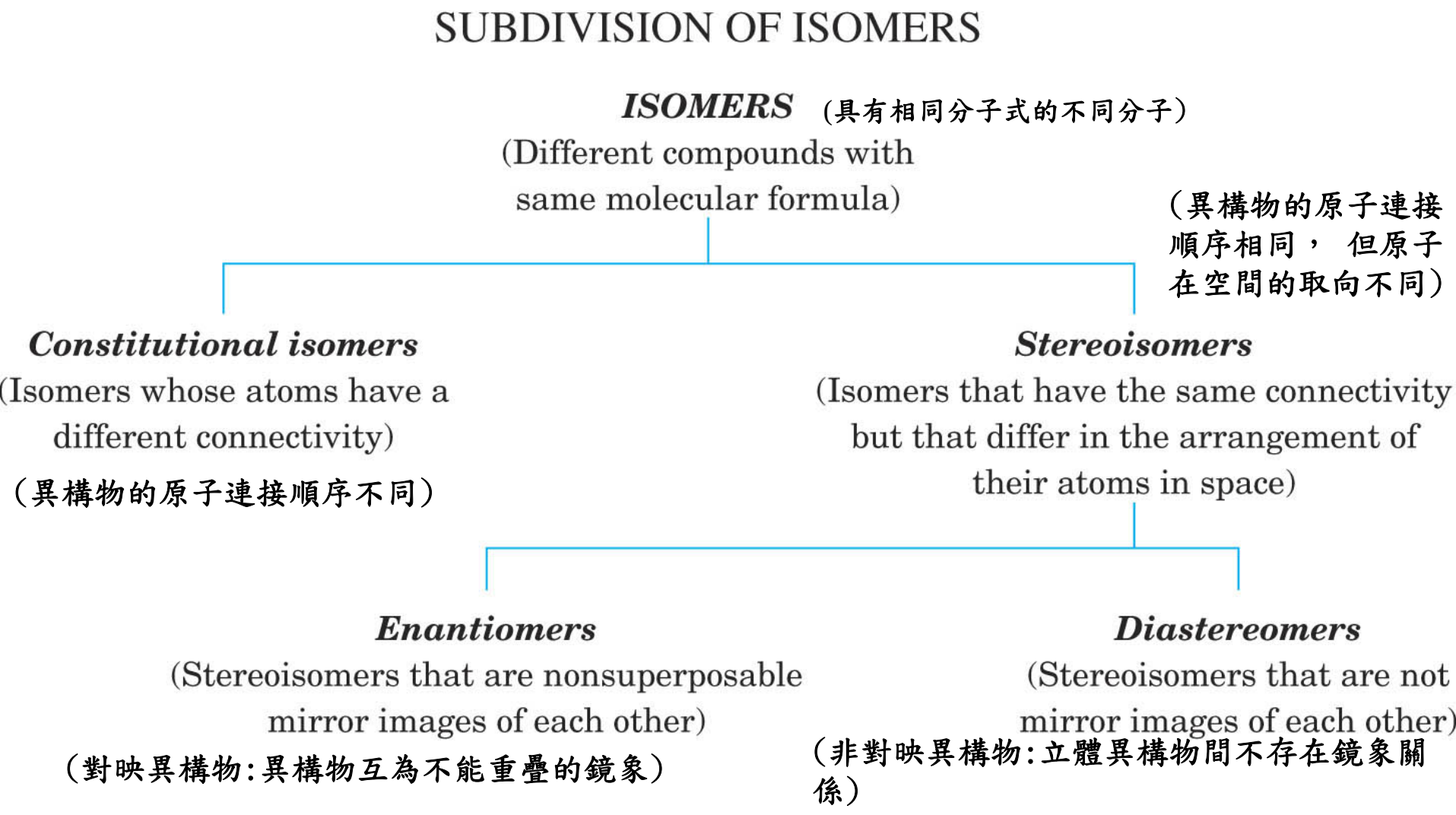
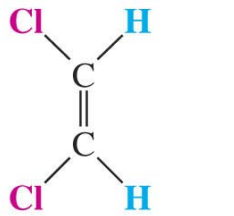
第5章 Stereochemistry: Chiral molecules（掌性分子)

