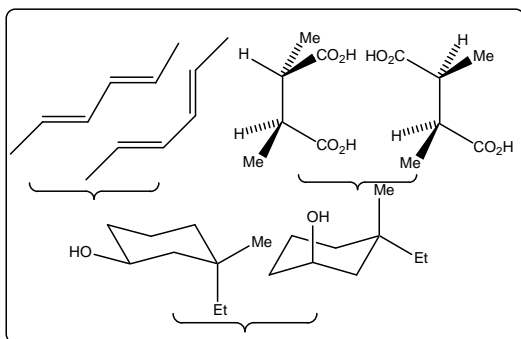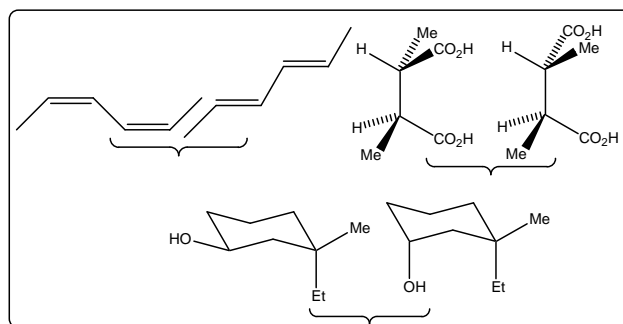# Conformational Analysis

Conformational analysis

• The different arrangements of the atoms in space that result from rotations of groups about single bonds are called *conformations* of the molecule.

• An analysis of the energy changes that a molecule undergoes as groups rotate about single bonds is called *conformational analysis*.
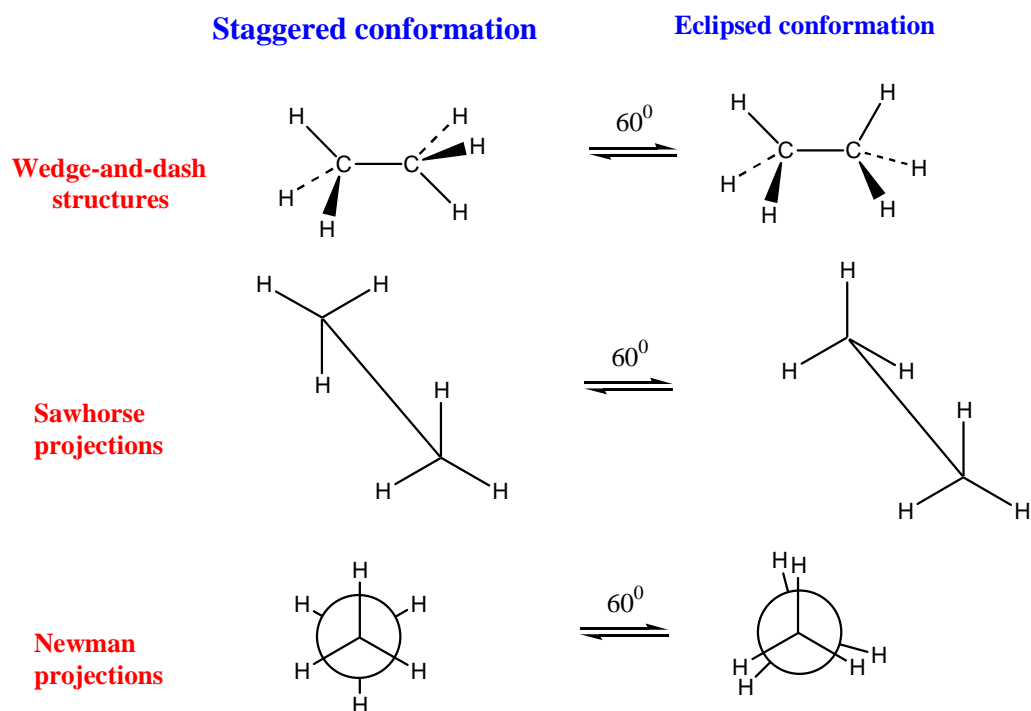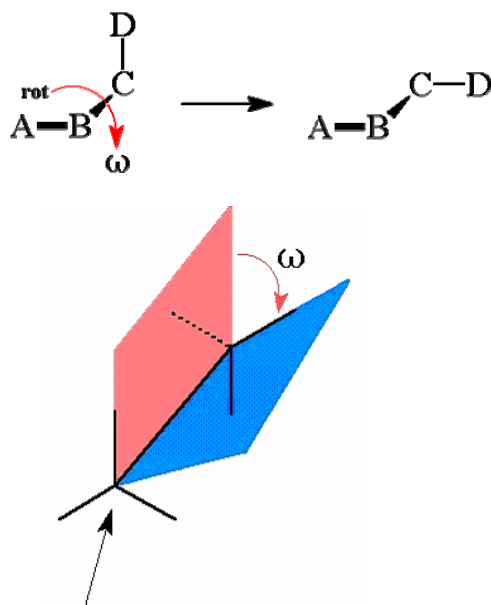

Different conformations

Different configurations

Conformations of ethane

Staggered conformation　　　**Eclipsed conformation**

Wedge-and-dash structures

60^0

Sawhorse projections

60^0

Newman projections

60^0

Torsion or Dihedral angle

The single parameter to differentiate conformers is an angle between two planes that contain atoms ABC and BCD in themselves. This dihedral angle ω is called a "**torsion**" angle and is most frequently used for specification of the type of conformations.

**Potential energy of ethane as function of torsion angles**

Potential energy of ethane as a function of the torsion angle.
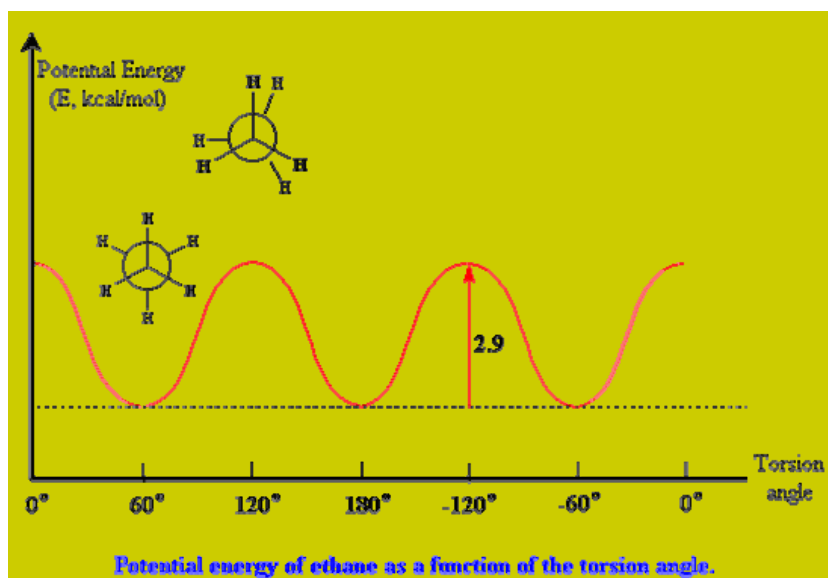
•staggered conformation has potential energy minimum
•eclipsed conformation has potential energy maximum
• staggered conformation is lower in energy than the eclipsed by
  2.9 kcal/mole (12 kJ/mole)

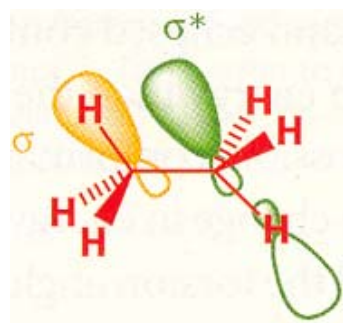**Why is the eclipsed conformation higher in energy than the staggered conformation?**

