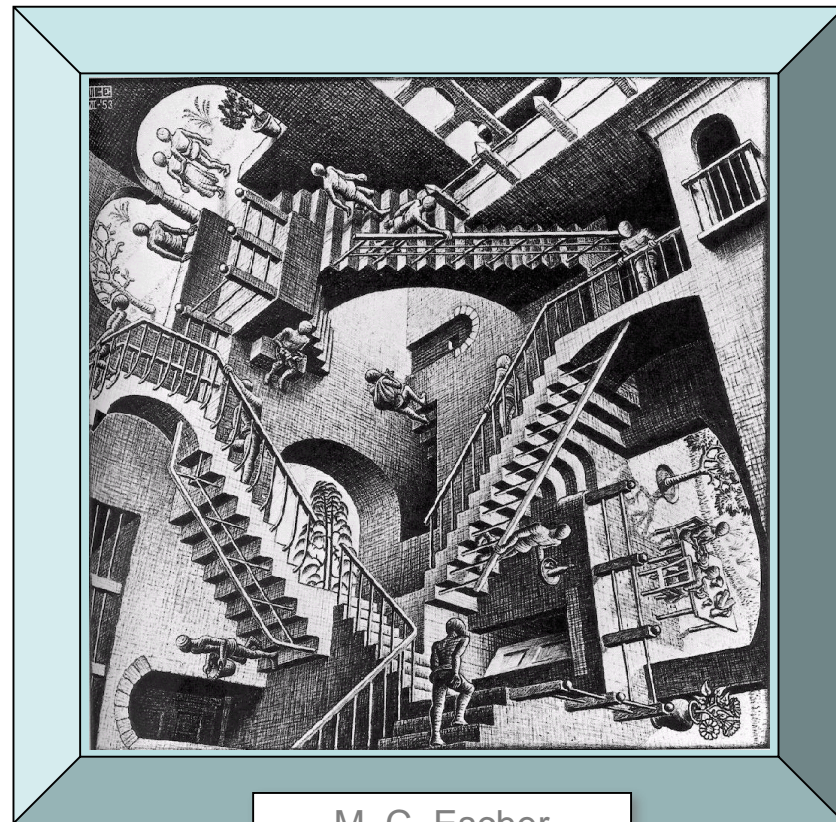


CHEM202

Stereochemistry

Lecture 1



M. C. Escher
Relativity

Conformation, Rings & Ring Strain

Tips and Suggestions

- Bring paper
- Pyramidal learning structure... you snooze you lose!
- If something is not clear get help
- NEF, don't get caught up

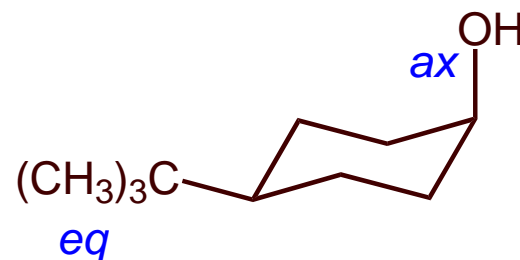
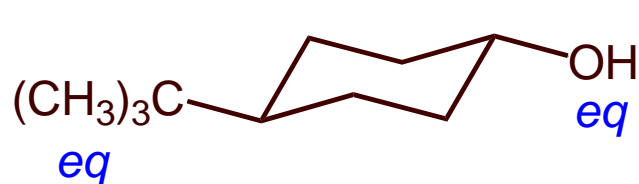
Aims of the Course

1. How does molecular shape and orientation of groups influence chemical reactivity?

CHEM 191 - typical reactions of functional groups

CHEM 111 - molecular shape (configuration & conformation)

This course - molecular shape does exert a secondary influence on the reactivity of functional groups



