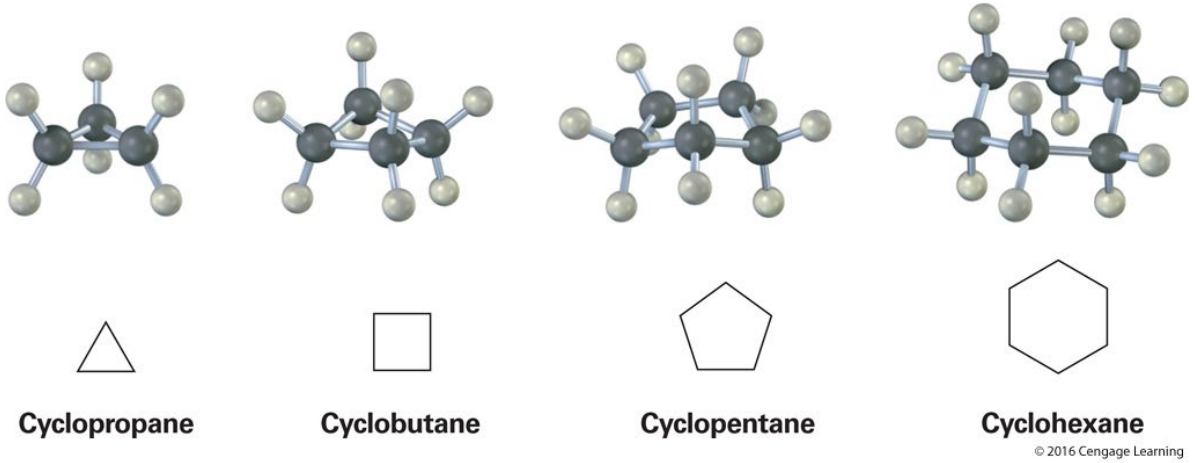
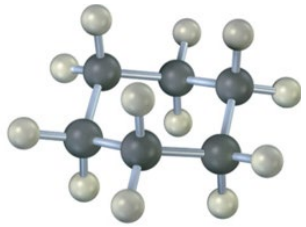
The musk gland of the male Himalayan musk deer secretes a substance once used in perfumery that contains cycloalkanes of 14 to 18 carbons.



Chapter 4: Organic Compounds:

Cyclo*alkanes* and Their *Stereochemistry*

Outline



Cyclohexane

Administrative

Naming cycloalkanes 4.1

Cis-trans isomerism in cycloalkanes 4.2

Stability of ***cyclo***alkanes: Ring strain 4.3

Conformations of cyclo**alkanes** **4.4**

Conformations of cyclo**hexane** **4.5**

Axial and equatorial bonds in cyclohexane 4.6

Conformations of monosubstituted cyclohexanes 4.7

Conformations of disubstituted cyclohexanes 4.8

Exam 1

Study tips:

- Finish HW-5 ≥ 48hrs before exam 1
  - Review/practice All Lecture worksheets Qs (make ppoint file)
  - Review all HW questions and put:
    - a) ✓ if got it correct
    - b) X if not so sure, (go back >1 hr later ~ review again until - got it)
    - 8pm - night before exam

      ~ Netflix or Amazon prime movie etc. ~ just relax ☺

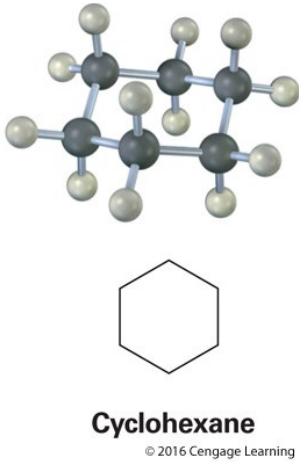
Most important: 1) Pace your self - study every day; 2) do your best NOT to cram ☺

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

Stability of ***cyclo***alkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane

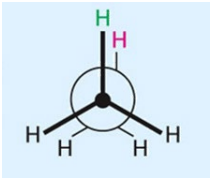
Conformations of monosubstituted cyclohexanes

Conformations of disubstituted cyclohexanes

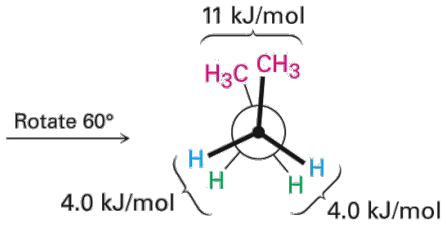
Conformations of polycyclic molecules

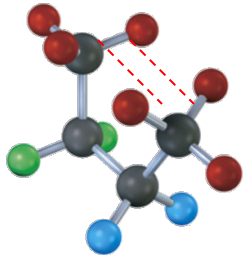
Organic structures ~ **STRAIN Energy:** **Summary**

Torsional strain: strain in a molecule caused by ***e-*** repulsion b/w eclipsed bonds (e.g. H-H)



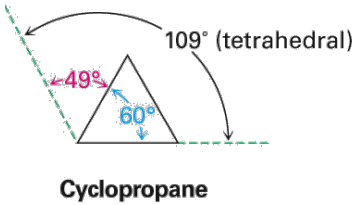
Steric strain: strain imposed on a molecule when 2 groups try to occupy same space ☹

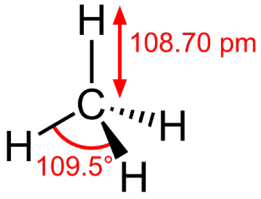




Angle strain: is induced in a molecule when **bond angles** are forced to deviate from the ideal 109° (tetrahedral value)

☹





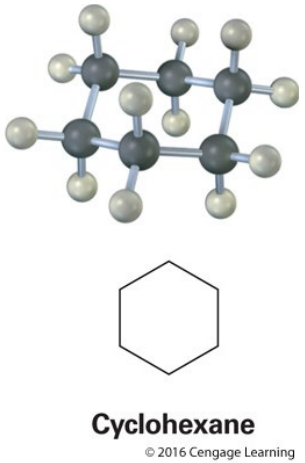
☺

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

Stability of cycloalkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane

Conformations of monosubstituted cyclohexanes

Conformations of disubstituted cyclohexanes

Conformations of polycyclic molecules

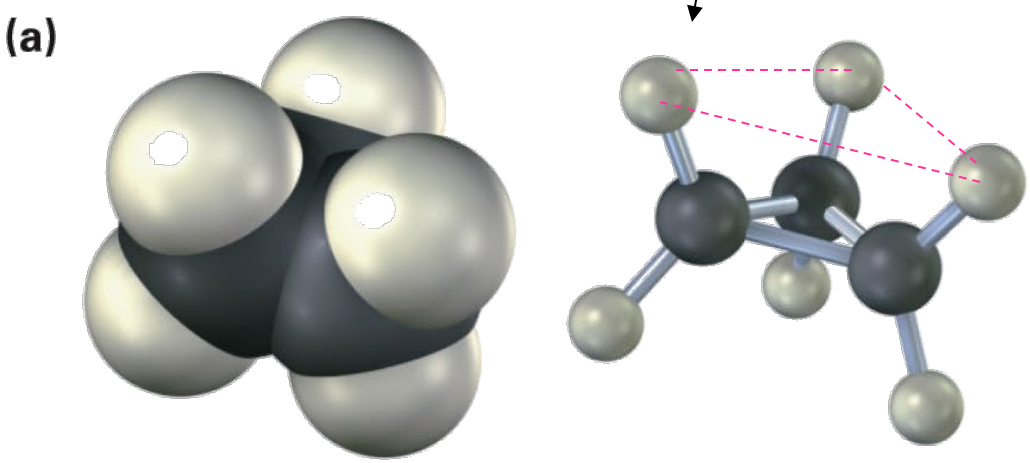
Conformations of ***Cyclo***alkanes

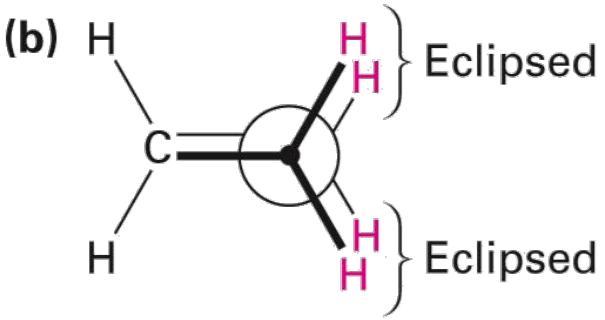
- Cyclo**propane**
  - Most strained of all rings b/c angle strain caused by C–C–C bond angles of 60°
    - Has considerable torsional strain

    a) Has bent bonds

    b) C–H bonds are eclipsed

Cyclopropane



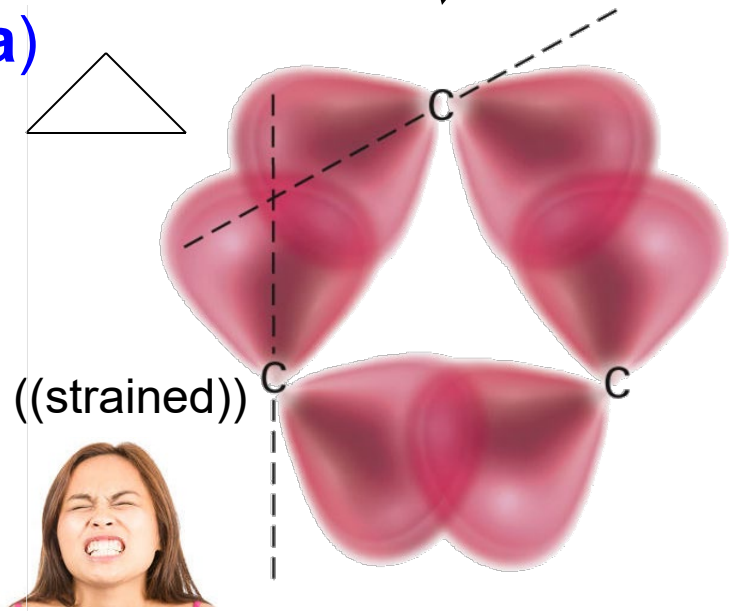


Conformations of ***Cyclo***alkanes

Thus ~ **a)** cyclo***propane*** bonds are

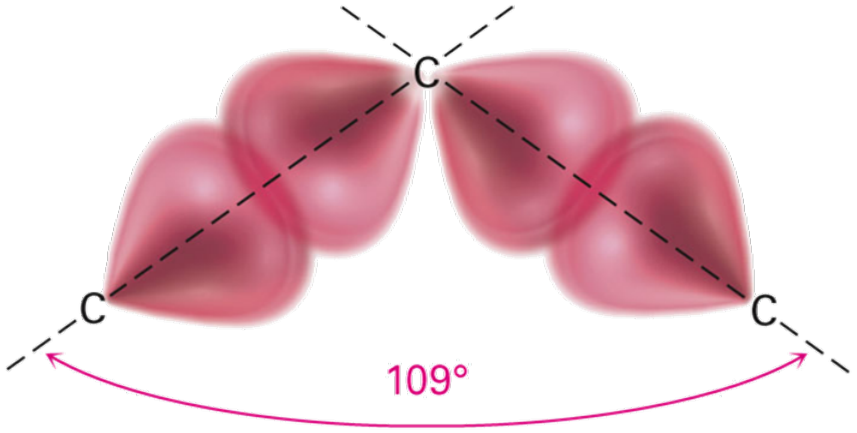
weaker & **more reactive** vs **b)** typical alkane bonds

a)