•The H-atoms are too small to get in each other's way-steric factors make up < 10% of the rotational barrier in ethane

Torsional strain

Caused by repulsion of the bonding electrons of one substituent with the bonding electrons of a nearby substituent
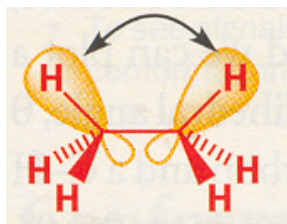

filled orbitals repel

- Stabilizing interaction between filled C-H σ bond and empty C-H σ^* antibonding bonding orbital

**The real picture is probably a mixture of all 3 effects**

- **The rotational barrier is (12 kJ/mol) small enough to allow the conformational isomers to interconvert million of times per second**
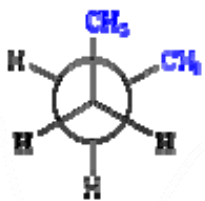
Conformations of butane

Potential energy of butane as a function of the torsion angle.
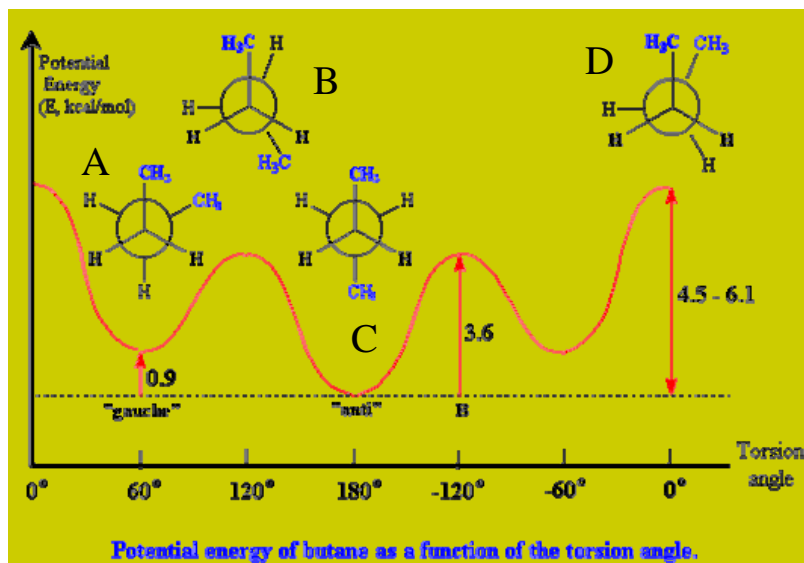
Potential energy of butane as a function of torsion angle

A ➜ "synclinal" or "gauche"
B ➜ "anticlinal"
C ➜ "anti-periplanar" or "anti"
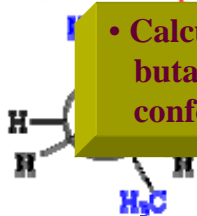D ➜ "syn-periplanar" or "fully eclipsed
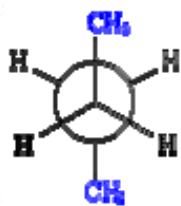
C ➔ "anti-periplanar" or "anti"

No torsional strain as the groups are staggered and CH_3 groups are far away from each other

A ➔ "synclinal" or "gauche"

van der Waals forces between two CH_3 groups are repulsive: the electron clouds repel each other which accounts for 0.9 Kcal/mole more energy compared to anti conformer

• **Calculations reveal that at room temperature ~72% of the molecules of butane are in the "anti" conformation, 28% are in "gauche" conformation**
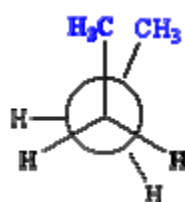
D ➔ "syn-periplanar" or "fully eclipsed"

Highest energy due to torsional strain and large van der waals repulsive force between the CH_3 groups


Conformations and Conformers

Butane can exit in an infinite number of **conformations** (6 most important have been considered), but has only 3 **conformers** (potential energy minima)-the two "gauche"conformations and the "anti" conformations

• **The preference for a staggered conformation causes carbon chains to orient themselves in a *zig zag* fashion, see structure of decane**
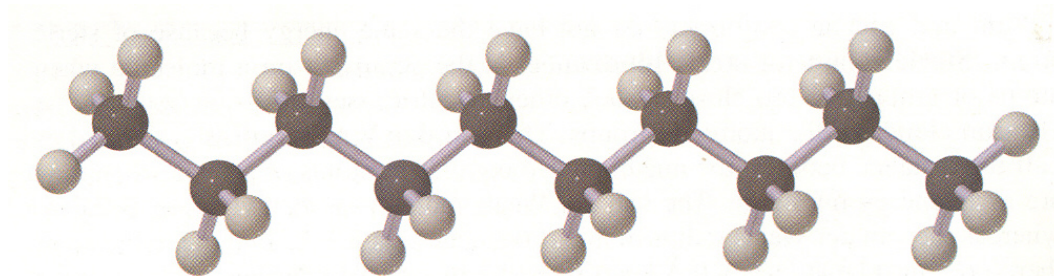
Cycloalkanes
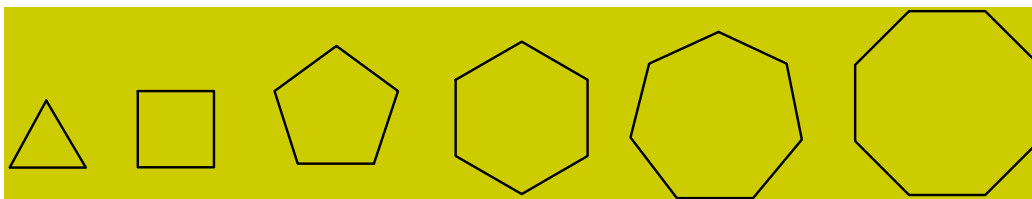
Is the energy per CH_2 is same in this series?

Is the energy per CH_2 is same in the straight chain alkanes?

$$CH_3\text{-}(CH_2)_n\text{-}CH_3$$

Does the value of n has an effect on combustion energy per CH_2?

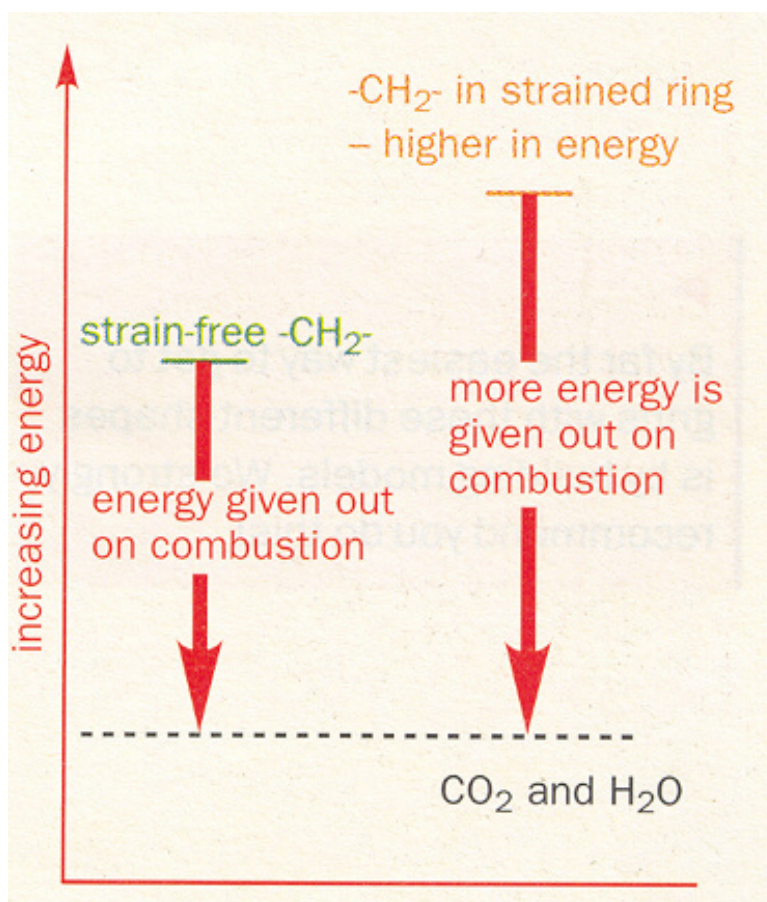## Heats of combustion for straight chain alkanes of formula $CH_3(CH_2)_nCH_3$