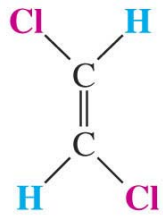
一）有機分子異構物(isomer)的分類



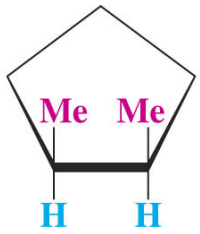
順，反異構物即互為 **diastereomers:**



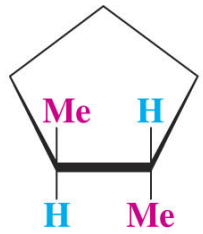
cis-1,2-Dichloroethene
($C_2H_2Cl_2$)



trans-1,2-Dichloroethene
($C_2H_2Cl_2$)



cis-1,2-Dimethylcyclopentane
(C_7H_{14})



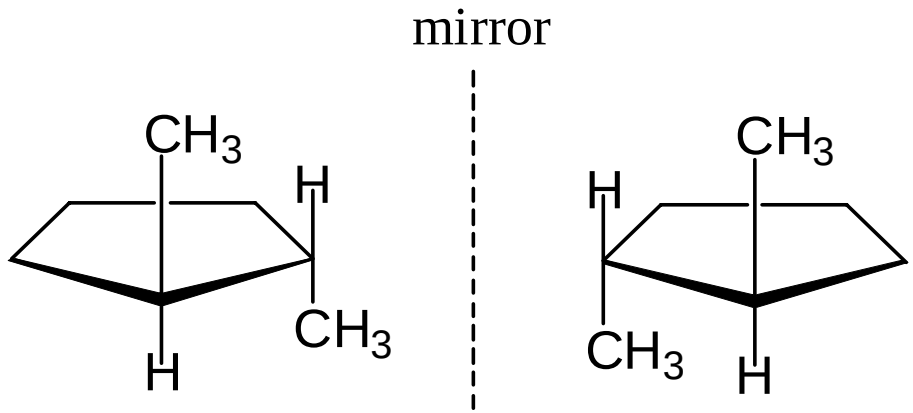
trans-1,2-Dimethylcyclopentane
(C_7H_{14})

二 ）掌性及掌性化和物

Chirality (掌性): the object is not superposable on its mirror image.

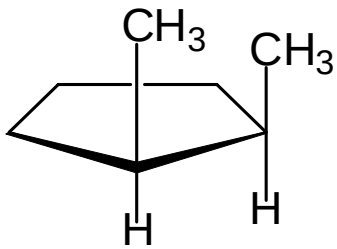
Chiral molecule: one that is not superposable on its mirror image.

Enantiomers: a chiral molecule and its mirror image are called a pair of enantiomers; their relationship is defined as enantiomeric



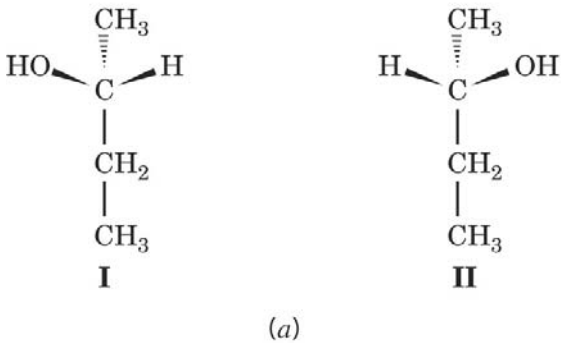
Enantiomers

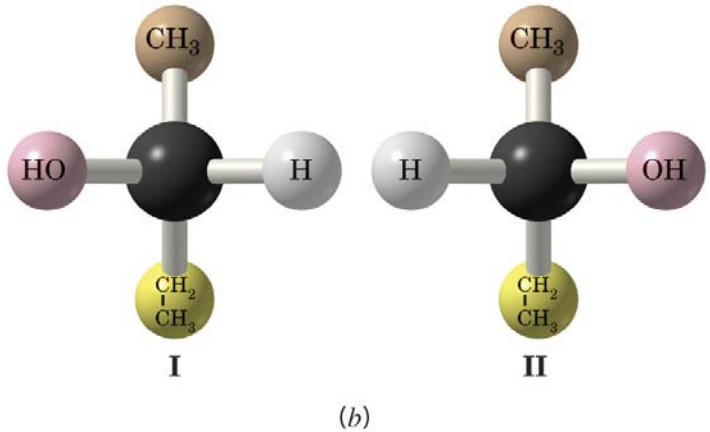
Think about:



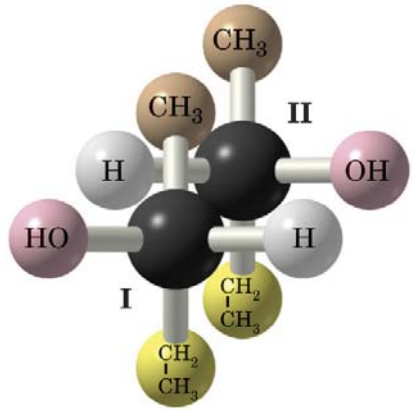
***Achiral molecule*: molecule that is superposable on its mirror image**

a) Molecules contains one sp^3 stereogenic center:





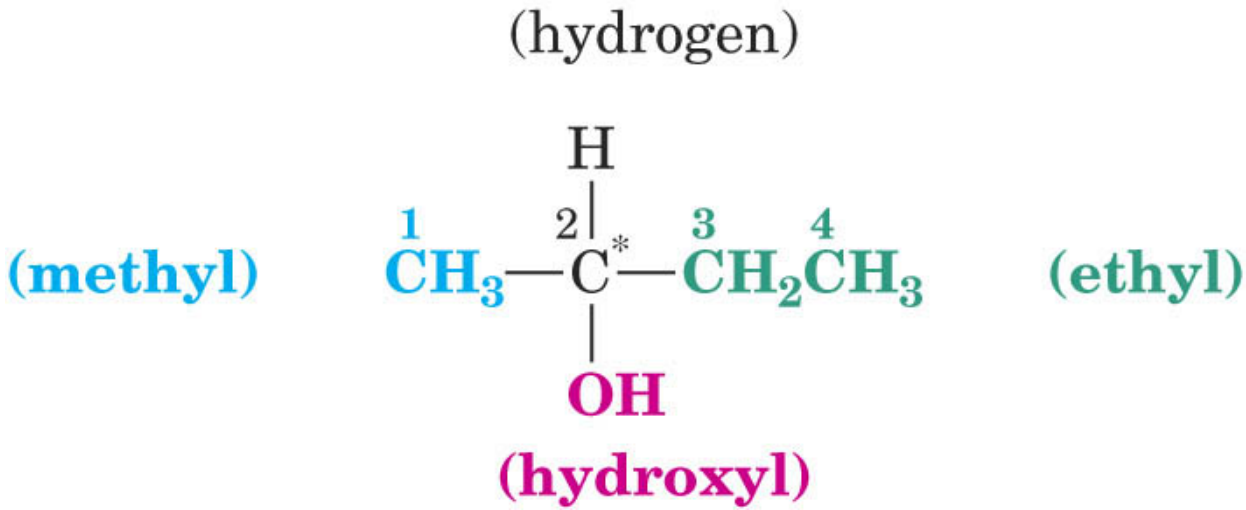
2-butanol

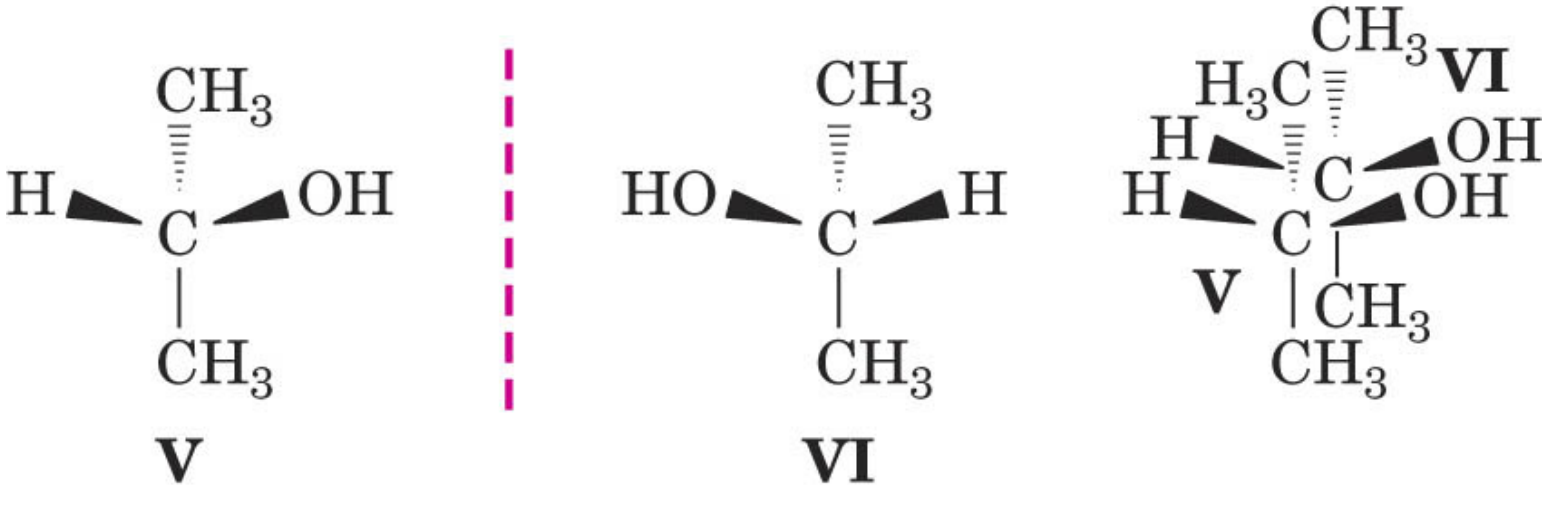


i) A molecule with a single tetrahedral carbon bonded to four different groups will always be chiral, the atom is called chiral atoms !!!

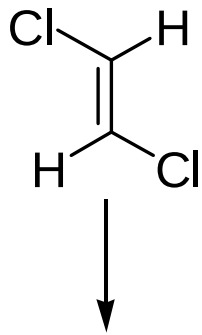
ii) Switching any two groups at the tetrahedral center leads to the another enantiomeric molecule with one tetrahedral carbon!!!

iii) Stereogenic center: An atom bearing groups of such nature that an interchange of any two groups will produce a stereoisomer (including both enantiomer and diastereomer) , designated with *.





Not chiral: achiral

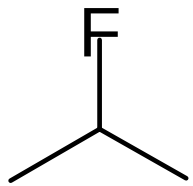


trigonal planar stereogenic carbon

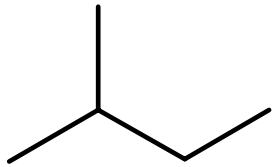
iv) Enantiomers do not interconvert spontaneously

Exercise on page 200: some molecules listed herein have a stereogenic center and some do not; if they do, write the three-dimensional formulas:

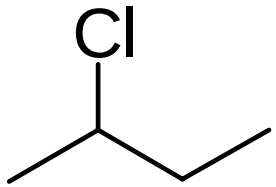
a) 2-Fluoropropane



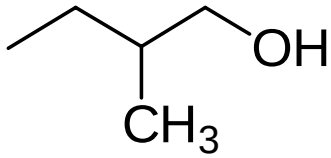
b) 2-Methylbutane

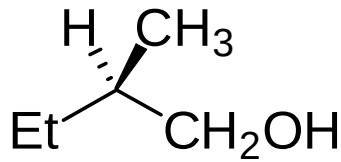


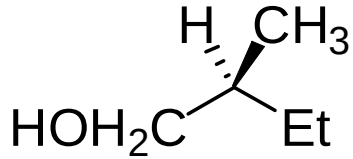
c) 2-Chlorobutane



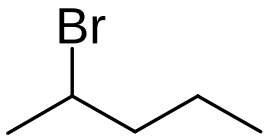
d) 2-Methyl-1-butanol

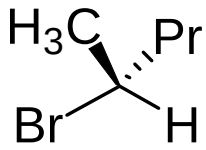


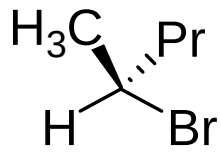




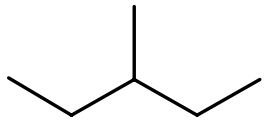
e) 2-Bromopentane



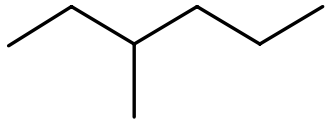


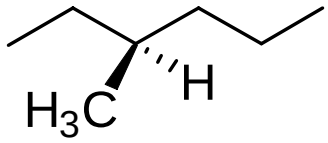


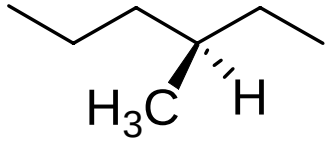
f) 3-Methylpentane



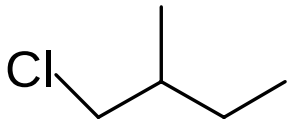
g) 3-Methylhexane

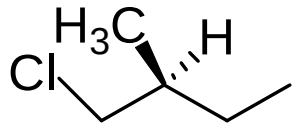


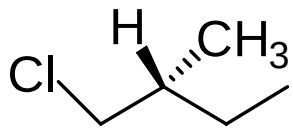




h)1-Chloro-2-methylbutane

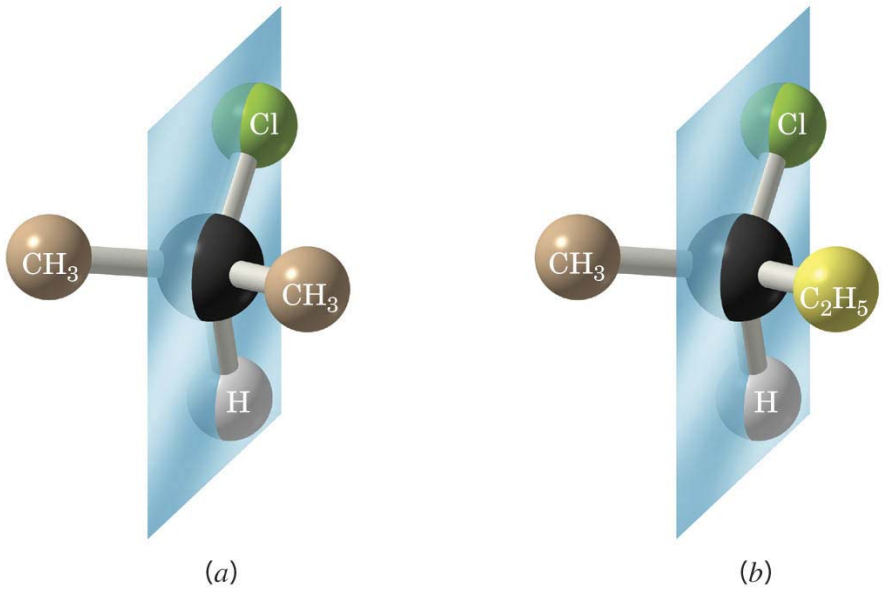






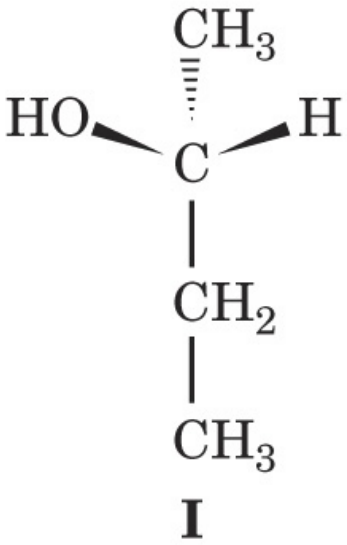
Tests for Chirality: Planes of Symmetry

Plane of symmetry: An imaginary plane that bisects a molecule in such a way that the two halves of the molecule are mirror images of each other. A molecule with a plane of symmetry cannot be chiral (achiral)

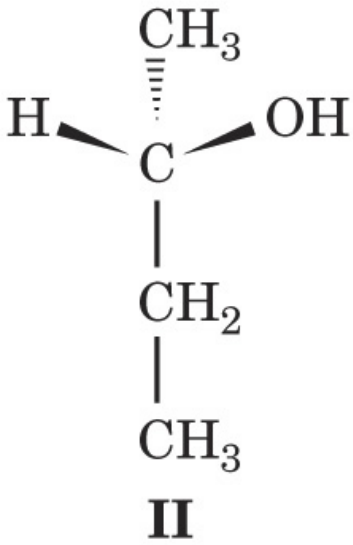


(*a*) (*b*)

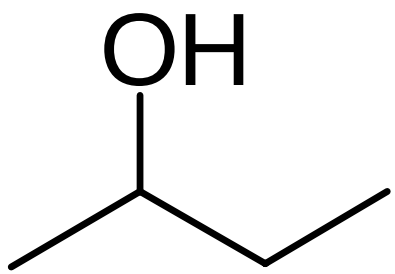
Enantiomers 之命名：*R* and *S* system (Cahn-Inglod-Prelog system)



