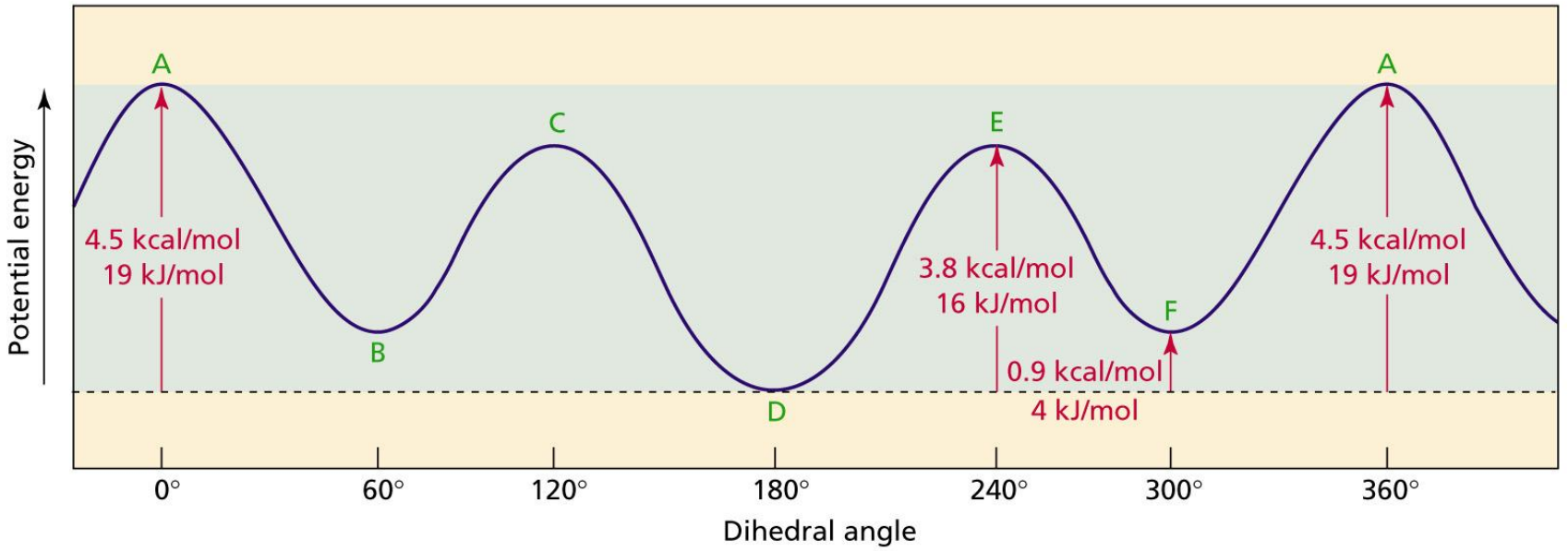
Different Conformations of Ethane

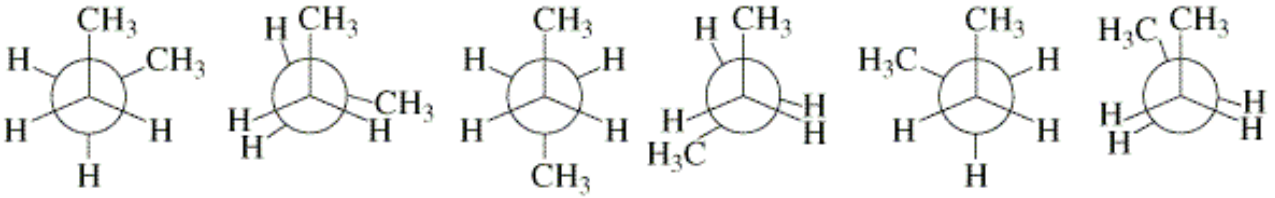


- A staggered conformer is more stable than an eclipsed conformer
- Torsional strain: repulsion between pairs of bonding electrons

Conformations of *n*-Butane

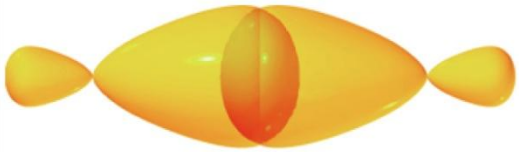
- Steric strain: repulsion between the electron clouds of atoms or groups



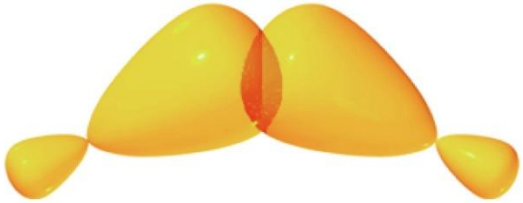


Cycloalkanes: Ring Strain

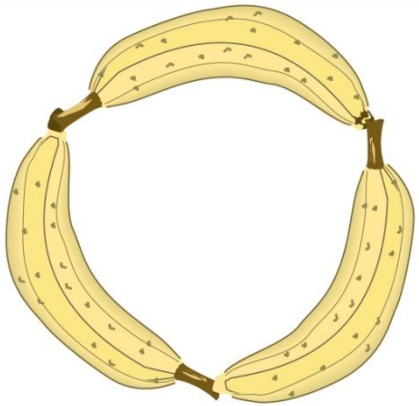
- Angle strain results when bond angles deviate from the ideal 109.5° bond angle



good overlap
strong bond
(a)



poor overlap
weak bond
(b)



banana bonds

The Shapes of Cycloalkanes: Planar or Nonplanar?

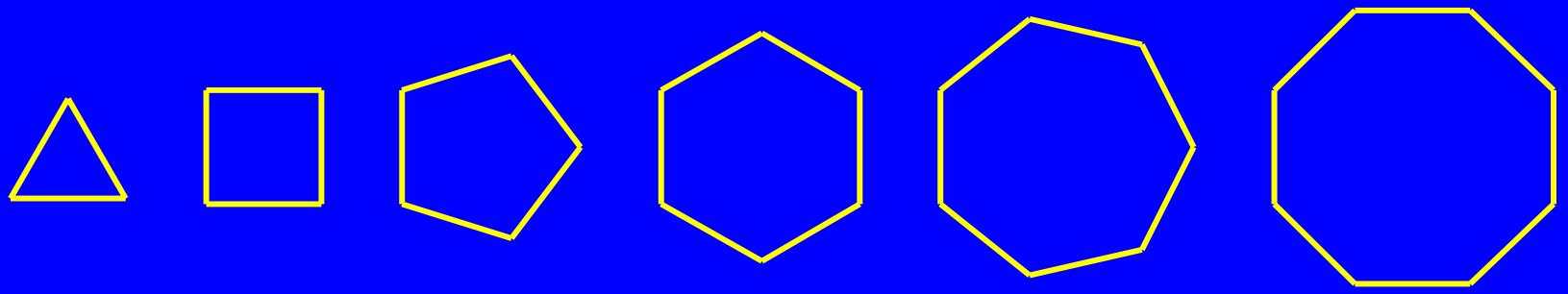
Adolf von Baeyer (19th century)

- Assumed cycloalkanes were planar polygons.
- Believed distortion of bond angles from 109.5° gives angle strain to some cycloalkanes.
- One for two is great in baseball.

Types of Strain

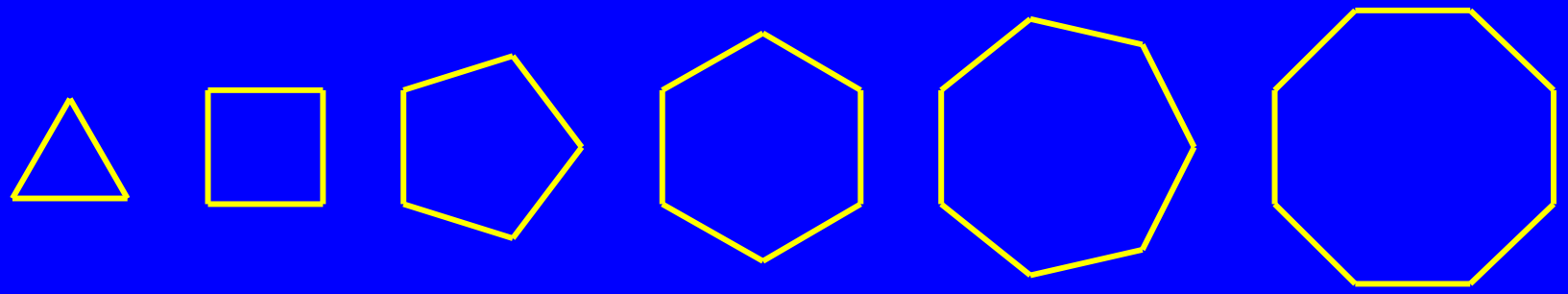
- *Torsional strain*
  strain that results from eclipsed bonds (measure of the dihedral angle)
- Van der Waals strain or (*Steric strain*)
  strain that results from atoms being too close together.
- *Angle strain* results from distortion of bond angles from normal values, for a tetrahedron 109.5^{o}

Measuring Strain in Cycloalkanes



- Heats of combustion can be used to compare stabilities of isomers.
- But cyclopropane, cyclobutane, etc. are not isomers.
- All heats of combustion increase as the number of carbon atoms increase.

Measuring Strain in Cycloalkanes



- Therefore, divide heats of combustion by number of carbons and compare heats of combustion on a "per CH_2 group" basis.

Heats of Combustion in Cycloalkanes

Cycloalkane	kJ/mol	Per CH_2
Cyclopropane	2,091	697
Cyclobutane	2,721	681
Cyclopentane	3,291	658
Cyclohexane	3,920	653
Cycloheptane	4,599	657
Cyclooctane	5,267	658
Cyclononane	5,933	659
Cyclodecane	6,587	659

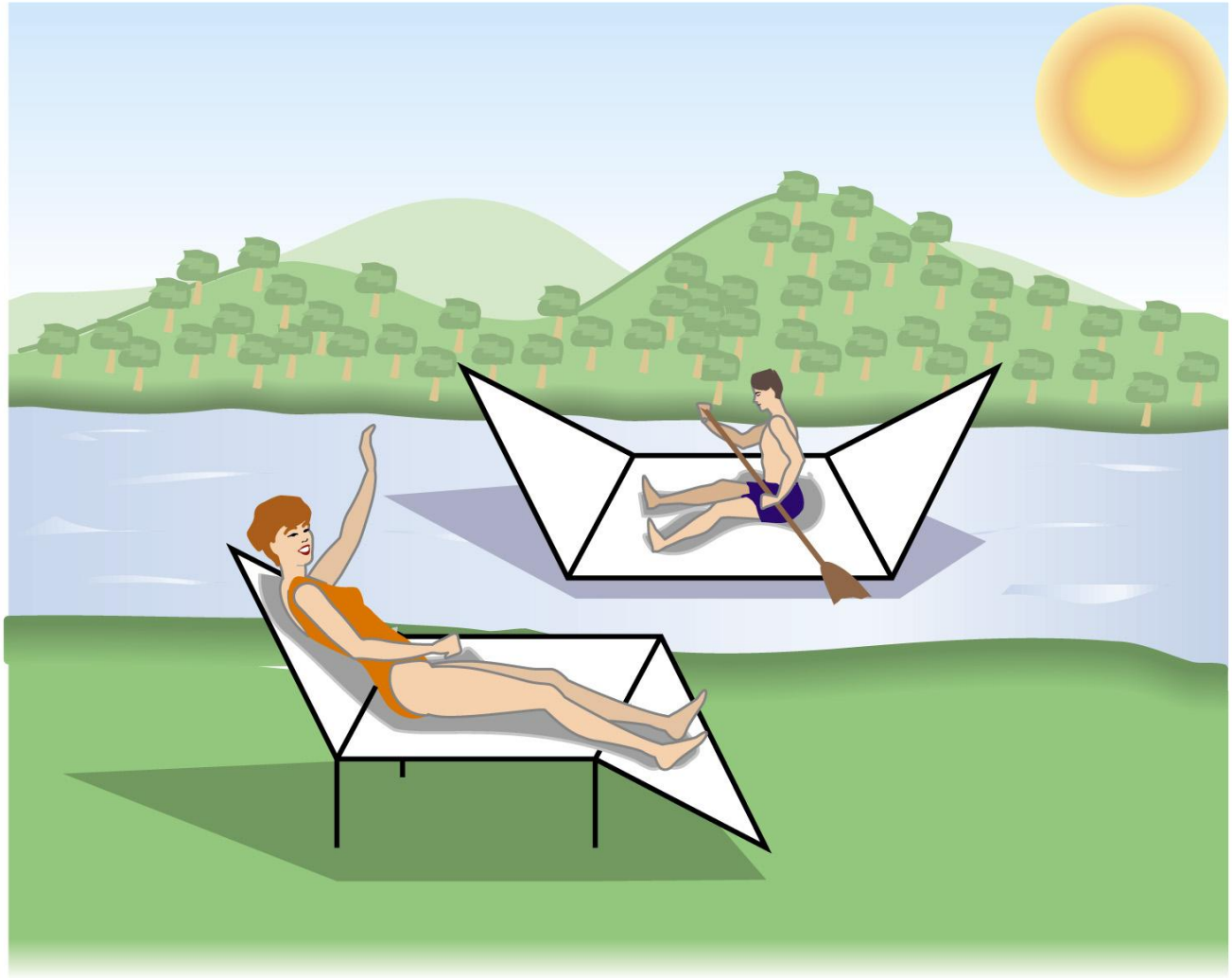
Heats of Combustion in Cycloalkanes

Cycloalkane	kJ/mol	Per CH_2
According to Baeyer, cyclopentane should have less angle strain than cyclohexane.		
Cyclopentane	3,291	658
Cyclohexane	3,920	653

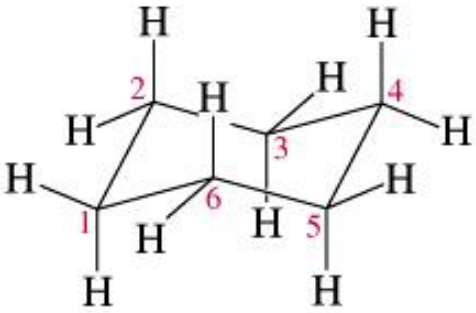
The heat of combustion per CH_2 group is less for cyclohexane than for cyclopentane. Therefore, cyclohexane has less strain than cyclopentane.

Conformations of Cyclohexane

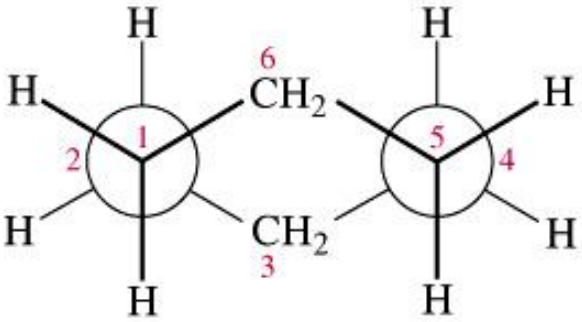
- Heat of combustion suggests that angle strain is unimportant in cyclohexane.
- Tetrahedral bond angles require nonplanar geometries.
- The chair and boat conformations.



