Damascus University
Faculty of Pharmacy
Pharmaceutical Organic Chemistry I

سيكلو ألكانات وكيميائيتها الفراغية

4. Cycloalkanes and their stereochemistry (chapter 4, McMurry)

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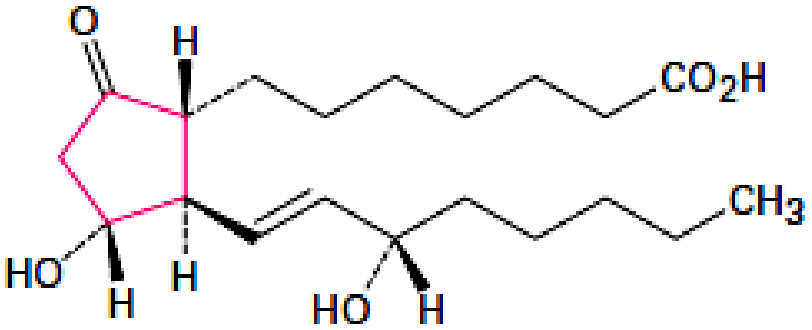
2016–2017

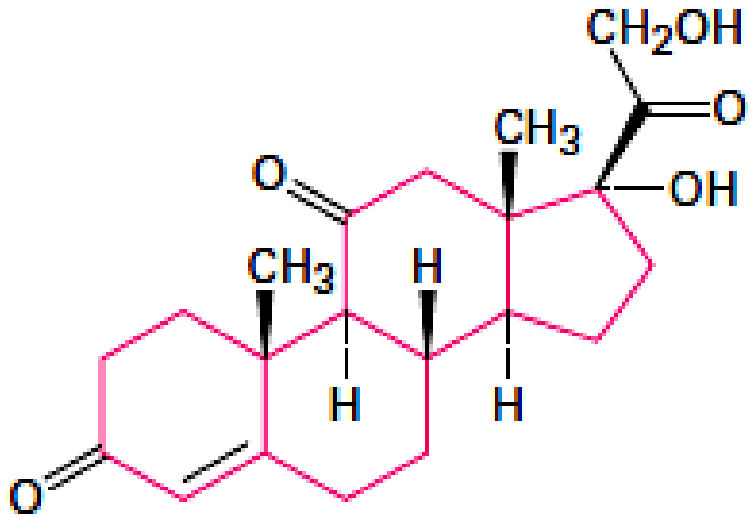
Cycloalkanes

سيكلو ألكانات

- Most organic compounds contain rings of carbon atoms such as Prostaglandins, Steroids, ….



Prostaglandin E_1

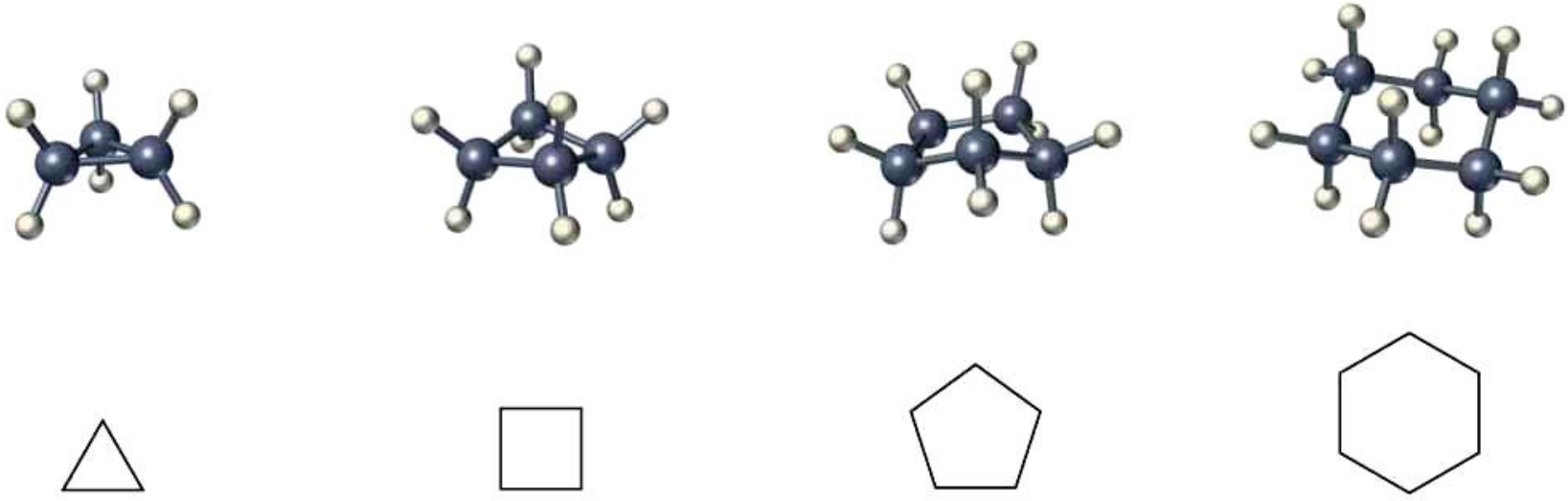


Cortisone

Naming cycloalkanes
تسمية سيكلوالألكانات

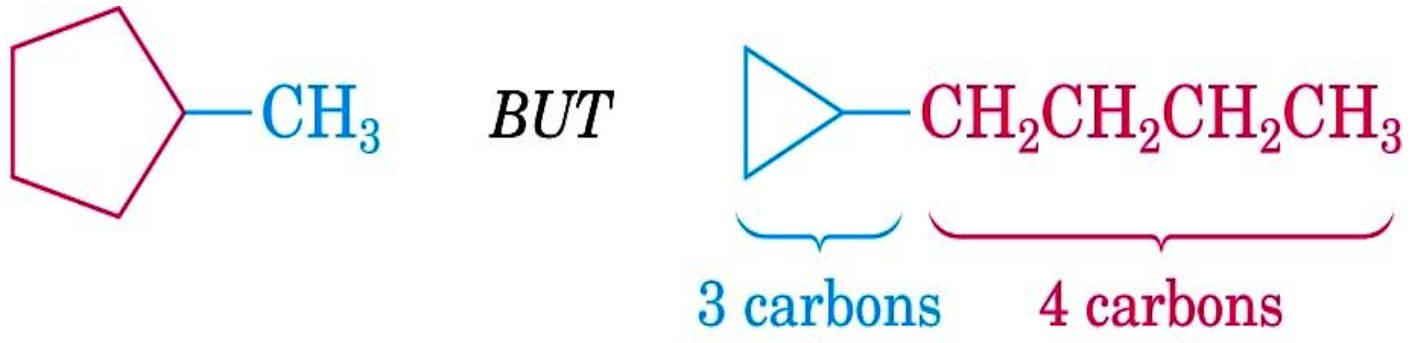
- Saturated cyclic hydrocarbons are called cycloalkanes, or alicyclic compounds (aliphatic cyclic). They Can be represented by polygons in skeletal drawings. General molecular formula : C_nH_{2n}

سيكلوألكانات هي فحوم هيدروجينية مشبعة حلقية ويطلق عليها أيضا المركبات الحلقية الأليفاتية alicyclic يتم تمثيلها على شكل مضلعات هيكلية وهي ذات الصيغة العامة C_nH_{2n}



Naming Alkyl-substituted Cycloalkanes
تسمية سيكلو الألكانات المستبدلة بألكيل

- Named as alkyl substituted cycloalkanes: example, methylcyclopentane. If the number of carbon atoms in the substituant is greater than the number in the ring, the parent name is the alkane
- تسمى باعتبارها ألكيل سيكلوألكان.
- إذا كان عدد ذرات الكربون في المتبادل أكبر من العدد في الحلقة يكون الاسم الأم هو الألكان أي أنها تسمى على شكل سيكلوألكيل ألكان



Methylcyclopentane

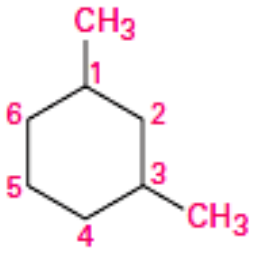
1-Cyclopropylbutane

Naming Alkyl- or halo-substituted Cycloalkanes

- Start at a point of attachment as C1 and number the substituents on the ring so that the *second* substituent has as low a number as possible.

Number the substituents and write the name .