Typical bent cyclopropane C–C bonds

b)

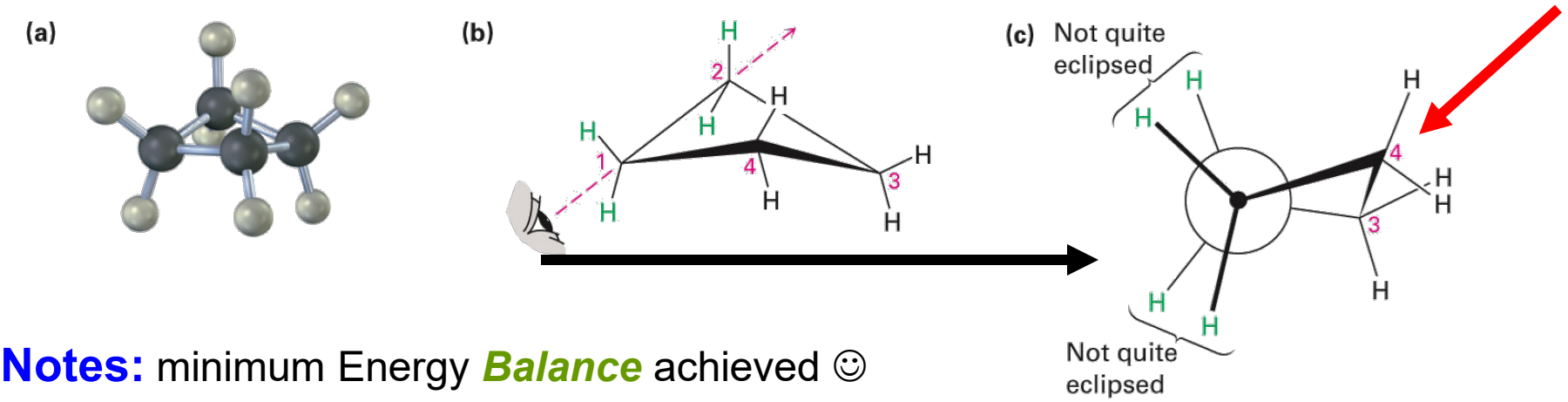


Typical alkane C–C bonds

Want to react more to relieve bond strain tension

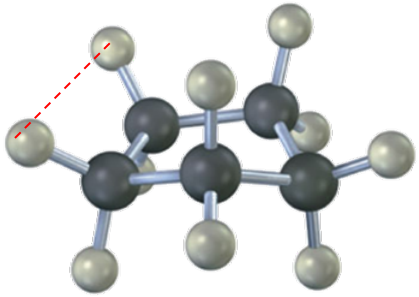
Conformations of ***Cyclo***alkanes

- Cyclo***butane***
  - Has less angle strain than cyclopropane
  - More torsional strain b/c of larger number of Hs,
    - and their proximity to each other
  - Slightly bent out of ***plane***,
    - one carbon atom (4) is about 25°above the plane
      - Increases angle strain but decreases *torsional strain*

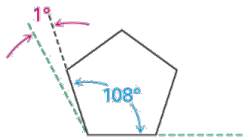


Notes: minimum Energy ***Balance*** achieved ☺

Conformations of ***Cyclo***alkanes



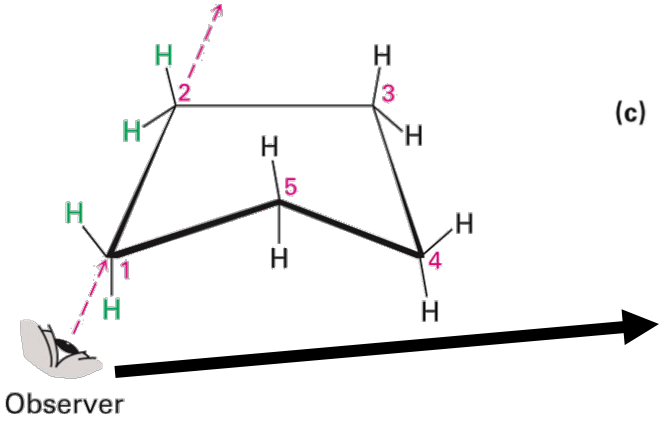
- Plain cyclo***pentane***:

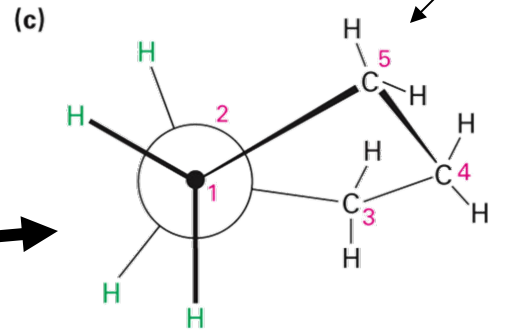


  - Mild angle strain but Large *torsional strain:*

- *to offset this…the molecule puckers (below)*
  - Non ***planar*** conformations strike balance b/w:
    - increased ***angle strain*** & decreased ***torsional strain***

- 4 carbon atoms are approx in the same *plane*:





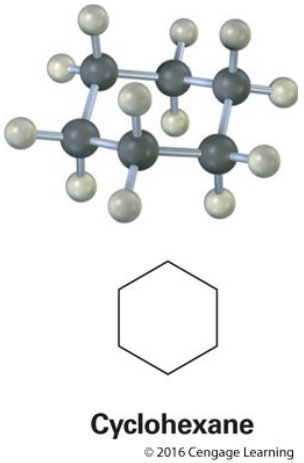
Fifth carbon atom (**5**) is bent *out of the plane*

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

Stability of cycloalkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane

Conformations of monosubstituted cyclohexanes

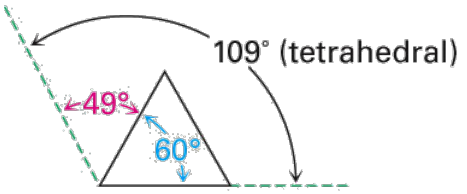
Conformations of disubstituted cyclohexanes

Conformations of polycyclic molecules

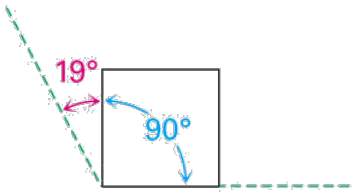
RECALL

Stability of Cycloalkanes: **Ring Strain**

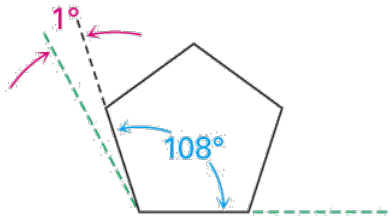
- **Larger rings** have many more possible conformations than smaller rings
  - More difficult to analyze (but less *angle strain* ☺)



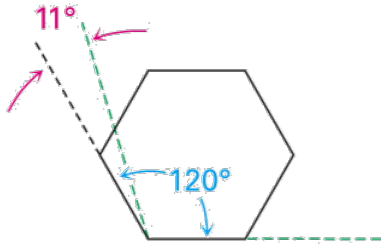
Cyclopropane



Cyclobutane



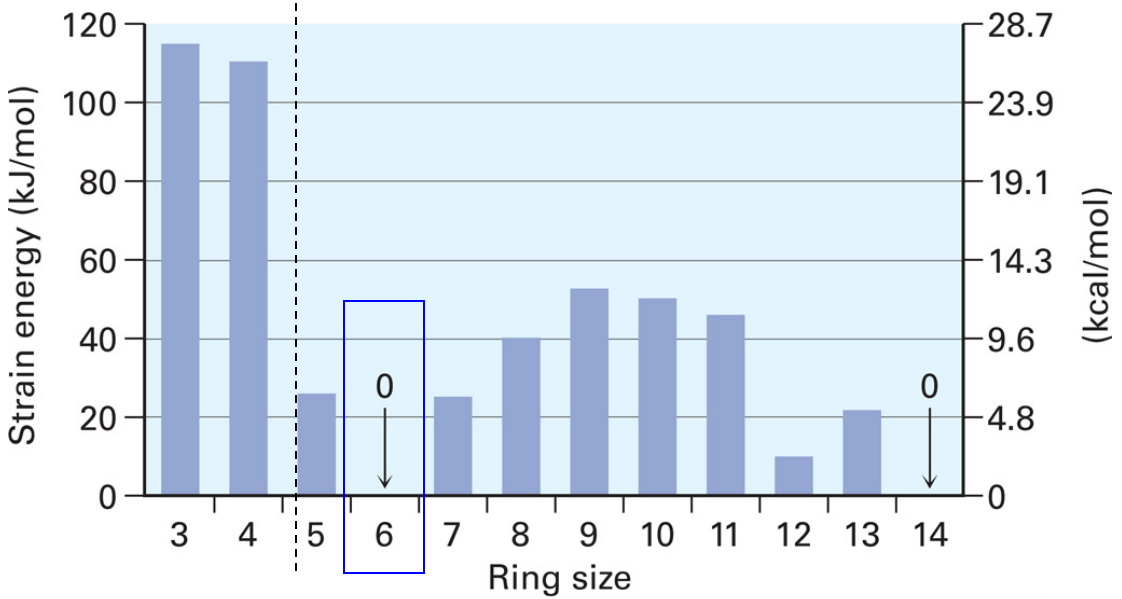
Cyclopentane



Cyclohexane

molecule

(((Strain E)))



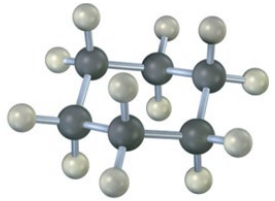
Conformations of ***Cyclo***hexane

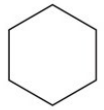
MOST COMMON ~ occur widely in **Nature**

– Adopts: ***"Chair" conformation***

– **most stable**

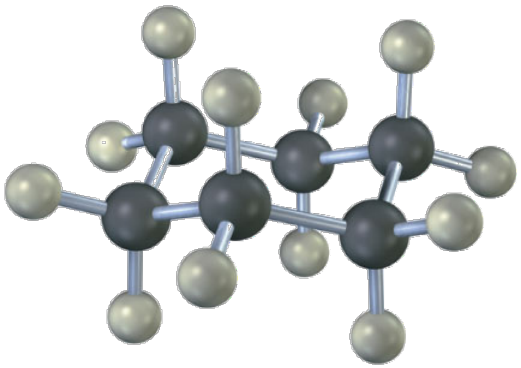
- Strain-free ☺, three-dimensional shape
- Has neither: *angle strain* or *torsional strain*