I



II

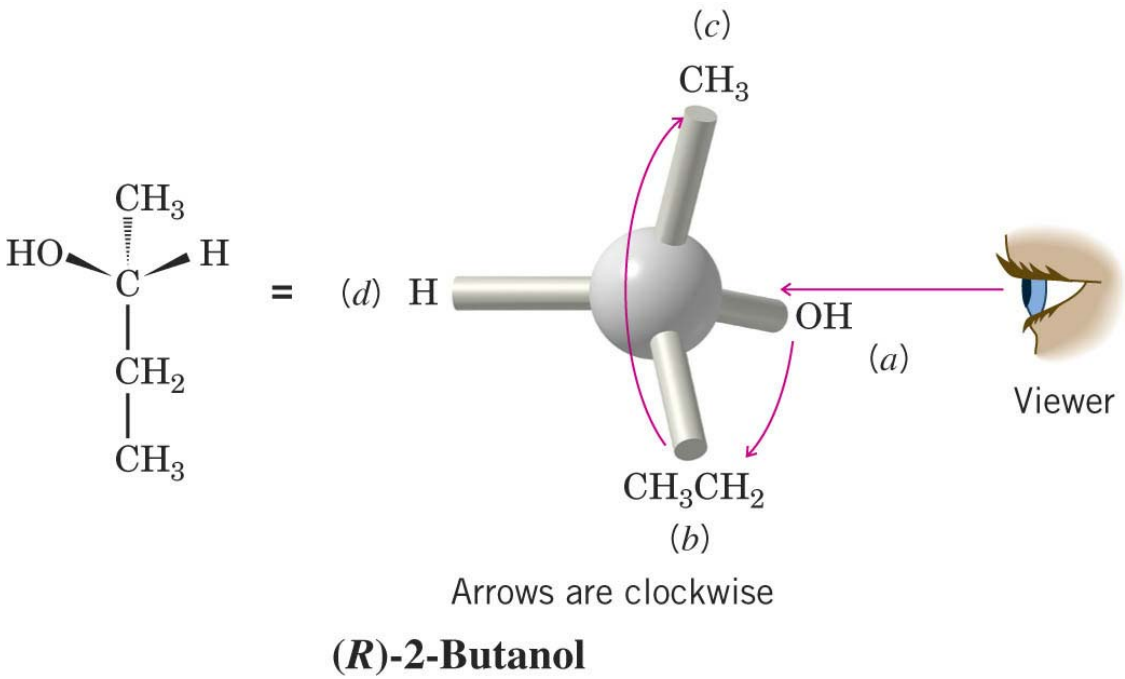


Configuration的命名原則:

1)對stereogenic center or chiral center上的基團，以原子序為基礎來編號:
OH為最大in this case.

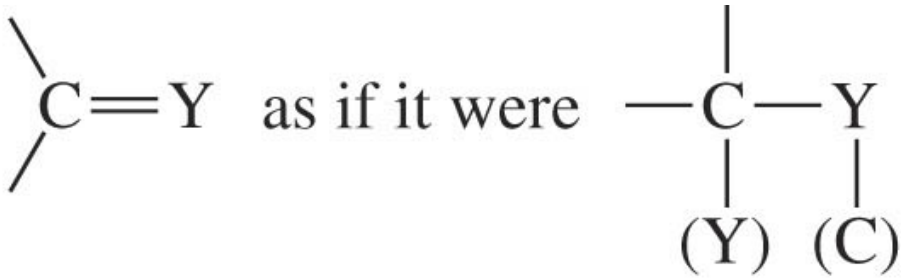
2) 如果與stereogenic center連接原子的原子序相同， 則追溯到有差別為止:
Et- will be the next in this case, (C, H, H) > (H, H, H).

