CHAPTER 6

STEREOCHEMISTRY I

Contents

- Cis-Trans Isomers and Conformations

Introduction

Stereochemistry (입체화학)

⇒ 3-diemsional structures of organic molecules

Isomer: different molecules with the same molecular formula

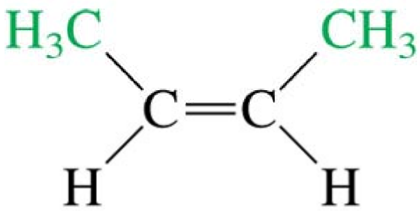
structural isomer: different connectivity

stereoisomers: same bonds but different 3-dimensional orientation of these bonds

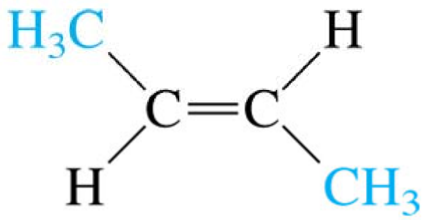
6.1 Cis-Trans isomers

cis ⇒ like groups on the same side
trans ⇒ like groups on the other side

- Isomers of 2-butene



cis-2-Butene



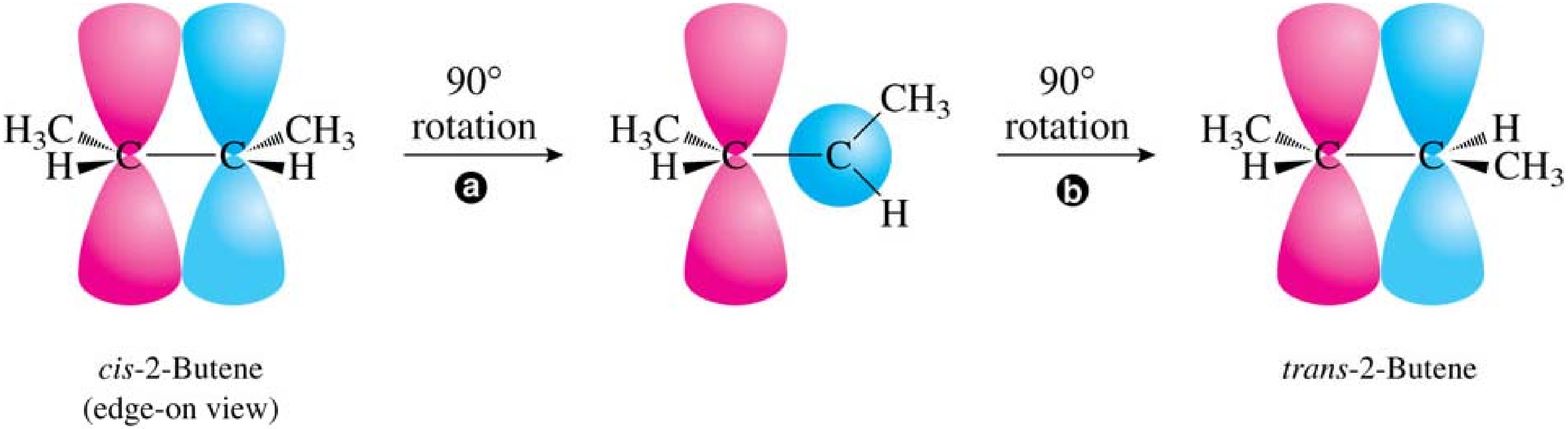
trans-2-Butene

0.33	Dipole moment (Debyes)	0
4°C	Boiling point	1°C
−139°C	Melting point	−106°C

Therefore cis and trans isomers are two different compounds
⇒ different shape, physical, and chemical properties

Is interconversion possible for cis-trans isomers? No!

only possible by breaking π bonds, while the problem is bond E of pi-bond is about 60 kcal/moe and the thermal E of RT is about 20 kcal/mol

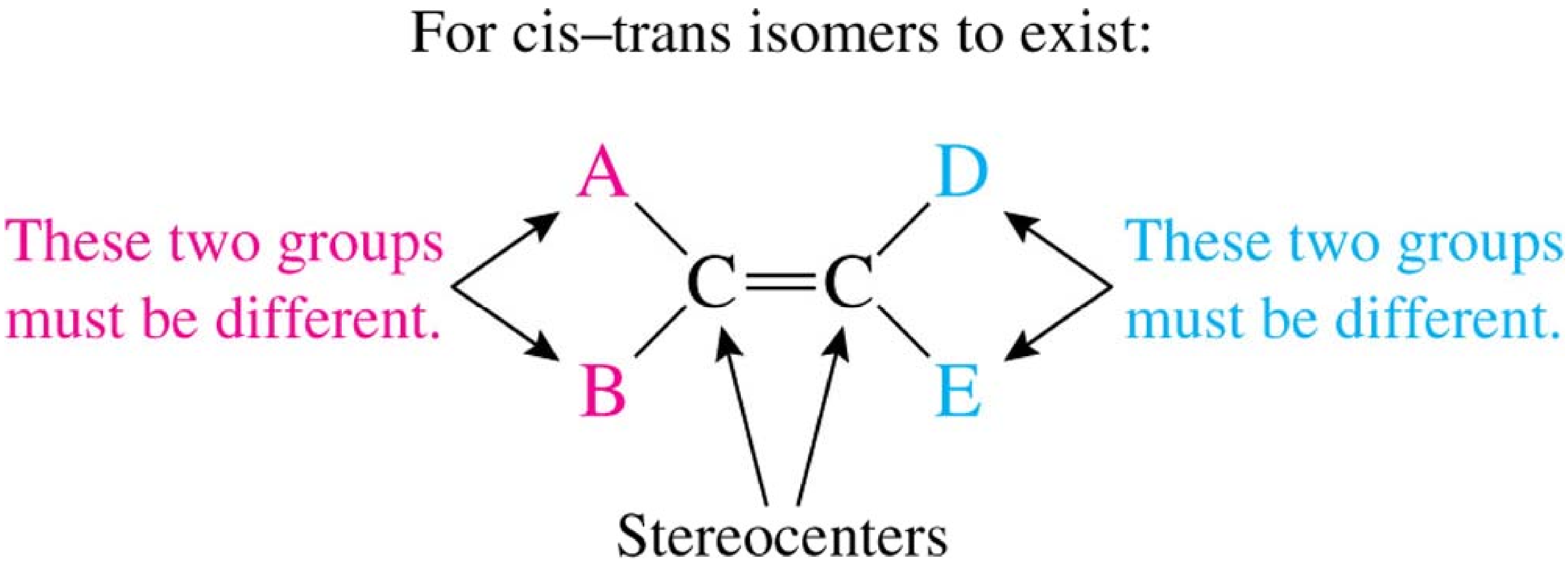


The *p* orbitals of the pi bond of *cis*-2-butene are in the plane of the page, and the plane defined by the atoms attached to the carbons of the double bond is perpendicular to the page. To convert to the *trans*-isomer, one of the carbons of the double bond must be rotated about the axis of the double bond.

ⓐ Rotation of the right carbon by 90° produces the middle structure. The plane defined by the left $CH_3—C—H$ is now perpendicular to the plane defined by the $CH_3—C—H$ on the right. The red *p* orbital on the left C is in the plane of the page, and the blue *p* orbital on the right C is pointed directly at you, so the two *p* orbitals are also perpendicular to one another. Therefore, there is no stabilizing overlap of these *p* orbitals—the pi bond has been broken.

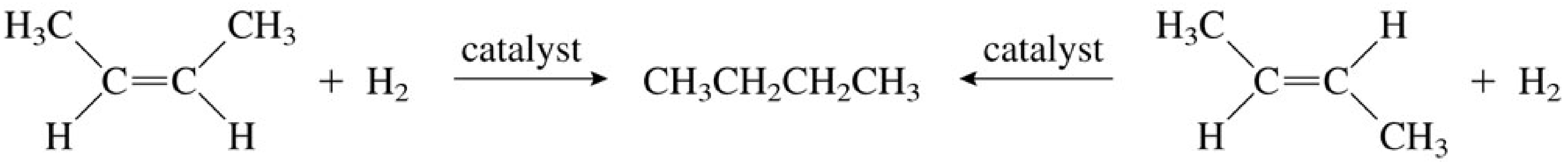
ⓑ An additional rotation of the right carbon by 90° produces *trans*-2-butene.

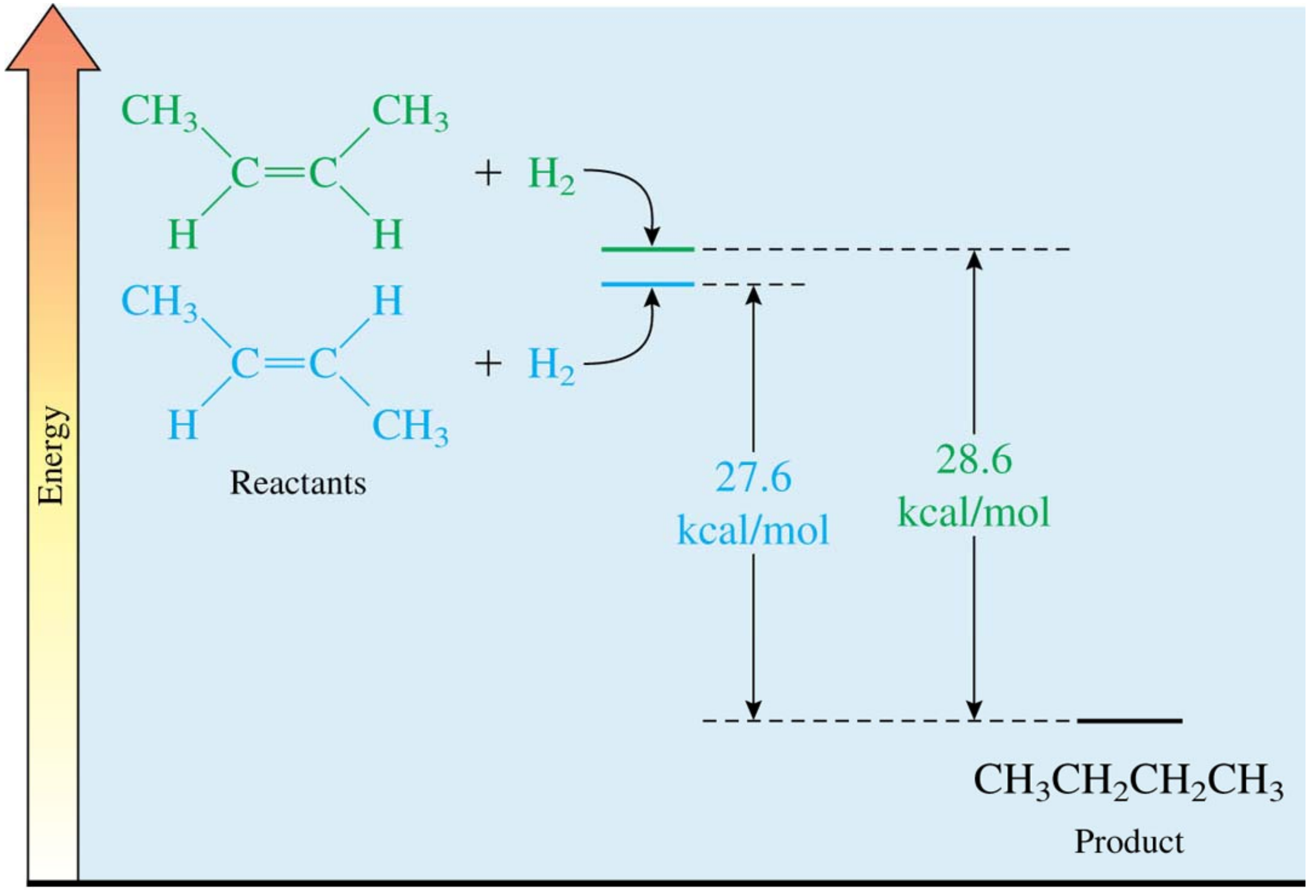
For an alkene to exhibit geometrical (cis-trans) isomerism, the two groups on one end of the double bond and the two groups on the other end of the double bond must be different.