Straight chain alkanes	n	-ΔHcombustion kJ mol^{-1}	Difference kJ mol^{-1}
ethane	0	1560	-------
propane	1	2220	660
butane	2	2877	657
pentane	3	3536	659
hexane	4	4194	658
heptane	5	4853	659
octane	6	5511	658
nonane	7	6171	660
decane	8	6829	658
undecane	9	7487	658
dodecane	10	8148	661

• the difference between any two in series very nearly constant at around –660 kJ/mole (energy per CH_2)
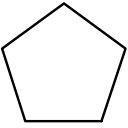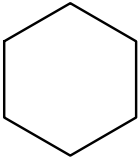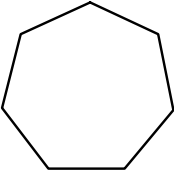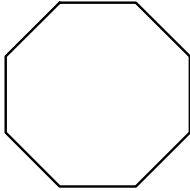
Therefore in cycloalkanes heat of combustion should be n X 658.7 kJ/mole.

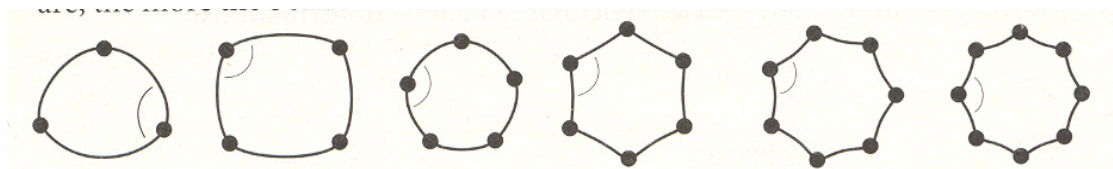**If there is some strain, more energy should given out on combustion**

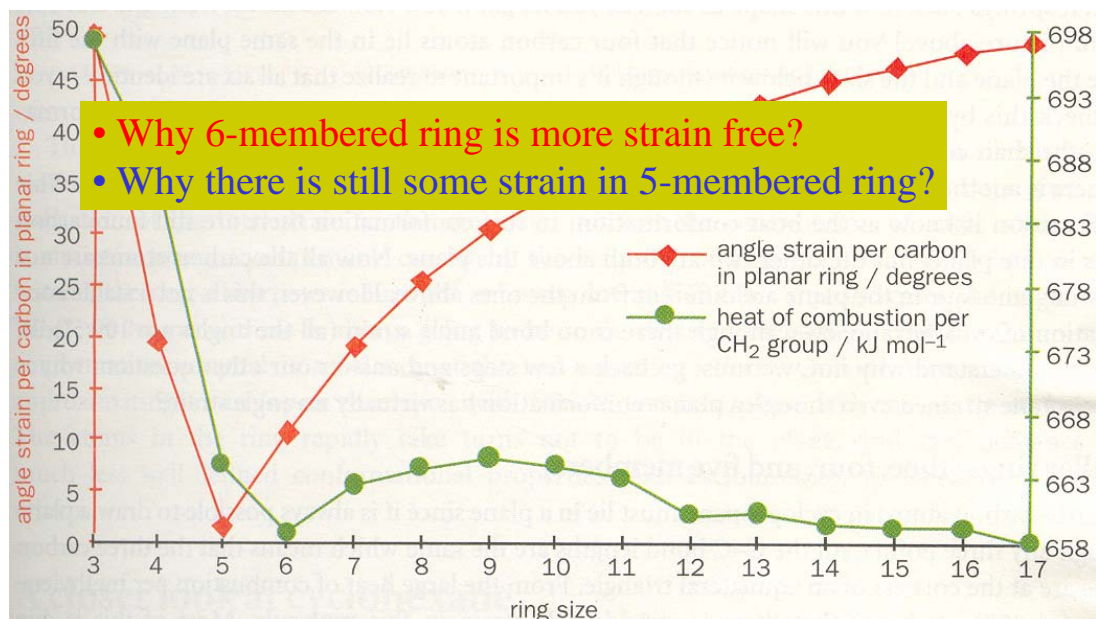-CH$_2$- in strained ring – higher in energy

strain-free -CH$_2$-

more energy is given out on combustion

energy given out on combustion

increasing energy

CO$_2$ and H$_2$O

Cycloalkanes:

Ring strain

ce per CH$_2$ 697	686	664	659	662.4	663.8 kJ mol^{-1}
Ideal angles 60°	90°	108°	120°	128.5°	135°
Deviation* 49.5° from 109.5°	19.5°	1.5°	-10.5°	-19°	-25.5°

* a measure of strain per C-atom

All internal angles 109.5 ^{0}

• Why 6-membered ring is more strain free?
• Why there is still some strain in 5-membered ring?