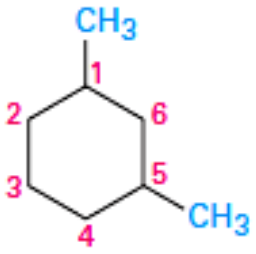
نعتبر الكربون C1 مرتبطا بالمتبادل الأول ثم الاستمرار بحيث يأخذ المتبادل الثاني أصغر رقم ممكن



1,3-Dimethylcyclohexane

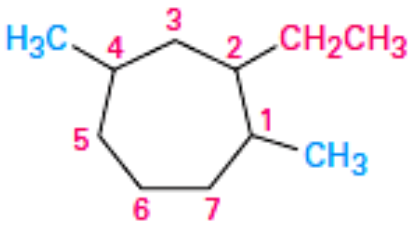
Lower

NOT



1,5-Dimethylcyclohexane

Higher



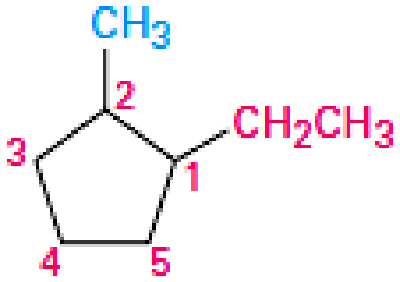
2-Ethyl-1,4-dimethylcycloheptane

Lower Lower

Naming Alkyl- or halo-substituted Cycloalkanes

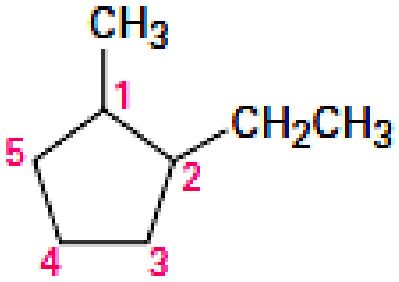
When two or more different substituents could receive the same numbers , number them by alphabetical priority

إذا كان بالإمكان اكتساب المتبادلات المختلفة أرقاما متماثلة يتم الترقيم وفق الأولوية الهجائية

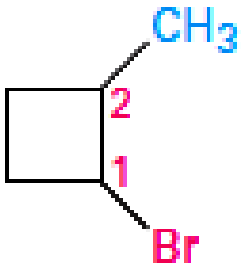


1-Ethyl-2-methylcyclopentane

NOT

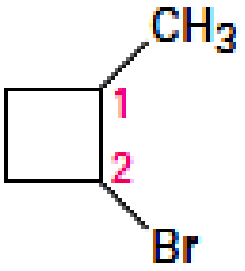


2-Ethyl-1-methylcyclopentane



1-Bromo-2-methylcyclobutane

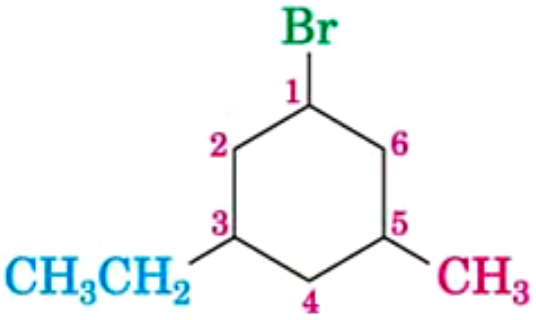
NOT

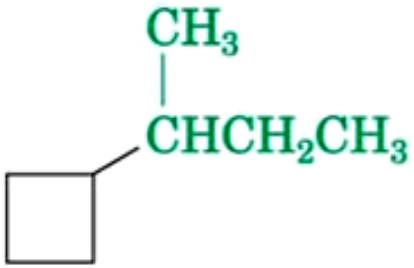


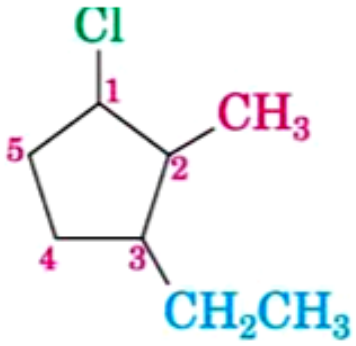
2-Bromo-1-methylcyclobutane

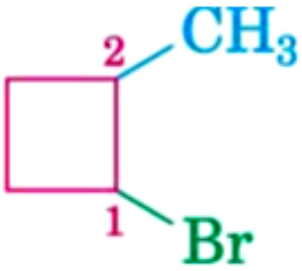
Naming Alkyl- or halo-substituted Cycloalkanes

Give the IUPAC names for the following cycloalkanes









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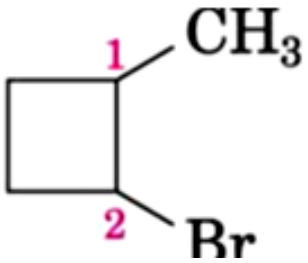


Pb 4.1 ,4.2

Problem 4.2

Draw structures corresponding to the following IUPAC names:

(a) 1,1-Dimethylcyclooctane (b) 3-Cyclobutylhexane

(c) 1,2-Dichlorocyclopentane (d) 1,3-Dibromo-5-methylcyclohexane

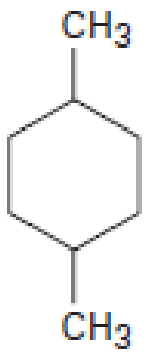
Problem 4.3

Name the following cycloalkane:

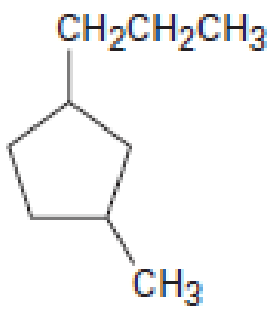
Problem 4.1

Give IUPAC names for the following cycloalkanes

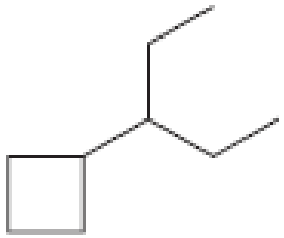
(a)



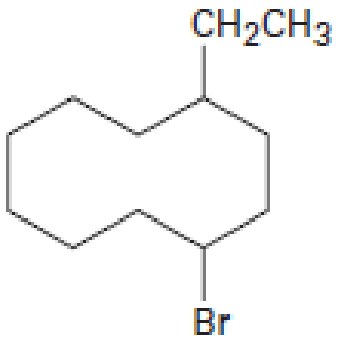
(b)



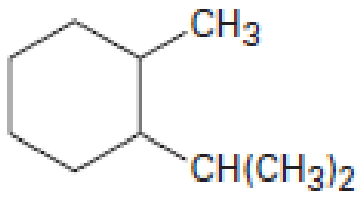
(c)



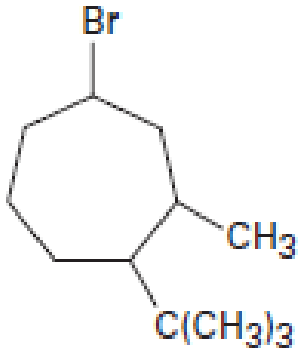
(d)



(e)



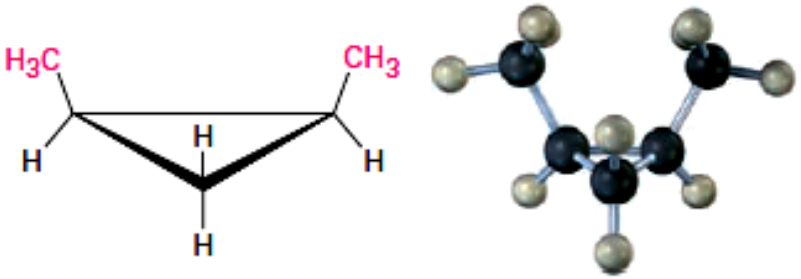
(f)



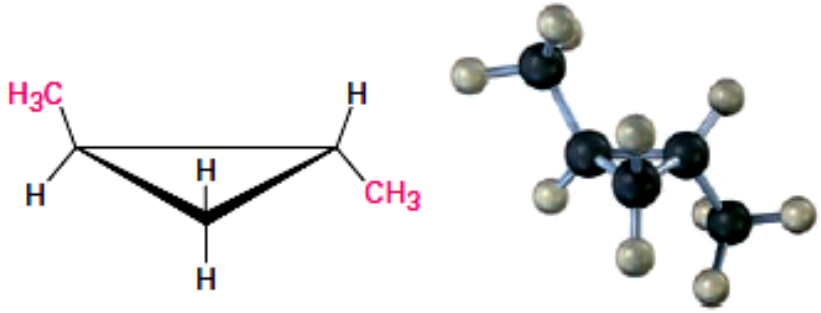
Cis-Trans Isomerism in Substituted Cycloalkanes التصاوغ مقرون- مفروق

- Rotation about C-C bonds in cycloalkanes is limited by the ring structure. As a result, isomerism is possible.
- For example, two different isomers (cis مقرون) and (trans مفروق) exist for 1,2-dimethylcyclopropane.
- Such isomers differ in three-dimensional orientation, are called stereoisomers متصاوغات فراغية

يؤدي وجود الحلقة إلى تقييد الدوران حول الروابط C-C مما يسمح بحصول التصاوغ مقرون مفروق ويطلق عليها متصاوغات فراغية stereoisomers أي تختلف عن بعضها بالبنية ثلاثية البعد