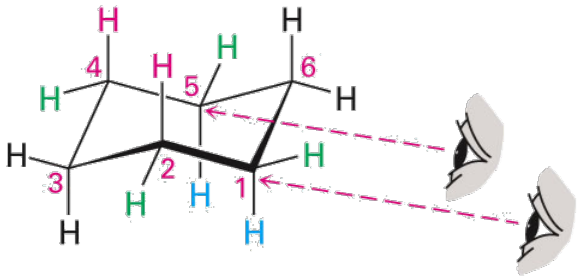
Cyclohexane

(a)

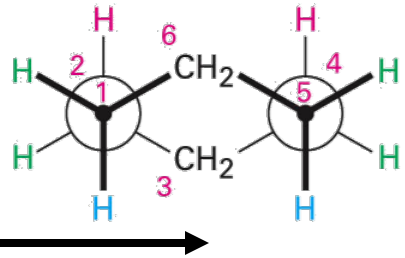


Chair conformation

(b)



(c)



staggered
(STABLE)

Steps to Draw ***Chair*** conformation of *Cyclo*hexane

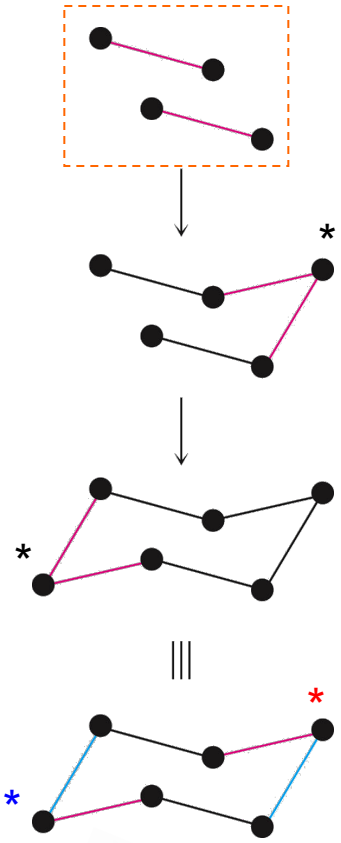
Please draw the steps ☺

1) Draw two parallel lines, slanted downward and slightly offset from each other with dots

- 4 of the cyclohexane carbons lie in a ***plane***.

2) Place the topmost carbon atom* above and to the right of the ***plane*** of the other 4, and connect the bonds.

3) Place the bottommost carbon* atom below and to the left of the plane of the middle four, and connect the bonds

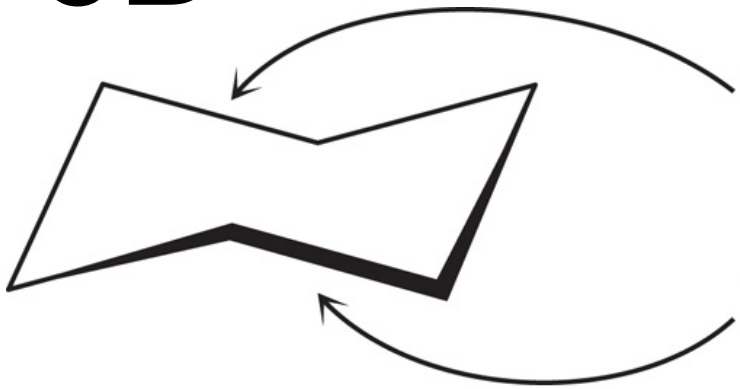


Note:

The bonds to the bottommost carbon* atom are ***parallel*** with the bonds to the topmost carbon.

Note: 3D

Please draw top portion here



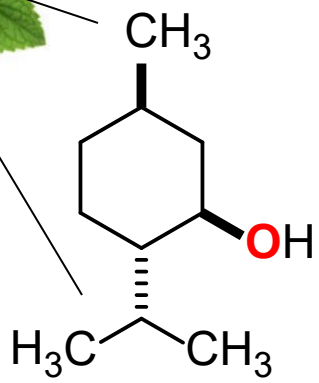
This bond is in back.

This bond is in front.

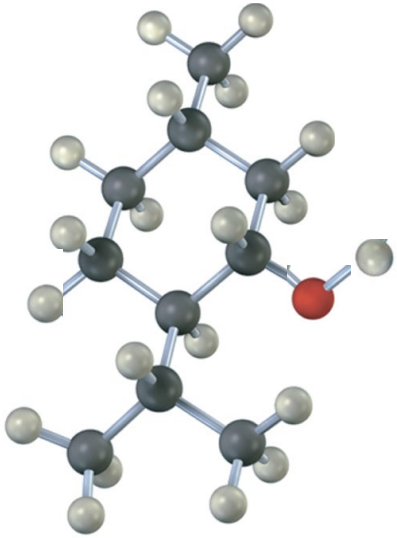
---

e.g.

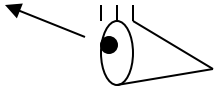
Top view



menthol



side view

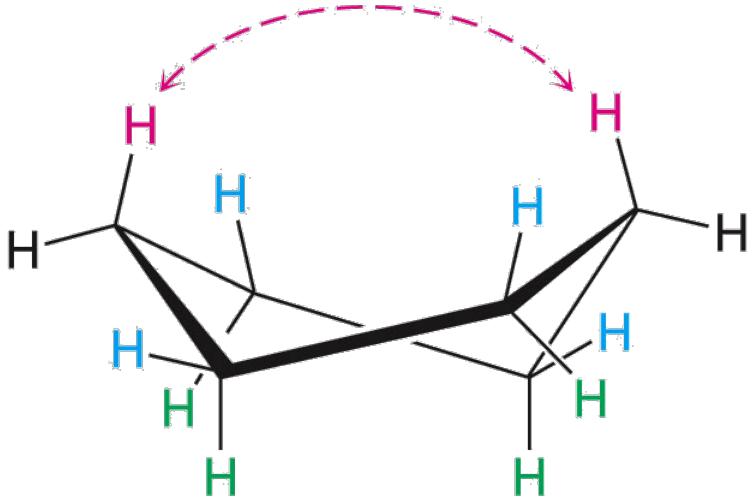


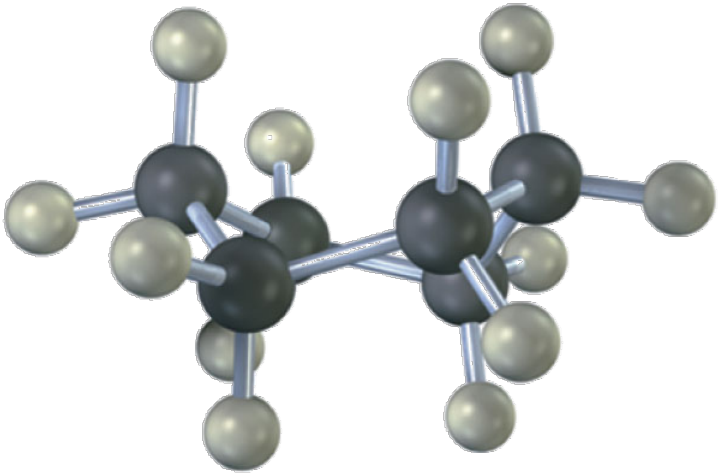
Chair form of
(-)-Menthol

Alternate Conformation of Cyclo**hexane**

twisting **"BOAT" conformation**

1) **Steric strain**





H ↔ H

H ↔ H

} **Torsional strain**

2)

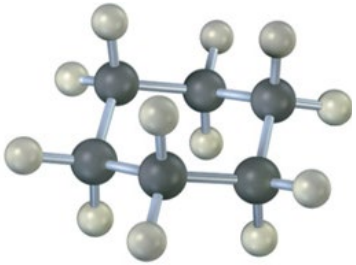
Twist-boat cyclohexane
(23 kJ/mol strain)

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

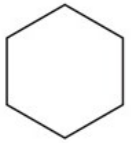
Stability of cycloalkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane



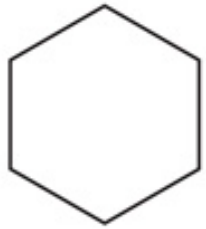
Cyclohexane

Conformations of monosubstituted cyclohexanes

Conformations of disubstituted cyclohexanes

Conformations of polycyclic molecules

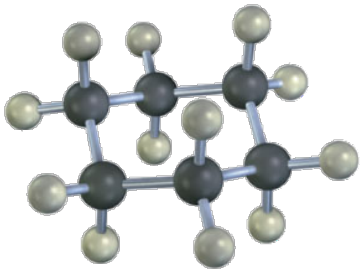
*Cyclo**hexane*** - *axial* & *equatorial* bonds

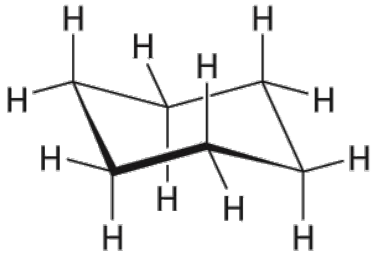


Cyclohexane

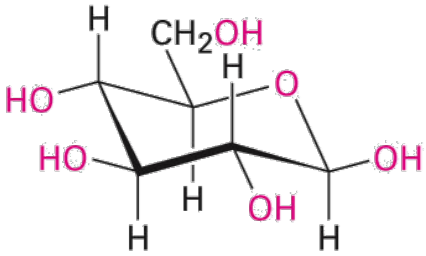
e.g.