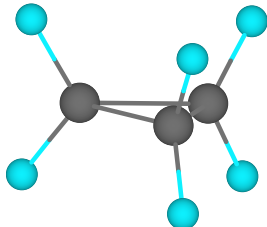- **strain and ce are more in the 3-membered ring.**
- **strain decreases with ring size and reaches a minimum for 5-membered ring.**
- **ce decreases with ring size and reaches minimum for 6-membered ring**
- **The ce increases, but not as quickly as the angle calculation suggested: it reaches a maximum at 9 and then decreases.**
- **ce remain constant from ~14, not increases steadily as the angle-strain suggests.**
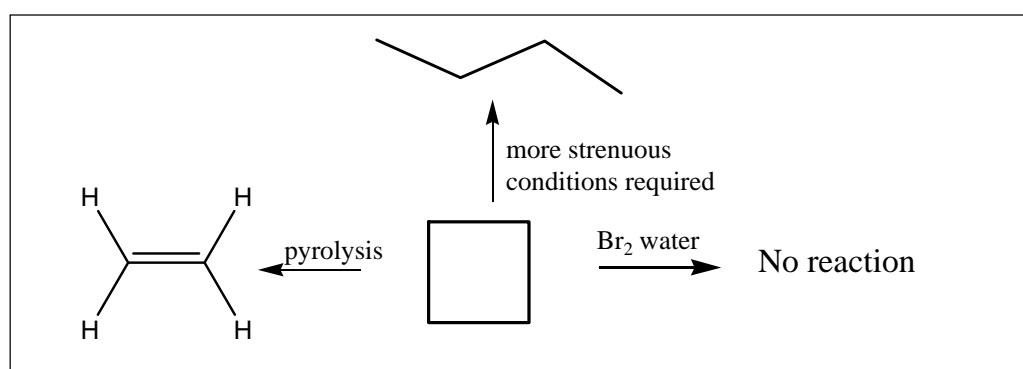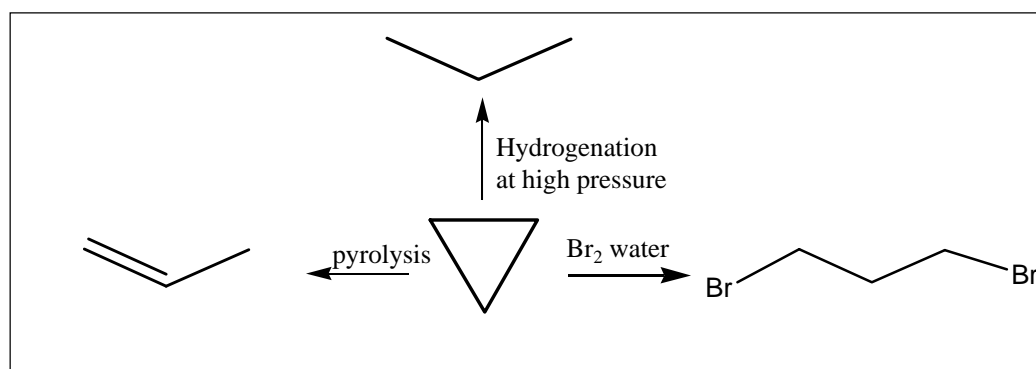
Cyclic compounds twist and bend to minimize the 3 different kinds of strain
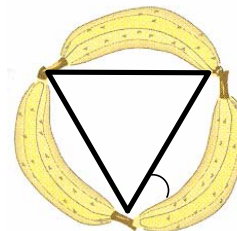**1. Angle strain   2. Torsional strain   3. Steric strain**

Cyclopropane

• banana bonds
poor orbital overlap

HCH 115°

Electron density diverts away
from the ring by 21°

•Torsional strain

For sp^3: 25% s & 75% p charector
Here the four hybrid orbitals of C are far from
equivalent

Good overlap
Strong bond

External orbitals: 33% S & 67% p ➔ sp^2
Internal orbitals: 17% S & 83% p ➔ sp^5
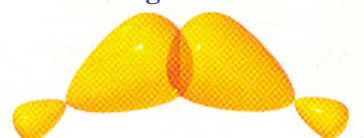
Poor overlap
Weak bond
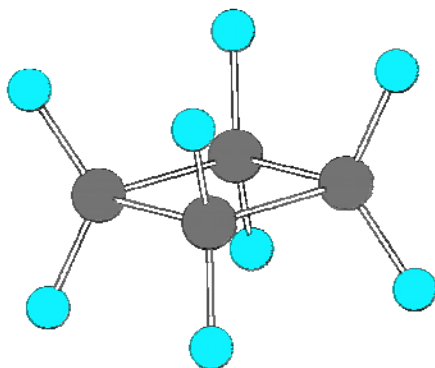
Cyclobutane

to reduce torsional angle

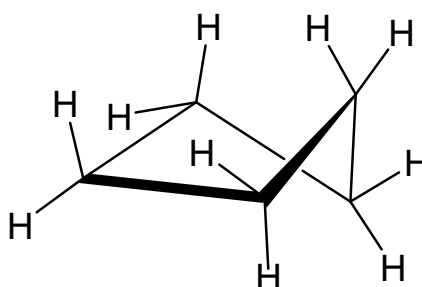**Cyclobutane**
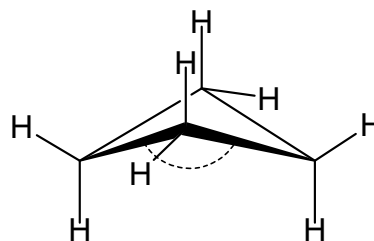
Interplanar angle 35°
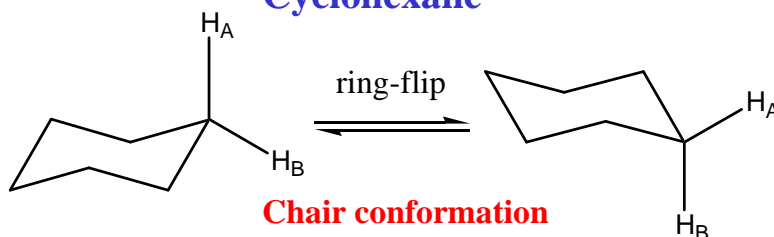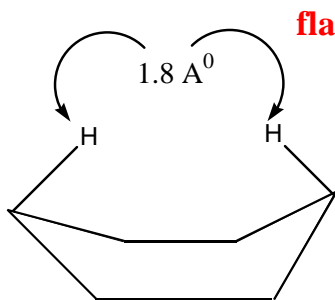
Cyclopentane
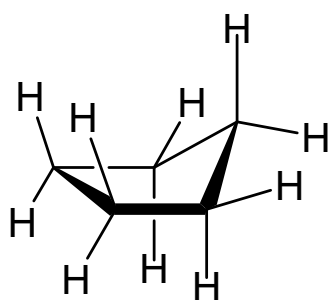
Envelope

Half chair

The energy difference is little

- one carbon atom is bent upwards
- The molecule is flexible and shifts conformation constantly
- Hence each of the carbons assume the pivotal position in rapid succession .
- The additional bond angle strain in this structure is more than compensated by the reduction in eclipsed hydrogens.
- With little torsional strain and angle strain, cyclopentane is as stable as cyclohexane.
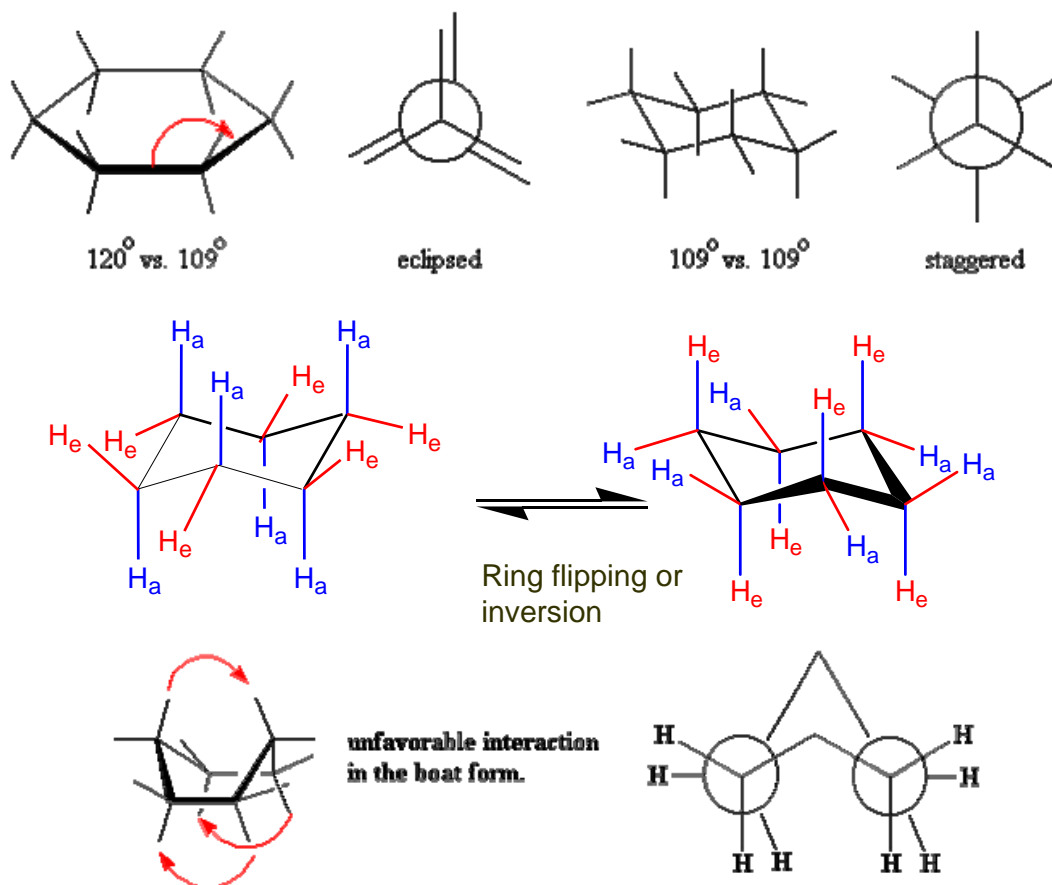
Cyclohexane