- The chair conformation of cyclohexane is free of strain



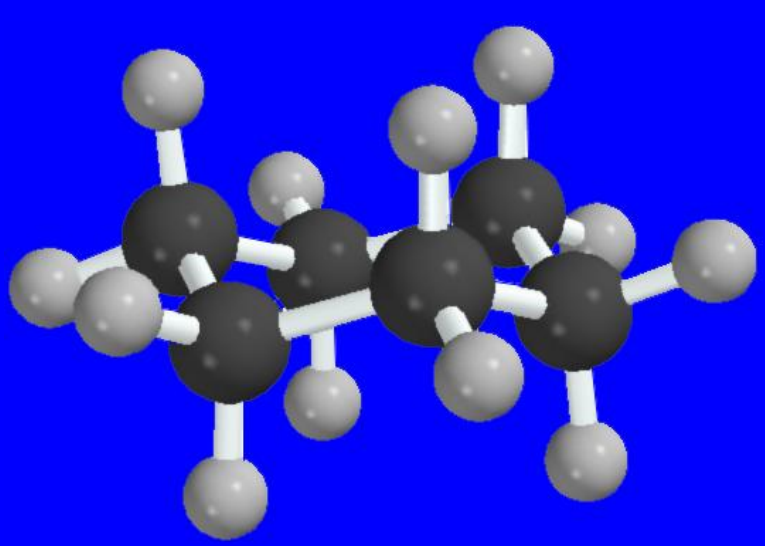
chair conformer of cyclohexane

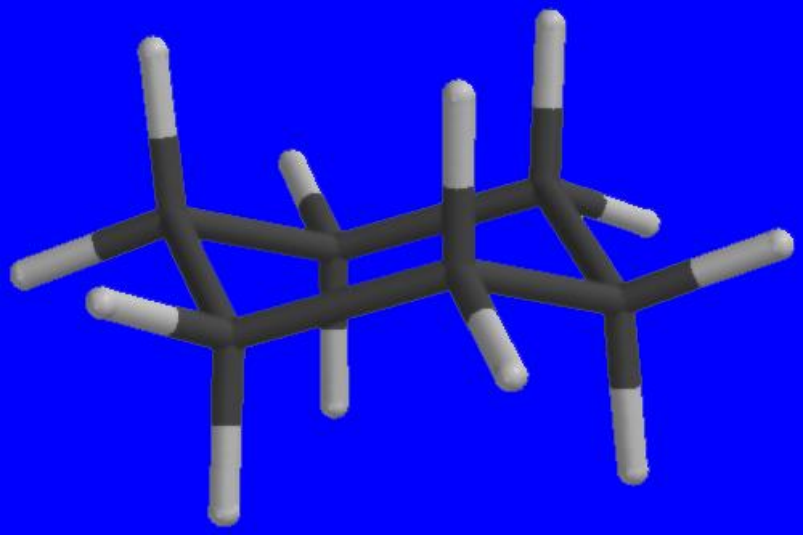


Newman projection of the chair conformer

ball-and-stick model of the chair conformer of cyclohexane

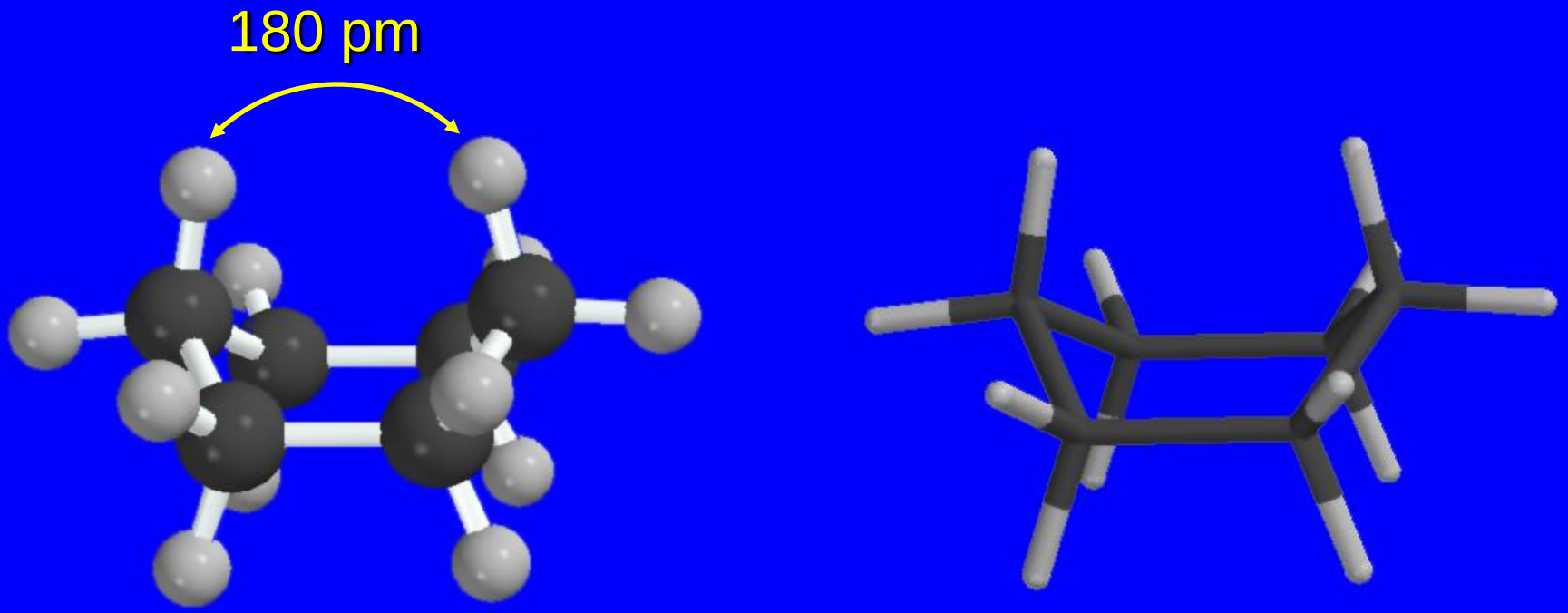
Chair is the most stable conformation of cyclohexane





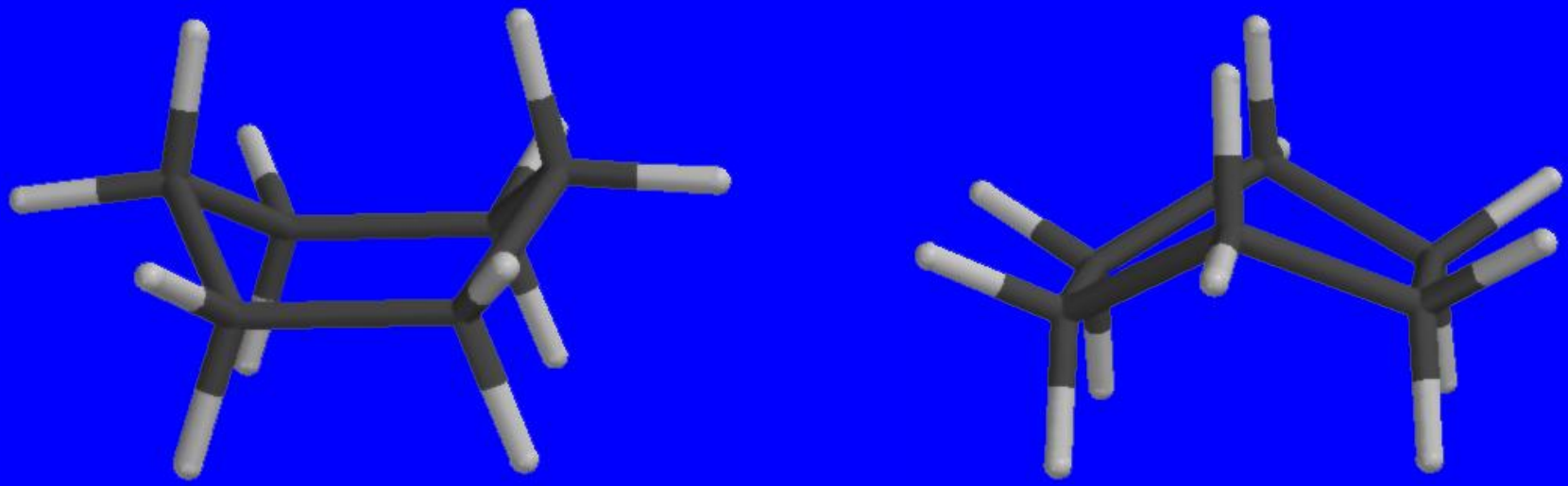
- All of the bonds are staggered and the bond angles at carbon are close to tetrahedral.

Boat conformation is less stable than the chair



- All of the bond angles are close to tetrahedral but close contact between flagpole hydrogens causes strain in boat.

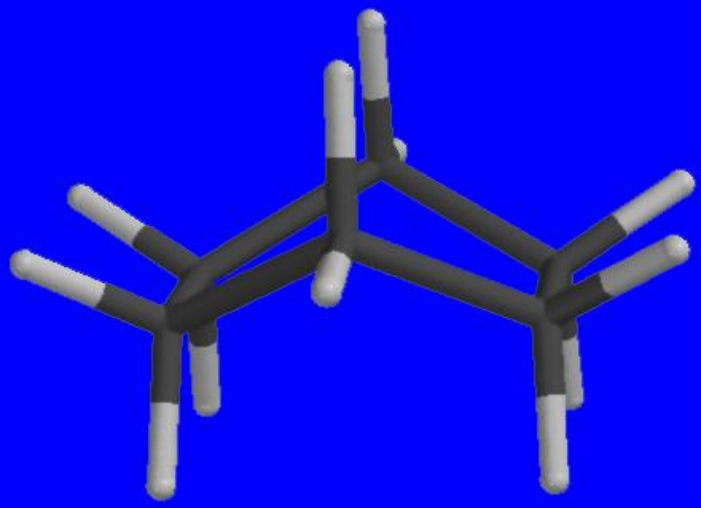
Boat conformation is less stable than the chair



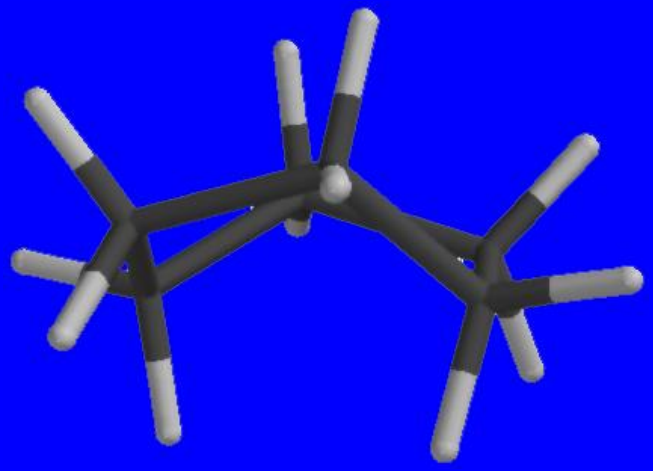
- Eclipsed bonds bonds gives torsional strain to boat.

Skew boat is slightly more stable than boat

Boat



Skew or Twist Boat



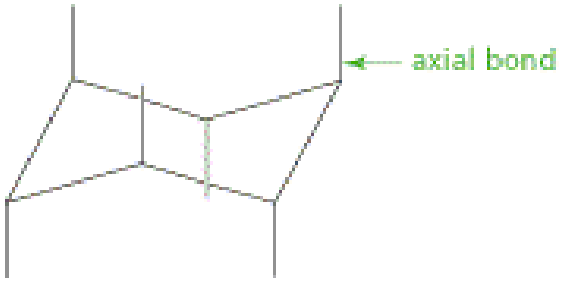
- Less van der Waals strain and less torsional strain in skew boat.

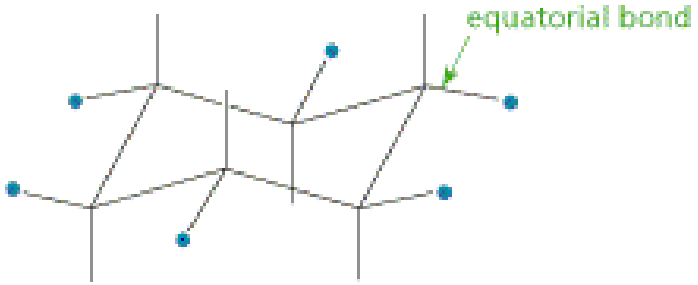
Generalization

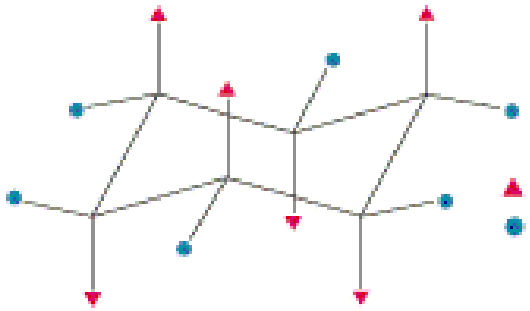
- The chair conformation of cyclohexane is the most stable conformation and derivatives of cyclohexane almost always exist in the chair conformation

Axial and Equatorial Bonds in Cyclohexane

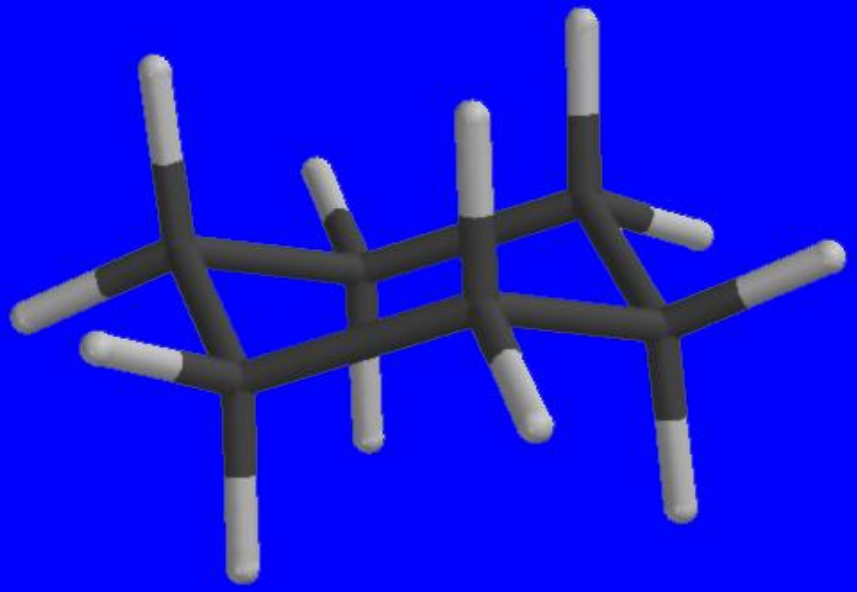
Drawing Cyclohexane



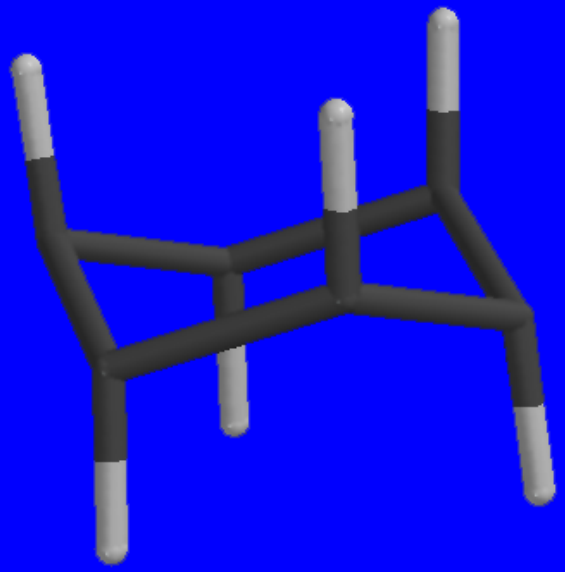




The 12 bonds to the ring can be divided into two sets of 6.