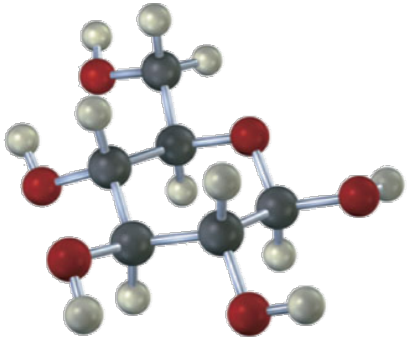
$C_6H_{12}O_6$





Cyclohexane
(chair conformation)



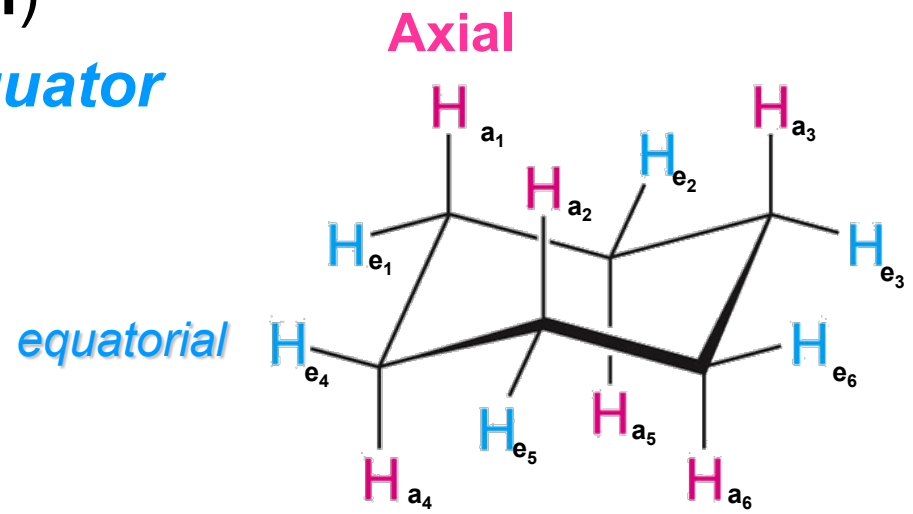


Glucose
(chair conformation)

RECALL: ***Chair*** form *most* **stable** form in **Nature**

*Cyclo**hexane*** - *Axial* & *Equatorial* bonds

- ***Chair*** conformation positions for *substituents* on the ring:
  - ***A**xial* positions (**Up/down**)
  - ***E**quatorial* positions ~ ***equator***



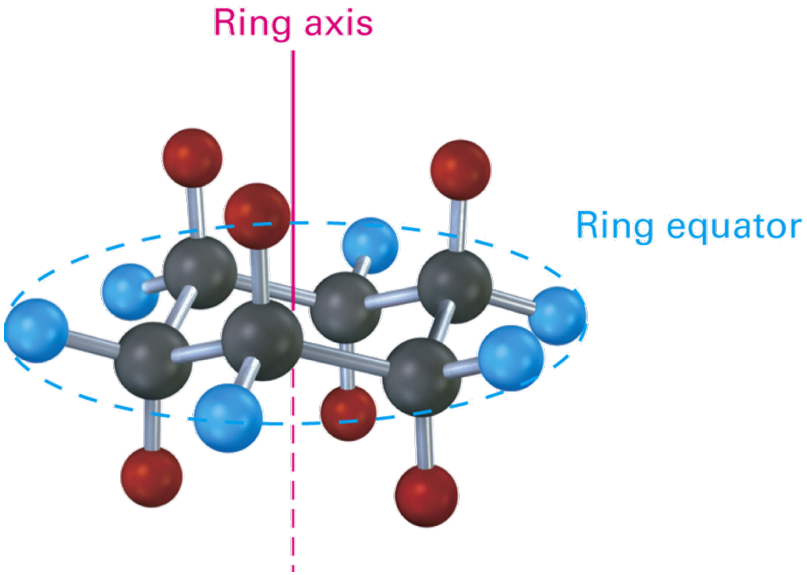


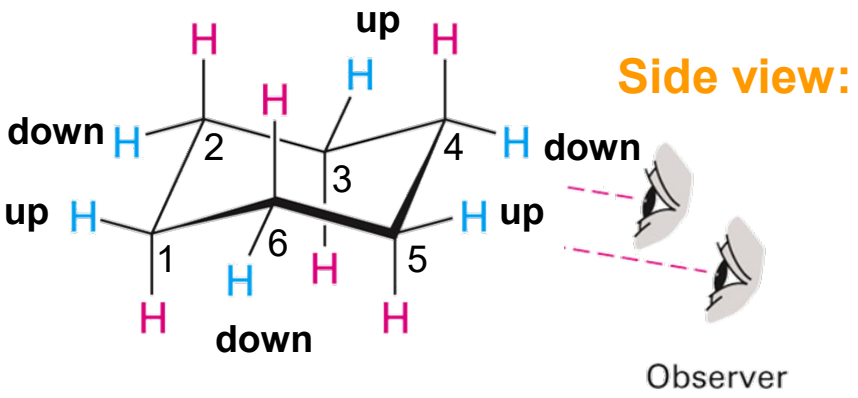
Figure 4.8

You draw please ☺

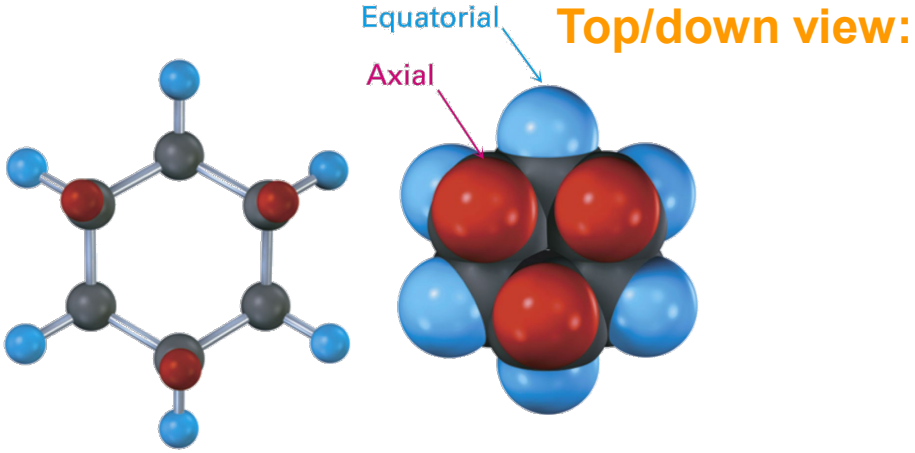
*Cyclo**hexane*** - *Axial* & *Equatorial* bonds

Each carbon atom in *cyclohexane* has:

one axial and one equatorial hydrogen



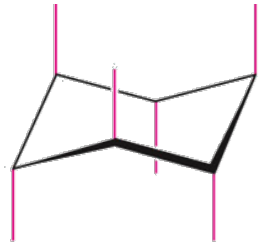
Each "***face***" of the ring has 3 ***axial*** and three ***equatorial*** **Hs** in an alternating arrangement



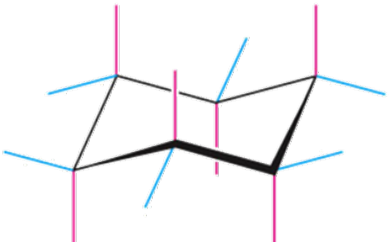
Procedure for Drawing *Axial* and ***Equatorial*** bonds in ***Chair*** Cyclo***hexane***

Please annotate your handout
Practice drawing…

Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up–down.



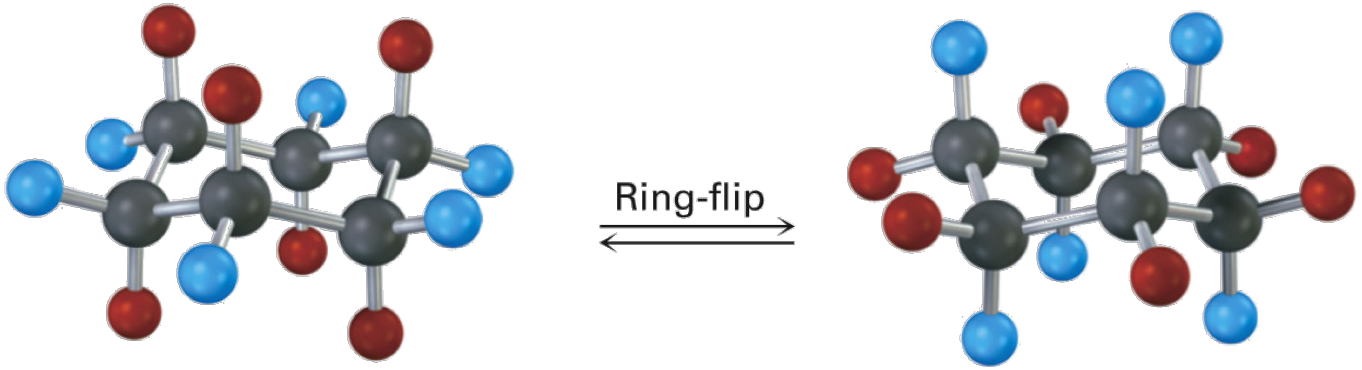
Equatorial bonds: The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alternate between sides around the ring.



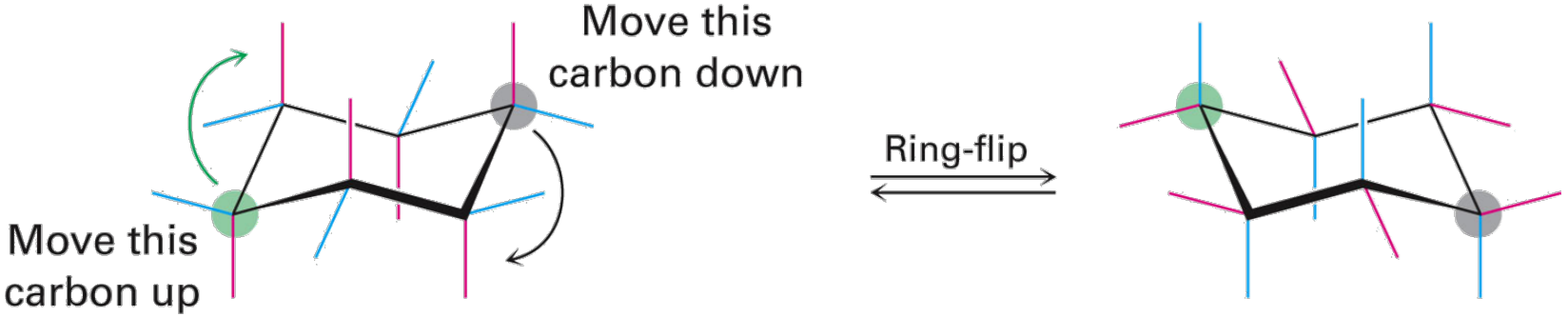
Completed cyclohexane

Conformational *Mobility* of ***Cyclo****hexane*

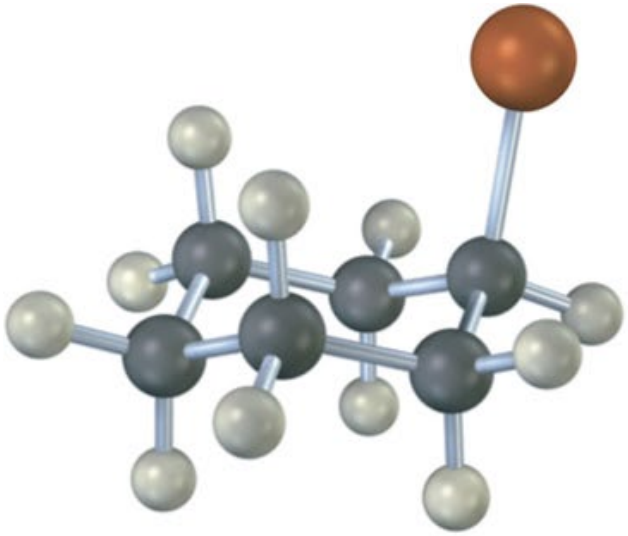
"Ring-flip" ~ ***Interconversion*** of chair conformations, resulting in the exchange of *axial* and *equatorial* positions

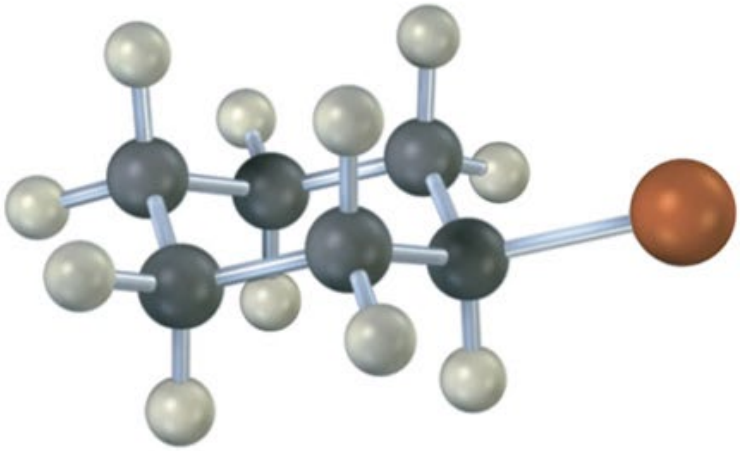


"Ring-flip"



e.g.