H_A

ring-flip

H_B

H_A

H_B

Chair conformation

flagpole h

$1.8 \ A^0$

H   H

Boat conformation

Su

boat conformation

120° vs. 109°   eclipsed   109° vs. 109°   staggered

H_a H_a H_e H_e H_e
H_e H_e H_e H_a H_e
H_e H_a H_a H_a H_a
H_e H_a H_e H_a
H_a H_a H_e H_e

Ring flipping or inversion

unfavorable interaction in the boat form.

H   H
H   H
H H   H H

Interconversions of Cyclohexane

Chair   Half Chair   Twist boat   boat

Erel=0.0 kcal/mol   Erel=10   Erel=5.5   Erel=6.5

Twist boat   Half Chair   Opposite sense Chair
Opposite sense

Planar Erel= very large >20 kcal/mol
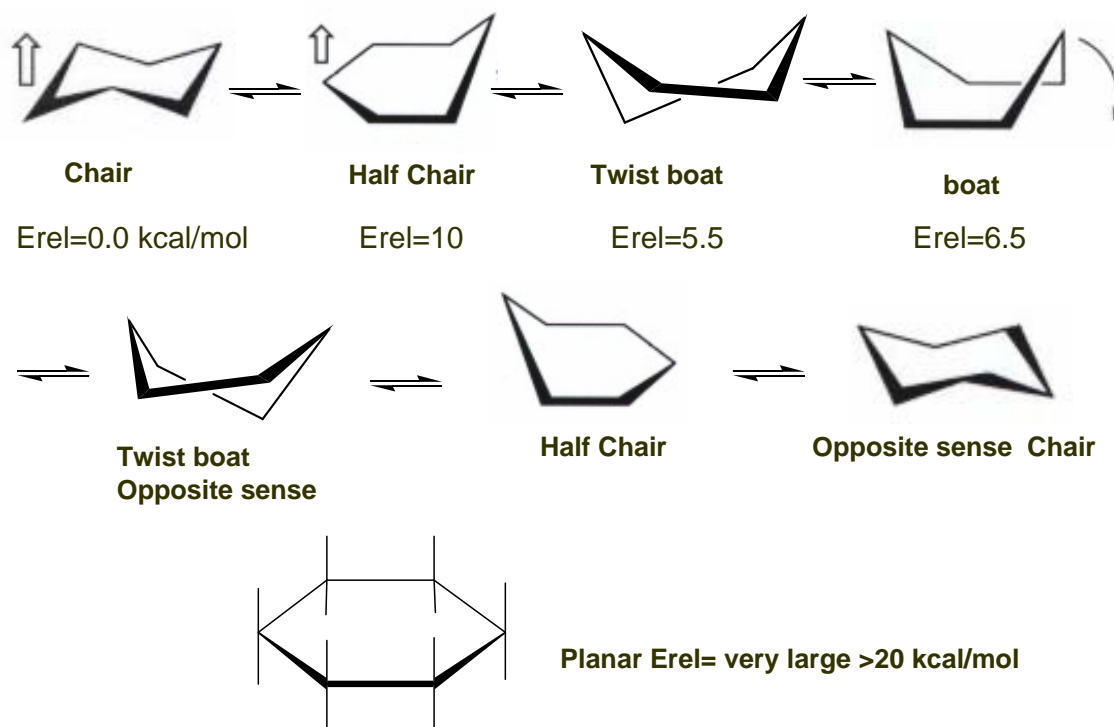
Cyclohexane energy profile for cyclohexane ring reversal

ΔH

Half chair

ΔH
10.7-11.5
(44.8 - 48.1)

boat

1-1.15
(4.2-6.3)

Twist boat

5.3 (22.2)

Half chair

4.7-6.2
(19.7-26.0)

chair   chair
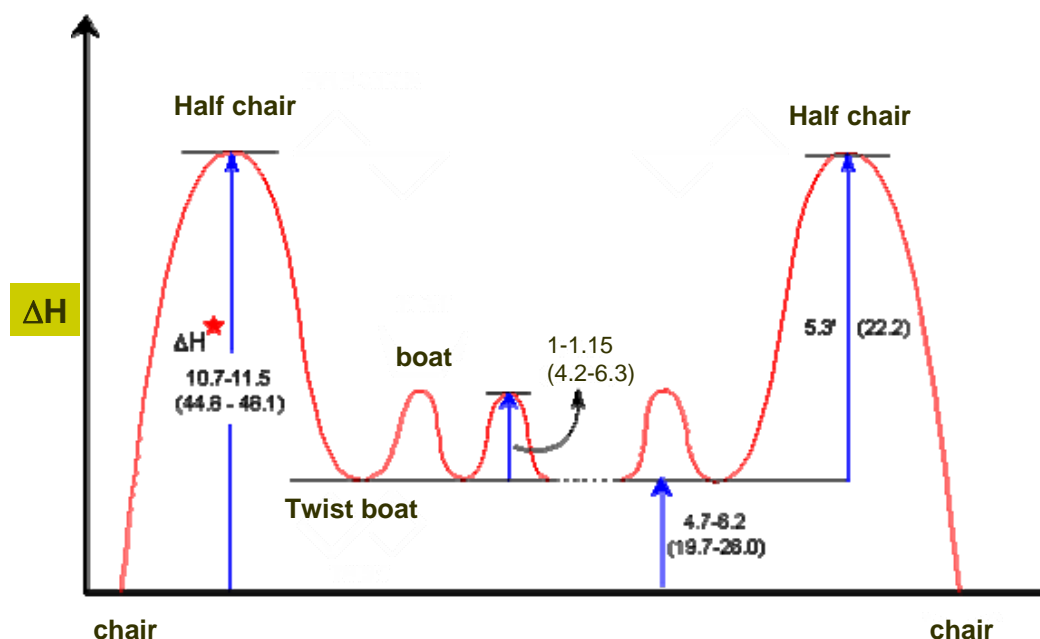
- **The energy difference between the chair, boat, and twist conformation of cyclohexane are low enough to make their separation impossible at r.t. At room temperature approx. 1 million inter-conversions occur in each second.**
- **More than 99% of the molecules are estimated to be in chair conformation at any given time**