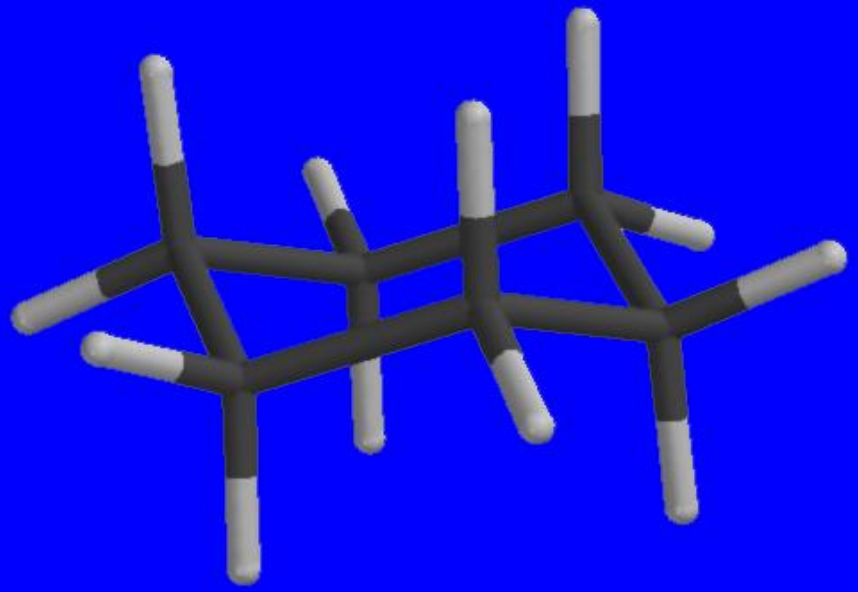


6 Bonds are axial

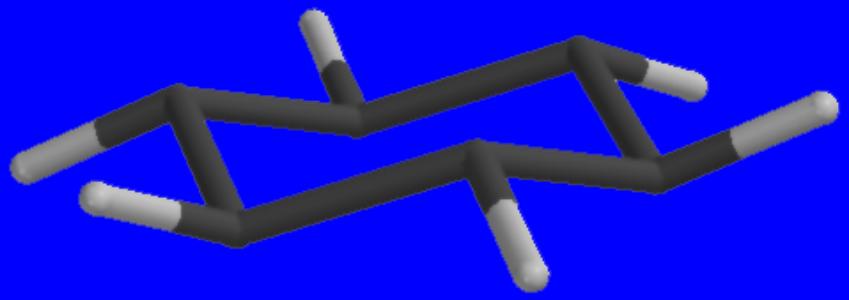


Axial bonds point "north and south"

The 12 bonds to the ring can be divided into two sets of 6.