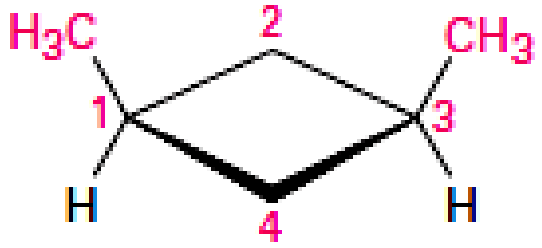


cis-1,2-Dimethylcyclopropane

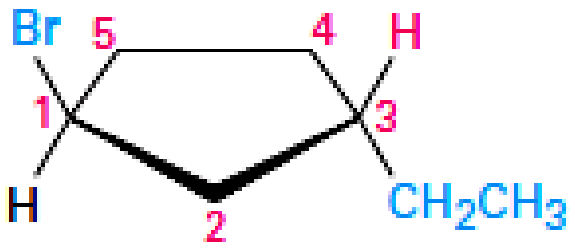


trans-1,2-Dimethylcyclopropane

Cis-Trans Isomerism in Cycloalkanes



cis-1,3-Dimethylcyclobutane

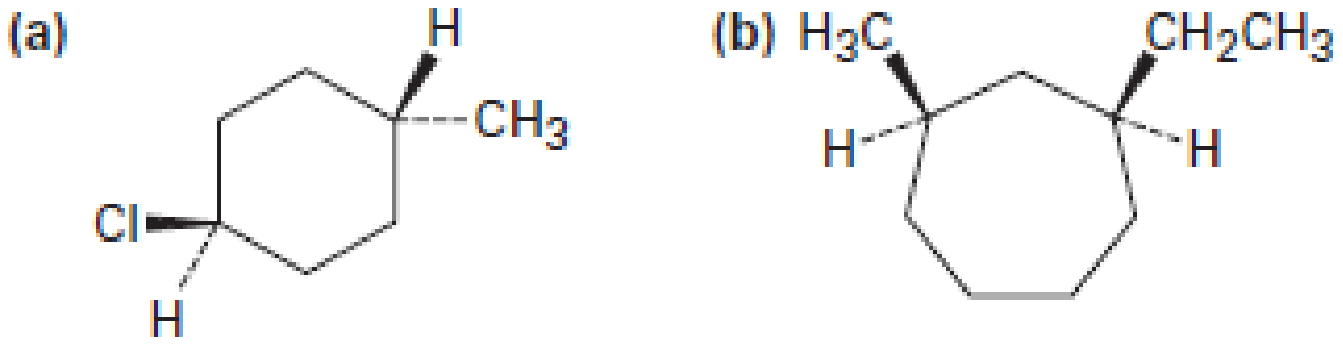


trans-1-Bromo-3-ethylcyclopentane

Pb 4.4- 4.6

Problem 4.4

Name the following substances, including the *cis- or trans-prefix:*



Problem 4.5

Draw the structures of the following molecules:

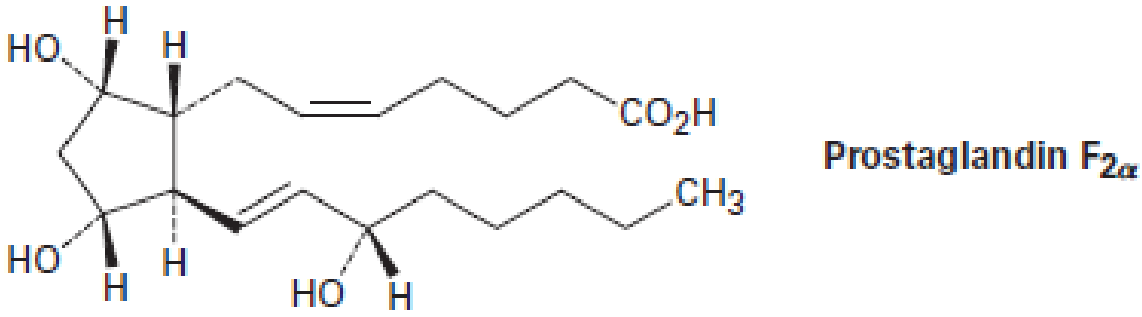
(a) trans-1-Bromo-3-methylcyclohexane

(b) cis-1,2-Dimethylcyclobutane

(c) *trans-1-tert-Butyl-2-ethylcyclohexane*

Problem 4.6

Prostaglandin F2α, *a hormone that causes uterine contraction during childbirth, has the* following structure. Are the two hydroxyl groups (-OH) on the cyclopentane ring cis or trans to each other? What about the two carbon chains attached to the ring?



Prostaglandin $F_{2\alpha}$

Stability of Cycloalkanes Ring strain
ثبات سيكلوالالكانات وإجهاد الحلقة

Cyclopropane is flat مسطح and is the most strained of all rings (has both angle and torsional strain). **Angle strain** - expansion or compression of bond angles away from most stable one (109.5^o). **Torsional strain**—the strain due to eclipsing of bonds on neighboring atoms

- Rings larger than 3 atoms are not flat.They can assume nonplanar conformations to minimize angle strain and torsional strain by ring-puckering. Larger rings have many more possible conformations than smaller rings

يملك سيكلو بروبان بنية مسطحة وهو أكثر الحلقات إجهادا(إجهادا زاويا وإجهاد فتل)

ينتج إجهاد الزاوية من كون الزوايا بين الروابط أكبر أو أصغر من الزاوية الأكثر ثباتا (109.5^o).

ينتج إجهاد الفتل من خسوف الروابط على الذرات المتجاورة .

الحلقات الأكبر من 3 ذرات هي غير مسطحة وتتبنى هيئات فراغية متجعدة للحصول على إجهاد زاوية أصغري.

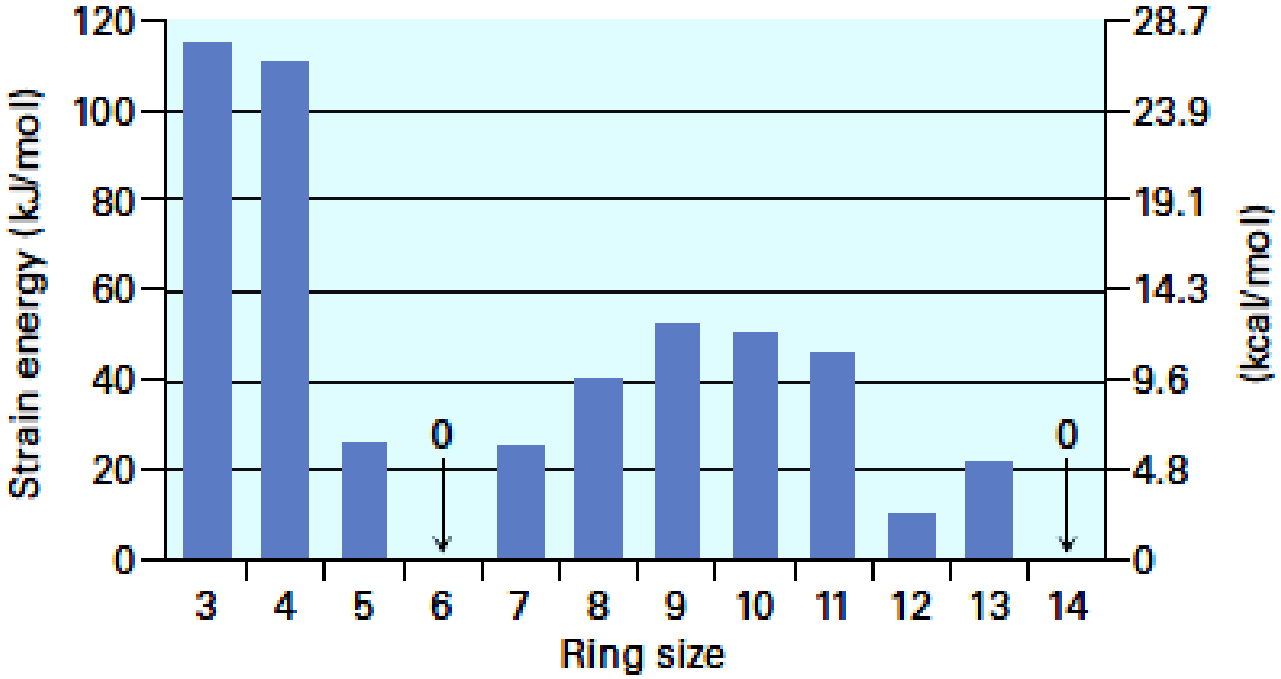
تستطيع الحلقات الأكبر تبني هيئات فراغية أكثر من الحلقات الصغيرة

Stability of Cycloalkanes Ring strain

ثبات سيكلوالالكانات وإجهاد الحلقة

- Rings with C_3 –C_5 are strained . Cyclohexane is strain – free
- Rings (C_7-C_{13}) rings are less strained than small rings (C_3,C_4).
- Rings with more than C_{14} are strain –free