Definition of stereocenter;

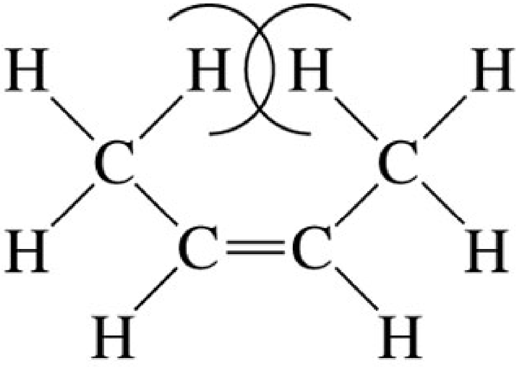
An atom at which the **interchange of two groups** produce a stereoisomer



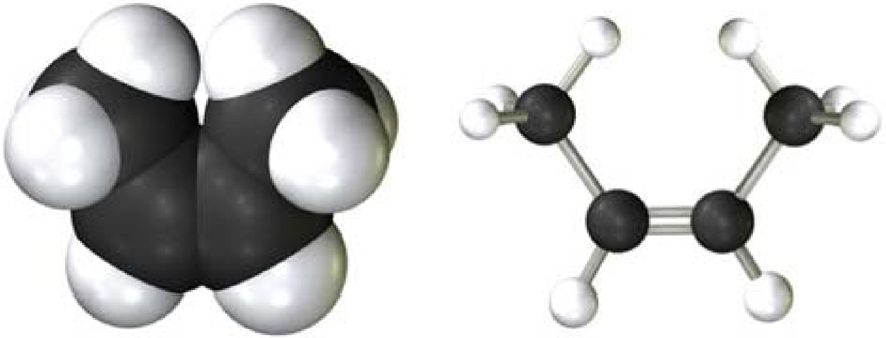


Different ΔH values, because trans isomer is more stable.
Why? Steric crowding or steric strain effect

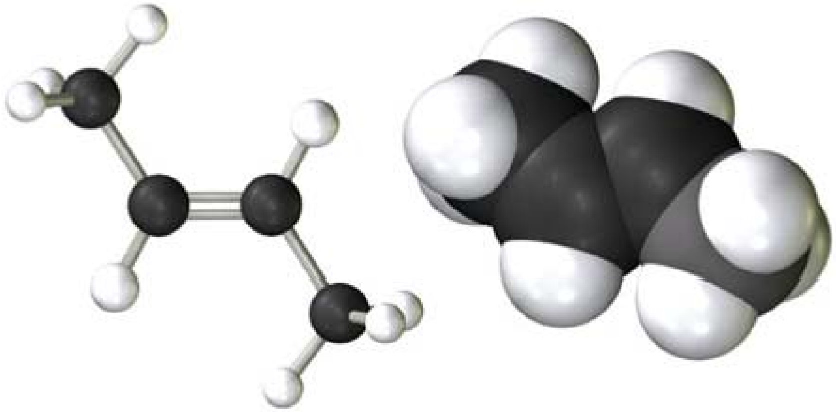
Steric (strain) effect



The planar geometry of the double bond causes a hydrogen on each of the methyl groups to be forced too close together, resulting in some steric strain.



cis-2-Butene



trans-2-Butene

Conclusions of 6.1

1. *Cis-trans* isomers -- two different comp'd

2. different shape, physical, and chemical properties

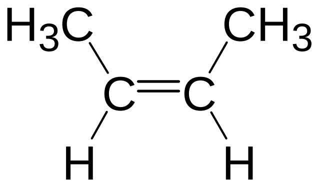
3. interconversion? -- only by breaking π bonds

4. *cis-* is sterically more hindered (higher steric hindrance), of larger steric strain, of higher energy, less stable

6.2 Designating The Configuration of Cis-Trans Isomers

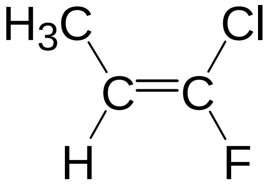
Configuration; 3-dimensional arrangement of groups about stereocenter in a molecule

Ex) *1. cis-trans* method of designation

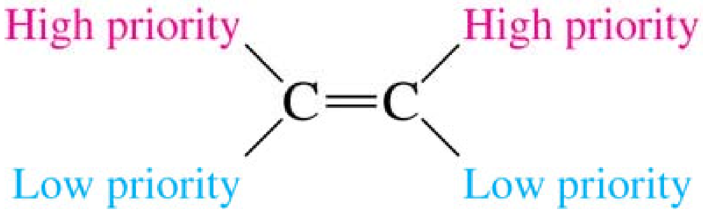


cis

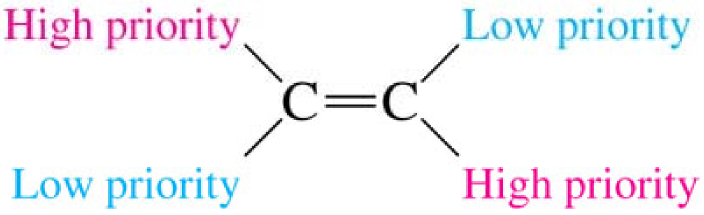
***2. Z-E* designation; *Z*usammen (together) vs *E*ntgegen (opposite)**



?



Z



E

similar to cis

similar to transe

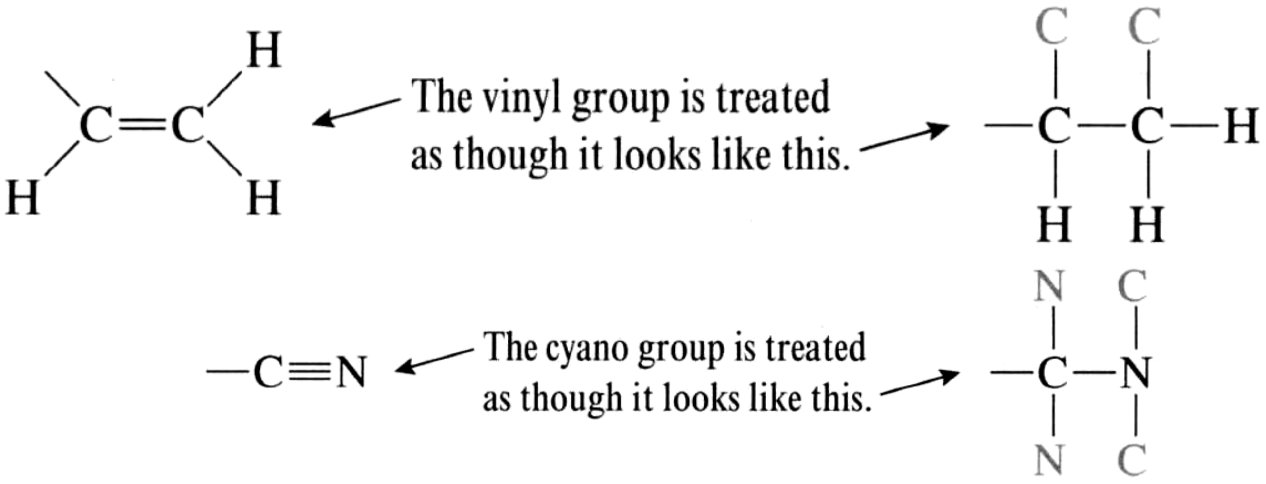
The priority *for Z-E* designation is determined by Cahn-Ingold-Prelog sequence rules

Rule 1: Of the two atoms on one carbon, the one with higher atomic number

Rule 2: If the two atoms are the same, compare the atoms attached to them

Rule 3: double bond = two single bond

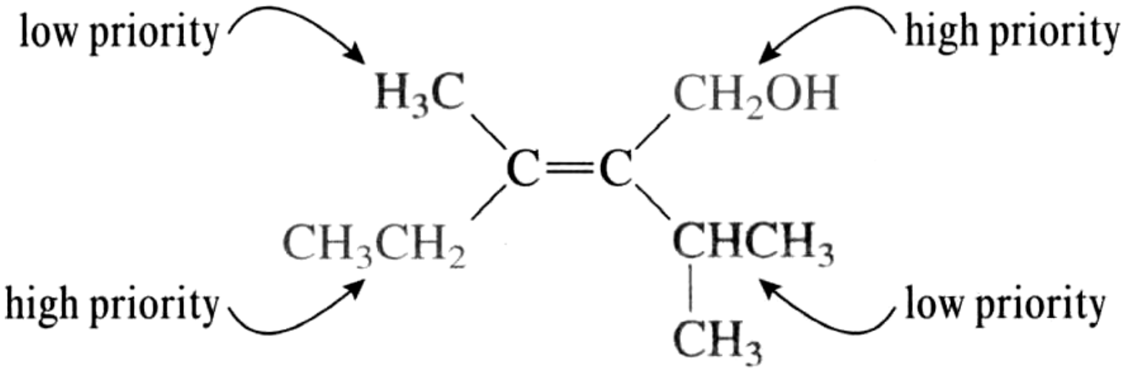
triple bond = three triple bond



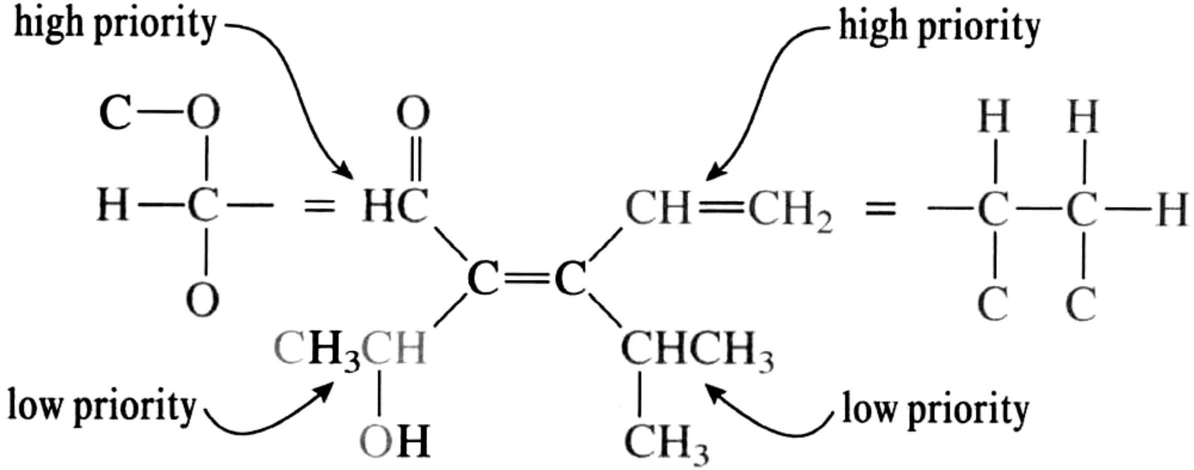
The vinyl group is treated as though it looks like this.

The cyano group is treated as though it looks like this.