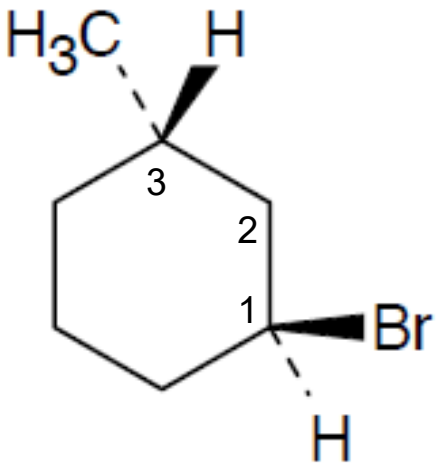
Ring-flip

Axial bromocyclohexane

Equatorial bromocyclohexane

RECALL

trans
(CH_3 to Br)

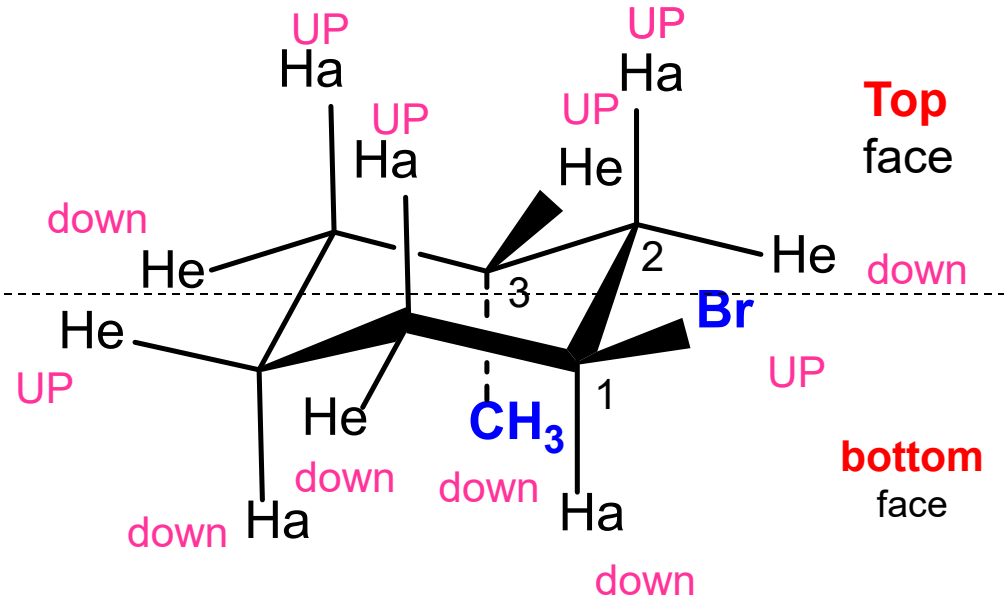


***trans*-1-Bromo-3-methylcyclohexane**

aka: the "*planar*" structure

"*Chair*" ***trans***

(**CH_3** to **Br**)



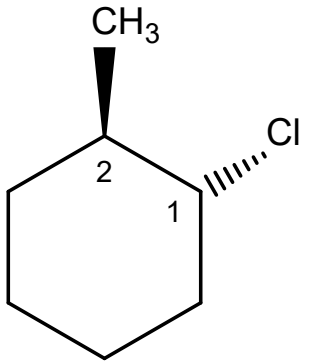
equatorial
(trans)

H_e = equatorial H
H_a = axial H

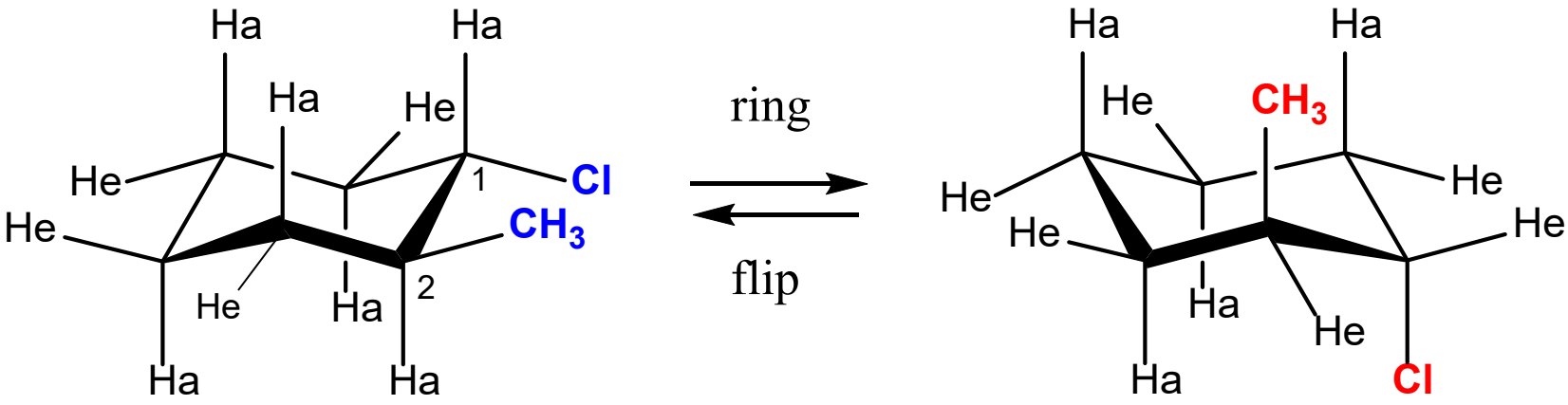
Challenge Question

Draw the two different ***chair*** conformations for

trans-1-**chloro**-2-**methyl**cyclohexane?



Hint: draw the ***planar*** structure of the compound above, then the 2 chair conformations below



equatorial (trans)

axial (trans)

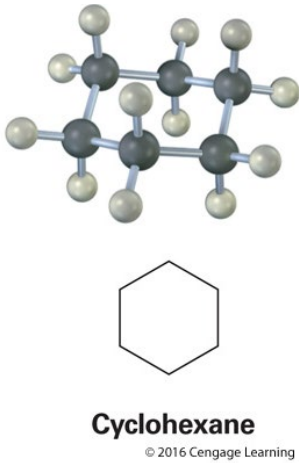
trans-1-Chloro – 2- methlycyclohexane

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

Stability of cycloalkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane

Conformations of ***Mono***substituted cyclohexanes

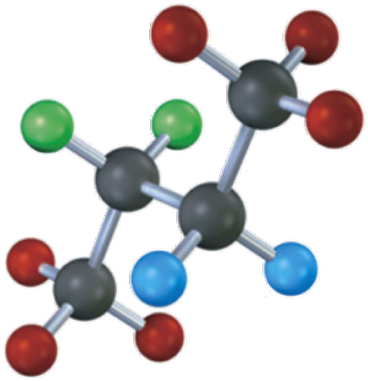
Conformations of disubstituted cyclohexanes

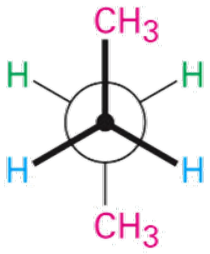
Conformations of polycyclic molecules

RECALL: *conformations*

NEWMAN
PROJECTION

Ball & Stick
PROJECTION

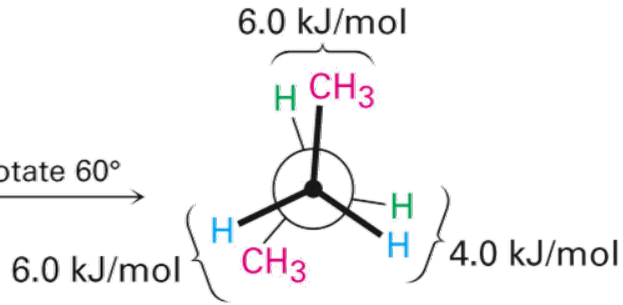




Butane—anti conformation (0 kJ/mol)

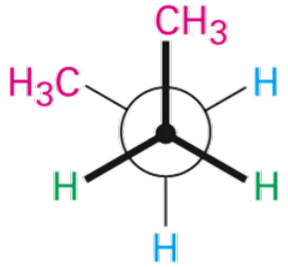
1) *ANTI*

Rotate 60°



2) *eclipsed*

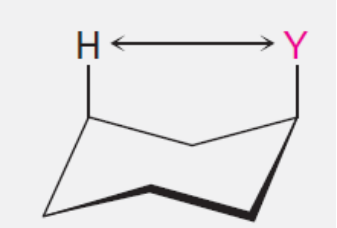
Butane—eclipsed conformation (16 kJ/mol)



3) *Gauche*

Gauche butane (3.8 kJ/mol strain)

Conformations of *Monosubstituted* Cyclo**hexanes**



NOTE: Cyclohexane ring rapidly flips b/w ***chair*** conformations at room temperature

The Two conformations of monosubstituted *cyclohexane* are **NOT** equally stable:

1)

Axial bromocyclohexane

2)