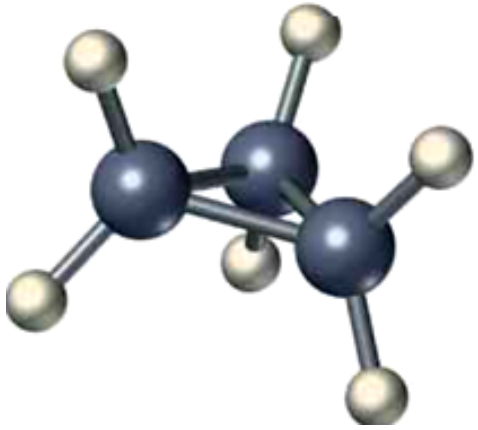
- الحلقات C_3 –C_5 حلقات مجهدة . سيكلوهكسان خالي من الإجهاد.
- والحلقات (C_7-C_{13}) أقل إجهادا من الحلقات الصغيرة .(C_3,C_4)
- الحلقات التي تحتوي على أكثر من C_{14} هي حلقات غير مجهدة

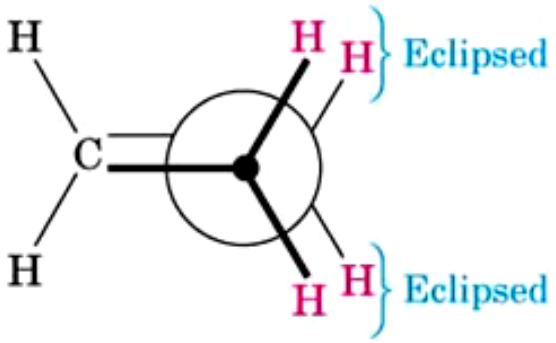


Conformation of Cyclalkanes
الهيئة أوالشكل الفراغي لسيكلوبروبان

• **Cyclopropane** is the most strained of all rings. Has planar مستوية structure (flat) . Angle strain is caused by its 60° C- C- C bond angles.
• Considerable torsional strain إجهاد فتل because the eclipsing C - H bonds on neighboring carbon atoms. **Total strain** الإجهاد الكلي **: about 115 kJ/mol**
• Cyclopropane bonds (bent bonds روابط منحنية) are weakerأ and more reactive than typical alkane bonds

•سيكلوبروبان هو أكثر الحلقات إجهادا ، له بنية مستوية ويملك إجهادا زاويا بسبب زوايا الروابط C- C- C 60 درجة. ويملك إجهاد فتل بسبب خسوف الروابط C – H على ذرات الكربون المتجاورة. ألإجهاد الكلي هو حوالي **115 kJ/mol** .
الروابط في سيكلوبروبان روابط منحنية وهي أضعف وأكثر تفاعلية من روابط الألكان





Problem 4.8

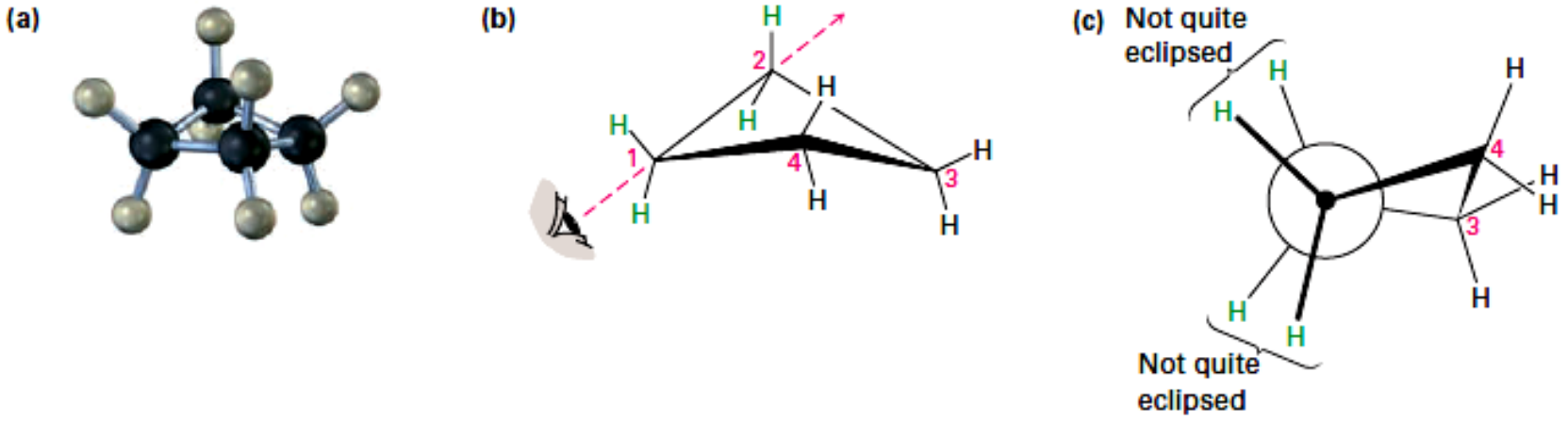
Each H ⟷ H eclipsing interaction in ethane costs about 4.0 kJ/mol. How many such interactions are present in **cyclopropane**? What fraction of the overall 115 kJ/mol (27.5 kcal/mol) strain energy of cyclopropane is due to torsional strain?

Problem 4.9

cis-1,2-Dimethylcyclopropane has more strain than trans-1,2-dimethylcyclopropane. How can you account for this difference? Which of the two compounds is more stable?

Conformation of Cyclobutane

- Ring not quite flat (Wing shape شكل جناح) but slightly bent out of plane; one carbon atom is about 25° out of plane. C-H bonds are partly eclipsed الروابط مخسوفة جزئيا .
- Less angle strain than cyclopropane (C-C-C bond angle about 90°)
- More torsional strain than cyclopropane, due to larger number of ring hydrogens.
- **Total strain is about 110kJ/mol**



Conformation of Cyclopentane

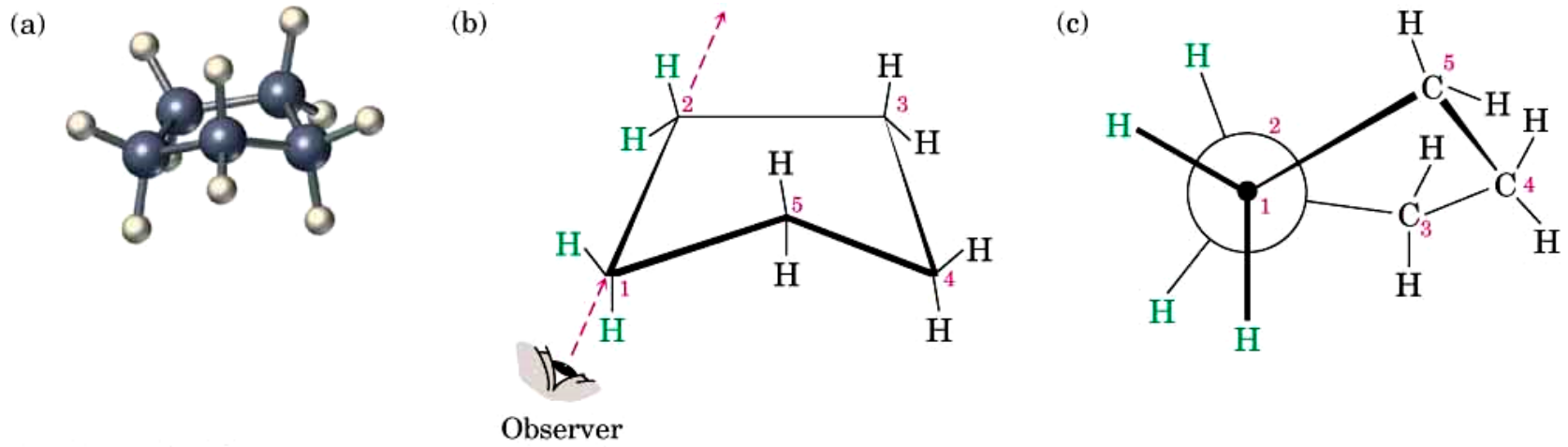
• Adopt puckered مجعدة, nonplanar غير مستوية conformation, a balance between increased angle strain and decreased torsional strain.

• Four carbon atoms are in a plane and the fifth carbon atom is above or below the plane (envelop shape شكل الظرف) .

• Too slight angle strain إجهاد زاوي ضعيف للغاية (C–C–C bond angles are near to 108°).

• Slight torsional strain إجهاد فتل ضعيف (C-H bonds are nearly staggered روابط متباعدة تقريبا).