Examples)



(*E*)-2-isopropyl-3-methyl-2-penten-1-ol

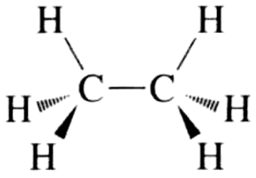


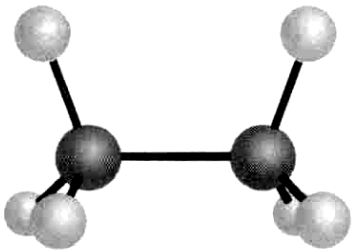
6.3 Conformations

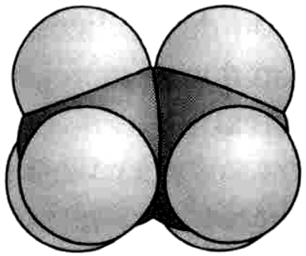
⇒ The various shapes of molecules by rotation about single bonds (rotation about the single bond is possible at RT)

Example; two possible conformations of ethane

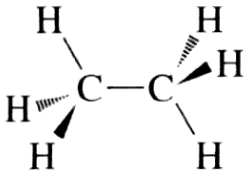
eclipsed conformation

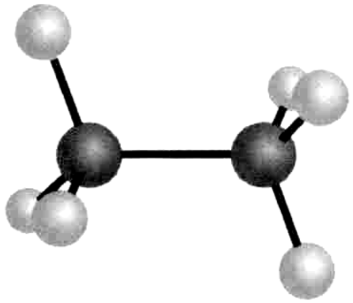


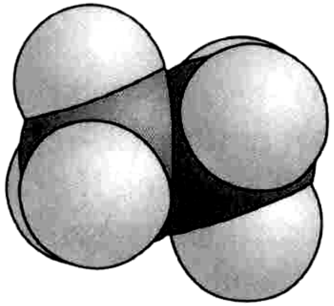




staggered conformation



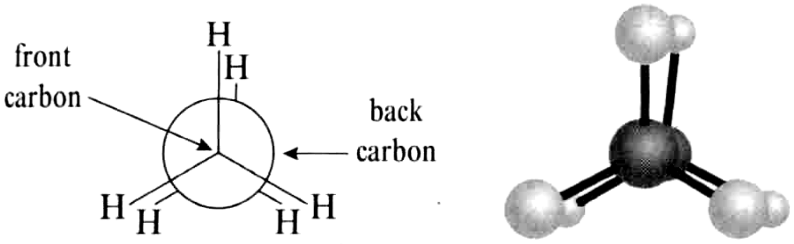




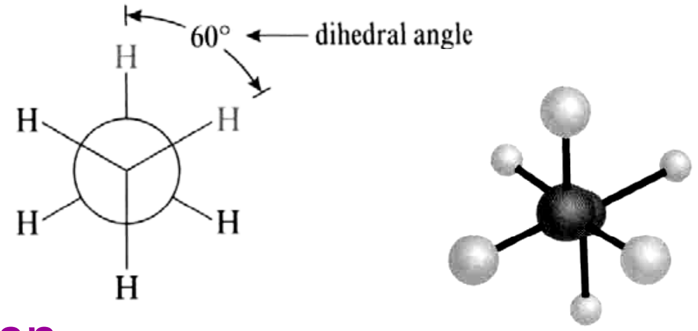
ball-and-stick model space-filling model

Newman projection of Ethane

eclipsed conformation

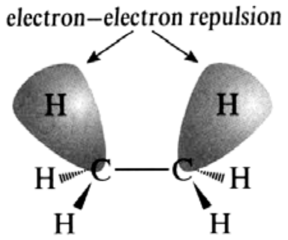


staggered conformation



eclipsed conformation is less stable than staggered conformation by 2.9 kcal/mol due to a electron-electron repulsion

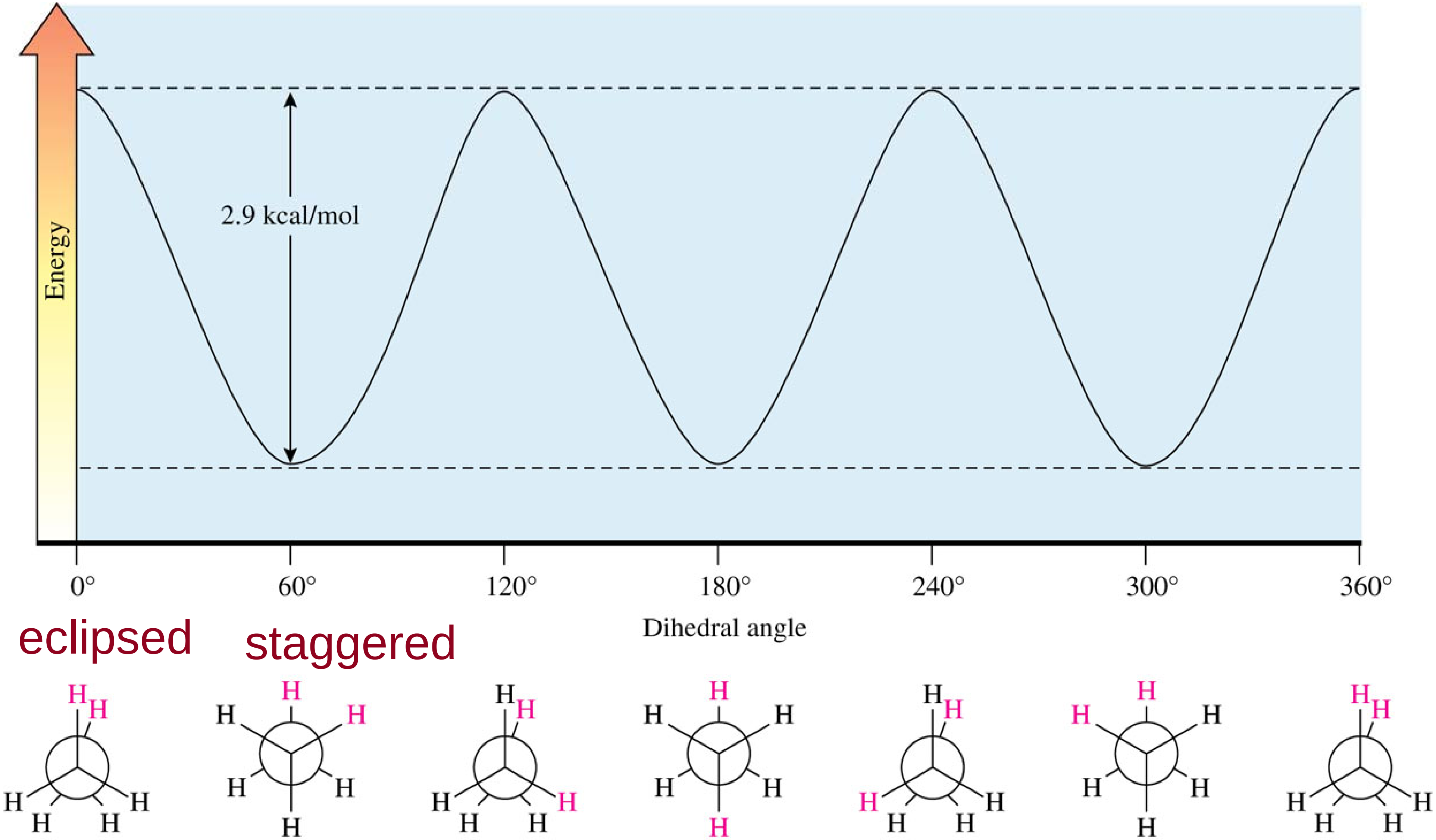
$\Rightarrow$ Eclipsing interaction of each = ~1 kcal/mol



Therefore free conformation changes between eclipsed and staggered occurs very rapidly at room temperature (20 kcal/mol).

conformational isomer (conformer)? rotational isomer?

Not separable -- not really an isomer!



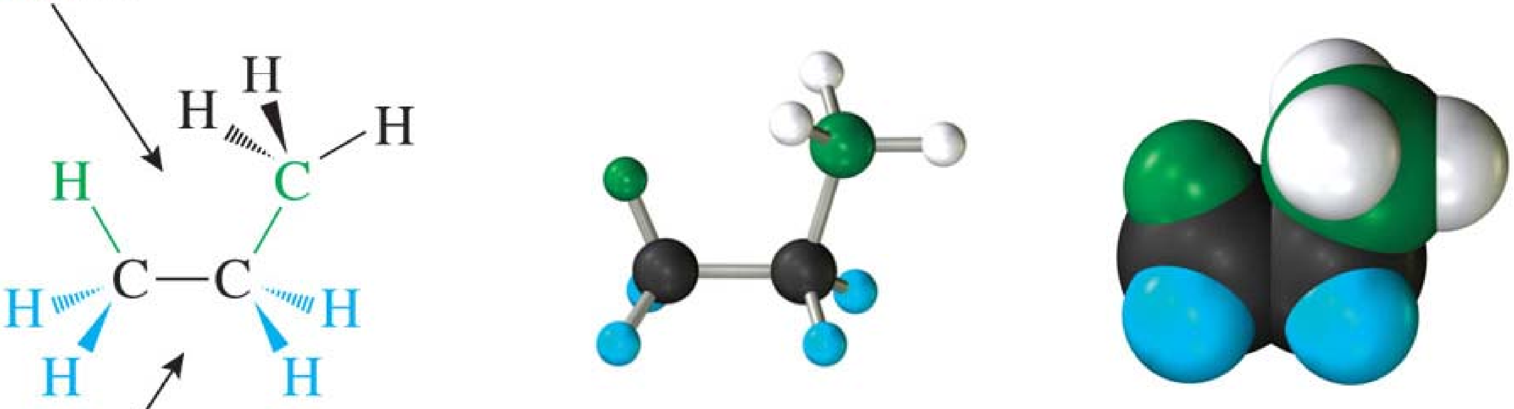
eclipsed

staggered

Example of propane

ΔE between eclipsed and staggered cnoformations = 3.3 kcal/mol > 2.9 for ethane because the CH_3 is larger than H.

3.3 = 1 + 1 + 1.3; 1.3 due to steric and torsional strain between H & CH_3



Propane that is eclipsed about one CC bond has one CH_3/H eclipsing interaction and

two H/H eclipsing interactions.

Propane

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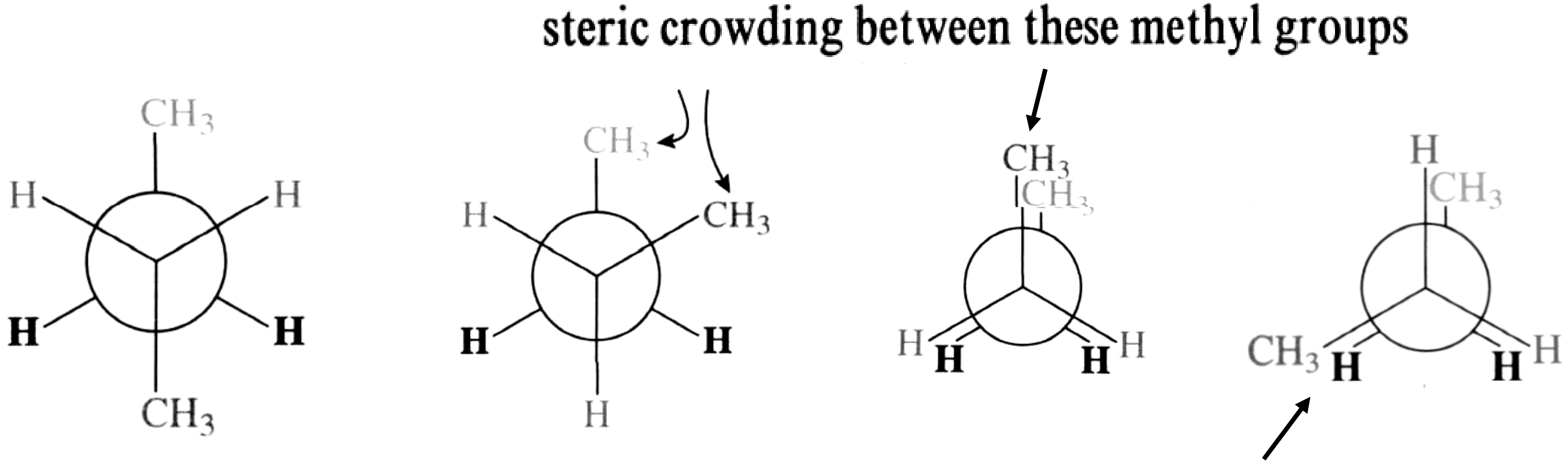
- Example of *n*-butane