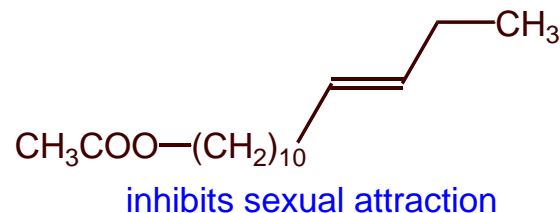
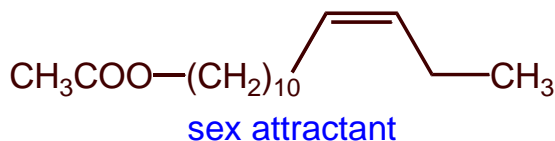
Trans-isomer:

Has a less hindered equatorial OH, will esterify faster than *cis*-isomer (ax-OH)

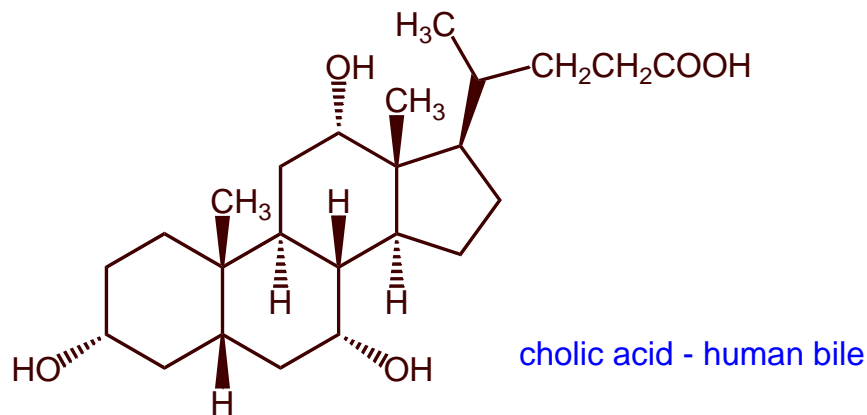
Aims of the Course, cont..

2. Can stereochemical principles be used in the design of selective syntheses?
- formation of one specific stereoisomer (*stereoselectivity*)