• **Total energy strain is 26kJ/mol.**



Problem 4.10

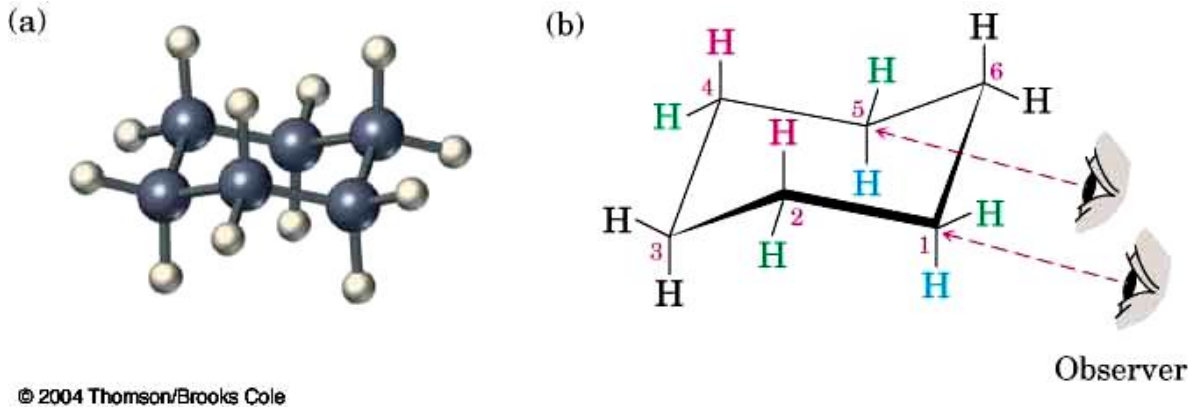
• How many H ←→ H eclipsing interactions would be present if cyclopentane were planar? (10)

• Assuming an energy cost of 4.0 kJ/mol for each eclipsing interaction, how much torsional strain would planar cyclopentane have? (40kJ/mol)

• Since the measured total strain of cyclopentane is 26 kJ/mol, how much of the torsional strain is relieved by puckering? (14 kJ/mol, 35% الإجهاد المحذوف)

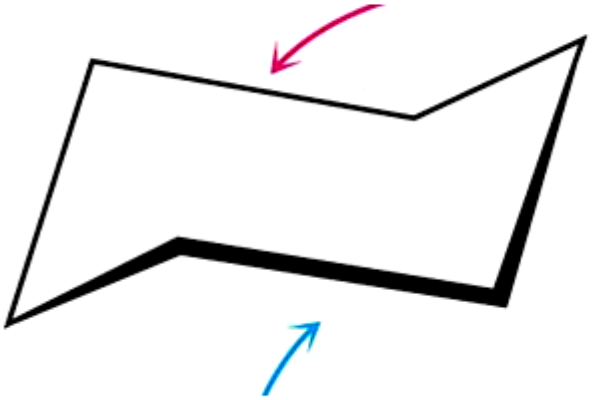
3.5 Chair Conformations of Cyclohexane

- No angle strain: bond angles; 109.5º .
- No torsional strain: staggered C-H bonds:(six axial hydrogens and six equatorial hydrogens ستة هيدروجينات محورية وستة استوائية) .
- Strain-free chair conformation كرسي خالي من الإجهاد.

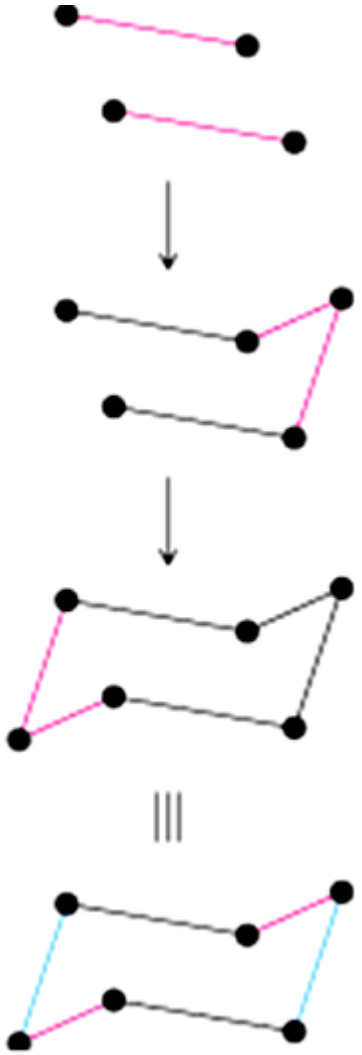


How to Draw Cyclohexane

This bond is in back



This bond is in front

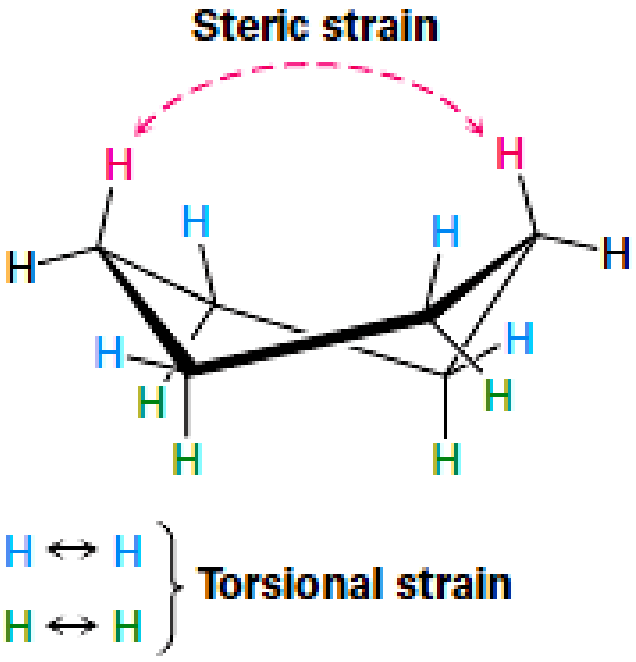


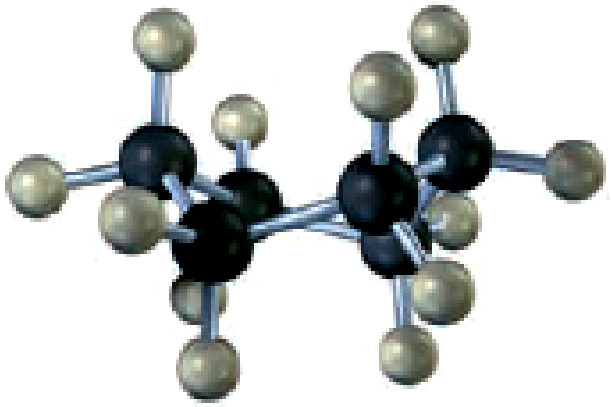
Other Conformations of Cyclohexane

• Other conformations less stable than chair conformations exist.

•Twist-boat قارب ملتوي conformation have both steric strain and torsional strain and is about 23 kJ/mol higher in energy than the chair conformation.

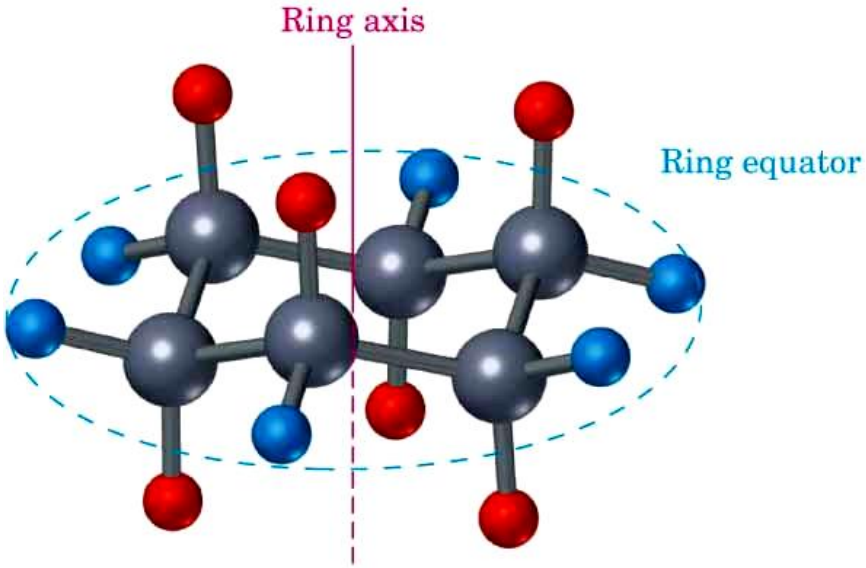
• Molecules can adopt the twist-boat geometry only under special circumstances

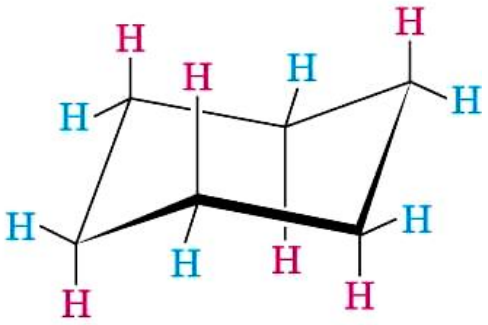


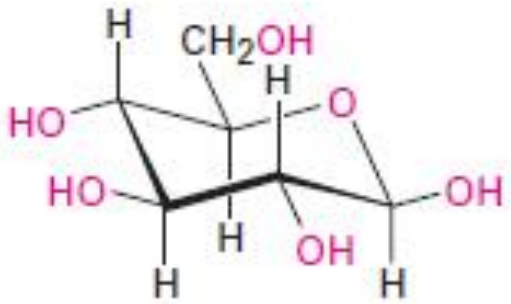


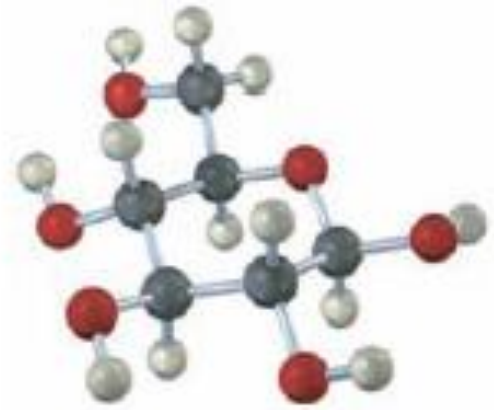
Twist-boat cyclohexane
(23 kJ/mol strain)