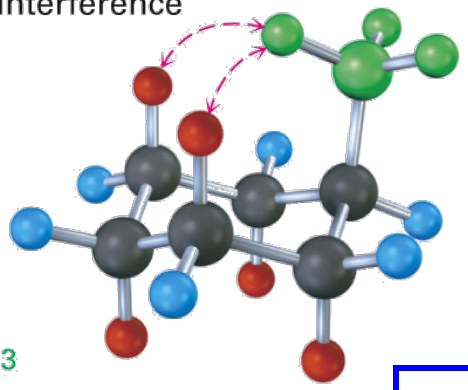
Equatorial bromocyclohexane

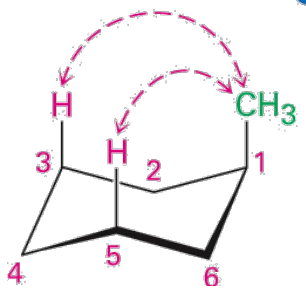
*Interconversion: **a**xial & **e**quatorial **Methy**lcyclohexane*

Axial conformer is ***less*** stable than the *Equatorial* by 7.6 kJ/mol

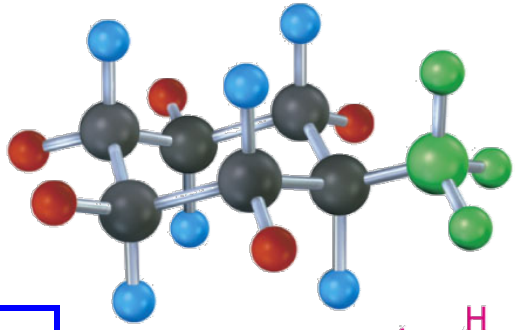
Why? ***b/c*** Steric interference

Axial

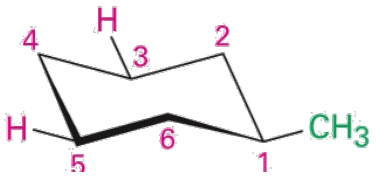


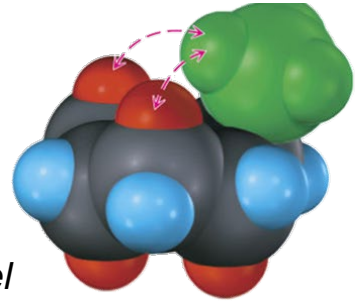


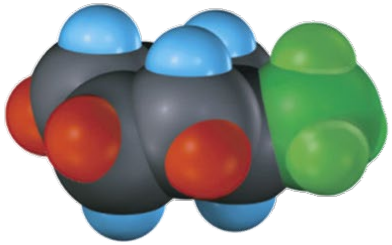
Ring-flip



Now ***Equatorial***





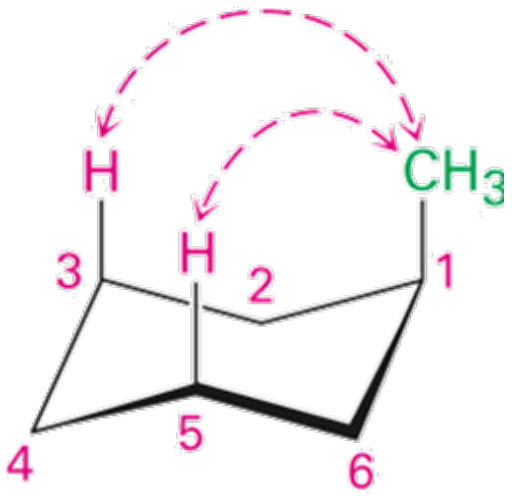


space filling model

Figure 4.13

aka: 1,3-***Di*axial** Interactions

Cause: *Steric strain*



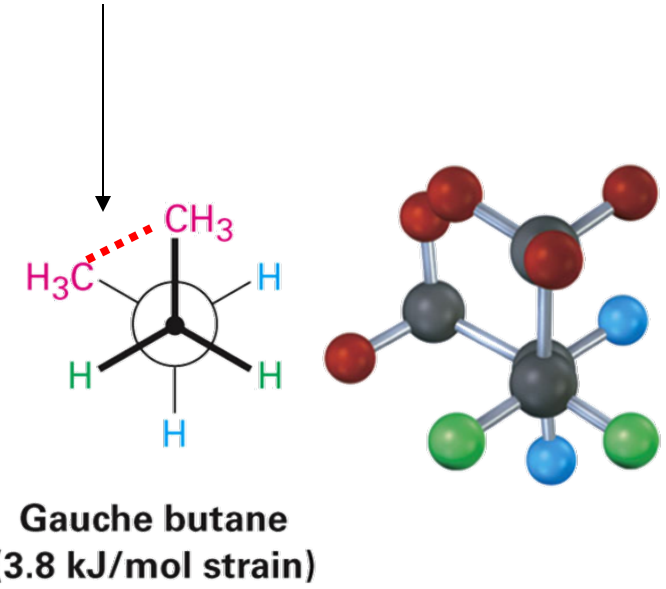
H atoms of the axial *methyl (CH_3)* group are too close to the axial **H** atoms on C3 and C5

Results in: 7.6 kJ/mol of ***steric strain***

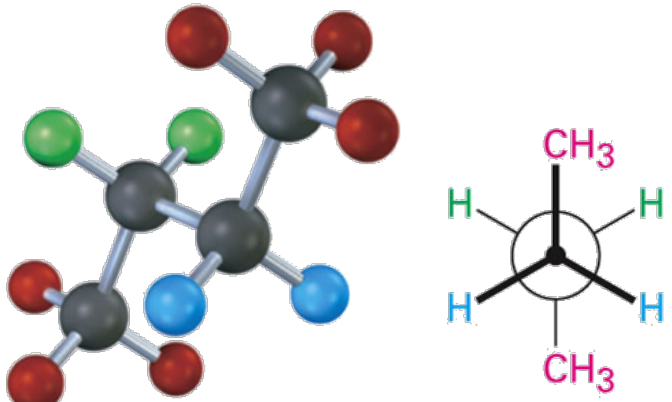
RECALL: *Gauche* ***butane*** interactions

a) ***Gauche*** butane is less stable than **b**) ***anti*** butane by 3.8 kJ/mol due to

steric interference b/w **H** atoms on the two methyl (CH_3) groups



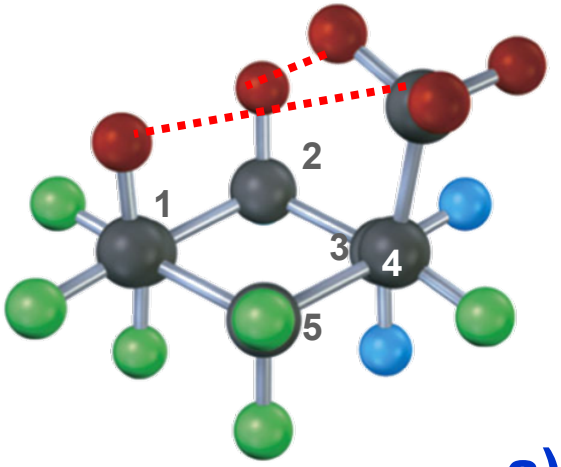
a) **Gauche butane (3.8 kJ/mol strain)**

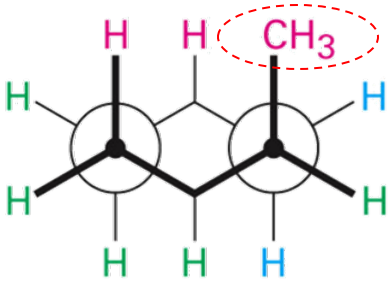


b) **Butane—anti conformation (0 kJ/mol)**

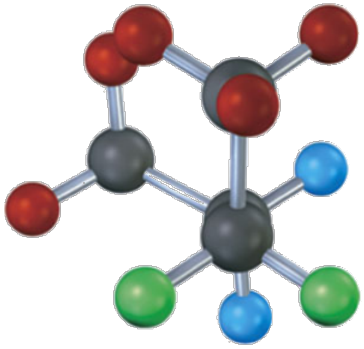
NOTE:

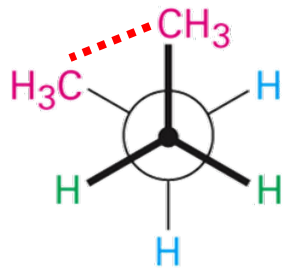
a) ***Axial*** methylcyclohexane and **b)** *Gauche* butane have similar ***steric interactions***





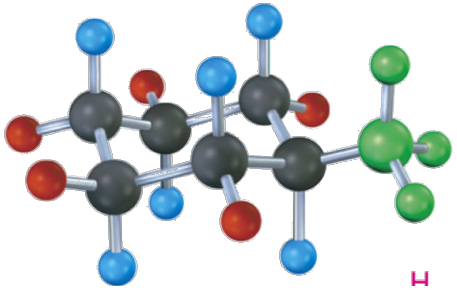
a) **Axial methylcyclohexane (7.6 kJ/mol strain)**





b) **Gauche butane (3.8 kJ/mol strain)**

However…



Equatorial methylcyclohexane has no such interaction ☺

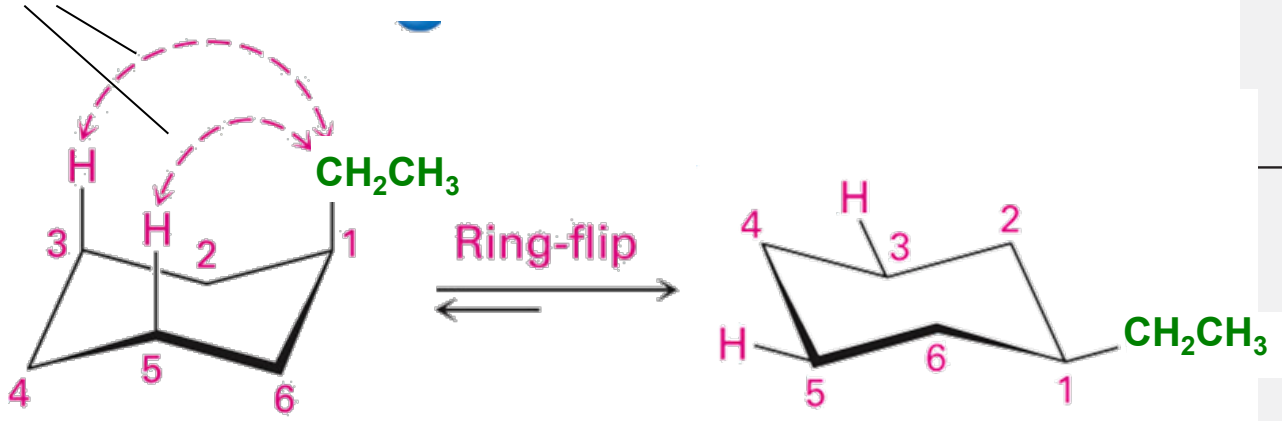
~ **More stable**

Confirming Your Knowledge

If given the following data set (Table 4.1), what is the energy difference (kJ/mol) b/w the ***axial*** and ***equatorial*** conformations of *Ethylcyclohexane*?