Red-banded leaf roller

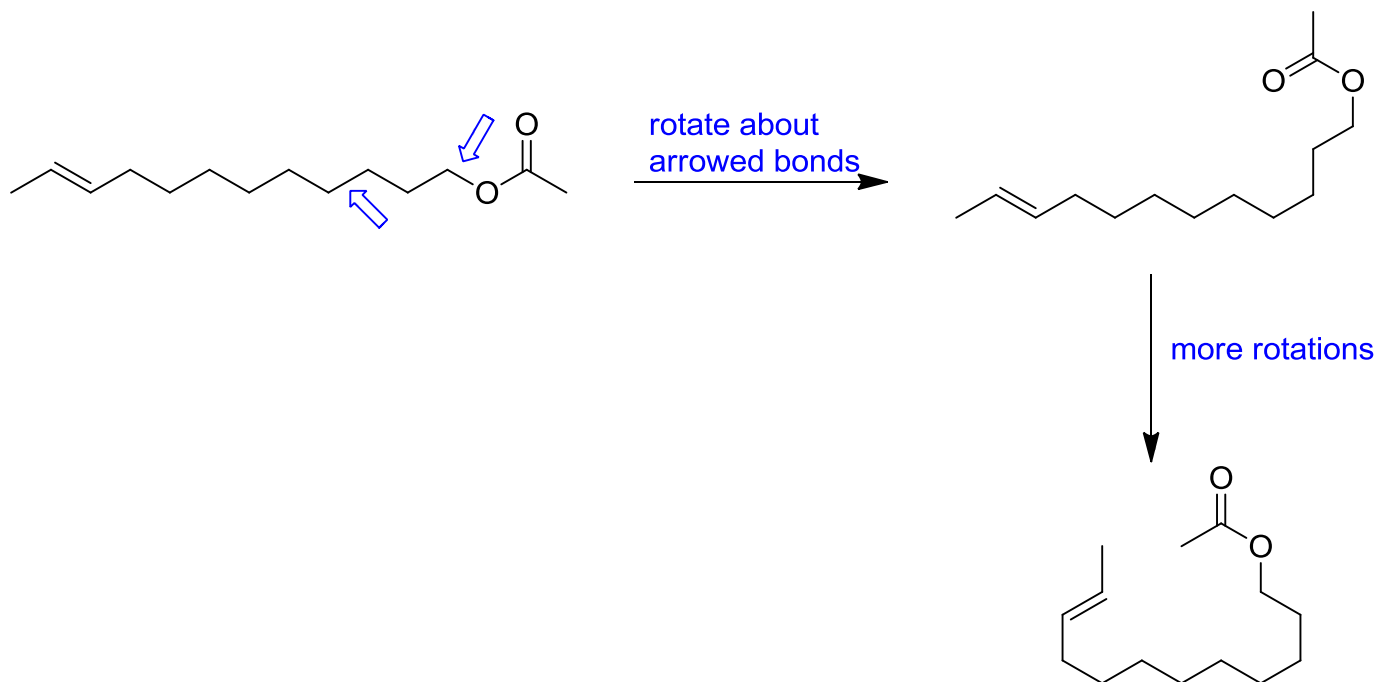


- manipulation of one of a set of potential reaction sites (*regioselectivity*)



The story so far

- Mainly interested in the shape of small localised atoms (think methyl group, ketone etc)
- On larger scale, shape is not so easily defined, rotation about single bonds is possible => lots of possible shapes (conformations)



- Flash back/quick review (Newman, saw-horse projections)

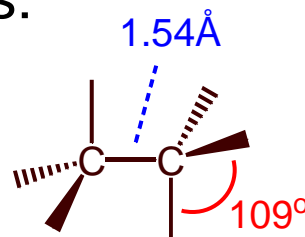
Conformation

Molecular shape dictated by:

- optimum bond lengths
- optimum bond angles for constituent atoms

e.g. C atom with 4 single bonds:

- bond angles $\sim 109^\circ$
- C-C bonds $\sim 1.54 \text{ \AA}$



- bond in plane of page
- bond to back
- ▴ bond to front

Deviations indicate some strain

Within these constraints, most molecules adopt various shapes by rotation about single bonds – gives various *conformations*

Conformation and Configuration

Change **conformation** \Rightarrow new shape

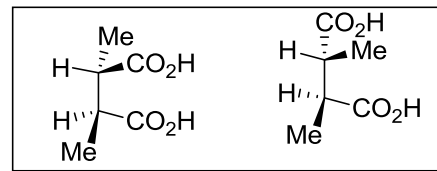
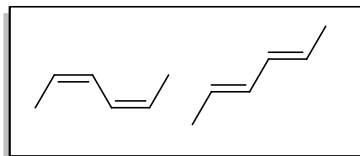
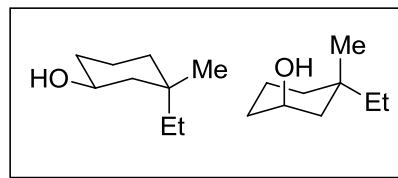
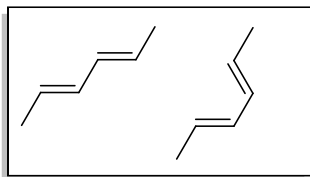
When the energy barrier is small you cannot isolate individual conformations, e.g. butane:

- *anti* form is preferred
- at room temperature have free rotation
- properties are those of the mixture of various forms

Change **configuration** \Rightarrow new substance, a *stereoisomer*

- different forms can be isolated
- have some physical differences:
 - *enantiomers* – non-identical mirror images – have different effect on plane polarised light
 - *diastereoisomers* – not mirror images – differ in most physical properties