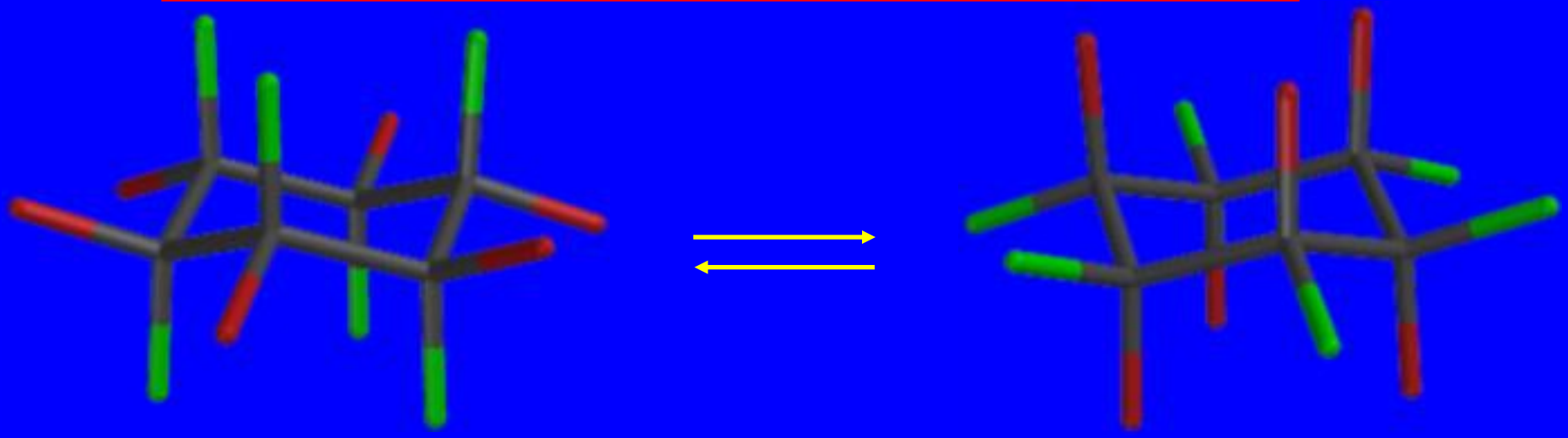
6 Bonds are equatorial



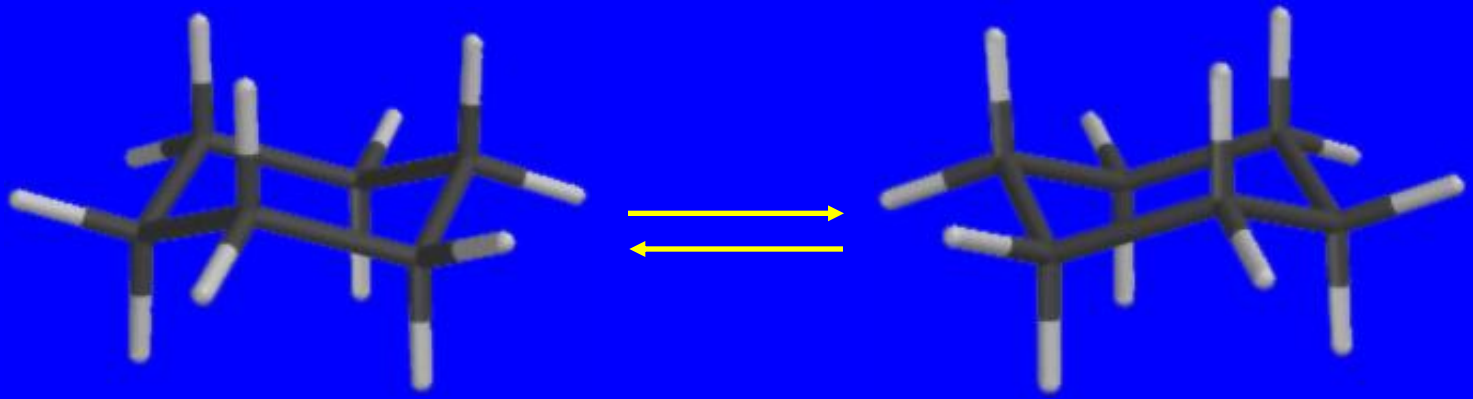
Equatorial bonds lie along the equator

Conformational Inversion (Ring-Flipping) in Cyclohexane

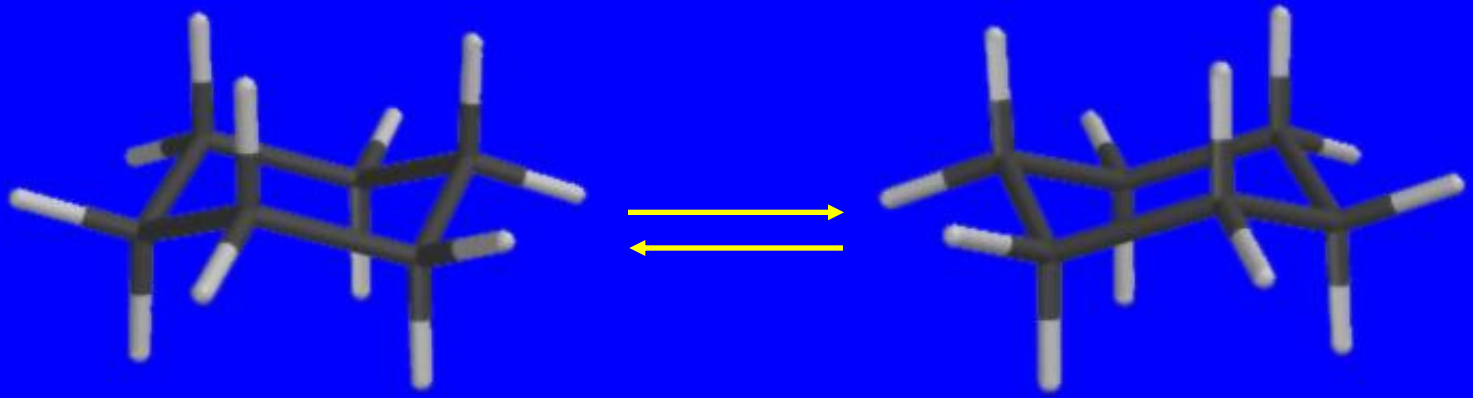
Conformational Inversion

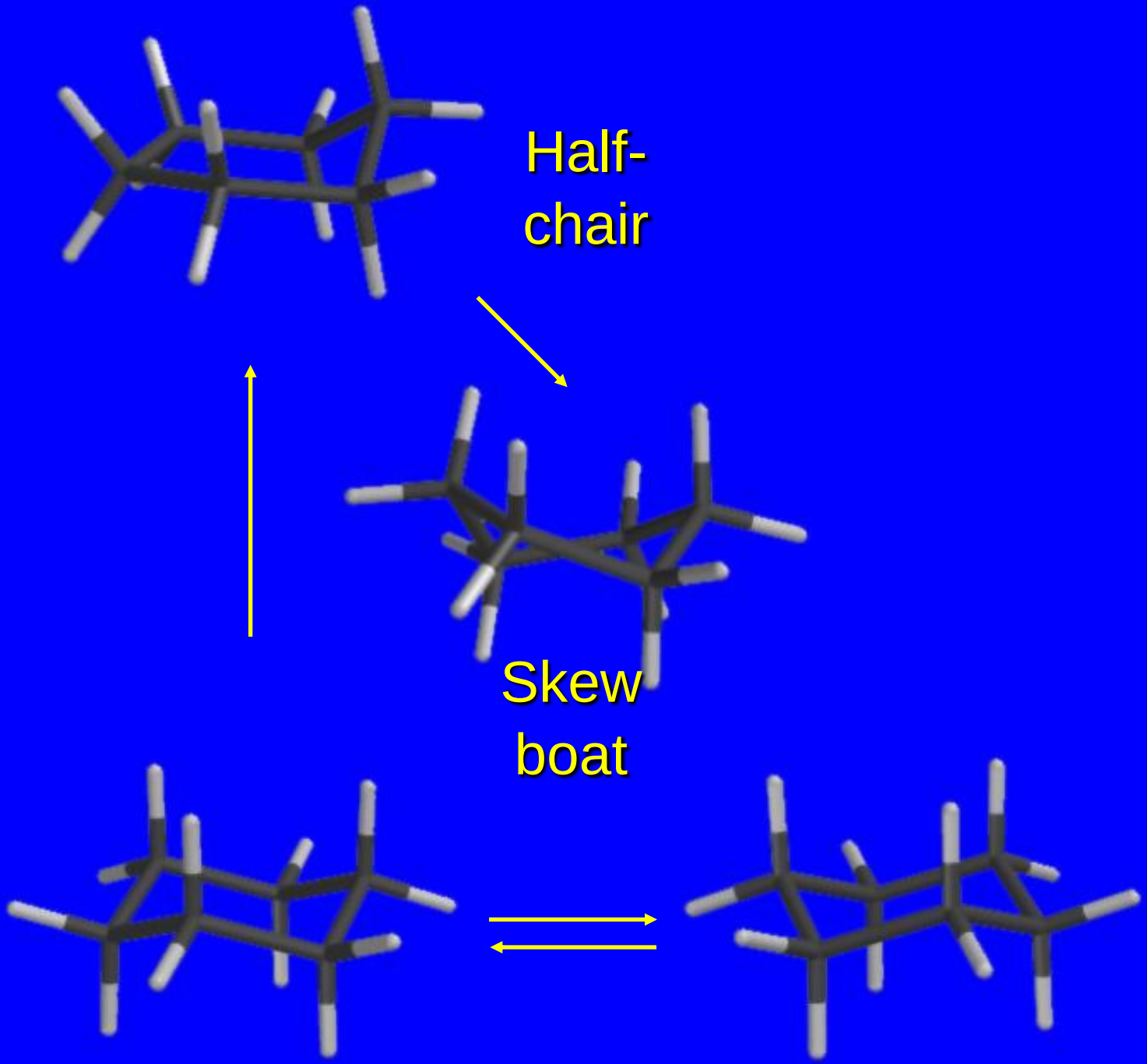


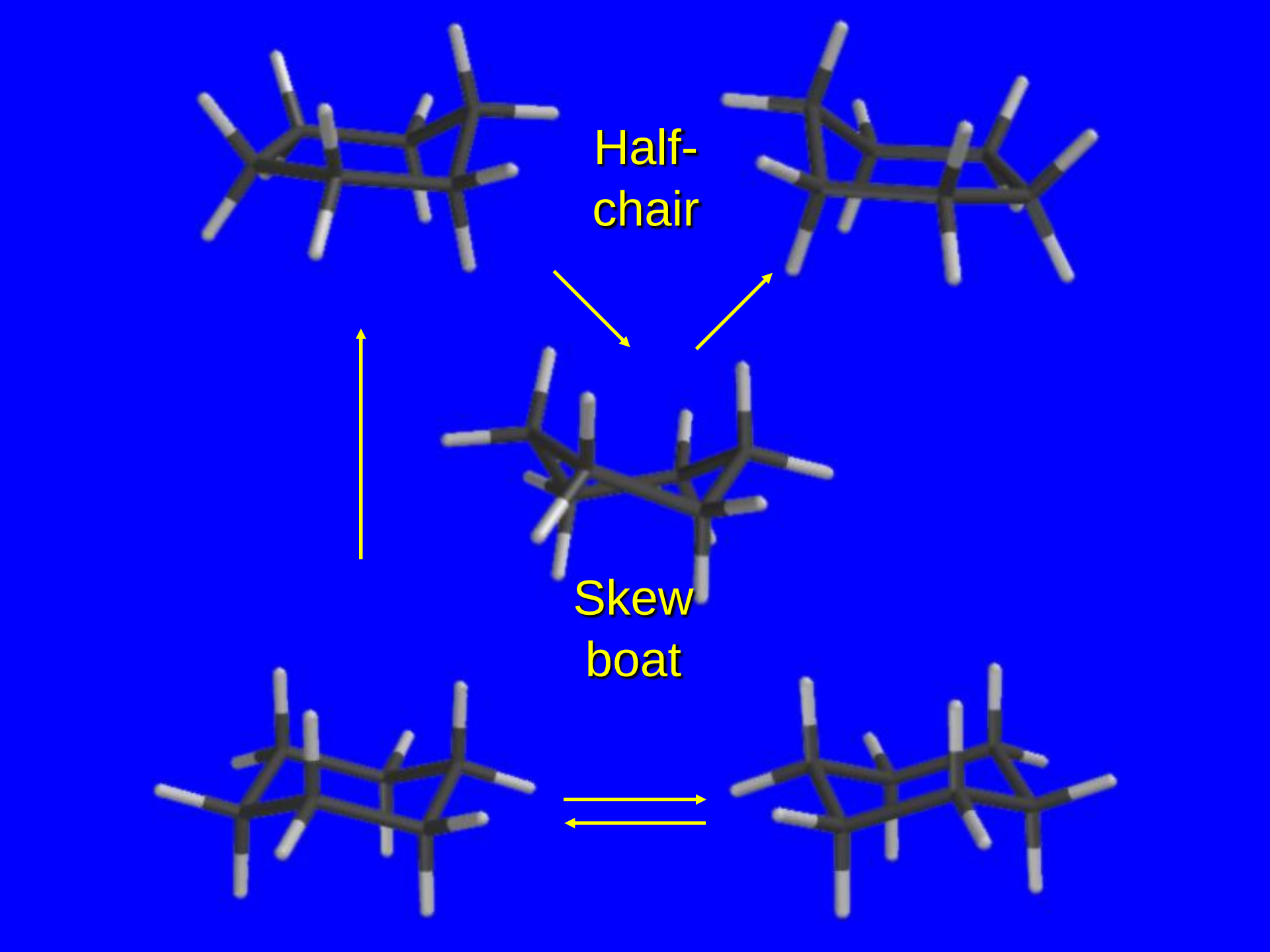
- chair-chair interconversion (ring-flipping)
- rapid process (activation energy = 45 kJ/mol)
- *all axial bonds become equatorial and vice versa*

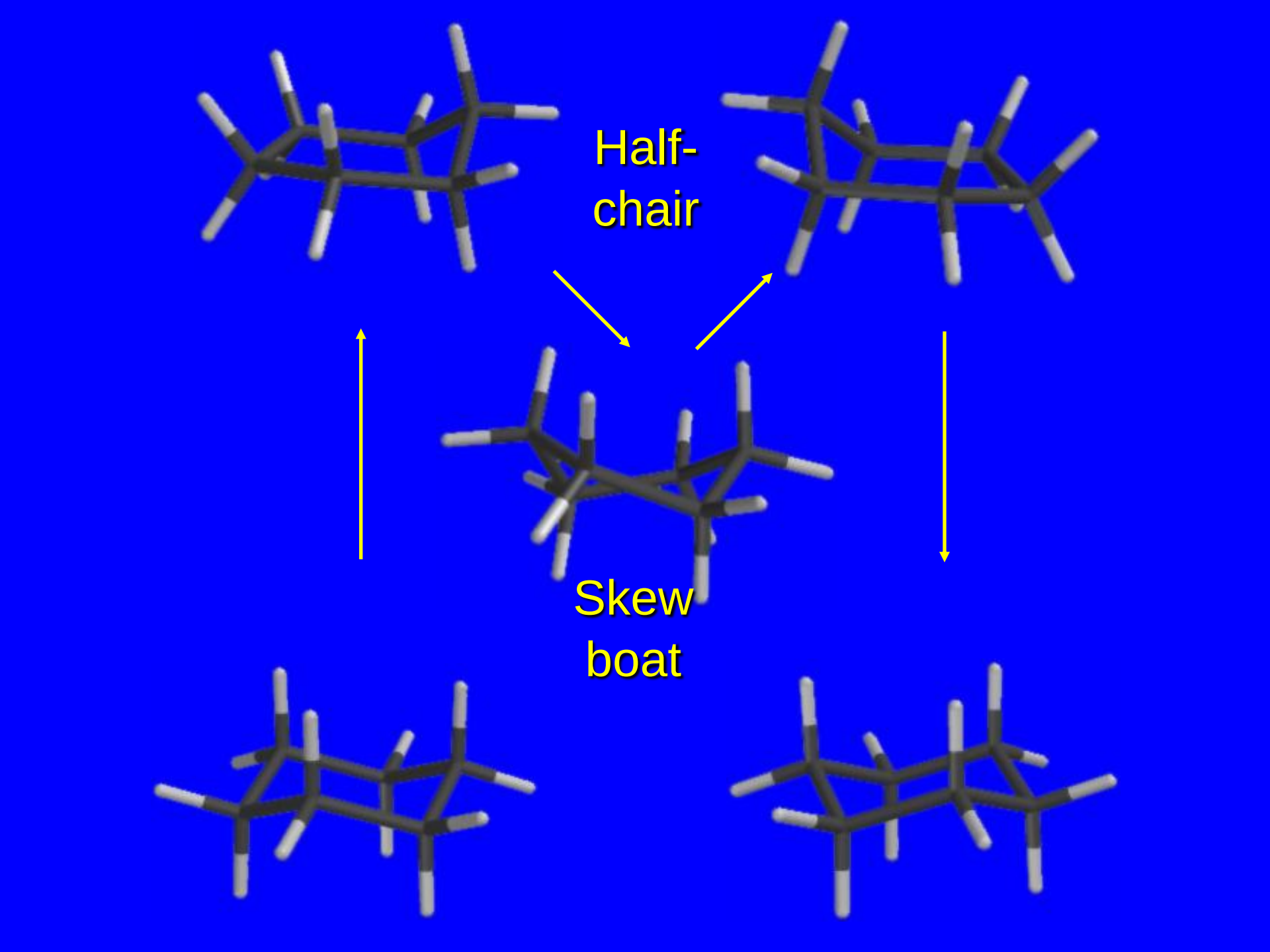


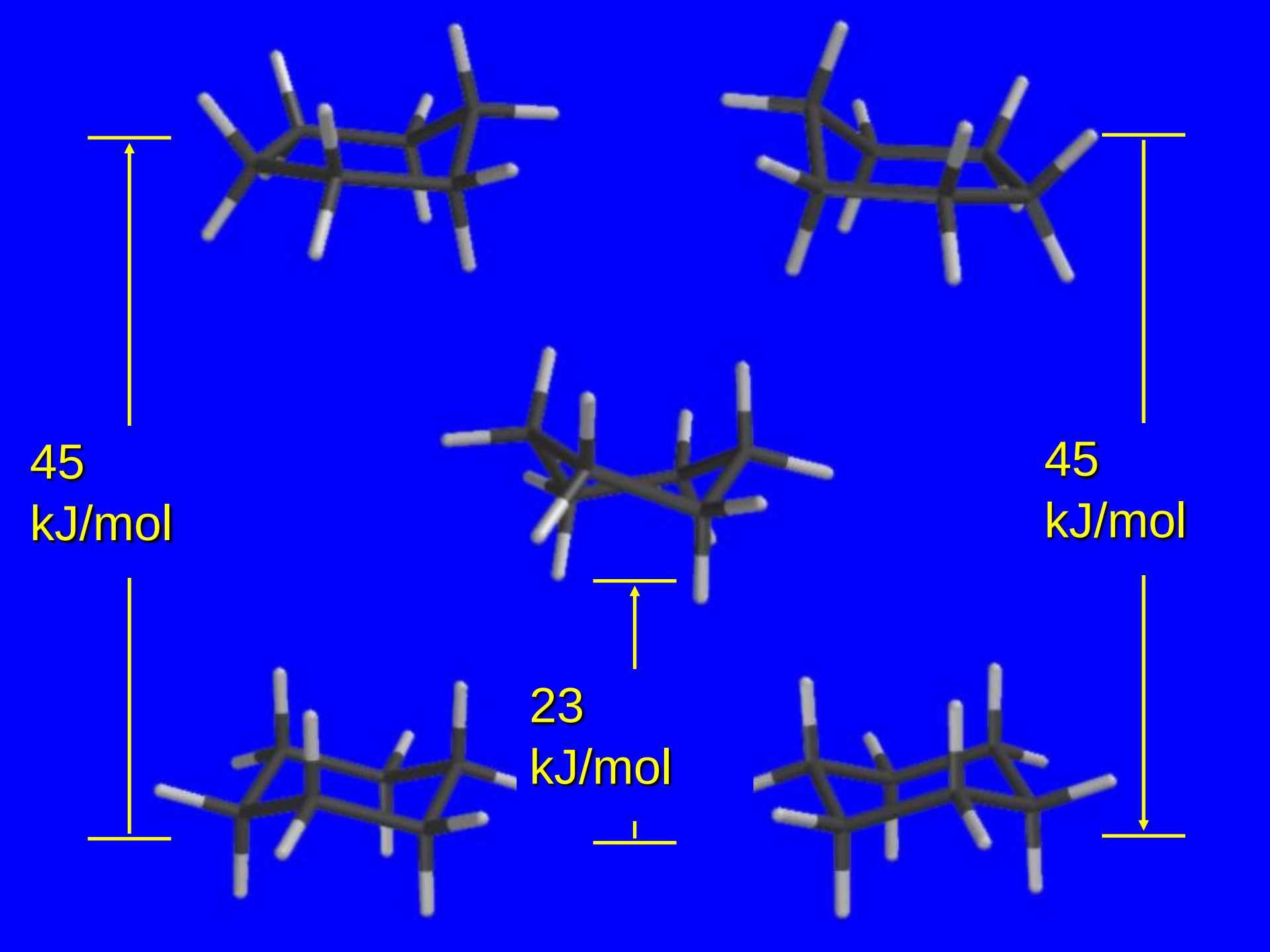
Half-chair



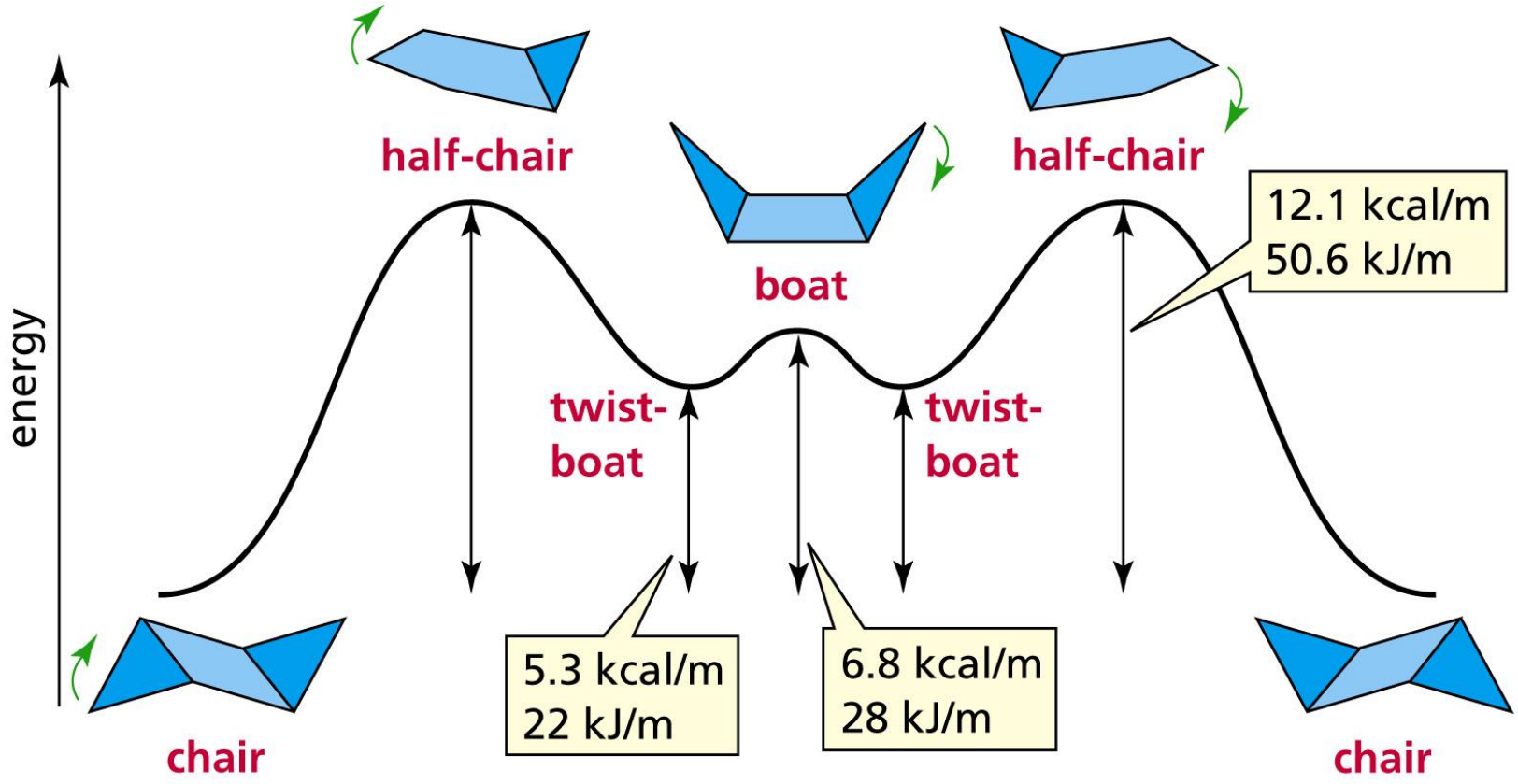

Half-
chair
Skew
boat


Half-
chair
Skew
boat


Half-
chair
Skew
boat


45
kJ/mol
45
kJ/mol
23
kJ/mol

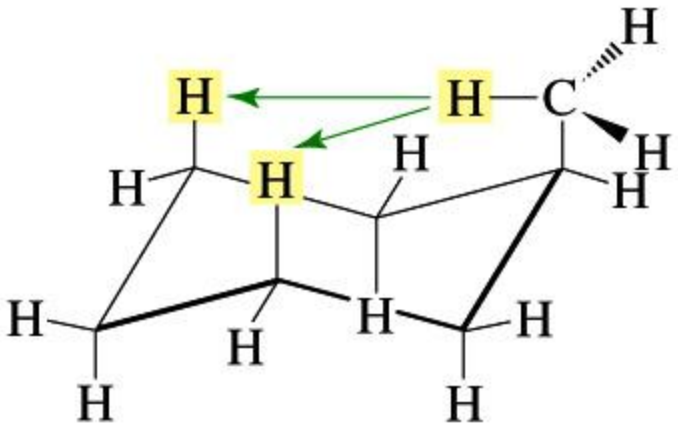
The Conformations of Cyclohexane and Their Energies