Monosubstituted cyclohexane
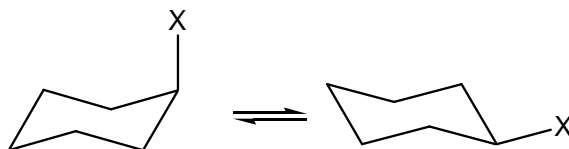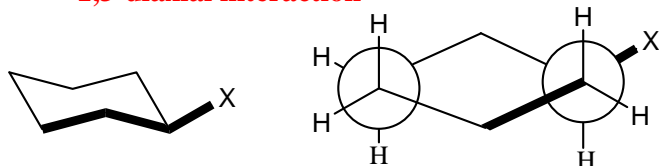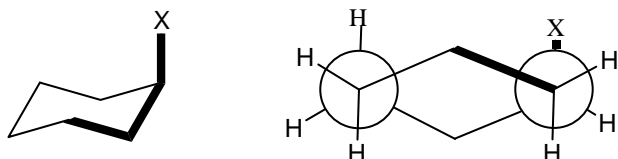

This conformation is lower in energy

Why?
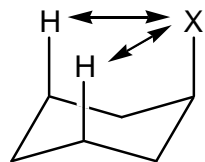
When X=CH$_3$, conformer with Me in axial is higher in energy by 7.3 kJ/mol than the corresponding equatorial conformer.
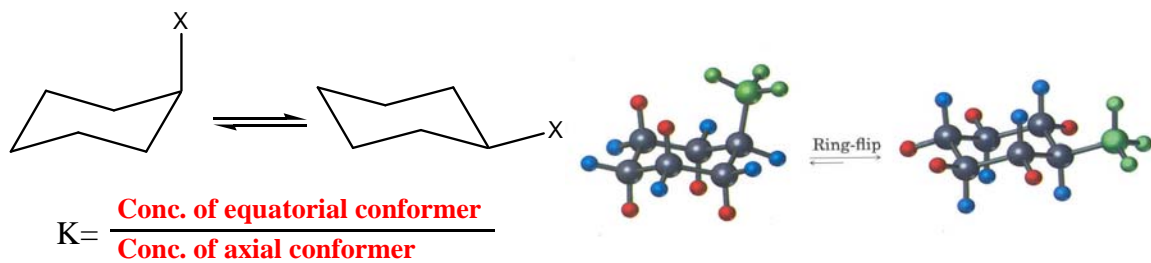**Result: 20:1 ratio of equatorial:axial conformer at 20^0 C**

1,3-diaxial interaction

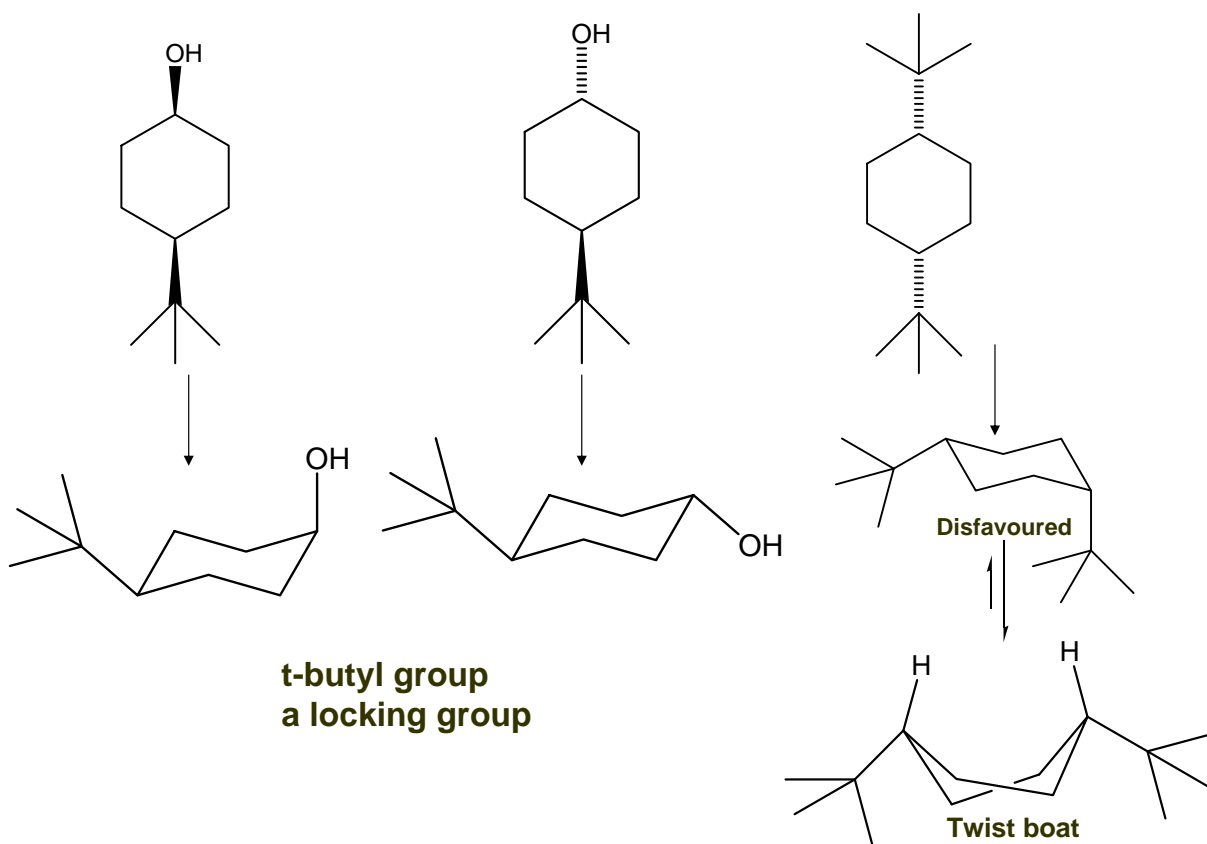

The black bonds are anti-periplanar
(only one pair shown)

The black bonds are synclinal (gauche)
(only one pair shown)

$$K= \frac{\text{Conc. of equatorial conformer}}{\text{Conc. of axial conformer}}$$

X	Equilibrium constant	Energy diff. between axial and equatorial conformers kJ/mol	% with substitutent equatorial
H	1	0	50
Me	19	7.3	95
Et	20	7.5	95
i-Pr	42	9.3	98
t-Bu	>3000	>20	>99
OMe	2.7	2.5	73
Ph	110	11.7	99