4.0 kJ/mol/each

Hint: draw them both (ring flip) and compare



axial

2 x 4.0 kJ/mol **= 8.0 kJ**

equatorial

= 0 kJ

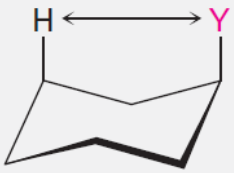


Table 4.1

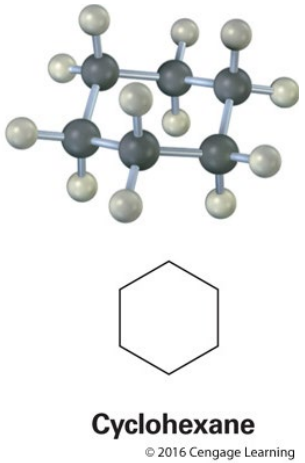
Y	1,3-Diaxial strain (kJ/mol)
F	0.5
Cl, Br	1.0
OH	2.1
CH_3	3.8
CH_2CH_3	4.0
$CH(CH_3)_2$	4.6
$C(CH_3)_3$	11.4
C_6H_5	6.3
CO_2H	2.9
CN	0.4

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

Stability of cycloalkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane

Conformations of monosubstituted cyclohexanes

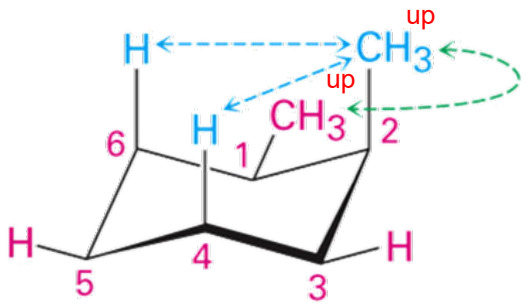
Conformations of **Di**substituted cyclohexanes

Conformations of polycyclic molecules

*"Con**formations**"* of **Di**substituted Cylco**hexanes**

Steric effects of both substituents (**CH_3**) are taken into account in both conformations (***cis*** or ***trans***)

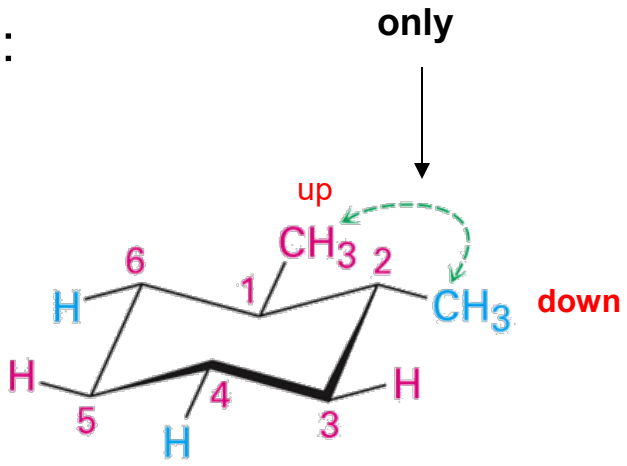
e.g. isomers of 1,2-dimethylcyclohexane:



1,2-dimethylcyclohexane

CH_3 ***same*** side "face" both in **UP** position

cis



1,2-dimethylcyclohexane

CH_3 ***opposite*** sides "faces"
CH3 = up, CH3 = down position

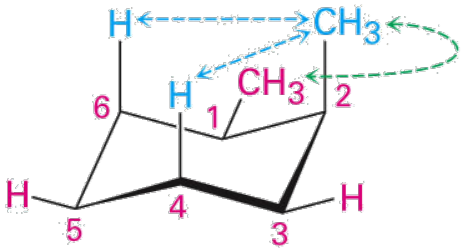
trans

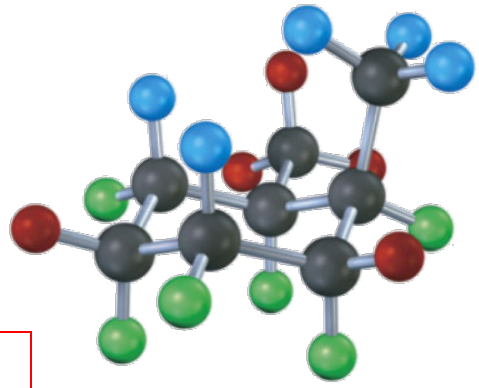
Conformations of: ***cis***-1,2-dimethylcyclohexane

***cis*-1,2-Dimethylcyclohexane**

One gauche interaction (3.8 kJ/mol)
Two $CH_3 \leftrightarrow H$ diaxial interactions (7.6 kJ/mol)

Total strain: 3.8 + 7.6 = 11.4 kJ/mol

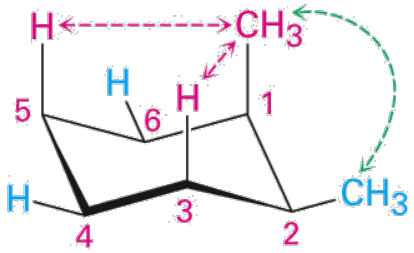


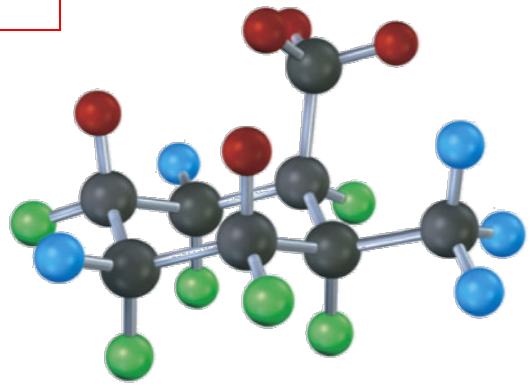


Ring-flip

One gauche interaction (3.8 kJ/mol)
Two $CH_3 \leftrightarrow H$ diaxial interactions (7.6 kJ/mol)

Total strain: 3.8 + 7.6 = 11.4 kJ/mol





NOTE: *Same* total strain ~ 11.4 kJ/mol

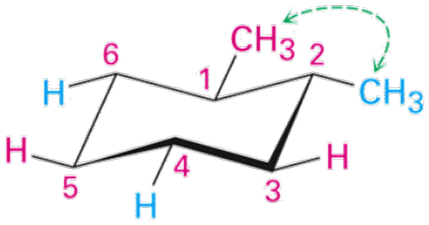
Conformations of: ***trans***-1,2-dimethylcyclohexane

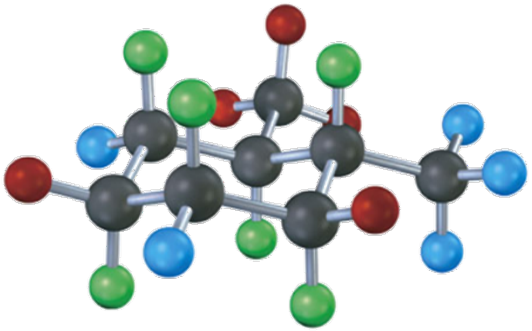
***trans*-1,2-Dimethylcyclohexane**

One gauche interaction (3.8 kJ/mol)

methyls (CH_3) ***equatorial…***

More Stable FORM



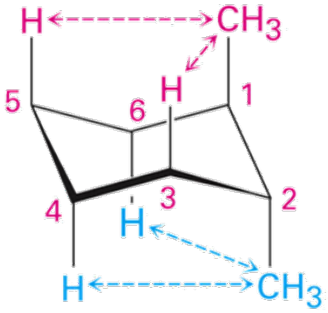


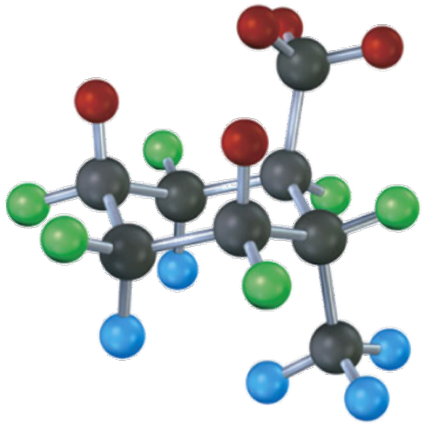
Ring-flip

Four $CH_3 \leftrightarrow H$ diaxial interactions (15.2 kJ/mol)

methyls (CH_3) ***axial…***

less stable FORM

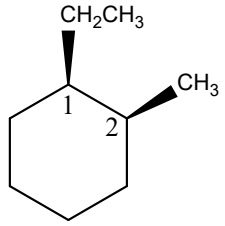




NOTE: *different total strain*: 3.8 kJ/mol vs 15.2 kJ/mol

Chem 3800
Lecture 8
Worksheet 3

Take Home Challenge (THC) Question

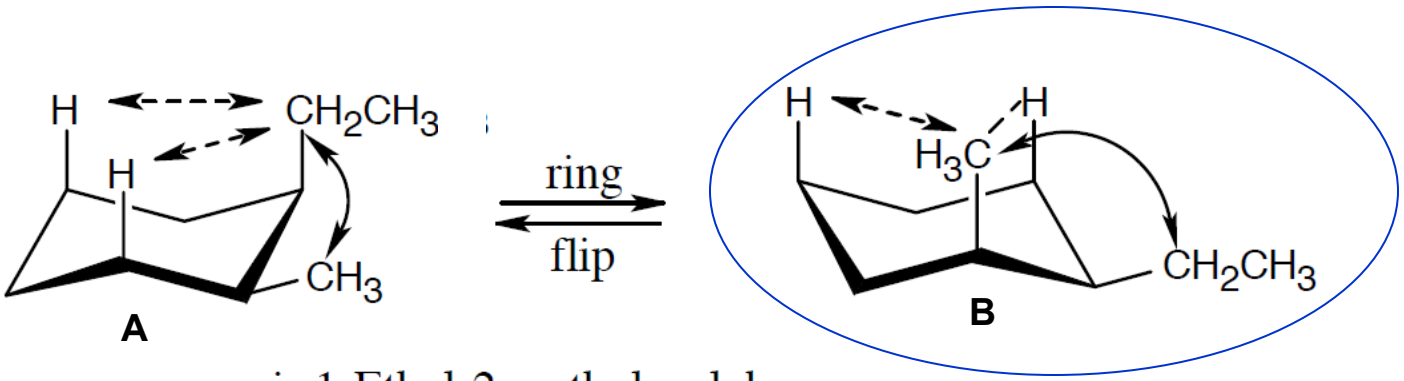


Hint:
Draw the planar structure
Then draw both chair forms.

a) Draw & circle the more stable chair conformation of:

cis-1-Ethyl-2-methylcyclohexane

b) estimate (using Table 4.1) the amount of *strain* in each?