4 possible comformations; see p190



Most stable
anti

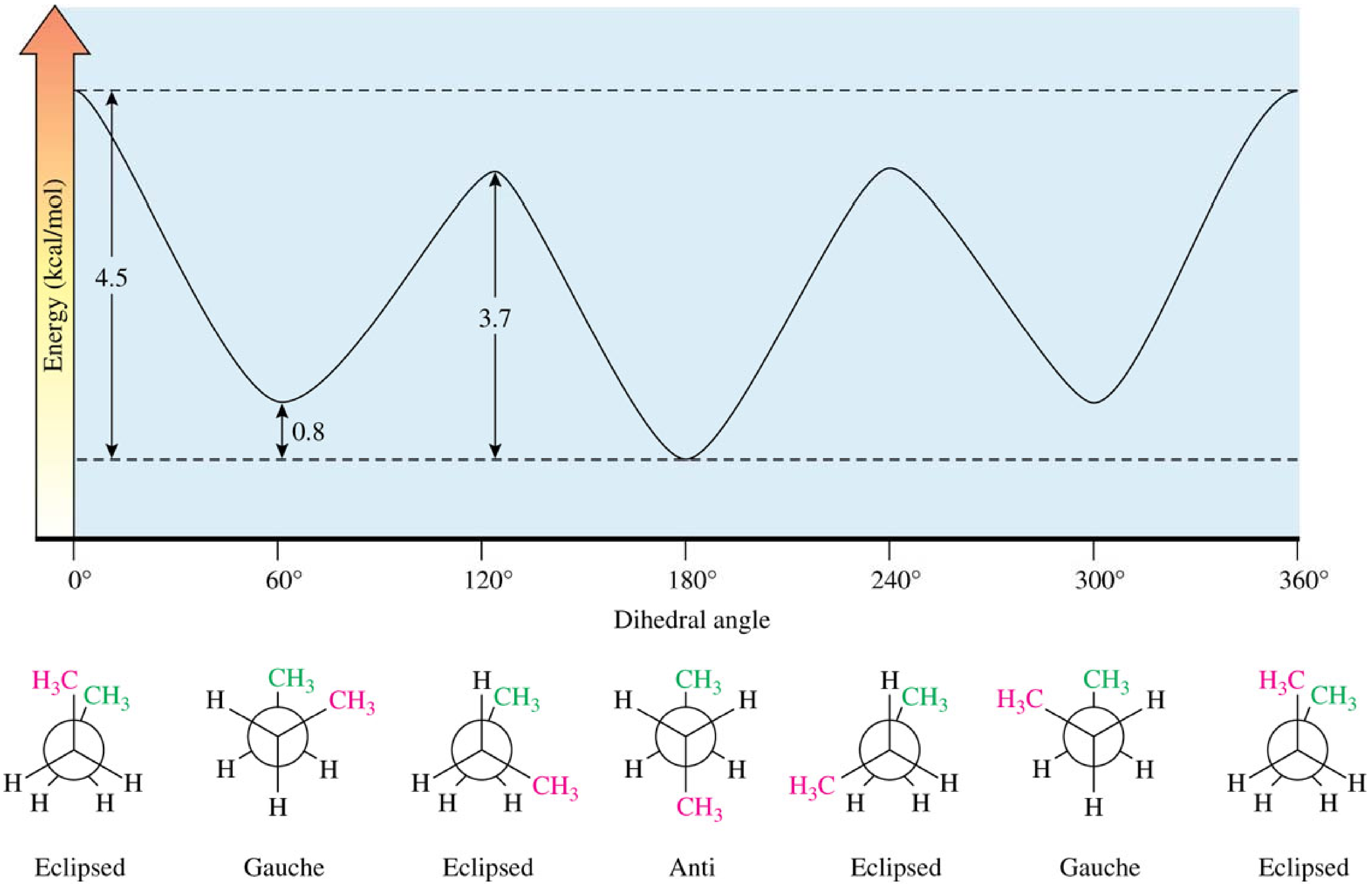
+ 0.8 kcal/mol
gauch

Least stable
+ 4.5 kcal/mol
eclipse

+ 3.7 kcal/mol
eclipse

4.5 = 1 + 1 + 2.5; 2.5 is due to CH_3 & CH_3 intxn

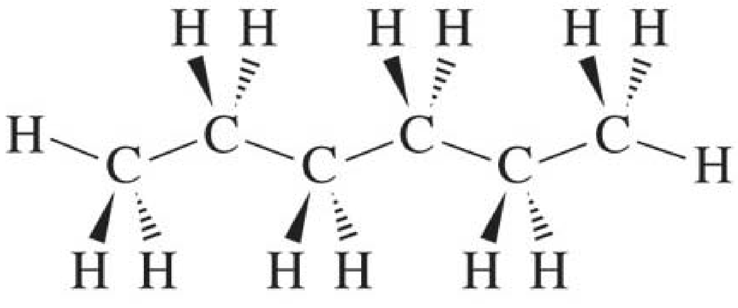
1 + 1.3 + 1.3 = 3.6 theoritical value



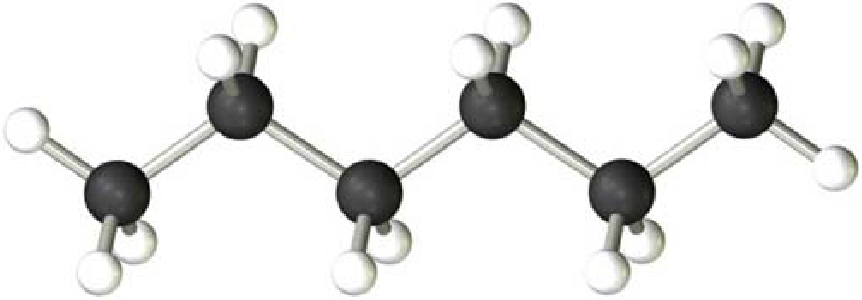
staggered staggered staggered

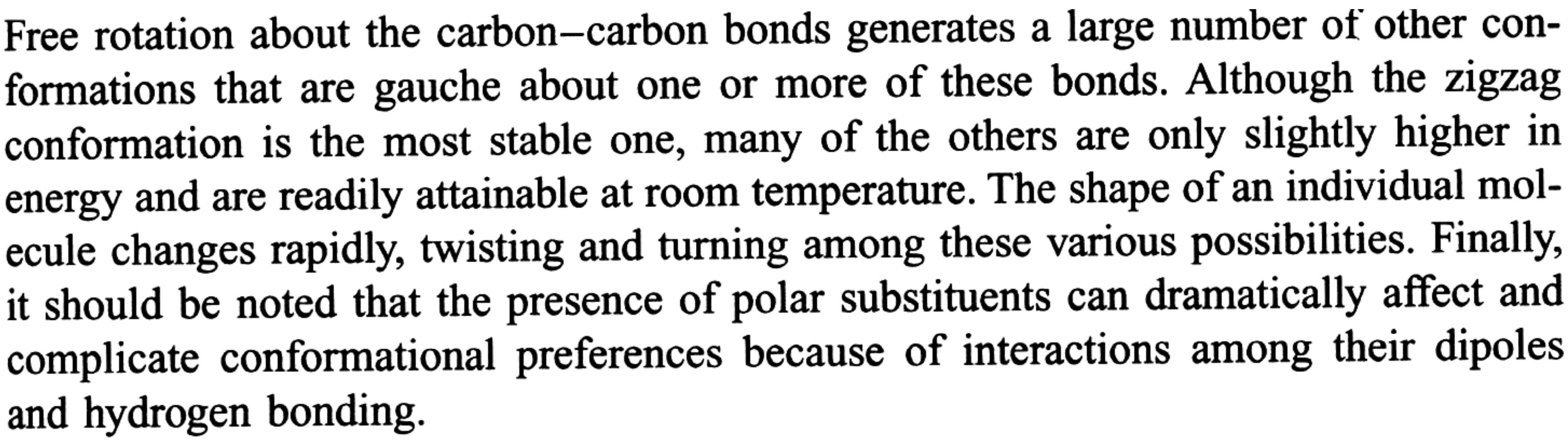
Linear longer alkane

⇒ **the most stable conformation is zig-zag conformation; anti about all the C-C bonds**



Hexane





Free rotation about the carbon–carbon bonds generates a large number of other conformations that are gauche about one or more of these bonds. Although the zigzag conformation is the most stable one, many of the others are only slightly higher in energy and are readily attainable at room temperature. The shape of an individual molecule changes rapidly, twisting and turning among these various possibilities. Finally, it should be noted that the presence of polar substituents can dramatically affect and complicate conformational preferences because of interactions among their dipoles and hydrogen bonding.

Configuration; **3-dimensional arrangement of groups about stereocenter in a molecule**

⇒ non-interconvertable

Ex) cis-trans isomers or Z-E isomers

Conformations :The various shapes of moleculse by rotation about single bonds

⇒ rotaion about the single bond is possible at RT

Ex) ***anti, gauch, eclipsed, staggered***

6.4 Conformations of Cyclic Molecules

Cycloalkanes

1. **less flexible than noncyclic alkanes.**
2. **less # of conformations available than noncyclic alkanes.**
3. **angle strain and torsional strain**

because their carbon chains are confined in the ring

How to calculate the strain energy;

Most stable ring

Ex) heat of combustion of cyclopropane per CH_2= 166.3 kcal/mol

heat of combustion of cyclohexane per CH_2= 157.3 kcal/mol

The difference, 8.9 kcal/mol, is the strain energy per CH_2.

8.9 x 3 = 26.7 kcal/mol is the total ring strain E.