4.6 Axial محوري and Equatorial استوائي Bonds in Cyclohexane





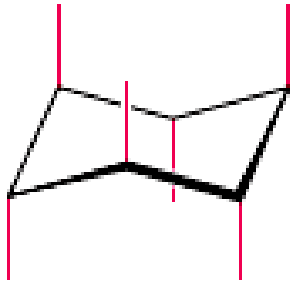




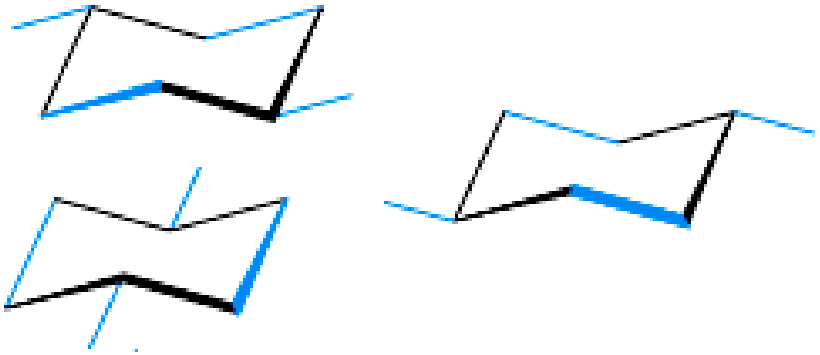
Glucose
(chair conformation)

Drawing the Axial and Equatorial Hydrogens

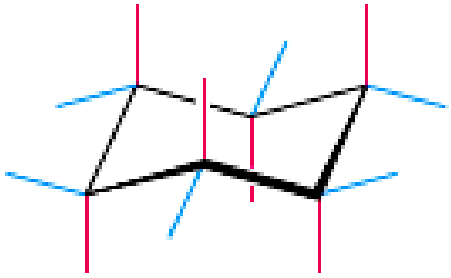
Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up–down.



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.

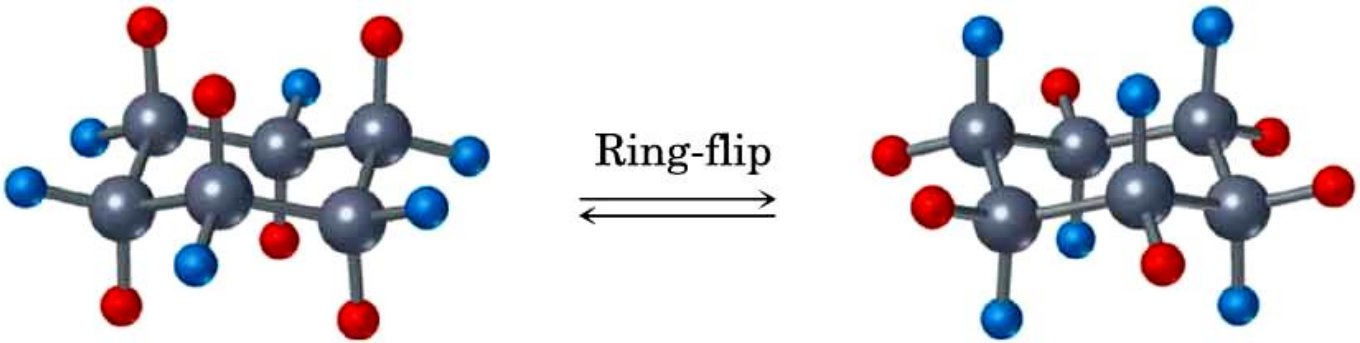


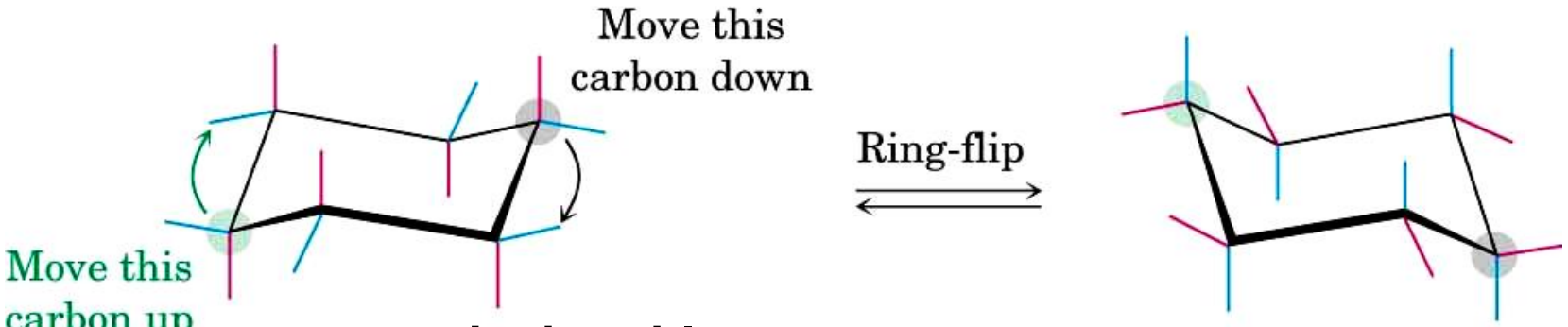
Completed cyclohexane



Ring flip انقلاب الحلقة of Cyclohexane

- Ring-flip انقلاب الحلقة : chair interconversion التحول كرسي-كرسي results in the exchange تبادل of axial and equatorial positions.
- The two conformers are equal in energy.
  المشكالان كرسي-كرسي متساويان في الطاقة





Worked problem 4.2
Problems 4.12, 4.13, 4.14

Drawing the Chair Conformation of a Substituted Cyclohexane

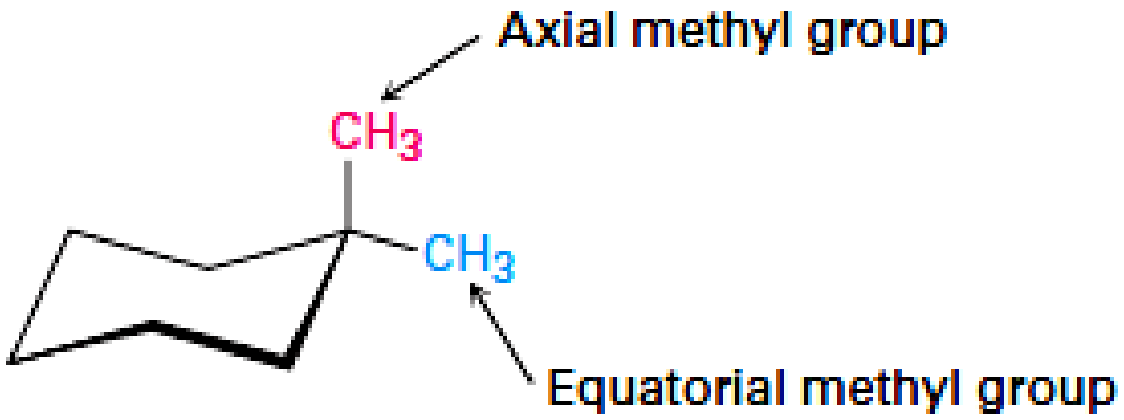
Worked Example 4.2

Draw 1,1-dimethylcyclohexane in a chair conformation, indicating which methyl group in your drawing is axial and which is equatorial.

Strategy

Draw a chair cyclohexane ring .put two methyl groups on the same carbon. The methyl group in the rough plane of the ring is equatorial, and the one directly above or below the ring is axial.