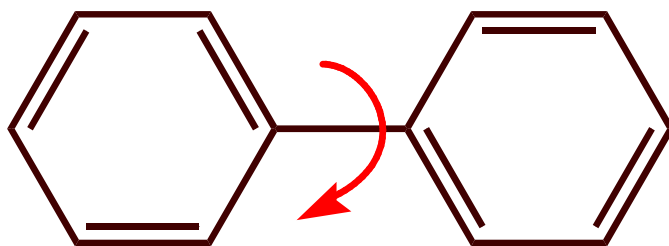
Putting it together



- Structures that can be interconverted simply by rotation are **conformations** of the same molecule.
- Structures that can interconverted only by breaking one or more bonds have different **configurations**, and are stereoisomers

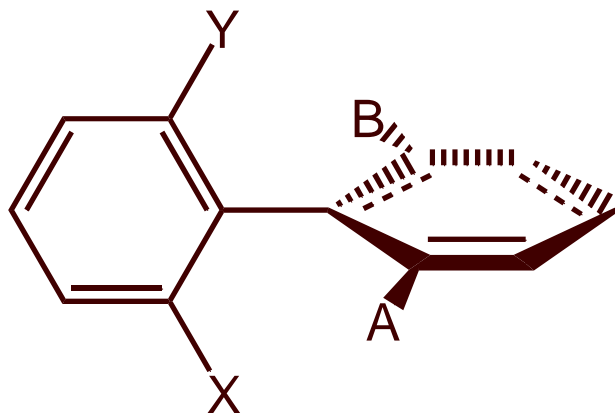
The Border Between Conformation and Configuration - 1

If the energy barrier is large ($> \sim 80 \text{ kJ mol}^{-1}$), the distinction between conformation and configuration blurs - e.g. biphenyl:



- Have free rotation about the C-C bond \Rightarrow many conformations
- But - with large groups in the *ortho*-positions, rotation can be blocked

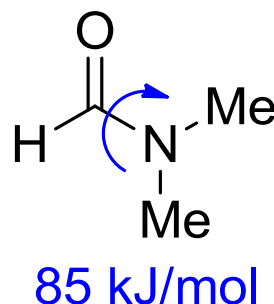
The Border Between Conformation and Configuration - 2



- If $X \neq Y$ and $A \neq B$ there is no plane of symmetry
- The molecule and its mirror image are enantiomers
- These enantiomers can only interconvert by rotation about the C-C bond
- If the energy barrier to rotation is large (large A, B, X and Y) enantiomers (conformations?) can be isolated

Rates and barriers: the guidelines (NEF!!)

- A barrier of 73 kJ/mol allows a rotation every second at 25 C
- Every 6 kJ/mol changes the rate at 25 C by a factor ~ 10
- To see signals in an NMR spectrum for two different conformations, they must interconvert $< \sim 1000 \text{ s}^{-1}$ (a barrier of roughly 55 kJ/mol at 25 C)



Can you draw the expected ^1H NMR spectrum of DMF?