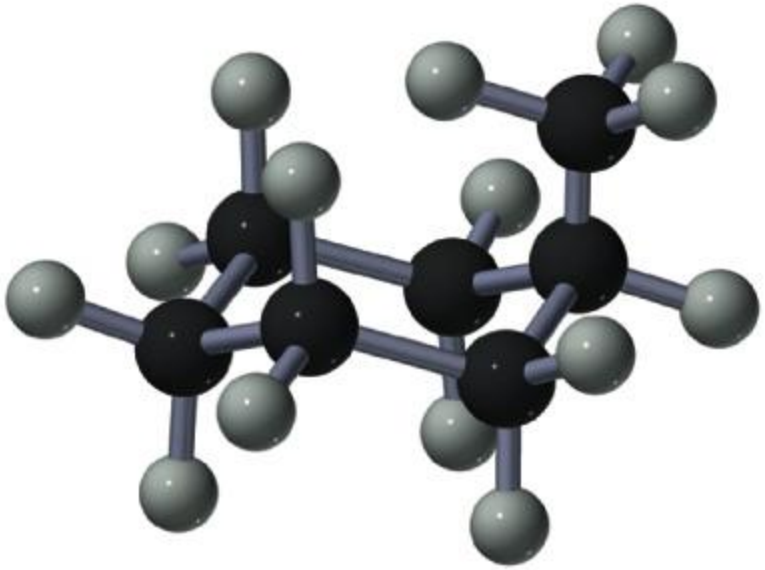
Conformational Analysis of Monosubstituted Cyclohexanes

- most stable conformation is chair
- substituent is more stable when equatorial

Steric Strain of 1,3-Diaxial Interaction in Methylcyclohexane

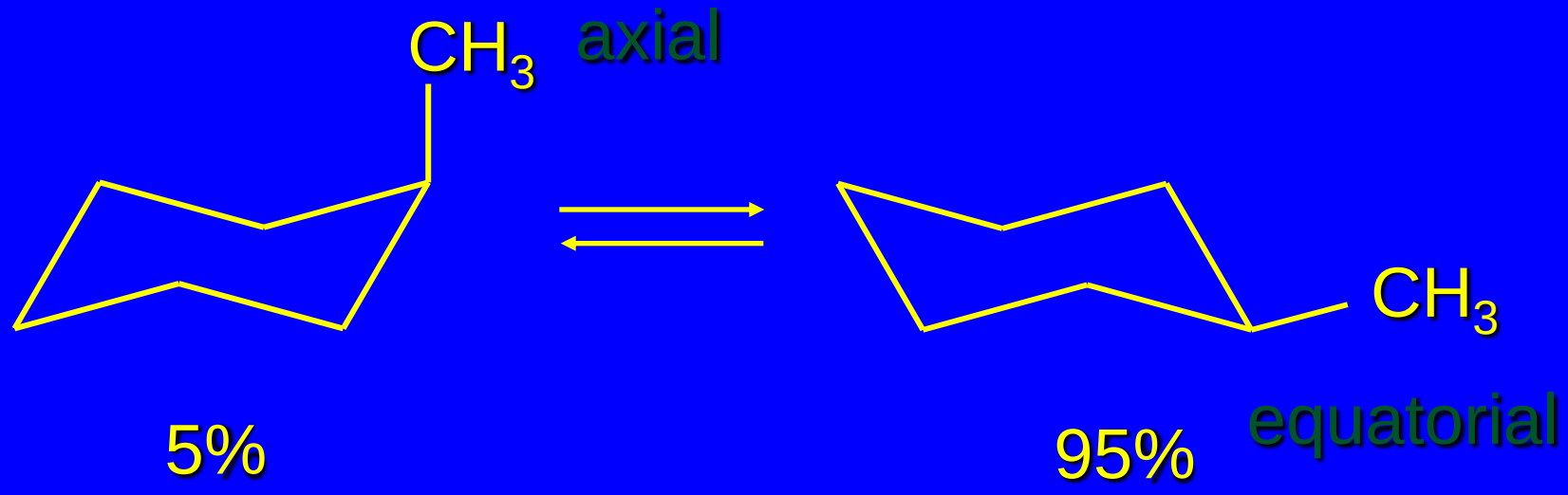


1,3-diaxial interactions



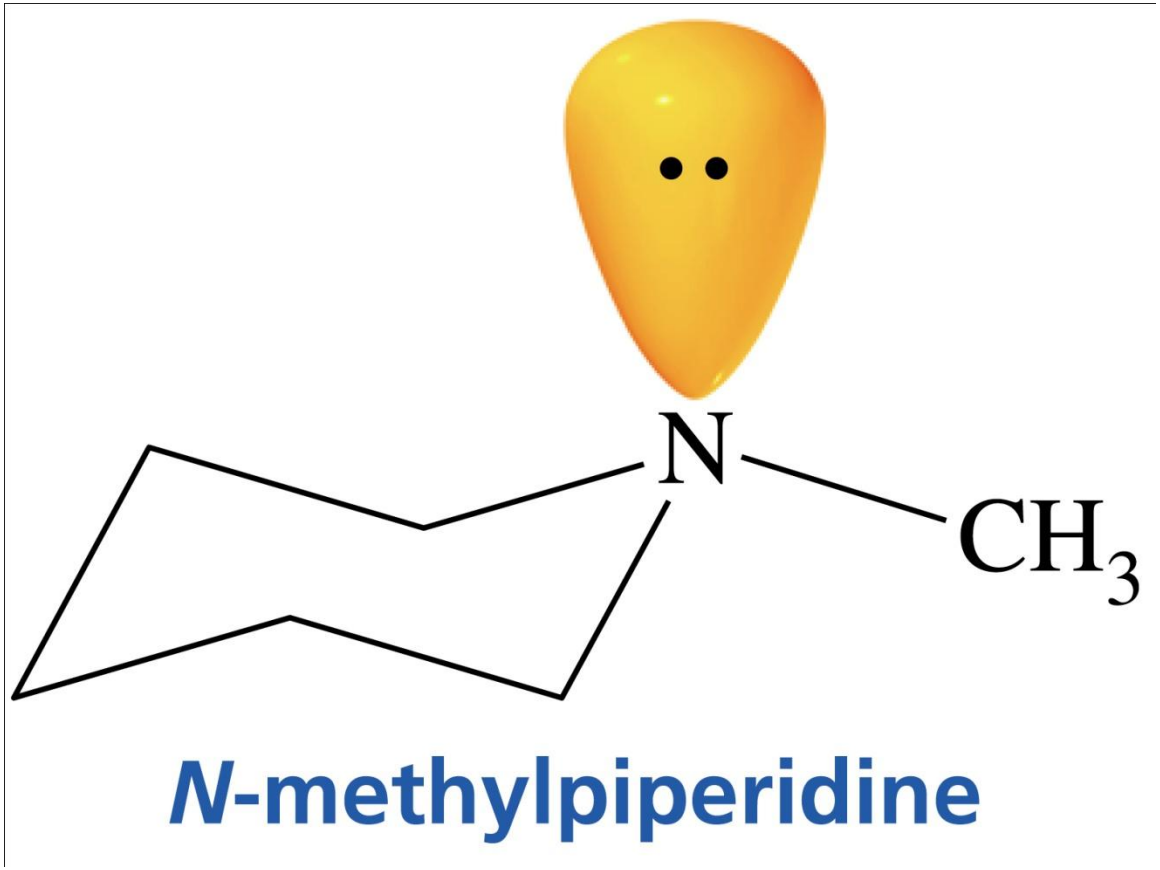
ball-and-stick model

Methylcyclohexane

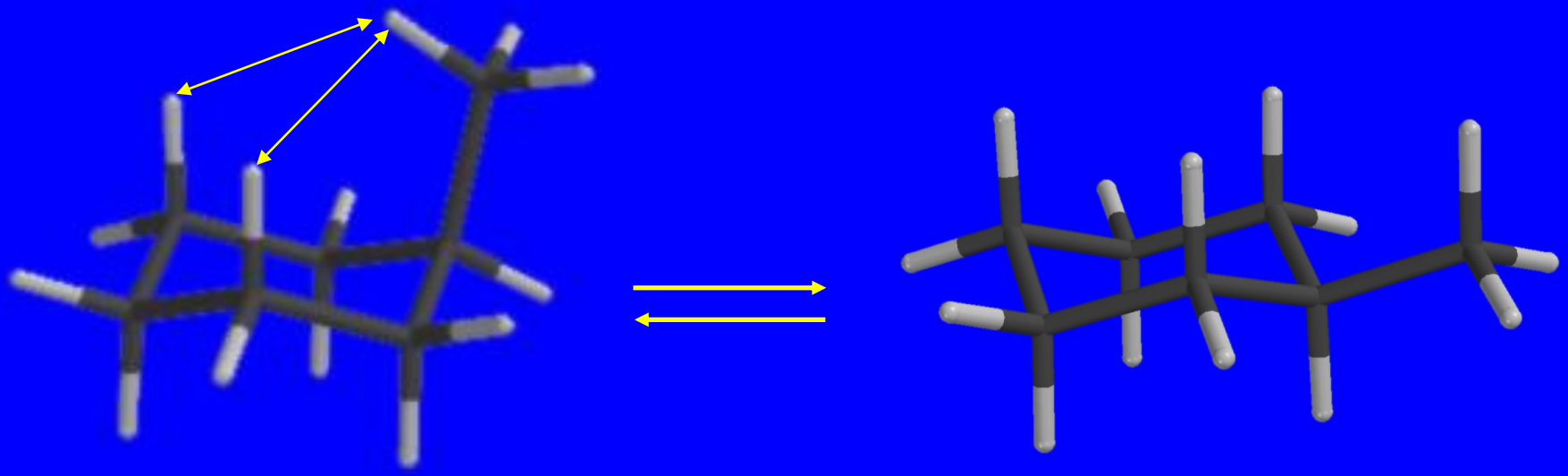


- Chair chair interconversion occurs, but at any instant 95% of the molecules have their methyl group equatorial.
- An axial methyl group is more crowded than an equatorial one.

- Is this the most stable conformer?



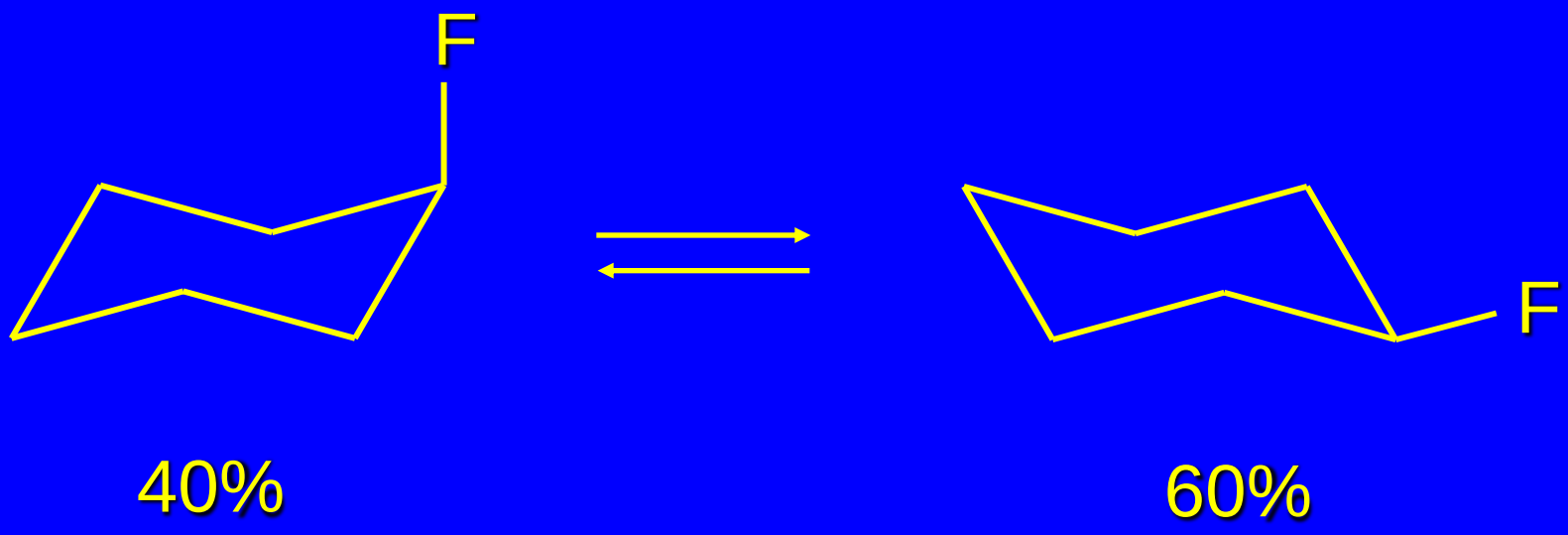
Methylcyclohexane



5% 95%

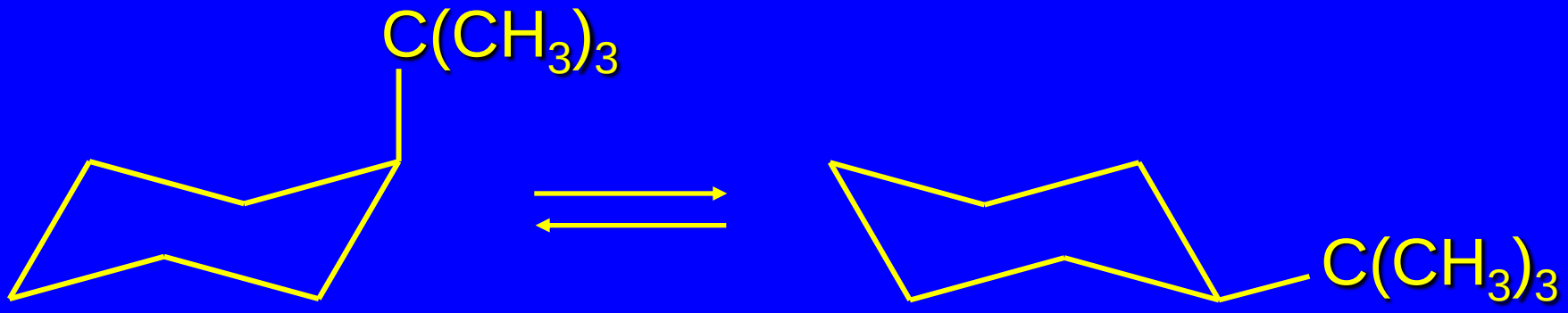
- Hydrogen atoms closer than 2.4 Angstroms will cause steric strain.
- This is called a "1,3-diaxial repulsion" a type of van der Waals strain or Steric strain.