Solution



Problem 4.12

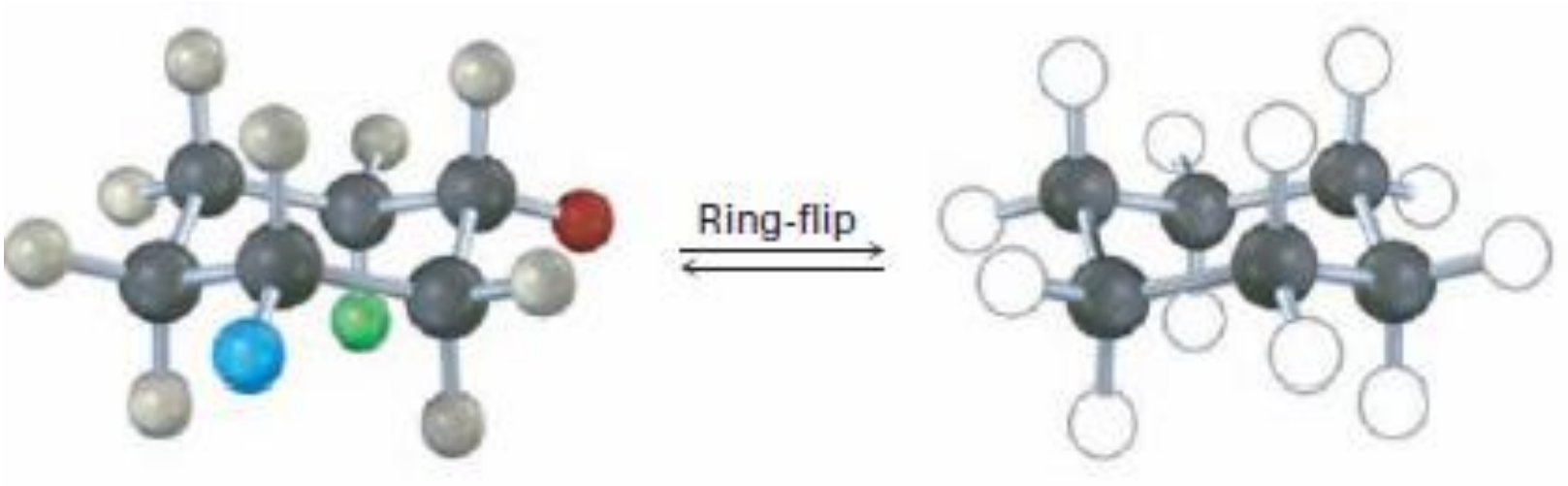
Draw two different chair conformations of cyclohexanol (hydroxycyclohexane), showing all hydrogen atoms. Identify each position as axial or equatorial.

Problem 4.13

Draw two different chair conformations of *trans-1,4-dimethylcyclohexane, and label all* positions as axial or equatorial.

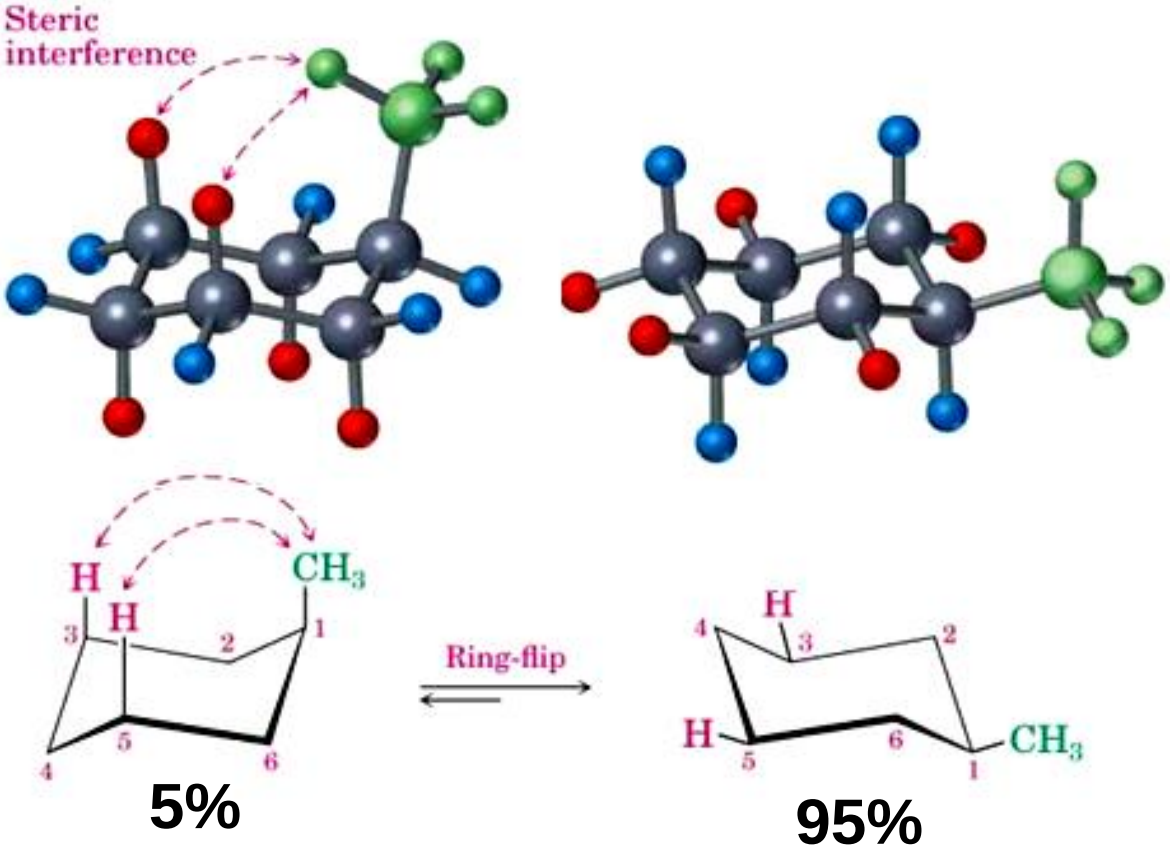
Problem 4.14

Identify each of the colored positions—red, blue, and green—as axial or equatorial. Then carry out a ring-flip, and show the new positions occupied by each color

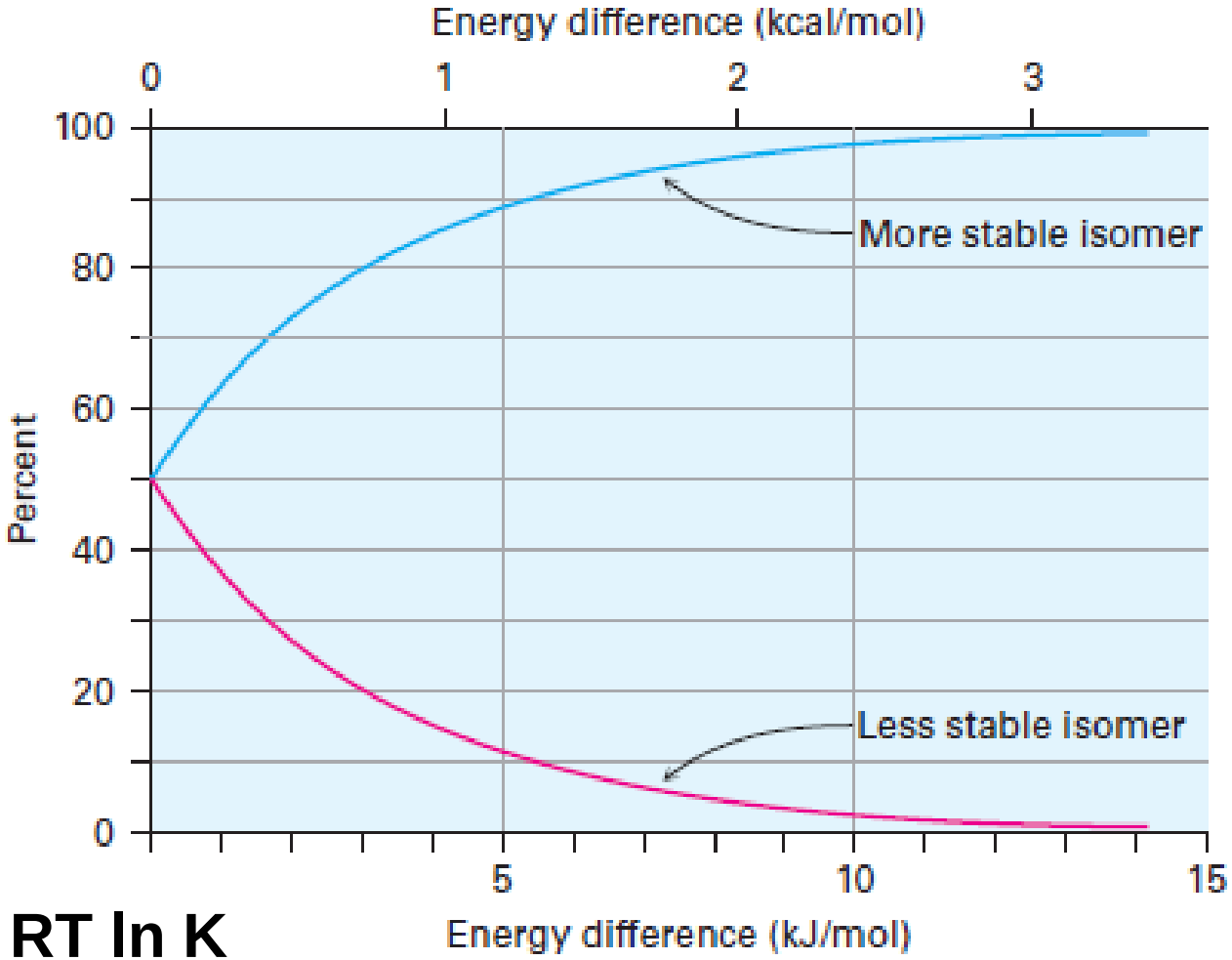


3.7 Ring-flip in methylcyclohexanes

- The two conformers are not equal in energy, and the methyl equatorial conformer is more stable than the axial one.
- The axial conformer المشكال المحوري is less stable because it has a steric strain (cost تكلفة أو قيمة : 2X 3.8 = 7,6 kJ/mol), due to 1,3-diaxial interaction محوري - تآثرثنائي المحور أو محوري.