Steric hindrance: 입체장애

분자내에 부피가 큰 원자단이 존재함 으로써 분자구조에 있어서도 정상에서 벗어나고, 분자의 반응성도 입체적인 장애를 받아 정상적인 반응을 하지 못하는 현상

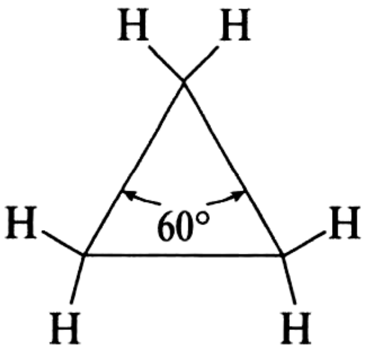
Tortional strain: 비틀림 변형

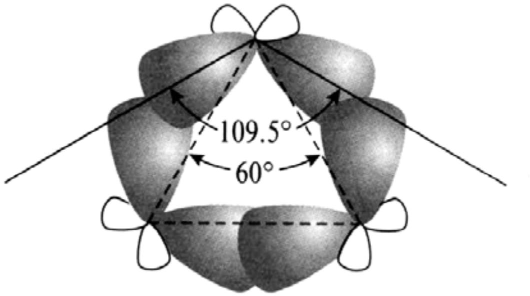
Table 6.1 Heats of Combustion and Strain Energies of Some Cycloalkanes

Ring Size	Heat of Combustion per CH_2	Strain Energy per CH_2	Total Ring Strain
3	166.3 (695.8)	8.9 (37.2)	26.7 (111.6)
4	163.9 (685.8)	6.5 (27.2)	26.0 (108.8)
5	158.7 (664.0)	1.3 (5.4)	6.5 (27.0)
6	157.4 (658.6)	0	0
7	158.3 (662.3)	0.9 (3.7)	6.3 (25.9)
8	158.6 (663.6)	1.2 (5.0)	9.6 (40.0)
9	158.8 (664.4)	1.4 (5.8)	12.6 (52.2)

ex) cyclopropane

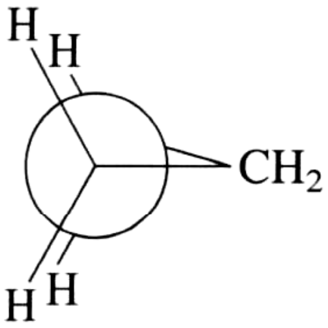
most strained; strain E per CH2 is 8.9 kcalo/mol, planar and, high angle strain (60° vs 109.5°)

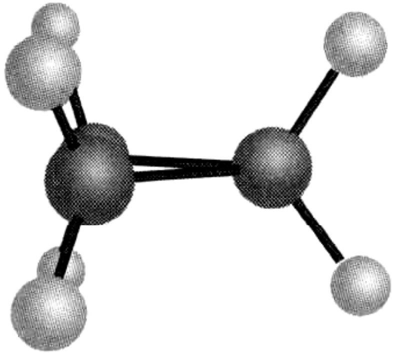




The orbitals forming the C—C bonds of cyclopropane

This decreased overlap increase the angle strain





high torsional strain, because it is the eclipsed conformation

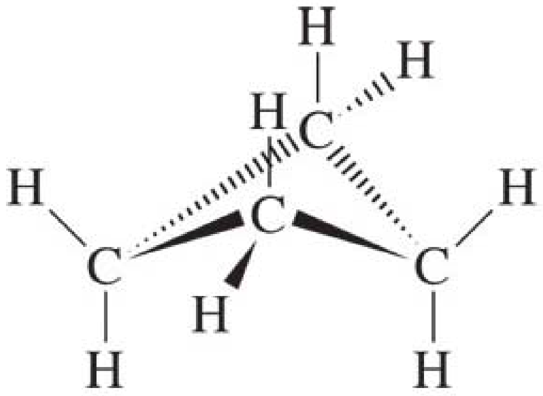
ex) cyclobutane

Strained, but not as much as cyclopropane

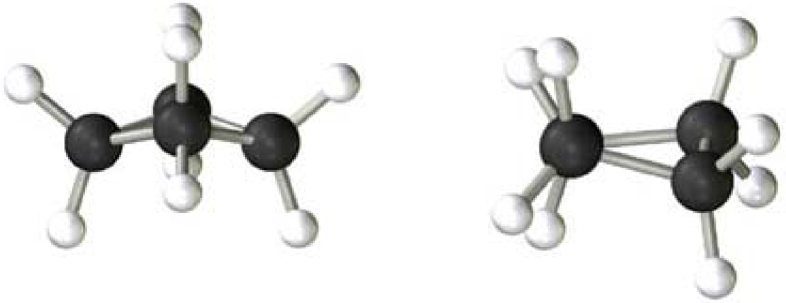
1. If planar, 90° bond angle and fully eclipsed, then very large tortional strain.
2. Distortion; increase the angle strain

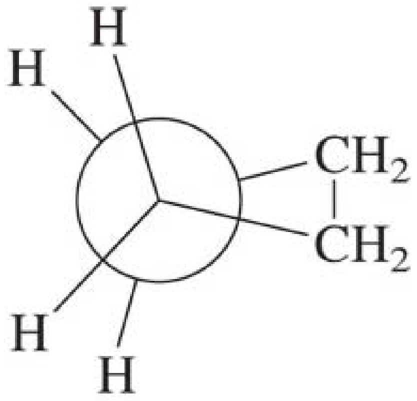
   decrease the torsional strain (somewhat staggered)

⇒ **2 has lower E than 1**



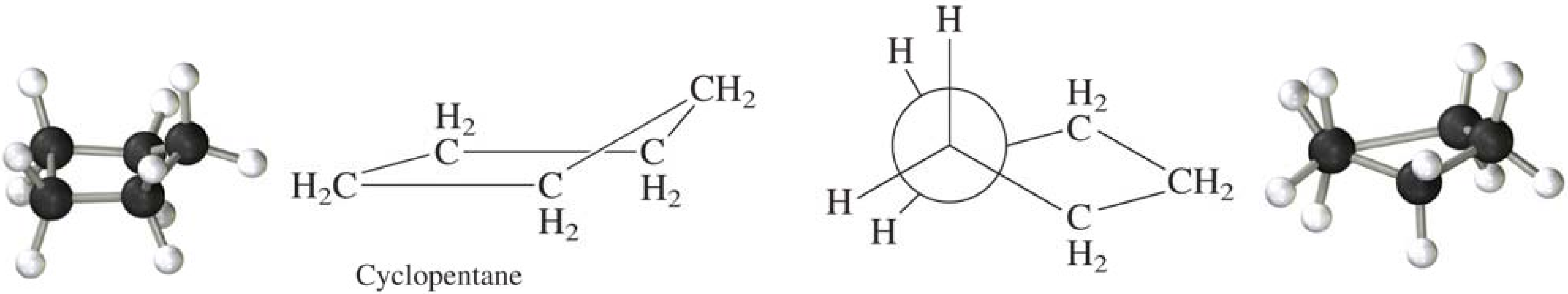
Cyclobutane





ex) cyclopentane

Also distorted to relieve the torsional strain



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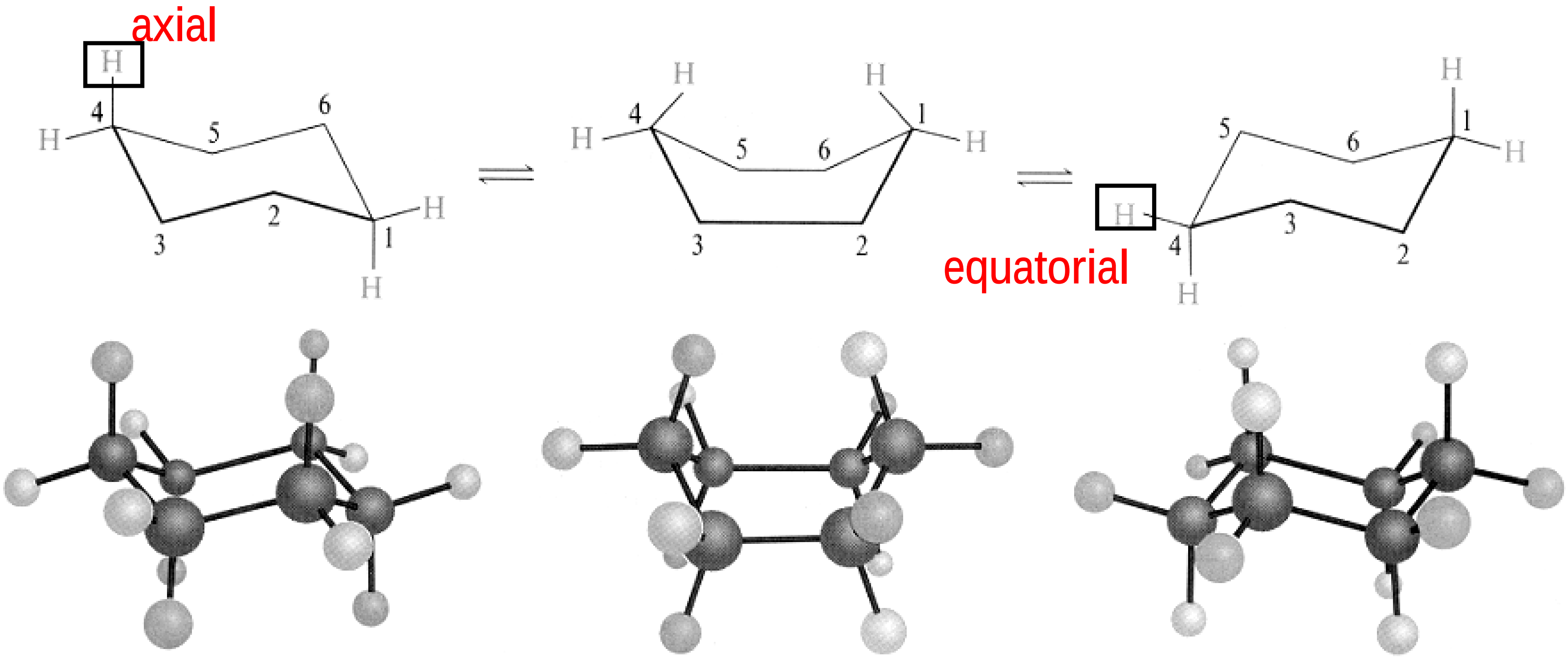
6.5 Conformation of Cyclohexane

1. Virtually strain-free

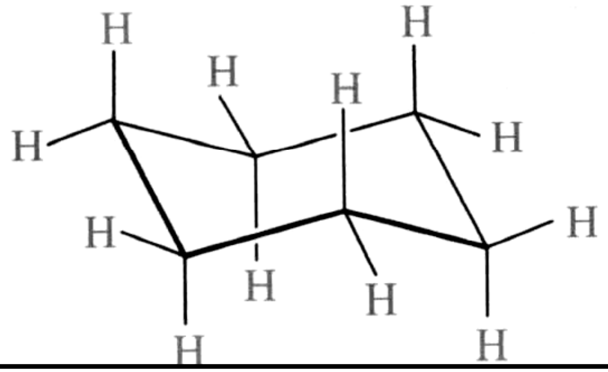
   chair and boat conformation (free of angle strain); not planer with 120° bond angle (fully eclipsed)

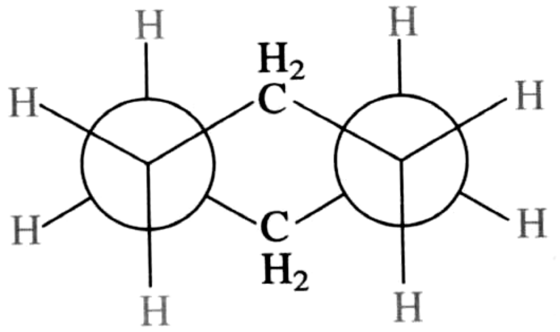
2. Abundant in nature or easily formed from chemical rxns.