Fluorocyclohexane



- Crowding is less pronounced with a "small" substituent such as fluorine.
- Size of substituent is related to its branching.

tert-Butylcyclohexane



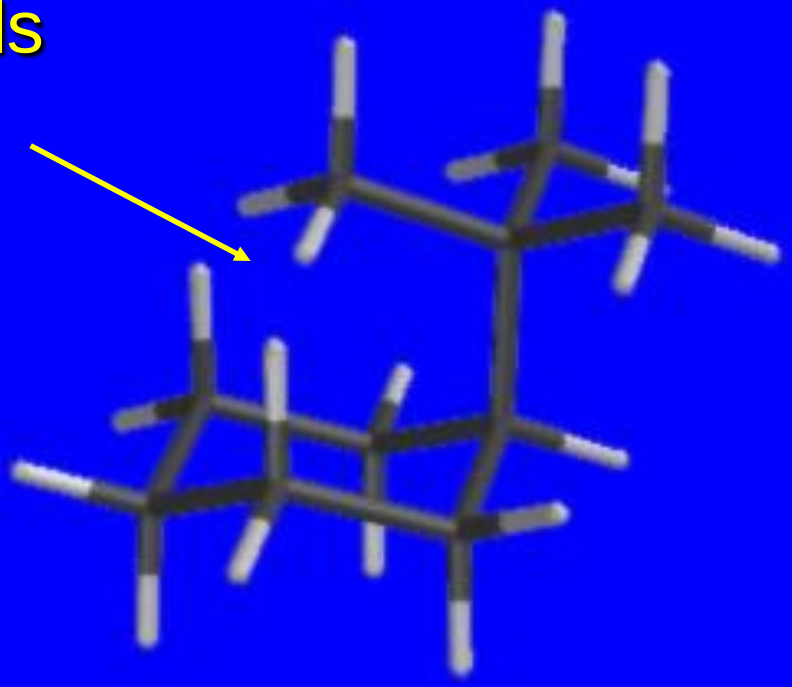
Less than 0.01%

Greater than 99.99%

- Crowding is more pronounced with a "bulky" substituent such as *tert*-butyl.
- *tert*-Butyl is highly branched.

tert-Butylcyclohexane

van der Waals strain due to 1,3-diaxial repulsions



- The larger the substituent on a cyclohexane ring, the more the equatorial substituted conformer will be favored

Table 2.10 Equilibrium Constants for Several Monosubstituted Cyclohexanes at 25 °C

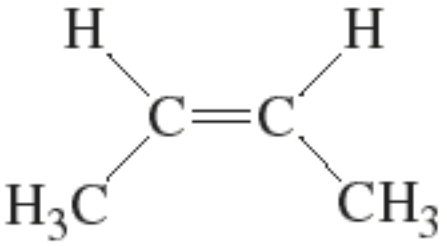
Substituent	Axial $\rightleftharpoons$ Equatorial (K_{eq})	Substituent	Axial $\rightleftharpoons$ Equatorial (K_{eq})
H	1	CN	1.4
CH_3	18	F	1.5
CH_3CH_2	21	Cl	2.4
$CH_3CH(CH_3)$	35	Br	2.2
$CH_3C(CH_3)_2$	4800	I	2.2
		HO	5.4

K_{eq} = [equatorial conformer]/[axial conformer]

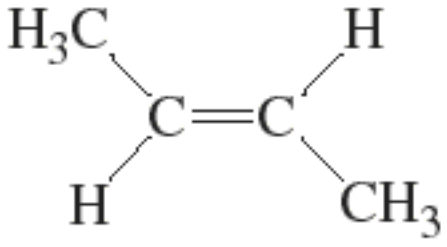
Disubstituted Cyclohexanes Cis-trans Isomerism

Cyclic Alkanes Stereochemistry

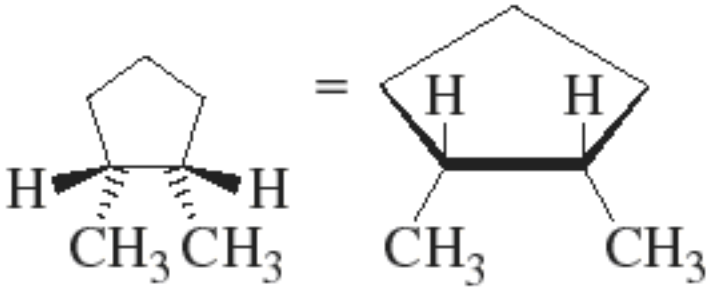
Cis -Trans Isomers



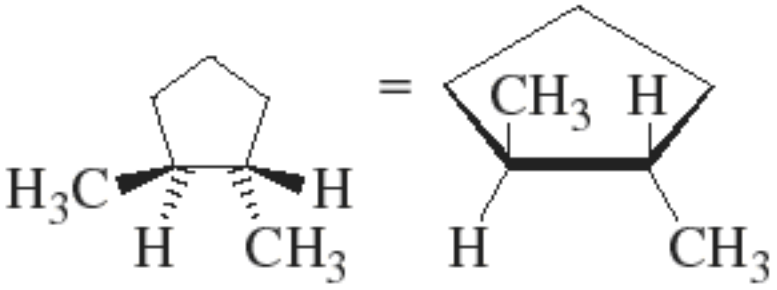
cis-2-butene



trans-2-butene

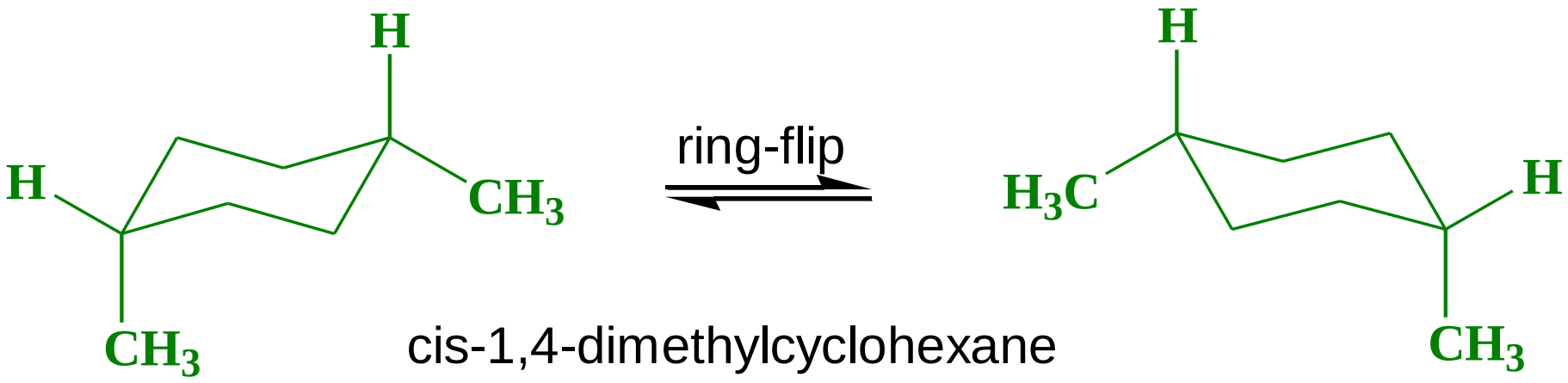


cis-1,2-dimethylcyclopentane



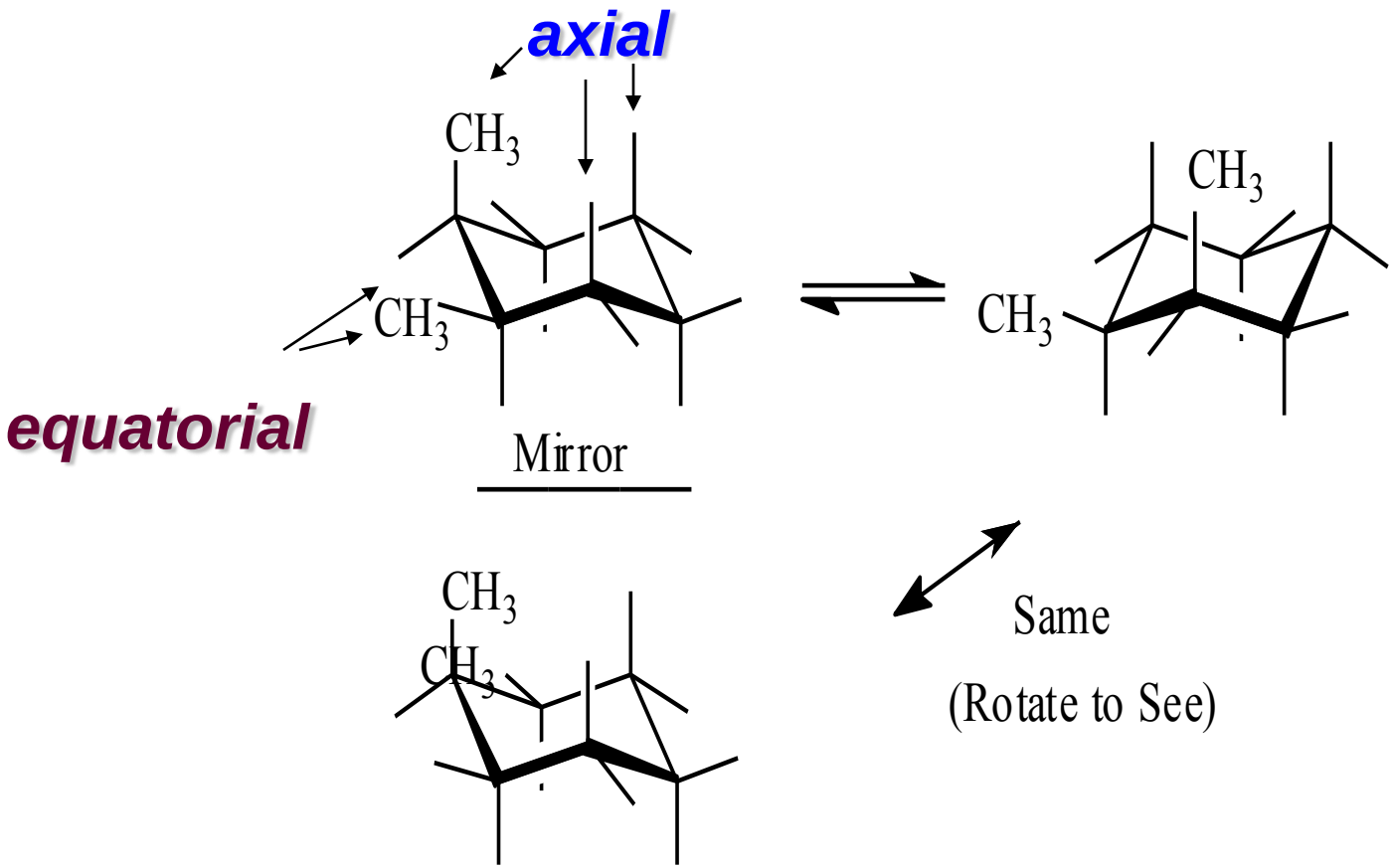
trans-1,2-dimethylcyclopentane

The Chair Conformers of *cis*-1,4-Dimethylcyclohexane



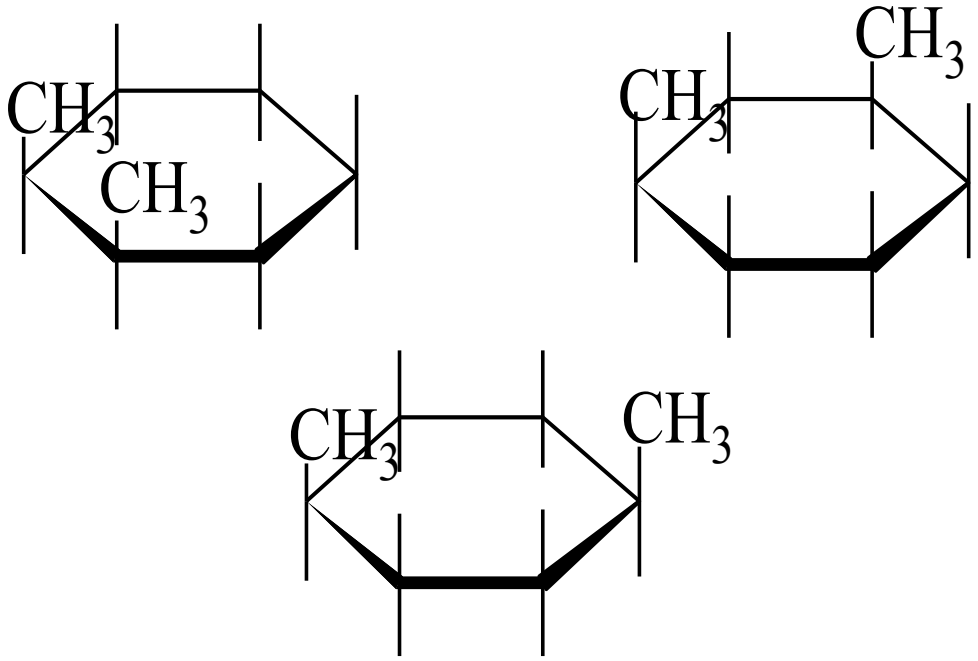
cis-1,4-dimethylcyclohexane

1,2-disubstituted-**cis**-cyclohexane Stereochemistry



Cyclohexane Stereochemistry

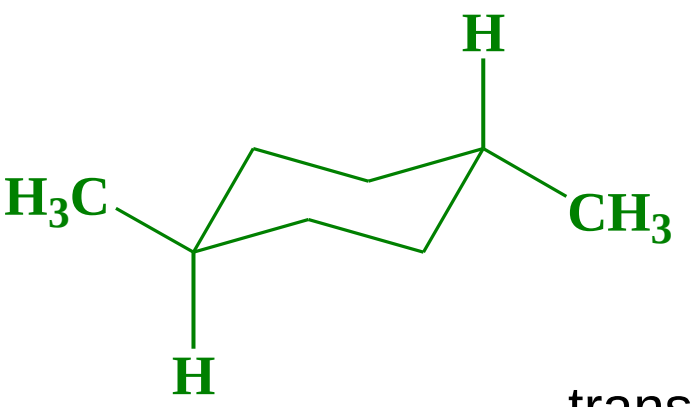
Drawings: Cis isomers & the need for perspective



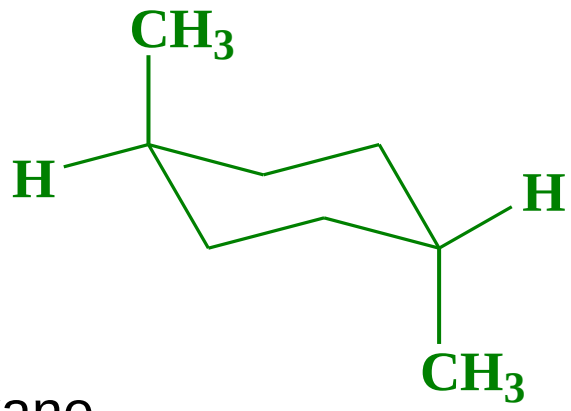
Are the methyl groups axial or equatorial?