Conformers percentage and energy difference

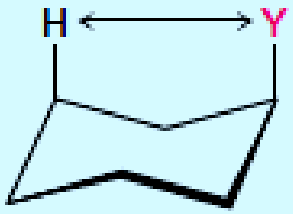


ΔE = - RT ln K

ΔE : energy difference between isomers. R:the gas constant

T : the Kelvin temperature. K : the equilibrium constant ثابت التوازن between isomers.

Table 4.1 Steric Strain in Monosubstituted Cyclohexanes



Y	1,3-Diaxial strain (kJ/mol)	1,3-Diaxial strain (kcal/mol)
F	0.5	0.12
Cl, Br	1.0	0.25
OH	2.1	0.5
CH_3	3.8	0.9
CH_2CH_3	4.0	0.95
$CH(CH_3)_2$	4.6	1.1
$C(CH_3)_3$	11.4	2.7
C_6H_5	6.3	1.5
CO_2H	2.9	0.7
CN	0.4	0.1

Pb 4.15- 4.17

Problem 4.15

What is the energy difference between the axial and equatorial conformations of cyclohexanol (hydroxycyclohexane)?

Problem 4.16

Why do you suppose an axial cyano (–CN) substituent causes practically no 1,3-diaxial steric strain (0.4 kJ/mol)? Use molecular models to help with your answer.

Problem 4.17

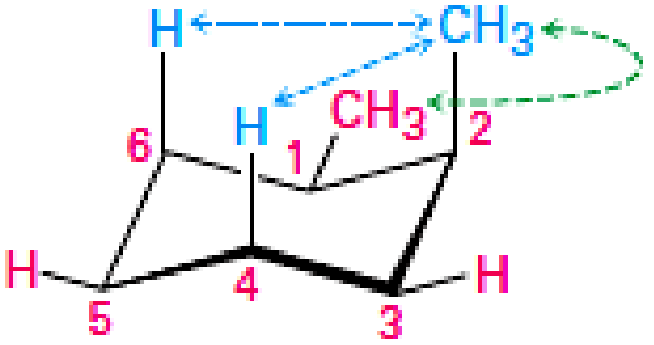
Look at Figure 4.12 on page 124, and estimate the percentages of axial and equatorial conformations present at equilibrium in bromocyclohexane.

3.8 Conformations of 1,2-Dimethyl Cyclohexane

- In *cis*- isomer both conformations are equal in energy

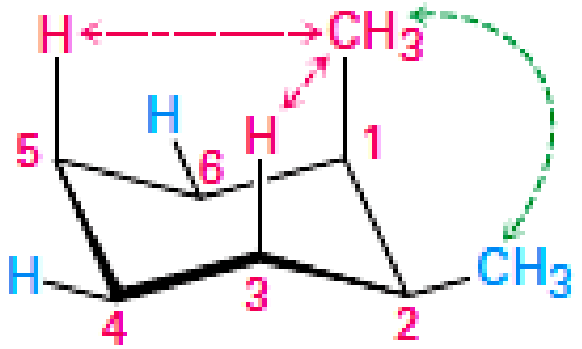
***cis*-1,2-Dimethylcyclohexane**

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

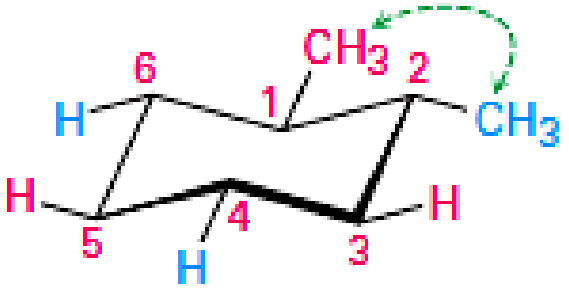


Conformations of 1,2-Dimethyl Cyclohexane

• The *trans*- isomer will exist almost exclusively (>99%) in the di-equatorial conformation

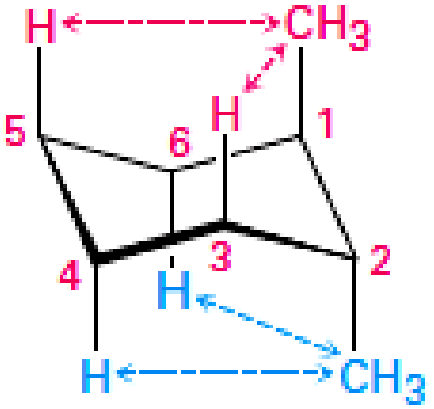
***trans*-1,2-Dimethylcyclohexane**

One gauche interaction (3.8 kJ/mol)

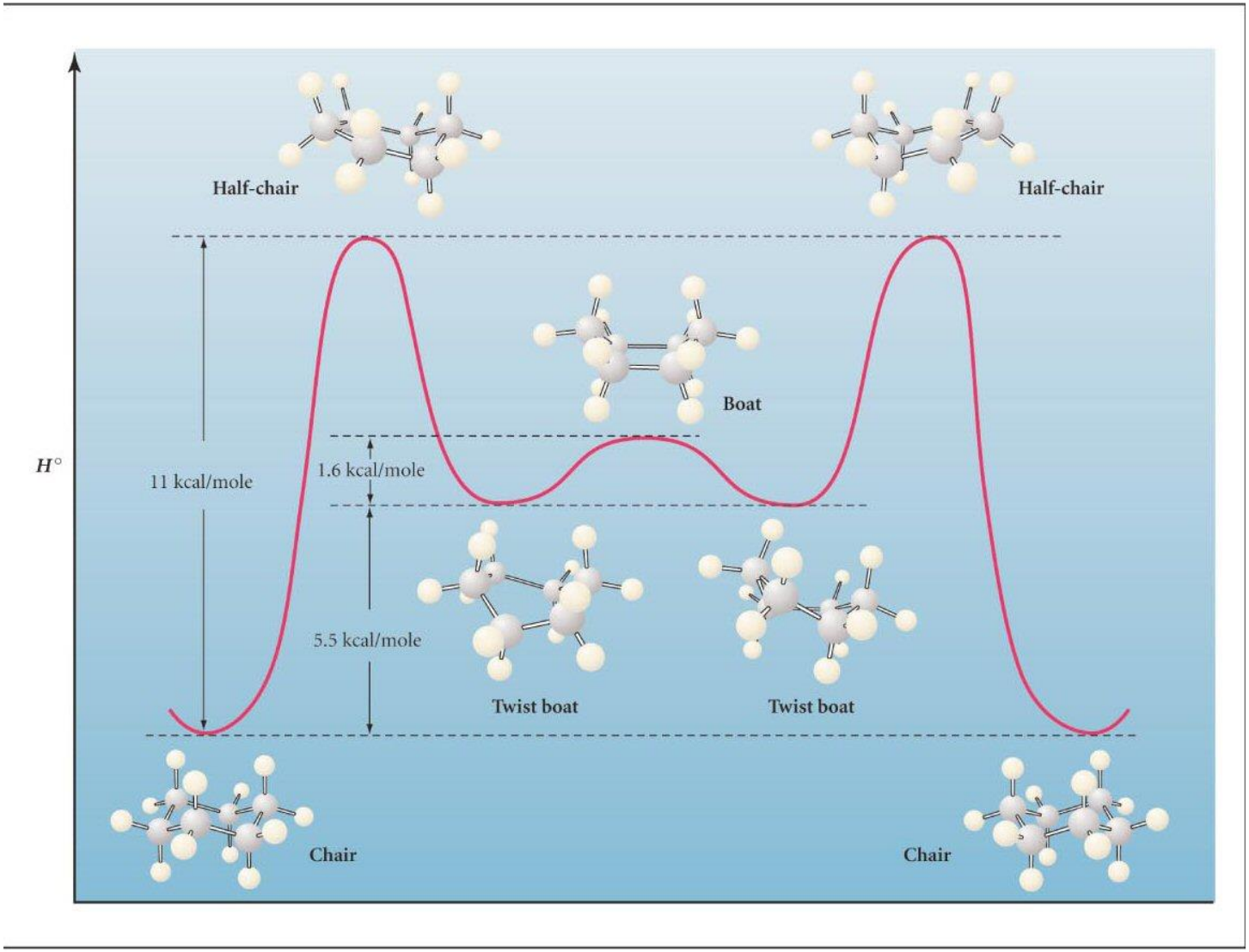


Ring-flip

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



المشاكيل الممكنة لسيكلوهكسان عند التحول كرسي- كرسي:
كرسي- نصف كرسي-قارب ملتوي- قارب



المشاكيل الممكنة لسيكلوهكسان عند التحول كرسي- كرسي:
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