Chair conformation boat conformation

Chair conformation

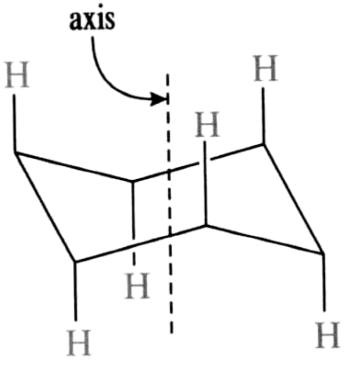




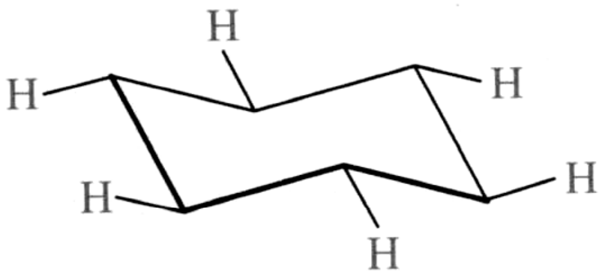
1. **All C-C-C bond angles are 109.5^o; no angle strain**

2. **All C-H bonds are perfectly staggered; no tortional strain**

Two different types of Hydrogens in chair conformation

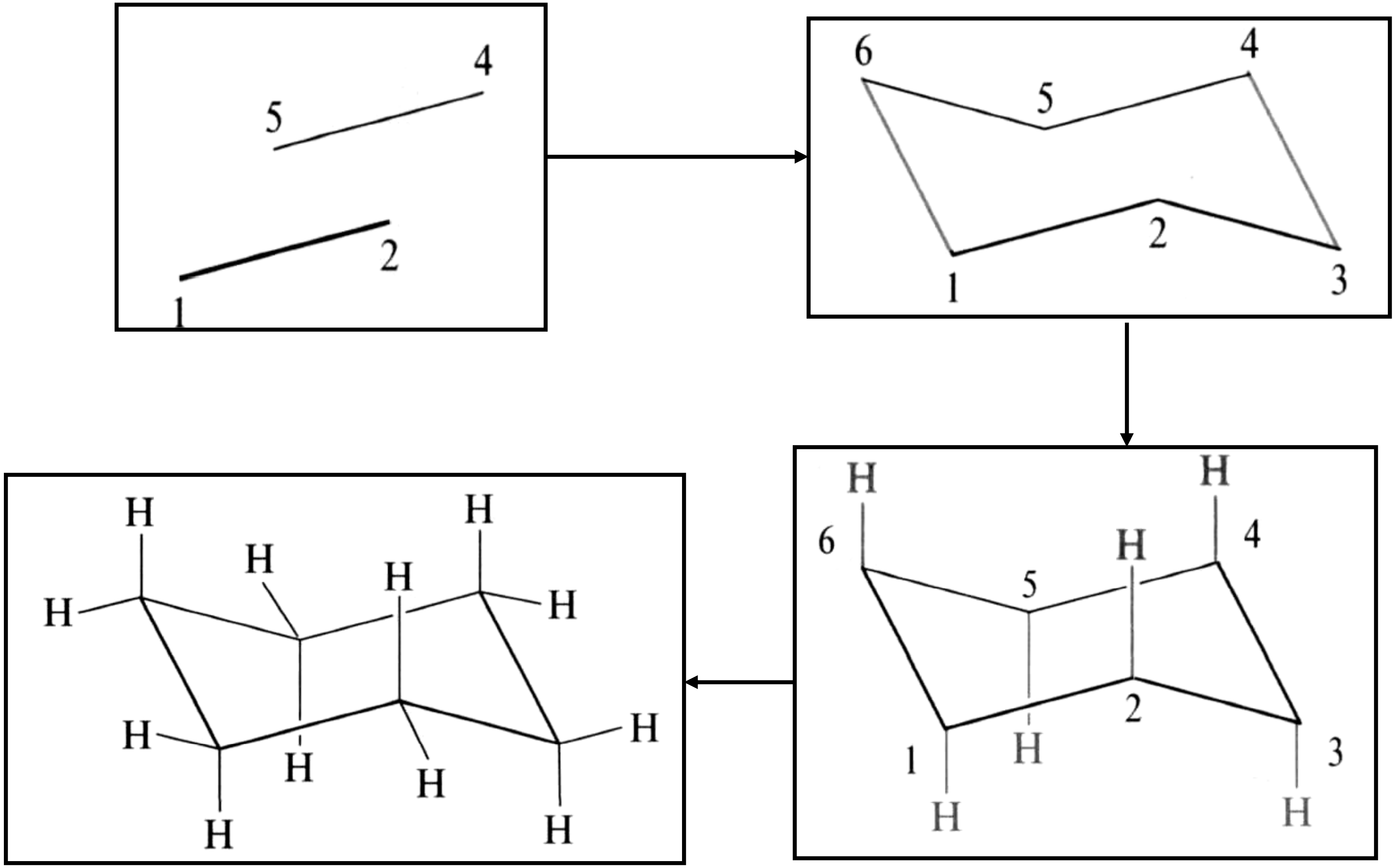


axial hydrogen

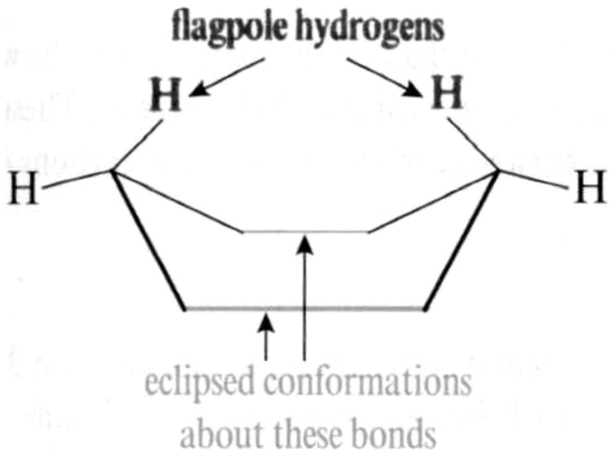


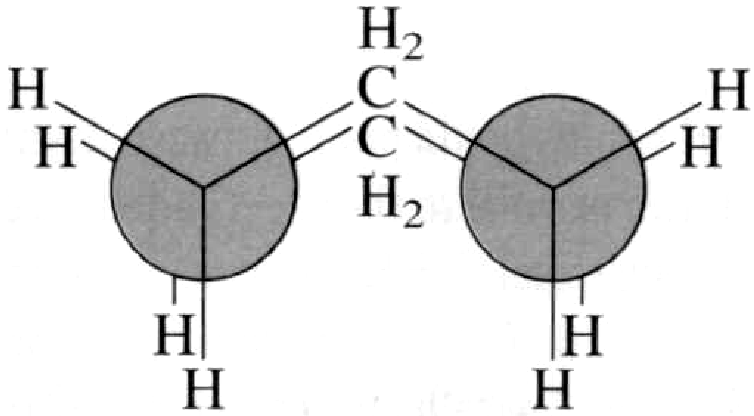
equatorial hydrogen

Steps for drawing chair conformation



Boat conformation

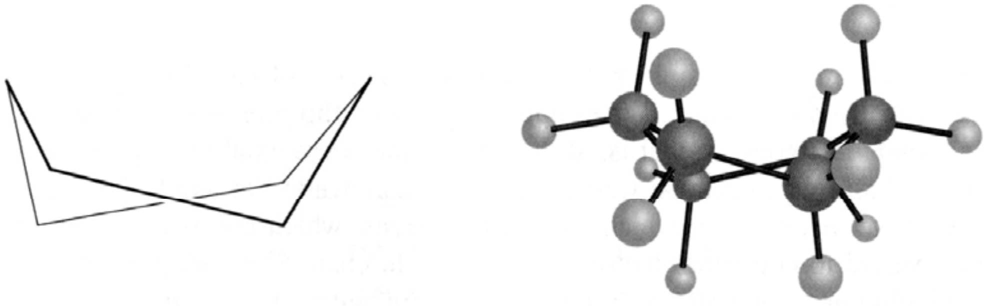




1. All C-C-C bond angles are 109.5^{o}; no angle strain
2. C-H bonds are eclipsed; torsional strain

less stable than the chair conformer by about 6 kcal/mol

Twisted boat conformation

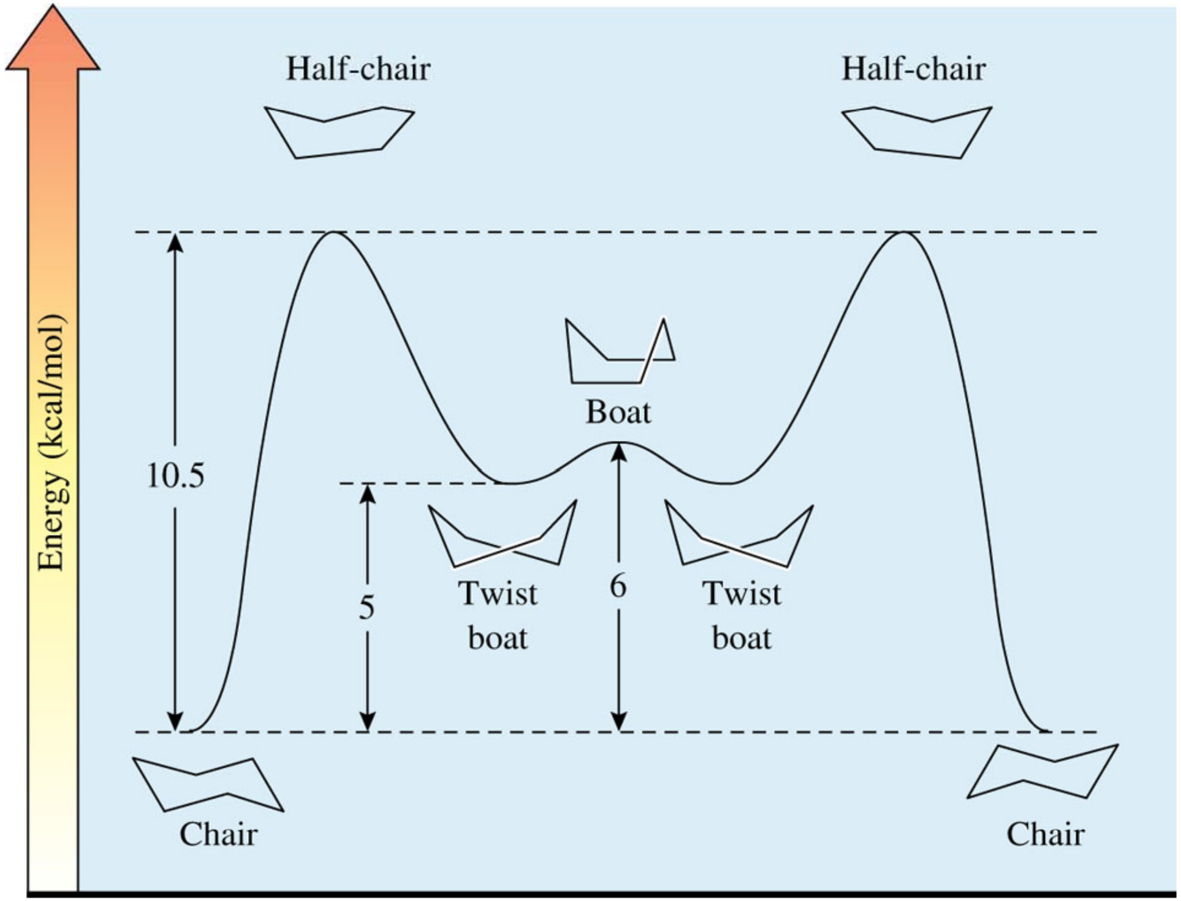


1. angle strain ↑
2. tortioanl strain ↓

less stable than the chair conformer by about 5 kcal/mol

Energy diagram for the ring flipping process

As energy availablr at RT is 20 kcal/mol, this flipping process happens 100,000 times per second.