Molecular Mechanics

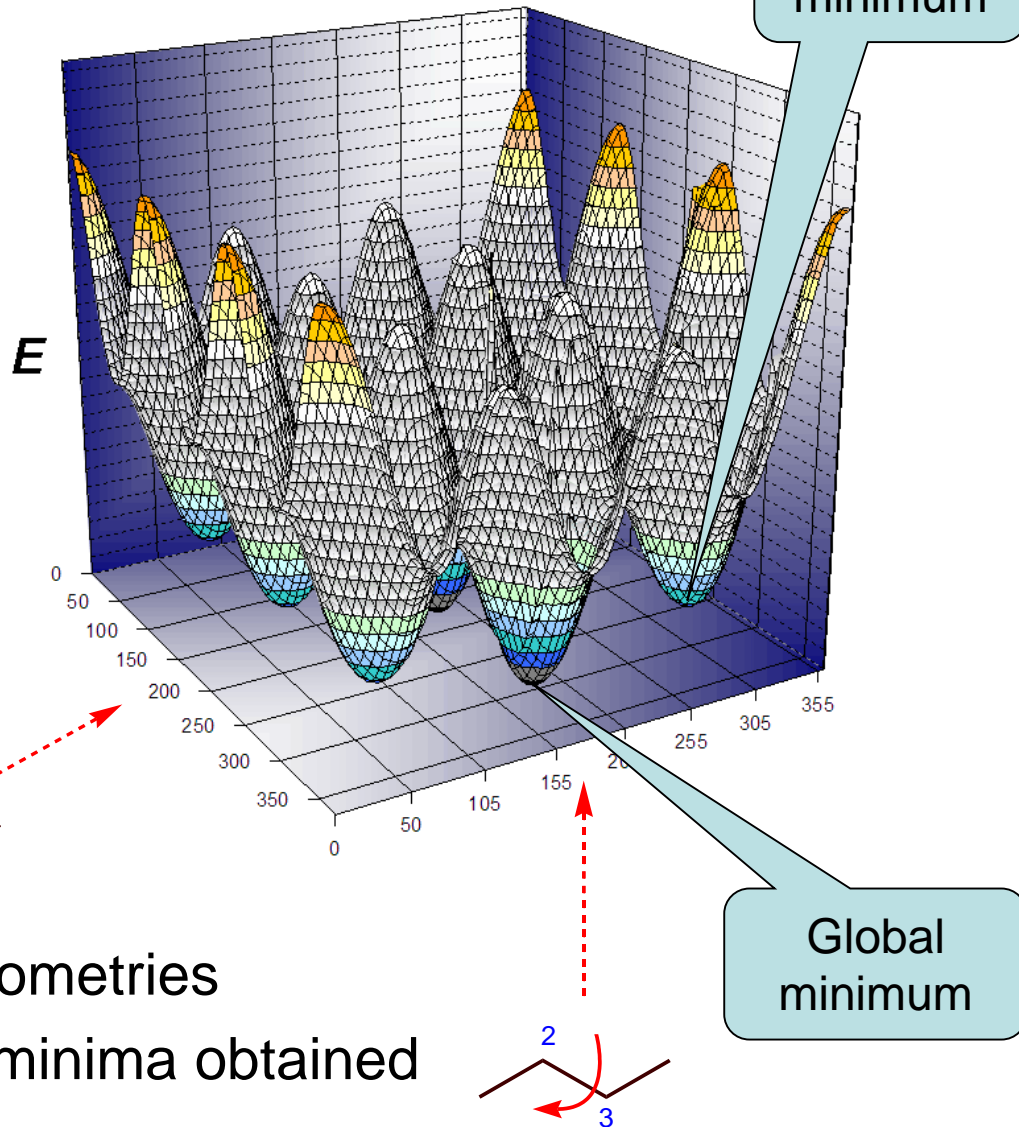
For molecules with >1 bond capable of free rotation:

- Difficult to assess relative energies of conformations
- Use computer programs that perform *molecular mechanics* calculations
- Procedure:
 - Draw approximate structure
 - The computer then:
 - Calculates a strain energy
 - Makes small change to the geometry and calculates a new strain energy
 - Repeats the process until any further changes always result in an increase in strain E
- Have found a *local minimum*

Energy Surface

- Picture of all conformations available
- Local minima lie in depressions
- Most favoured conformation - *global minimum*

e.g. for butane (2 different C-C bonds):



To find global minimum:

- Use many different starting geometries
- Compare energies of all local minima obtained
- Called *conformational searching*

Cyclic Molecules

Represent as regular polygons

Each unspecified vertex is a C with enough H to give 4 bonds

Name by adding *cyclo* to alkane name

Molecular shapes dictated by minimisation of:

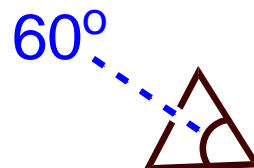
- *Bond Angle Strain* - bond angles will be as close as possible to the ideal
- *Torsional Strain* - adjacent bonds will be as close to staggered as possible
- *Van der Waals Interactions* - close approach of non-bonded atoms will be avoided if possible

(a) Bond Angle Strain

Only significant in smaller rings

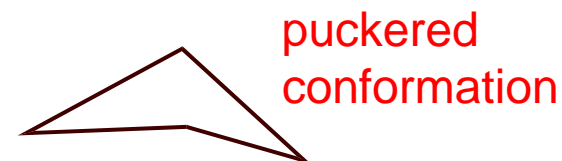
Cyclopropane:

- must be planar
- bond angles within ring are 60° - considerable strain



Cyclobutane:

- 90° bond angles if planar
- slight bending makes angles a little larger
- non-planar structure with considerable bond angle strain



Higher cycloalkanes:

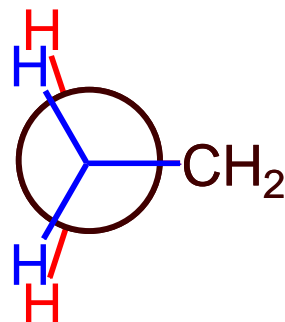
- all non-planar
- relatively unstrained bond angles, close to 109°

(b) Torsional Strain - 1

Resistance to bond twisting

Cyclopropane:

- planar
- all bonds eclipsed
- high torsional strain

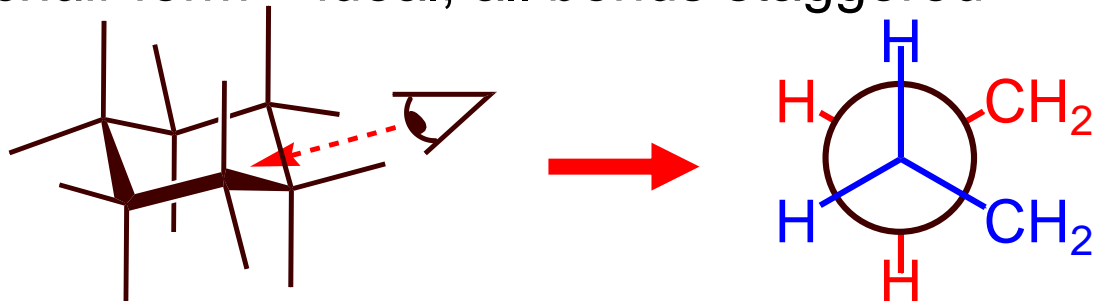


Cyclobutane - nearly planar, almost eclipsed

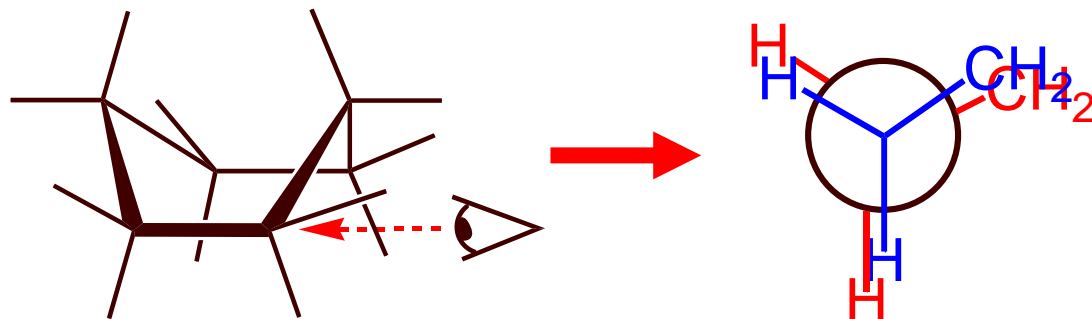
(b) Torsional Strain - 2

Cyclohexane:

- *chair* form – ideal, all bonds staggered



- *boat* - 2 sides with eclipsing bonds



Higher cycloalkanes:

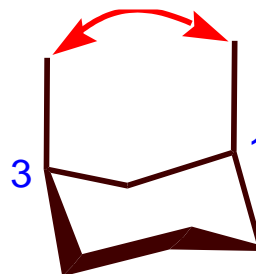
- many conformations with most bonds staggered
- usually can't have all bonds fully staggered

(c) Van der Waals Interactions - 1

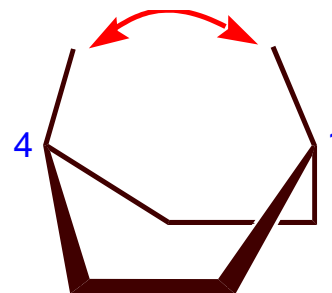
3 to 5 membered rings - no significant interactions between groups across the ring

Cyclohexane:

- chair - 1,3-diaxial interactions

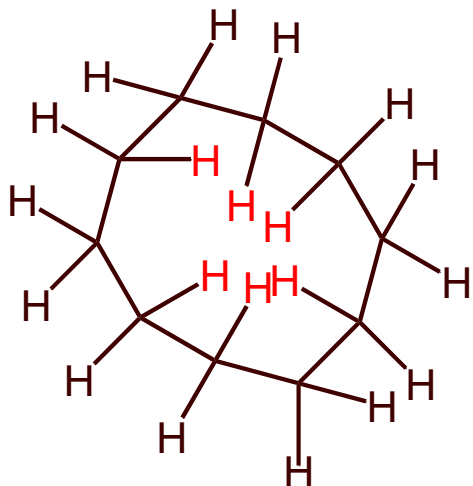


- boat - stronger 1,4-flagpole interactions



(c) Van der Waals Interactions - 2

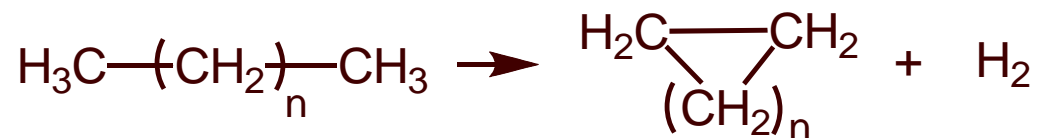
- 7 to 10-membered rings - quite severe interactions - e.g. cyclodecane:



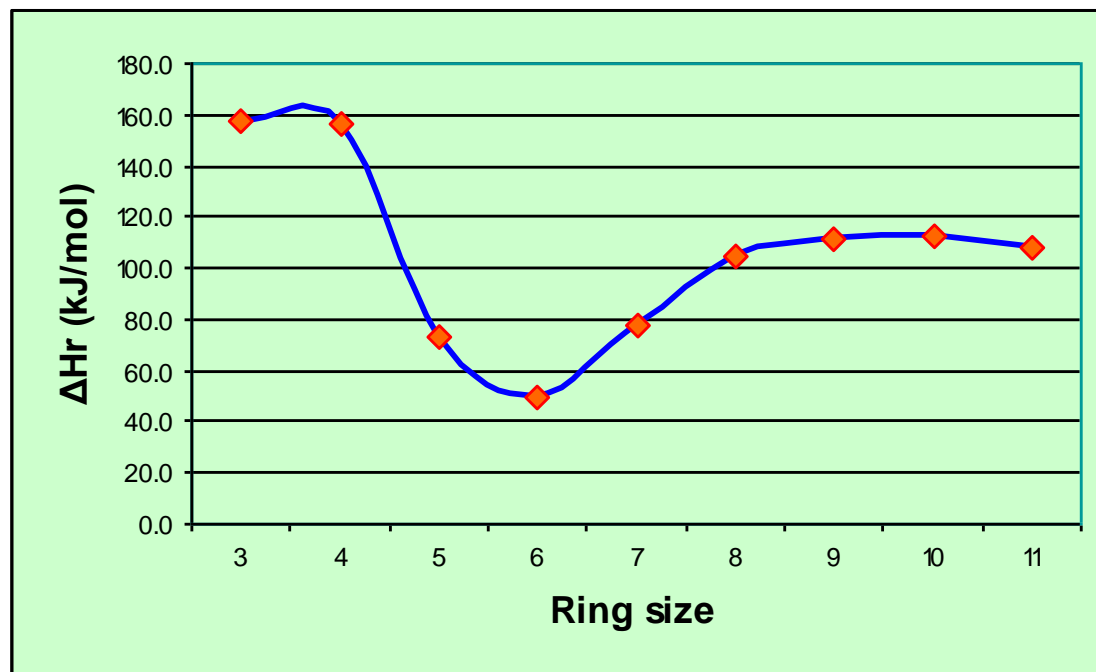
- > 10 membered:
 - more space in centre of ring
 - interactions less severe