Preferred Conformations
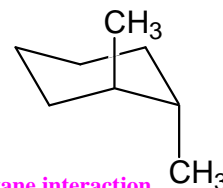

t-butyl group
a locking group

Disfavoured

Twist boat

Write preferred conformation for
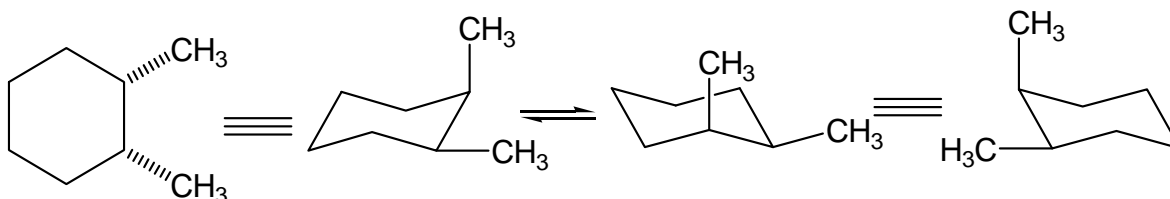

favoured
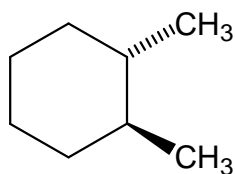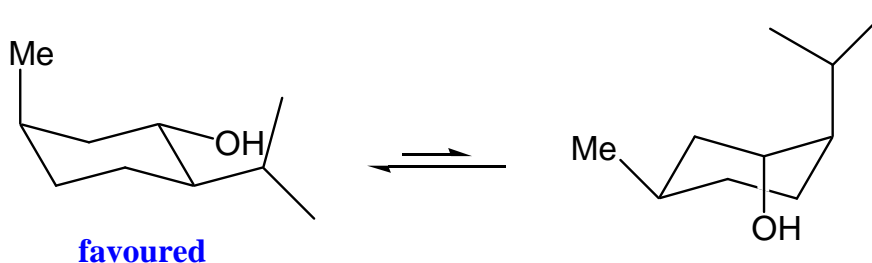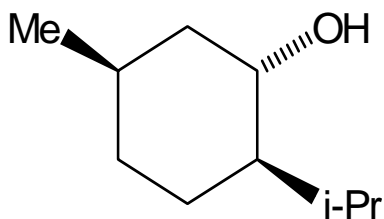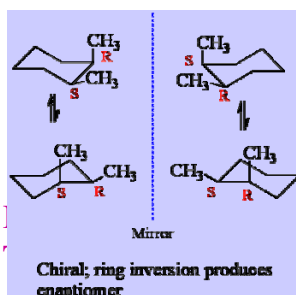
1 gauche-butane interaction
0.9 kcal/mol

4 gauche-butane interaction
4 x 0.9 kcal/mol = 3.6 kcal/mol

Difference in stability between the conformational isomers ⟶ 3.6 - 0.9 = 2.7 kcal/mol
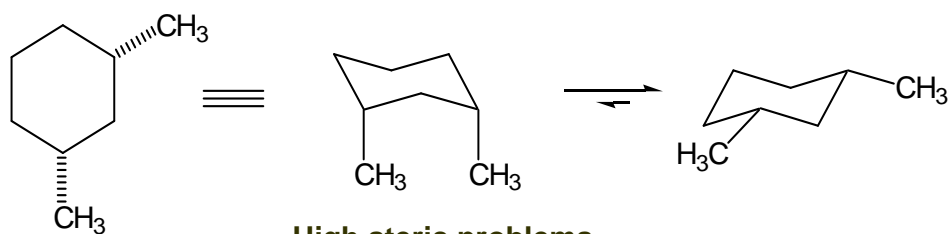
Diastereomeric, chiral and therefore resolvable

This has 3 gauche-butane interactions

Enontiomeric, chiral and not resolvable
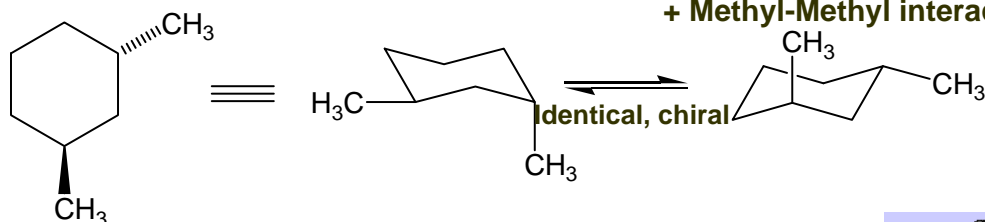
Chiral; ring inversion produces enantiomer

but since barrier of conversion is low to allow separation. is inseparable and hence the compound is optically inactive.
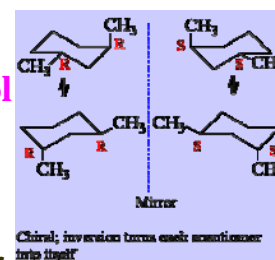
Diasteromers, achiral

CH$_3$

CH$_3$

CH$_3$

CH$_3$ CH$_3$

H$_3$C   CH$_3$

High steric problems
Unstable by ~ 5.5 kcal/mol (4 x 0.9 = 3.6 kcal/mol
+ Methyl-Methyl interaction)

CH$_3$

CH$_3$

CH$_3$

CH$_3$

H$_3$C   CH$_3$

CH$_3$

CH$_3$

Identical, chiral

It is a resolavable molecule
2-gauche-butane interaction = 1.8 kcal/mol

CH$_3$ CH$_3$
R   S
CH$_3$ CH$_3$

CH$_3$ CH$_3$
R   R   S   S
CH$_3$ CH$_3$

Mirror

Chiral; inversion turns each enantiomer into itself

cis-isomer is stable than trans isomer

CH$_3$

CH$_3$

CH$_3$

Identical, achiral

H$_3$C   CH$_3$ CH$_3$

CH$_3$ CH$_3$

2-gauche-butane interaction, 2 x 0.9 = 1.8 kcal/mol

CH$_3$

CH$_3$

CH$_3$ **Diastereomers, achiral**

CH$_3$ CH$_3$

CH$_3$

CH$_3$

H$_3$C   CH$_3$
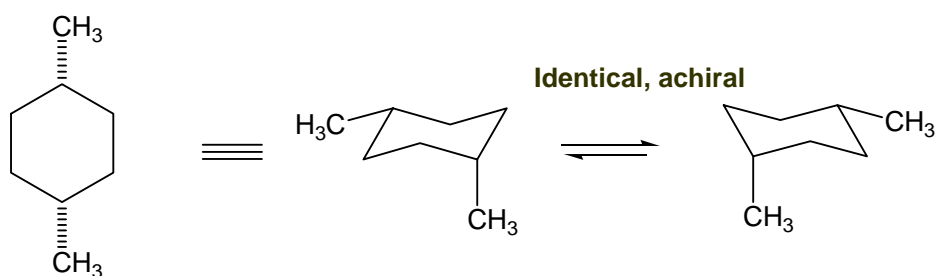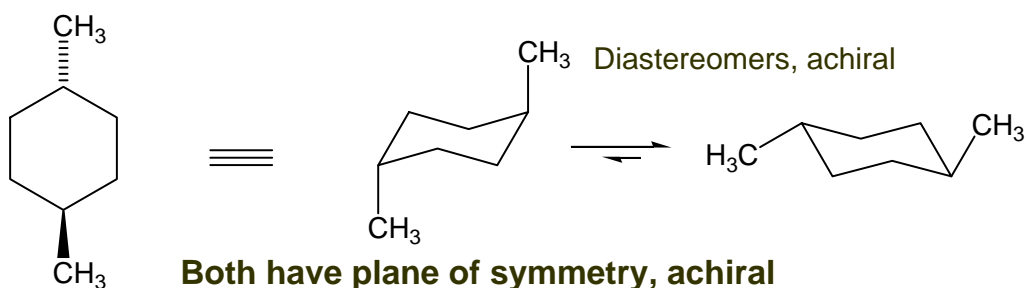
Both have plane of symmetry, achiral

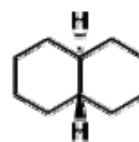Trans is stable than cis

DECALIN

Ring junctions
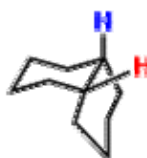("bridgeheads")
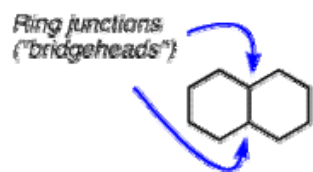
Decalin core structure
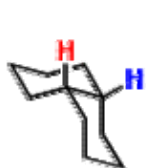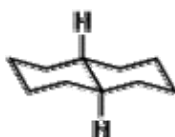(ambiguous stereochemistry)
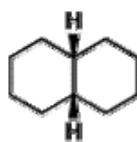
cis-decalin