6.6 Conformations of other rings

7 membered ring; cycloheptane

⇒ nonplanar

⇒ a little higher (angle and torsional) strain than C6, closer to cyclopentane (C5)

8 to 11 membered rings

⇒ very small angle and torsional strain

⇒ transannular strain (interior of the ring) arises

⇒ similar total strain to those of C5 and C7, but not so popular

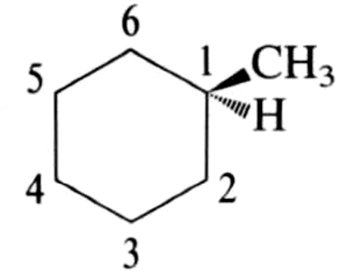
12 membered and larger

⇒ not popular (hard to make the larger rings)

⇒ strain-free

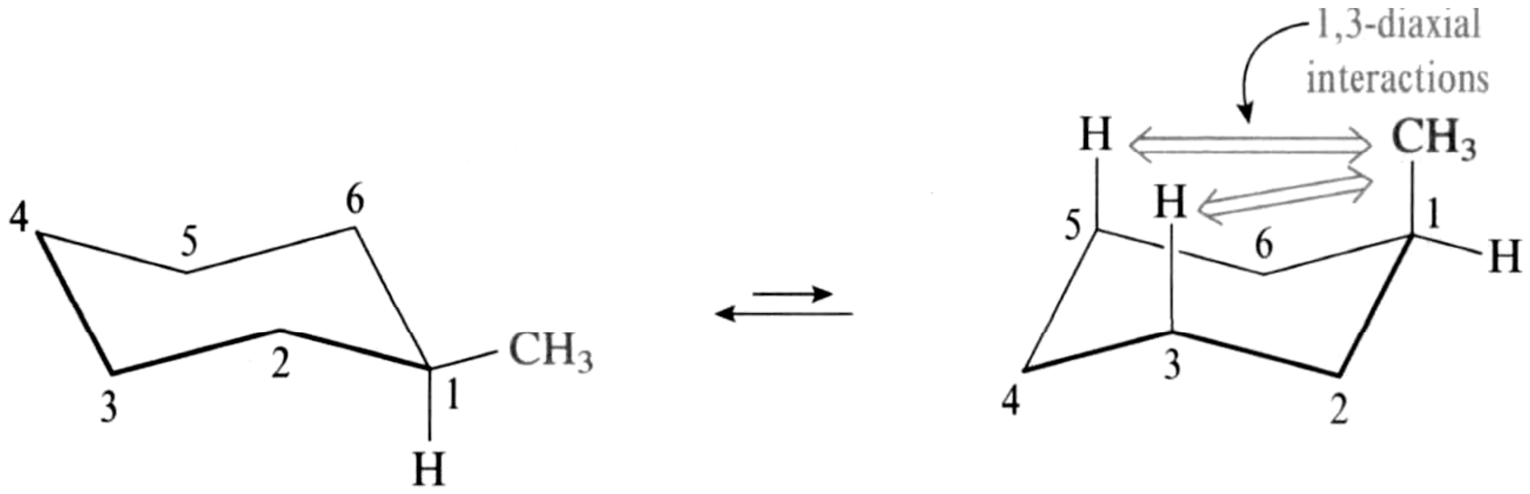
Benzene: planar molecule with no angle atrain

6.8 Conformations of cyclohexane with 1 substituent



Ex) Methylcyclohexane

1. 2 chair conformations are not identical
2. Methyl group in the axial position is has higher steric strain than that in the equatorial position.



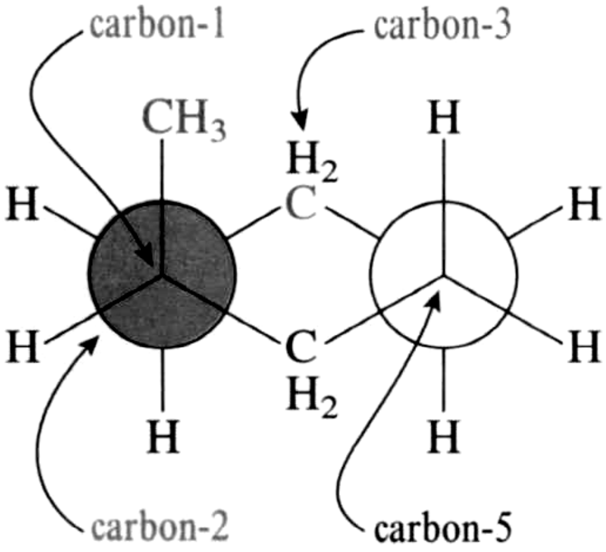
1.7 kcal/mol less stable

$\Delta G^o = -RT \ln K$

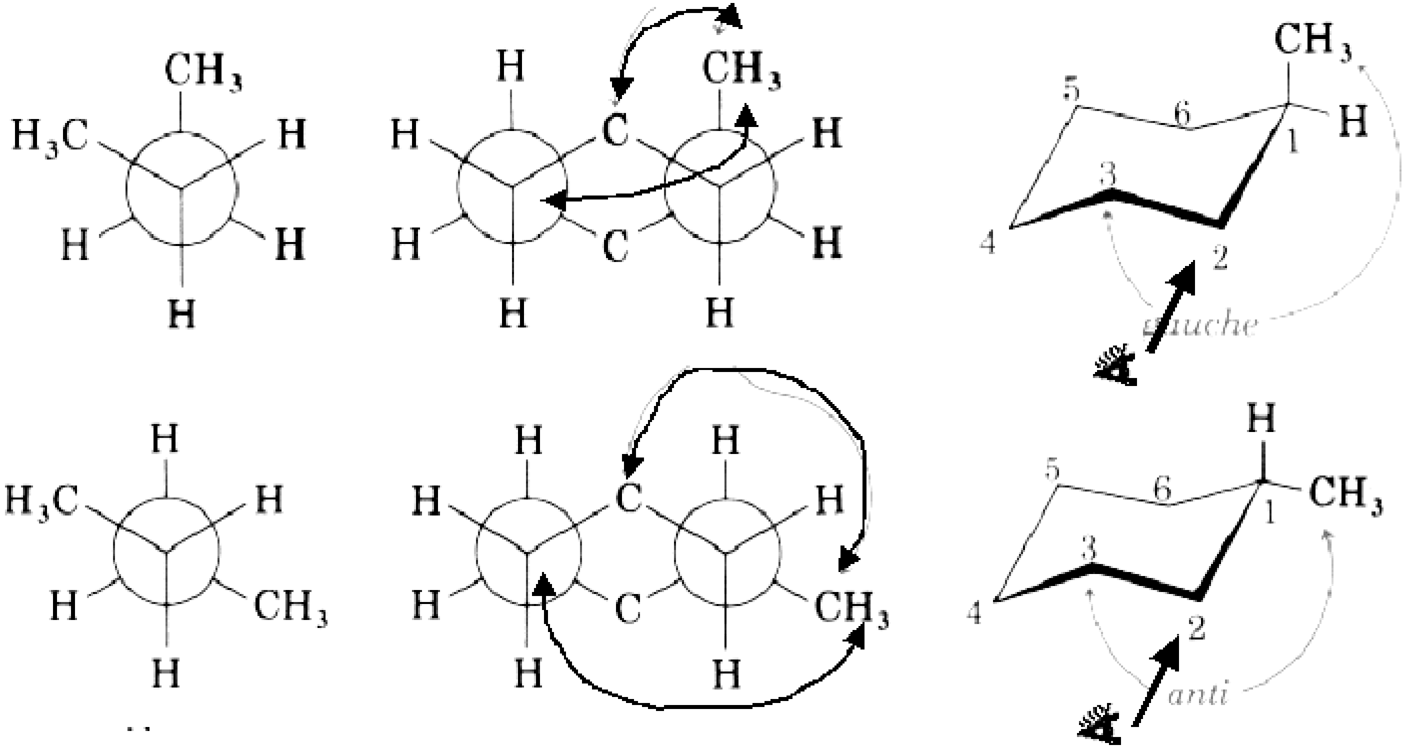
Then 95%;methyl in equatorial

5%; methyl in axial

Problem 6.8



In butane gauch intxn destabilize the conformer by 0.8 kcal/mol (p196). Then there are two gauch intxn between methyl& C3 and methyl & C5; 0.8 x 2 = 1.6 (Close to 1.7 kcal/mol)



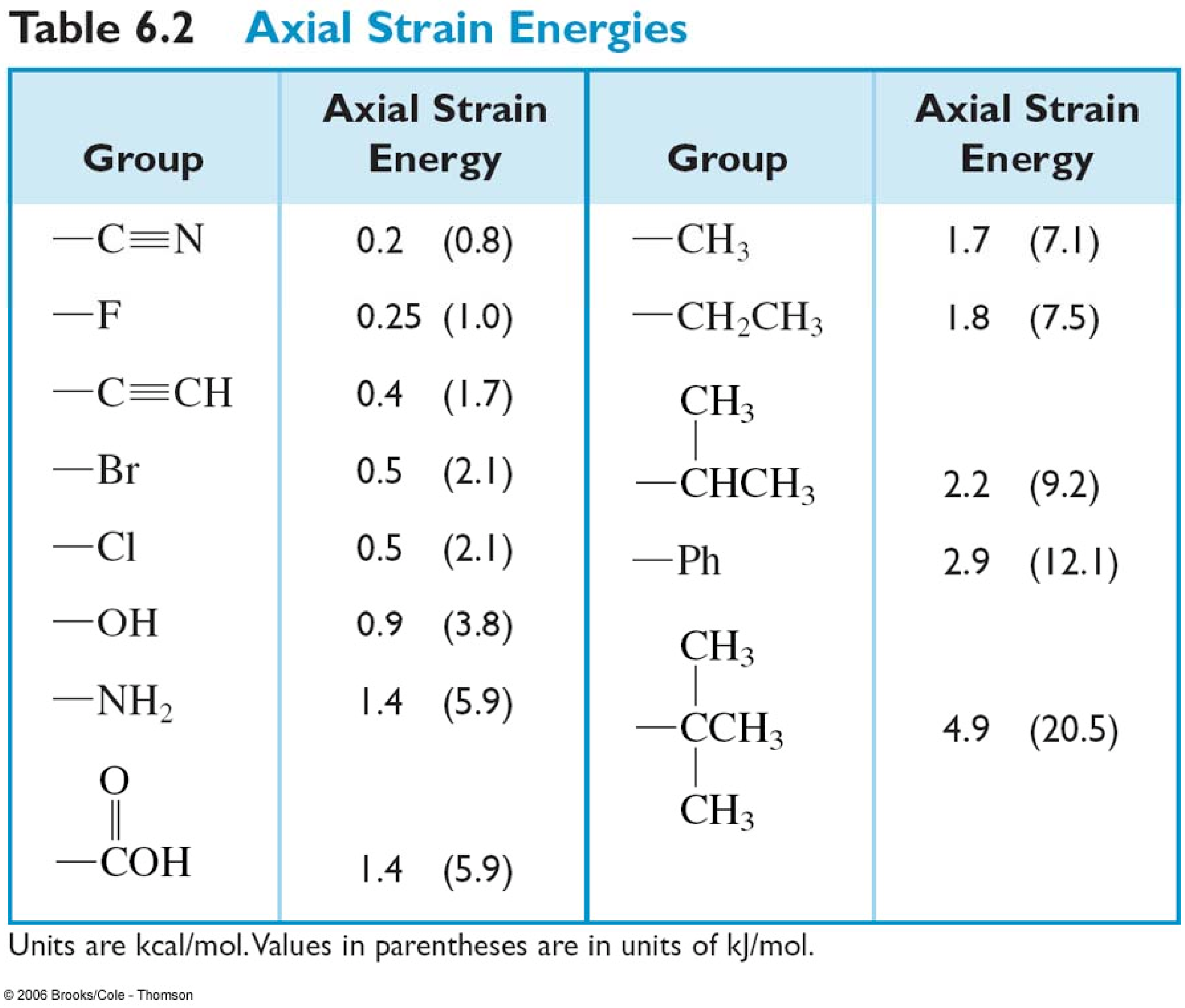


Table 6.2 Axial Strain Energies

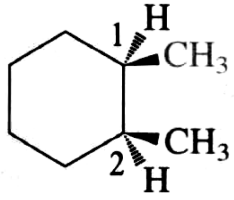
Group	Axial Strain Energy	Group	Axial Strain Energy
$-C\equiv N$	0.2 (0.8)	$-CH_3$	1.7 (7.1)
$-F$	0.25 (1.0)	$-CH_2CH_3$	1.8 (7.5)
$-C\equiv CH$	0.4 (1.7)	$-\overset{\overset{CH_3}{\vert}}{C}HCH_3$	2.2 (9.2)
$-Br$	0.5 (2.1)	$-Ph$	2.9 (12.1)
$-Cl$	0.5 (2.1)	$-\underset{\underset{CH_3}{\vert}}{\overset{\overset{CH_3}{\vert}}{C}}CH_3$	4.9 (20.5)
$-OH$	0.9 (3.8)		
$-NH_2$	1.4 (5.9)		
$-\overset{\overset{O}{\Vert}}{C}OH$	1.4 (5.9)		

Units are kcal/mol. Values in parentheses are in units of kJ/mol.