Strain Variation with Ring Size

Considerable variation in strain energy. For:



Ring size	Calc ΔH_r /kJ mol ⁻¹
3	157.3
4	156.4
5	73.5
6	49.3
7	78.1
8	104.9
9	111.5
10	112.9
11	107.5



Striking feature – low strain energy of the cyclohexane ring system

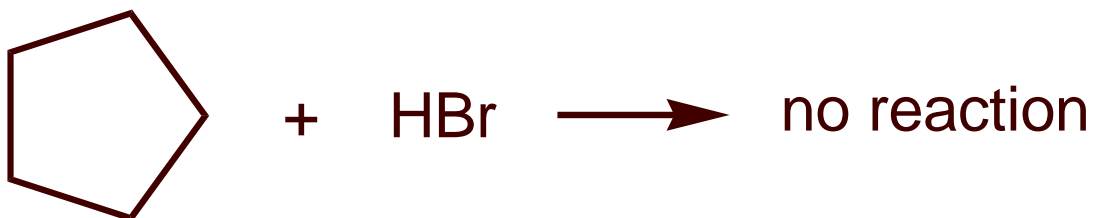
6-membered rings feature very strongly in organic chemistry

Cyclopropanes Behave Like Alkenes

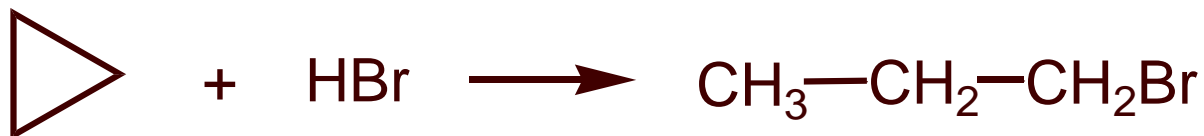
- An alkene undergoes addition reactions:



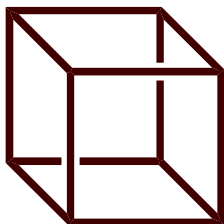
- Typical alkanes do not:



- Cyclopropane adds HBr:



Cubane – a Highly Strained Molecule



- First synthesised in 1964
- ~2x density of petrol
- Large amount of energy released on combustion
- Potential as a rocket fuel
- More recently – octanitrocubane synthesised. One of the most potent explosives known

Favoured Ring Size Varies

The 6-membered ring is not always the most favoured

Some influential factors:

- Atoms other than C may have different preferred bond angles
- Divalent ring atoms:
 - have no bonds to become involved in eclipsing
 - have no attached groupings – less van der Waals interaction
 - planar conformations may be feasible
- Interactions between charged or partially charged centres

Molecular modelling is again very helpful

<https://www.youtube.com/watch?v=717vb7kLKKk>