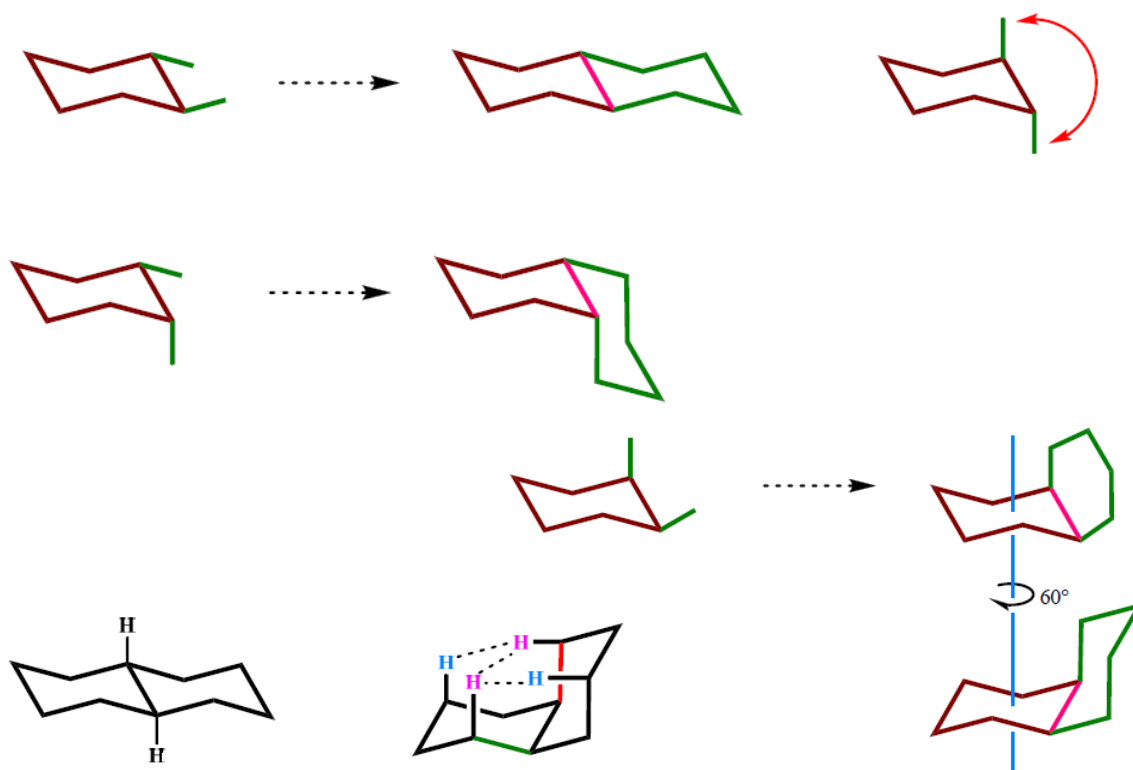*trans*-decalin

cis-decalin
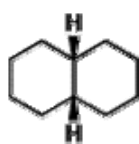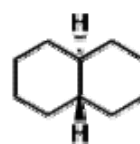
Ring flip occurs

trans-decalin

Would lead to breakage of C-C bond

Ring flip will not occur

60°

cis-decalin   trans-decalin

Why is the eclipsed conformation higher in energy than the staggered conformation?

van der Waals distance

Distance between molecules r ⟶

E
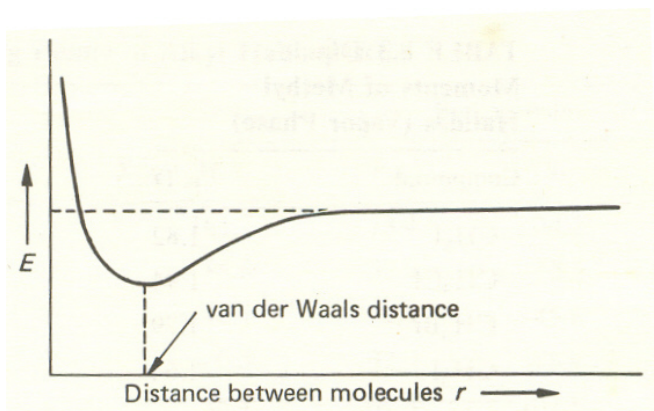
As two nonpolar groups approach each other, the van der Waals attractive force increases to a maximum, then decreases and becomes repulsive
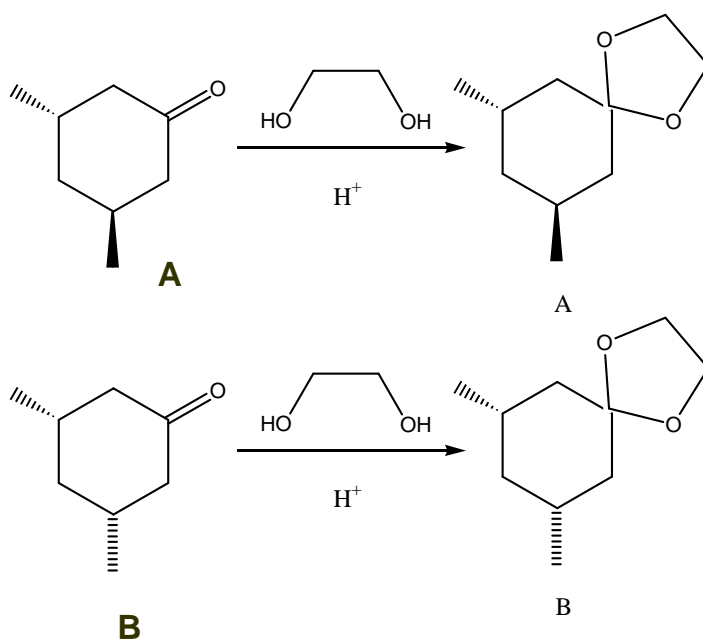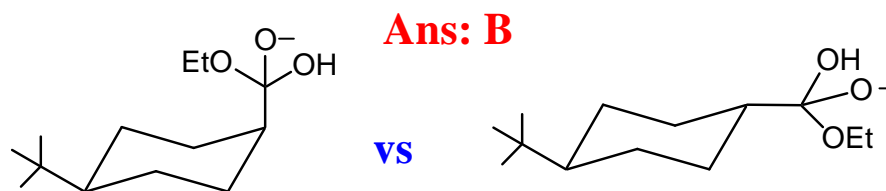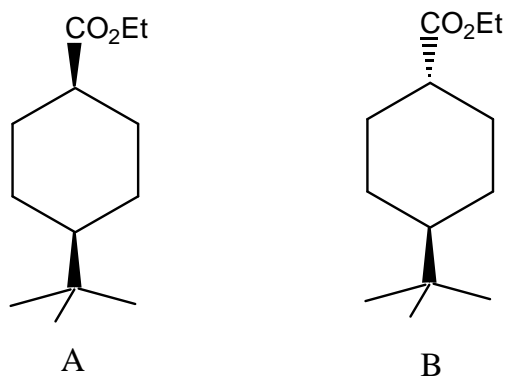
The van der Waals radius→ one-half the distance between two equivalent atoms at the point of the energy minimum

van der Waals radii, A^0			
H	N	O	F
1.2	1.5	1.4	1.35
CH$_2$	P	S	Cl
2.0	1.9	1.85	1.8
CH$_3$			Br
2.0			1.95
			I
			2.15

It is more difficult to form an acetal of compound A than of B.
Why?

A

B

Which compound should saponify faster (A or B)?

A

B

Ans: B

vs