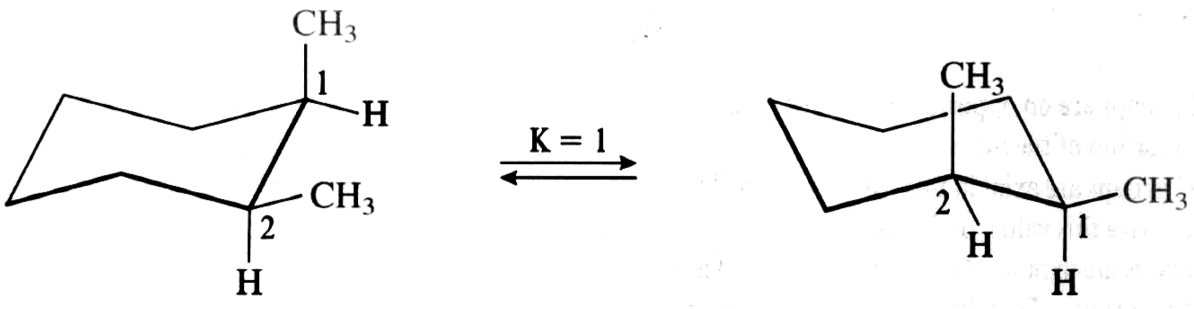
larger the size, the larger the value.

6.9 Conformations of cyclohexane with 2 or more substituents

Ex) 1,2-dimethylcyclohexane; *trans*-isomer is more stable by 1.7 kcal/mol

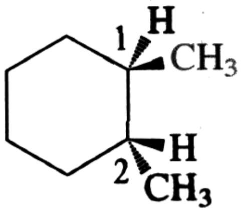


cis-

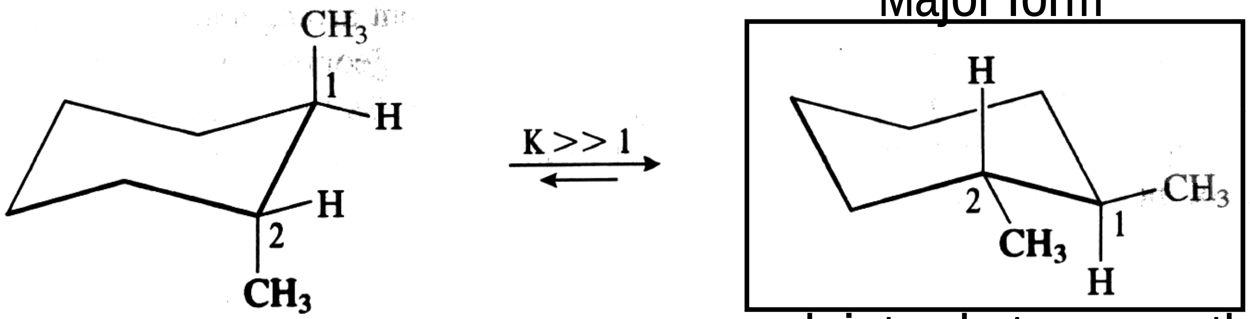


axial strain E of methyl (Table 6.2) = 1.7 kcal/mol
gauch intxn between two methyl groups = 0.8 kcal/mol
total 2.5 kcal/mol

Major form



trans-



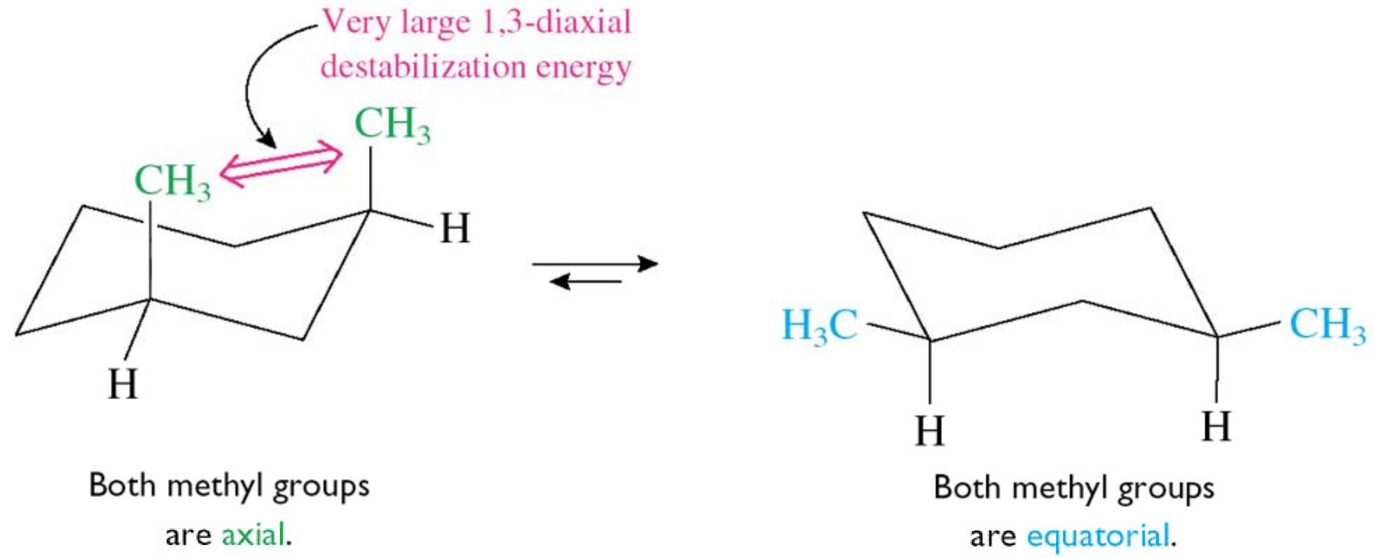
axial strain E of two methyl = 2 x 1.7
total 3.4 kcal/mol

gauch intxn between methyl groups = 0.8
total 0.8 kcal/mol

Ex) 1,3-dimethylcyclohexane;

cis-isomer is more stable because it has a conformation with both methyl groups equatorial

cis-



Both methyl groups are axial.

Both methyl groups are equatorial.

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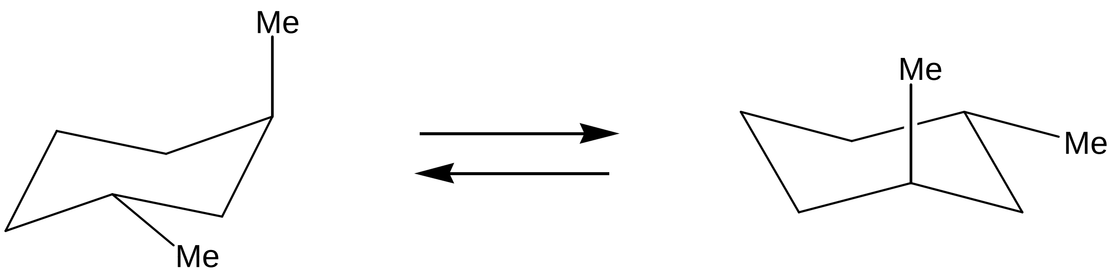
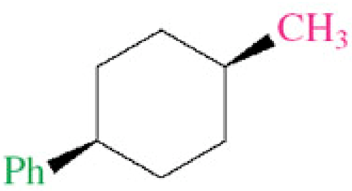
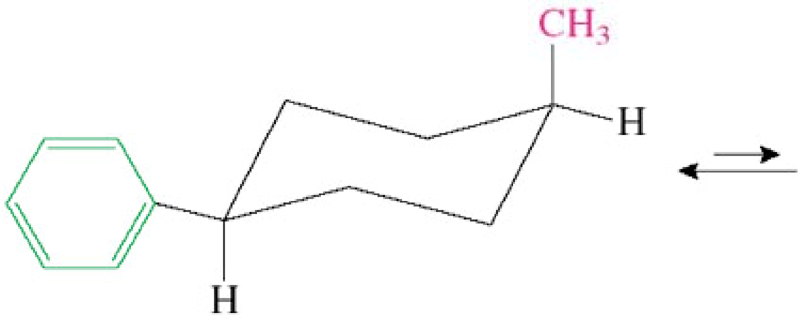
trans-



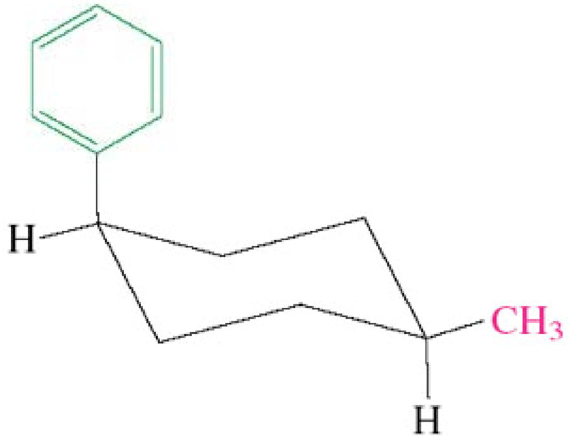
ex) 1-methyl-4-phenylcyclohexane; *cis*-isomer is more stable.



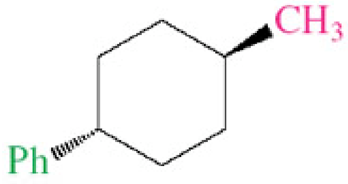
cis-1-Methyl-4-



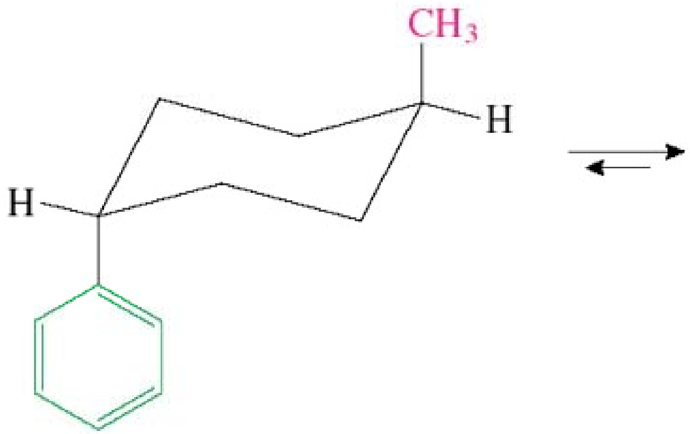
This conformation has an axial methyl and an equatorial phenyl. It has 1.7 kcal/mol



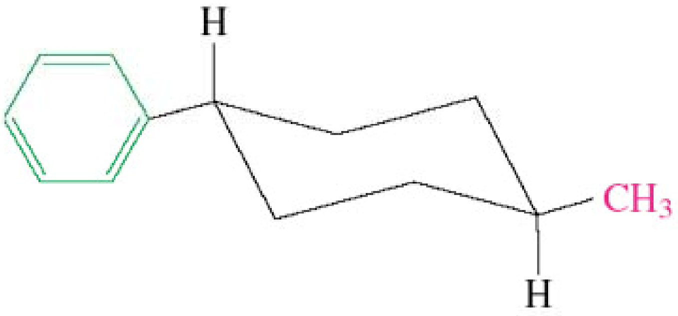
This conformation has an axial phenyl and an equatorial methyl. It has 2.9



trans-1-Methyl-4-phenylcyclohexane



This conformation has both groups axial. It has a total strain energy of 1.7 + 2.9 = 4.6 kcal/mol (19.2 kJ/mol).



This conformation has both groups equatorial. It has no strain energy.