What is the actual conformational shape of the cyclohexane ring?

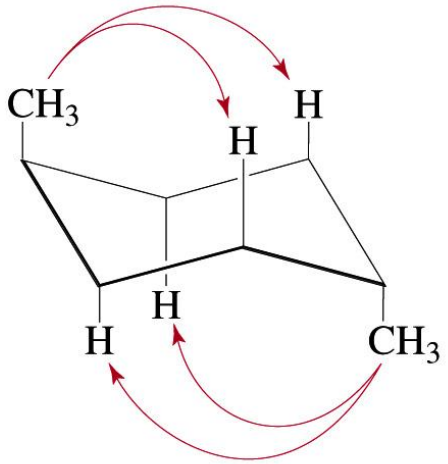
The Chair Conformers of *trans*-1,4-Dimethylcyclohexane



ring-flip



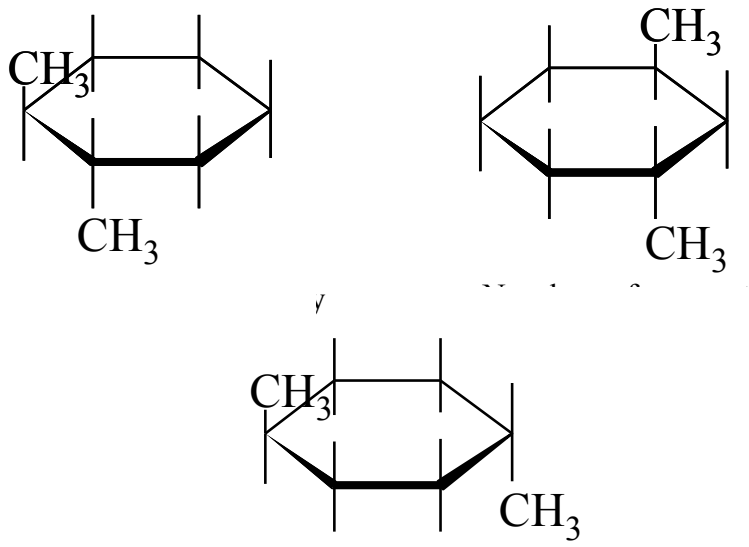
trans-1,4-dimethylcyclohexane



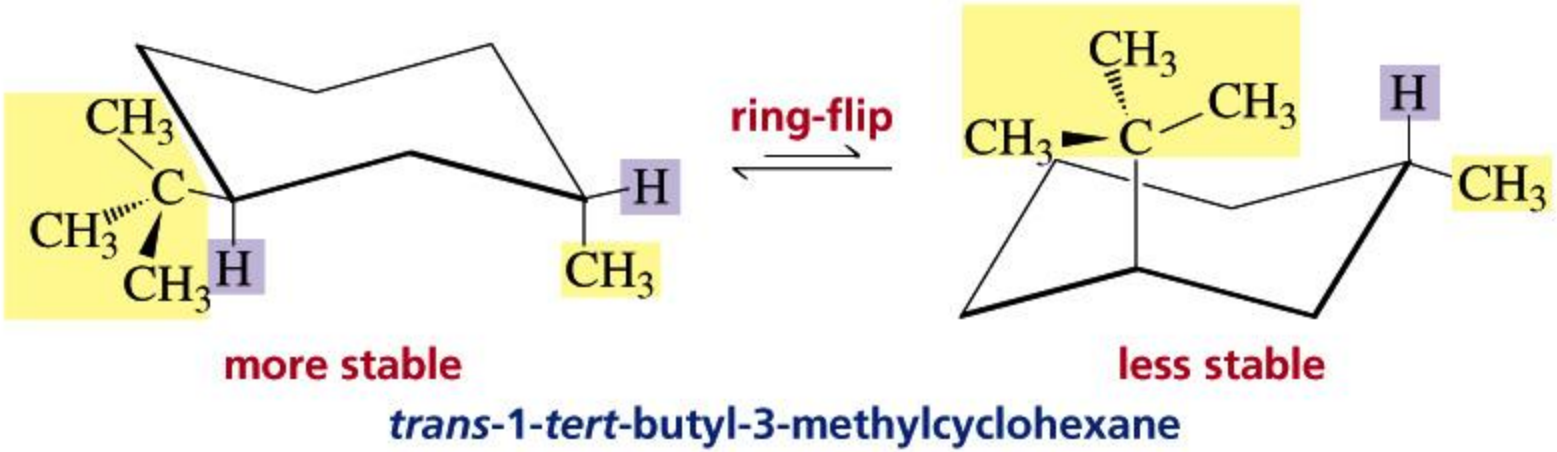
This chair conformer has four 1,3-diaxial interactions.

Cyclohexane Stereochemistry

Trans isomers



1-*tert*-Butyl-3-Methylcyclohexane



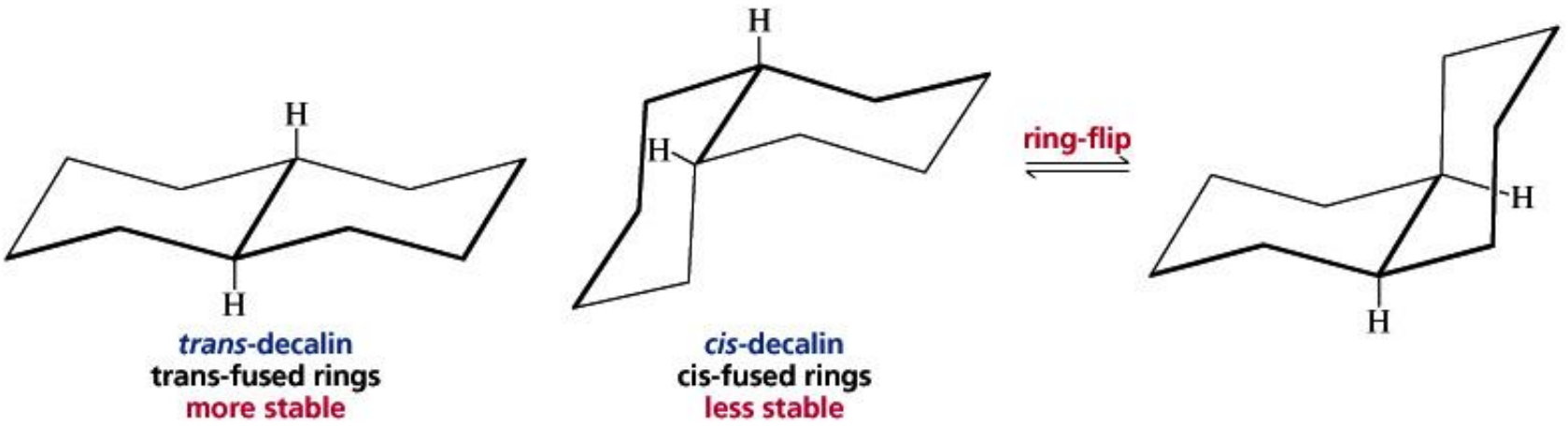
Cyclohexane Stereochemistry

Cis -Trans Isomers

Position	*cis*	*trans*
1,2	*e,a or a,e*	*e,e or a,a*
1,3	*e,e or a,a*	*a,e or e,a*
1,4	*e,a or a,e*	*e,e or a,a*

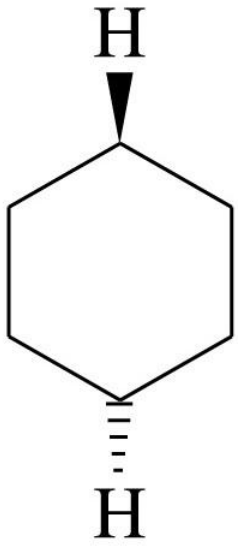
Complete the Table: a = axial; e = equatorial

Conformations of Fused Rings



- Trans-fused cyclohexane ring is more stable than cis-fused cyclohexane ring

trans-decalin



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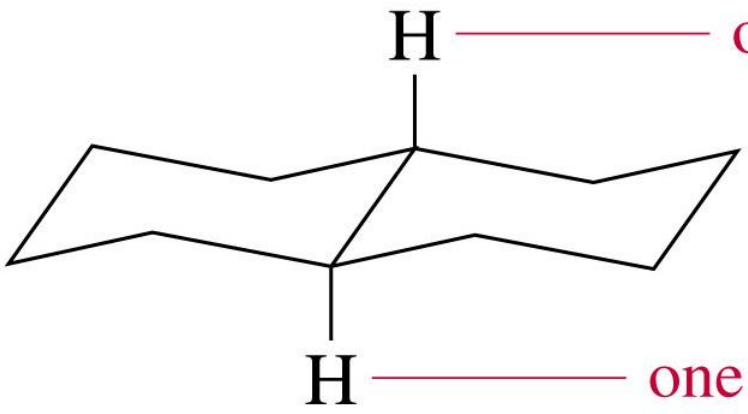
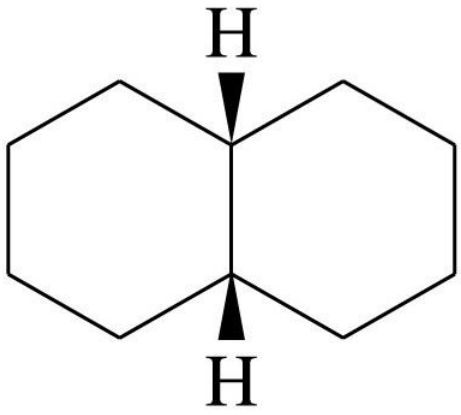


one hydrogen up

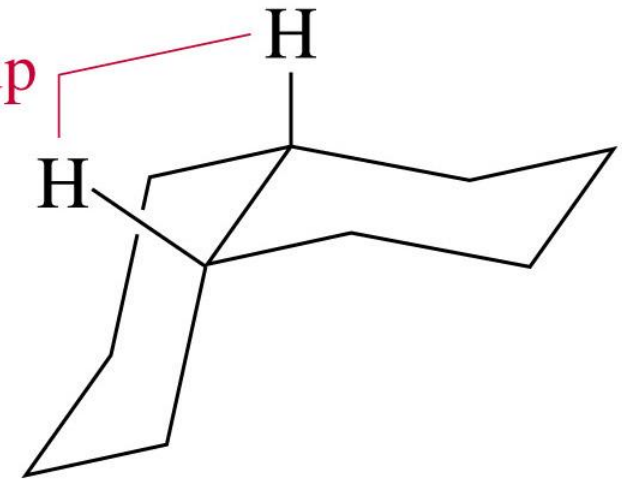
one hydrogen down

cis-decalin

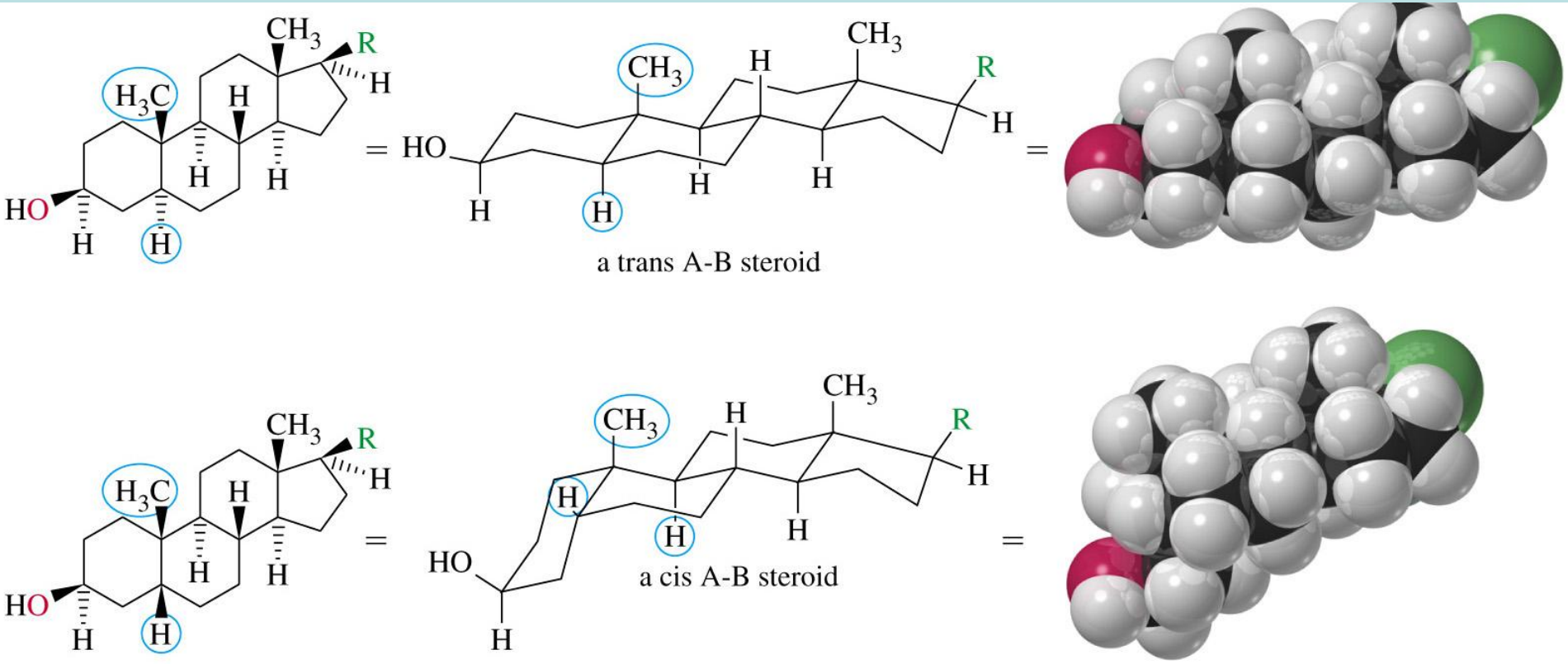


=

both hydrogens up

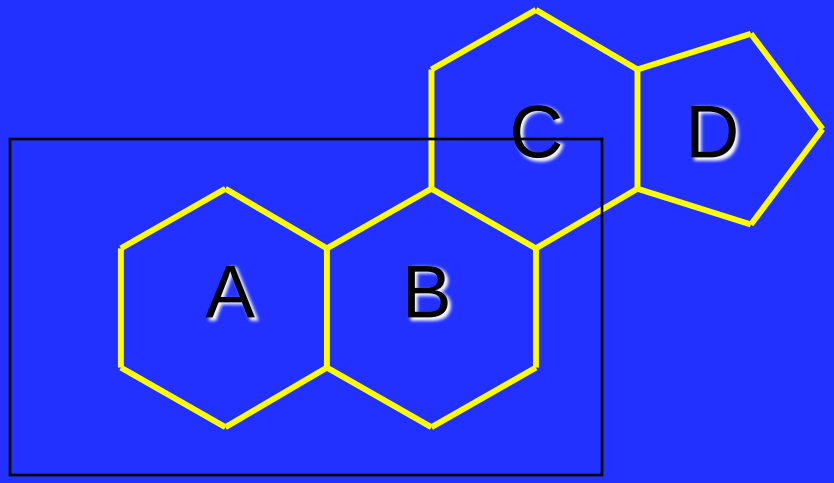


Steroids


CH3
R
H3C
H
HO
H
H
H
H
=
HO
CH3
H
CH3
R
H
H
H
H
H
a trans A-B steroid
=
CH3
R
H3C
H
HO
H
H
H
=
CH3
H
CH3
R
H
H
H
HO
H
a cis A-B steroid
=