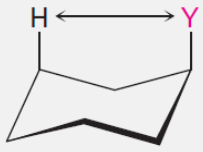
cis-1-Ethyl-2-methylcyclohexane

1 X CH_3 ↔ CH_2CH_3 **gauche** = 3.8 kJ/mol
2 X 4.0 kJ/mol (H–CH_2CH_3) = 8.0 kJ/mol
TOTAL: = **11.8**

1 X CH_3 ↔ CH_2CH_3 **gauche** = 3.8 kJ/mol
2 X 3.8 kJ/mol (H–CH_3) = 7.6 kJ/mol
TOTAL: = **11.4**

NOTE: **gauche** interaction strain ~ 3.8 kJ/mol

Table 4.1



1,3-Diaxial strain

Y	/mol)
F	0.5
Cl, Br	1.0
OH	2.1
CH_3	3.8
CH_2CH_3	4.0
$CH(CH_3)_2$	4.6
$C(CH_3)_3$	1.4
C_6H_5	6.3
CO_2H	2.9
CN	0.4

HW- 4: Due 9-25

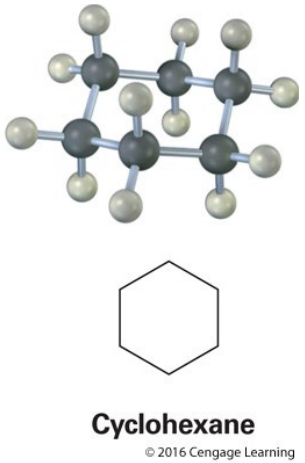
1, 2, 4-7, 9, 11, 12-15, 18, 30, 35-39, 42, 45

Outline

Naming cycloalkanes

Cis-trans isomerism in cycloalkanes

Stability of cycloalkanes: Ring strain



Conformations of cyclo**alkanes**

Conformations of cyclo**hexane**

Axial and equatorial bonds in cyclohexane

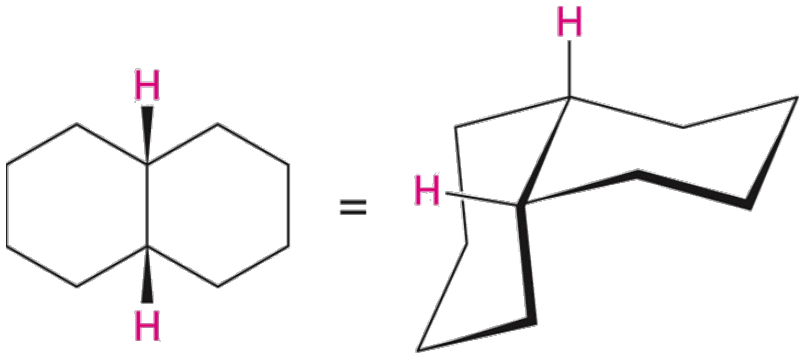
Conformations of monosubstituted cyclohexanes

Conformations of **Di**substituted cyclohexanes

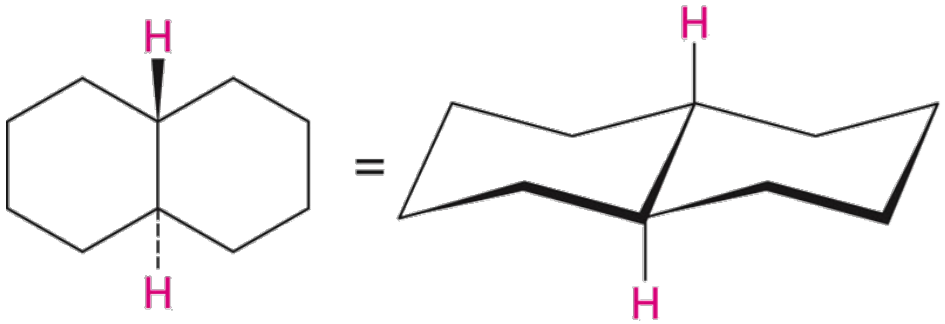
Conformations of **poly**cyclic molecules

Figure 4.17 – Representations of *cis*- and *trans*-**decalin**

consists of 2 cyclohexane rings joined



***cis*-Decalin**



***trans*-Decalin**

NOTES: NOT interconvertible by ***ring-flips*** or other rotations

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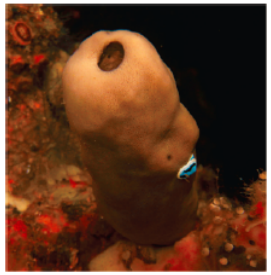
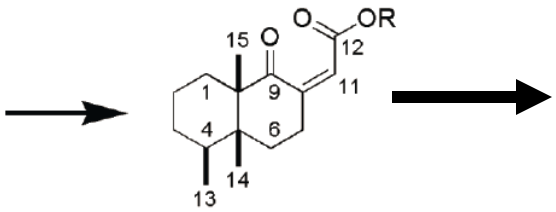
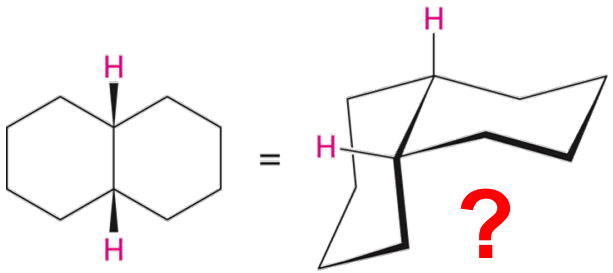


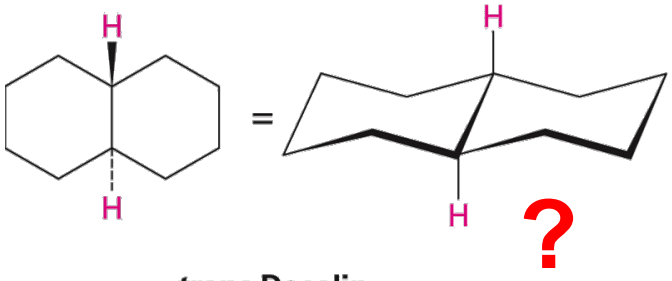


aignopsanoic acid A (**1**) R = H
methyl aignopsanoate A (**2**) R = CH_3

T. brucea - Trypanosomiasis
(African Sleeping sickness)



cis-Decalin



trans-Decalin

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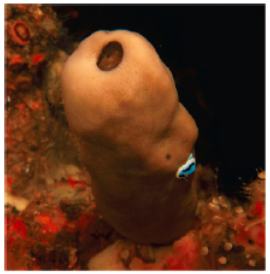

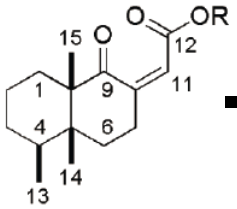

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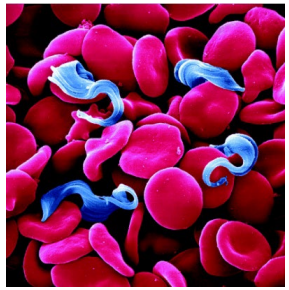
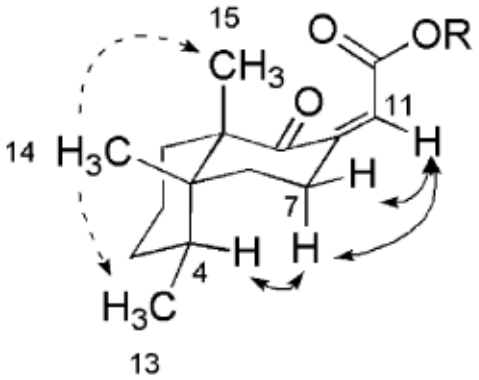
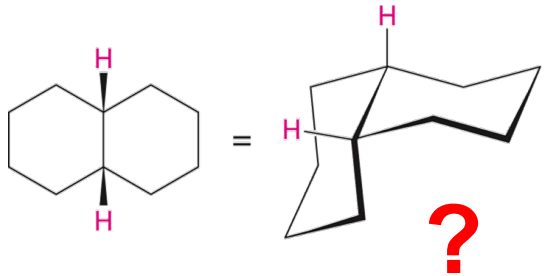


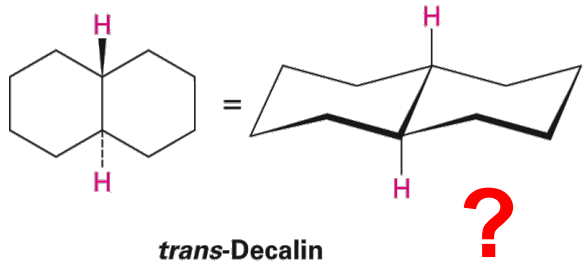
Using NMR (MRI) Confirms ☺:



→ NOESY
⇢ 1D NOE



cis-Decalin



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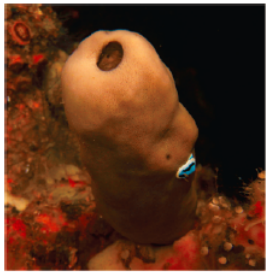

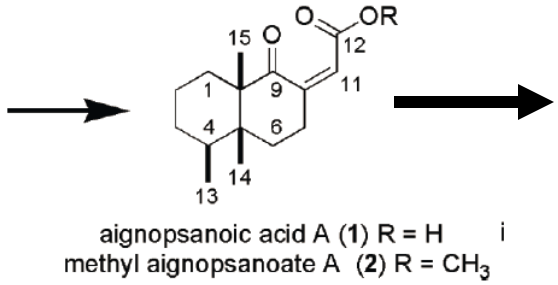

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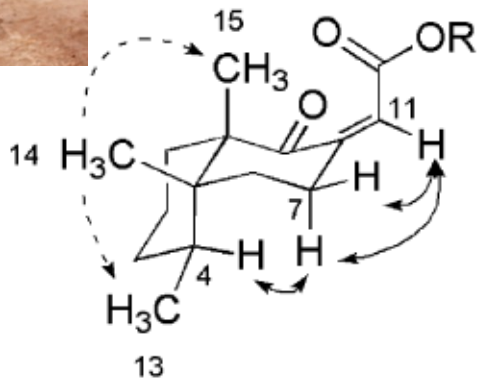

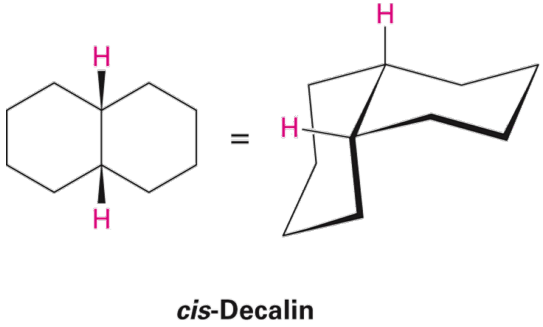

cis-Decalin

The *Aignopsanes:*
a hopeful therapeutic lead
that can one day serve as a cure

→ NOESY
⇢ 1D NOE

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