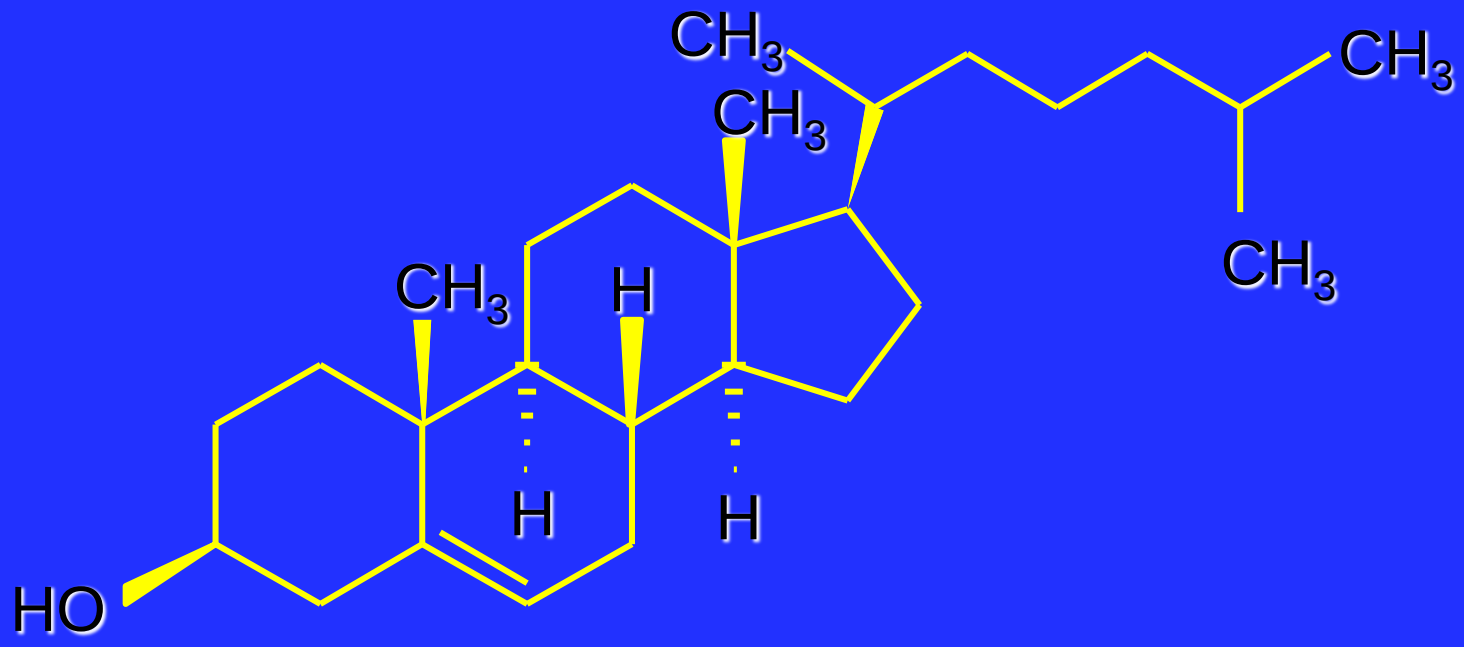
Structure of Steroids

Decalin-like



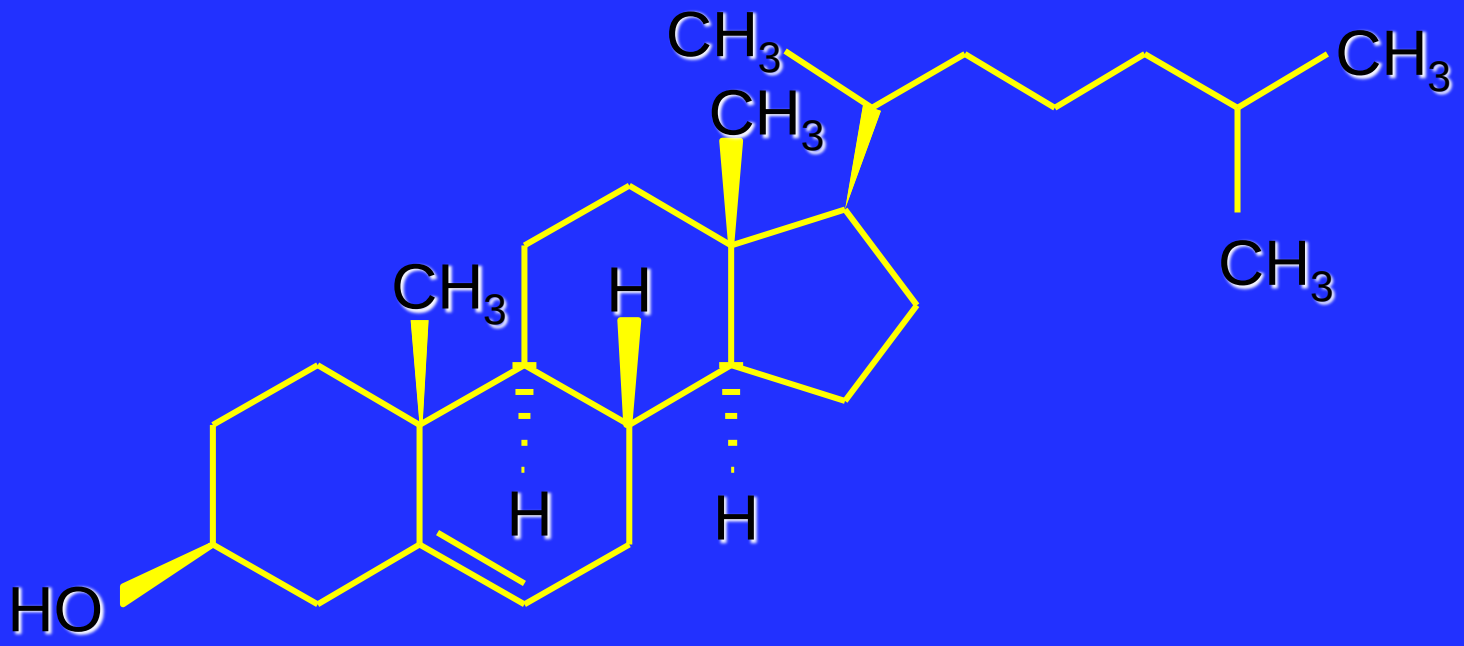
- Fundamental framework of steroids is a tetracyclic carbon framework.
- Cholesterol is an important steroid found in all plants and animals.

Structure of Cholesterol



- What principal function is present?
- Is the A/B ring system cis or trans?

Cholesterol



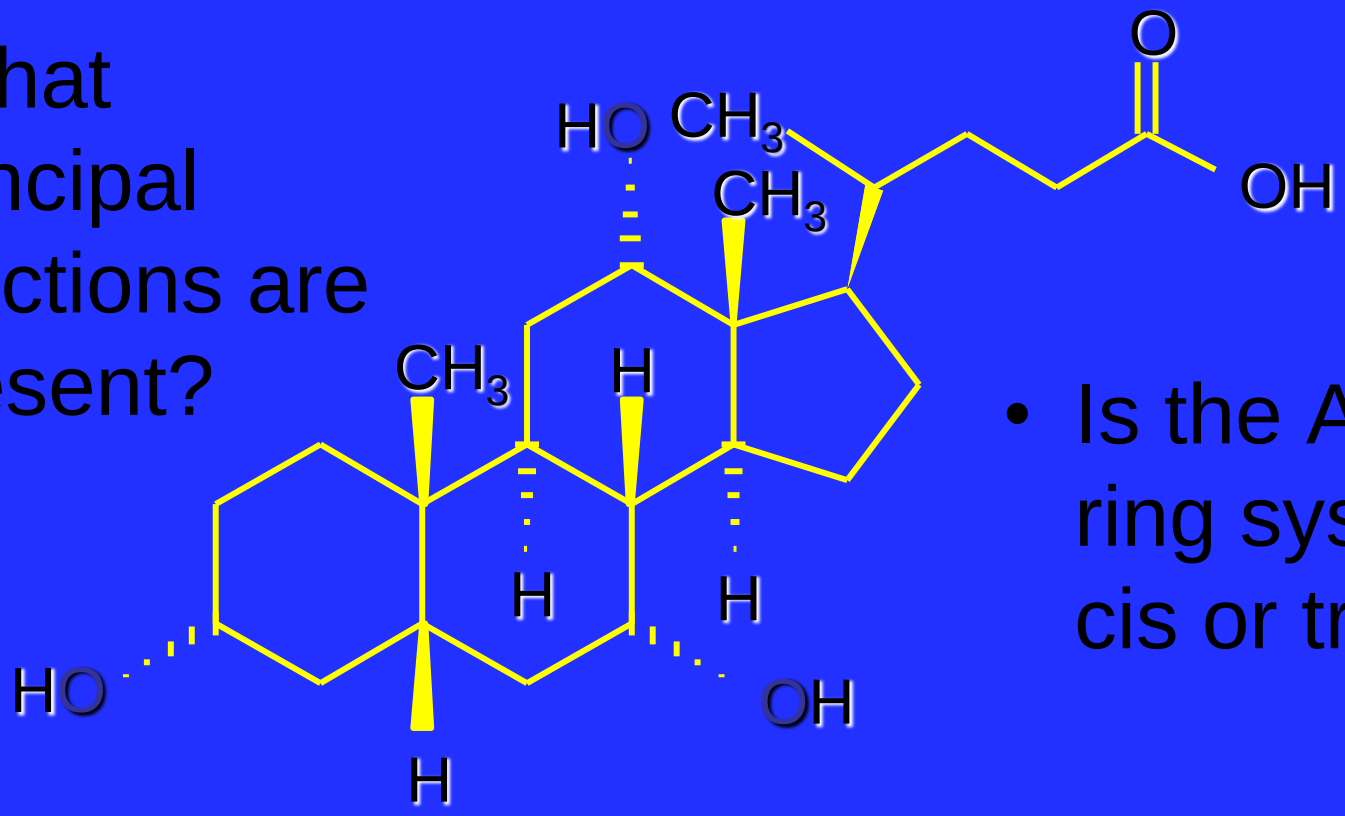
- Cholesterol is essential to life. It is the biosynthetic precursor to a large number of important molecules: Vitamin D Bile acids Corticosteroids Sex hormones

Vitamin D_3

- Insufficient sunlight can lead to a deficiency of vitamin D_3, interfering with Ca^{2+} transport and bone development. Rickets may result; as well as very bad moods.

Cholic Acid

•What principal functions are present?



- Is the A/B ring system cis or trans?

•Oxidation in the liver degrades cholesterol to produce Cholic acid which is the most abundant of the bile acids.

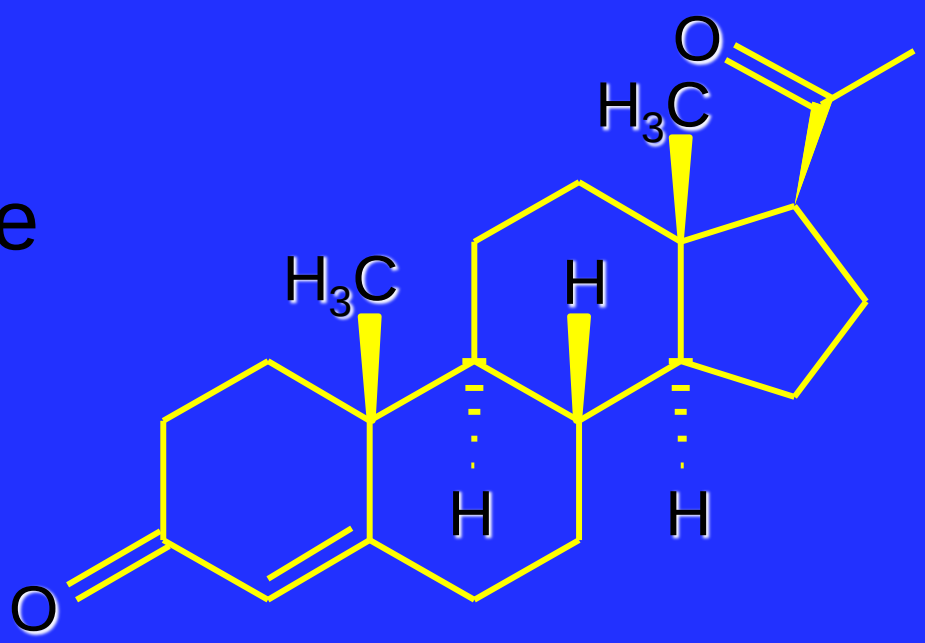
Cortisone

•What principal functions are present?

•Corticosteroids are involved in maintaining electrolyte levels, in the metabolism of carbohydrates, and in mediating allergic reactions by suppressing the immune system..

Progesterone

•What principal functions are present?



- Supresses ovulation during pregnancy.