3）將分子旋轉， 使最小的取代基遠離我們：

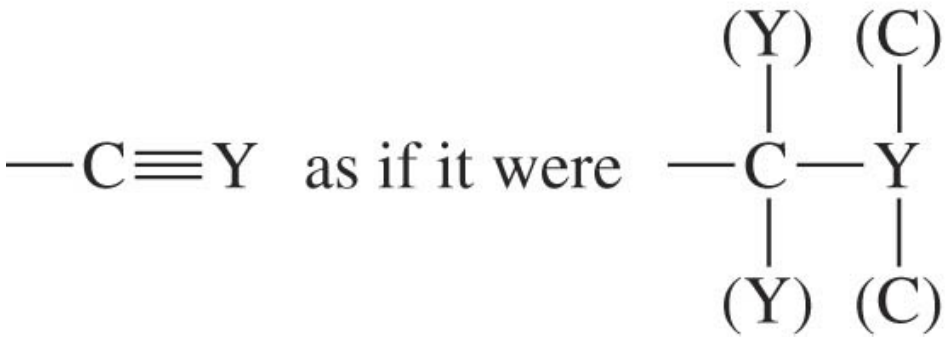


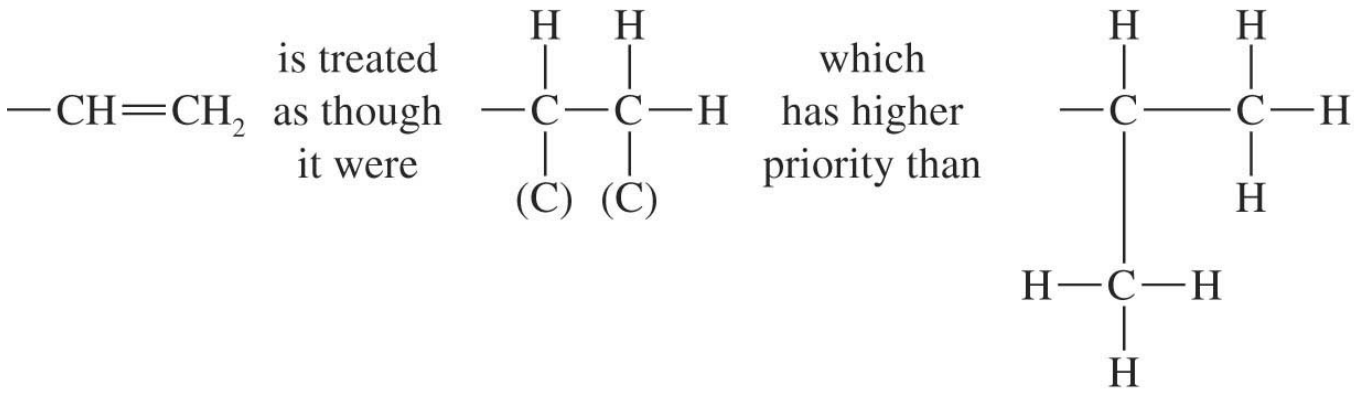
(*R*)-2-Butanol

4) Groups with double or triple bonds are assigned priorities as if their atoms were duplicated or triplicated:


C=Y
as if it were
C
Y
(Y)
(C)

and


—C≡Y
as if it were
(Y)
(C)
C
Y
(Y)
(C)


—CH=CH2
is treated as though it were
H
H
C
C
H
(C)
(C)
which has higher priority than
H
H
C
C
H
H
H
C
H
H

Exercise on page 206:

A) List the groups from highest to lowest priority:

-Cl > -SH > -OH > H;

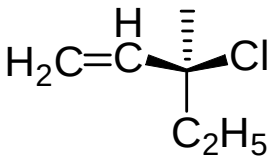
-CH2Br > -CH2Cl > -CH2OH > -CH3;

-OH > -CHO > CH3 > H

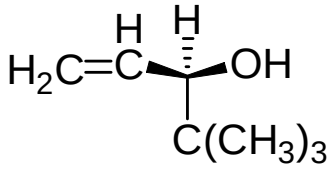
-C(CH3)3 > -CH=CH2 > -C(CH3)3 > H

-OCH3 > -N(CH3)2 > CH3 > H

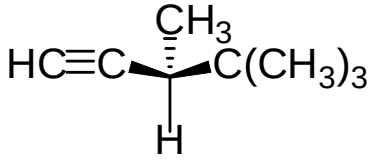
B) Assign (*R*) or (*S*)



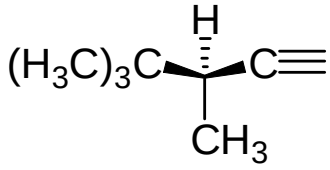
(*S*)



(*R*)

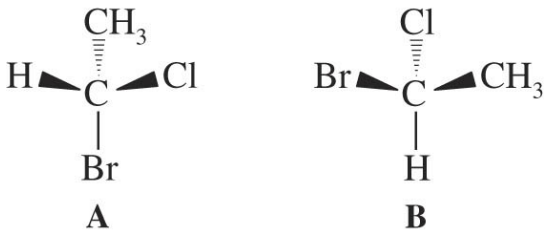


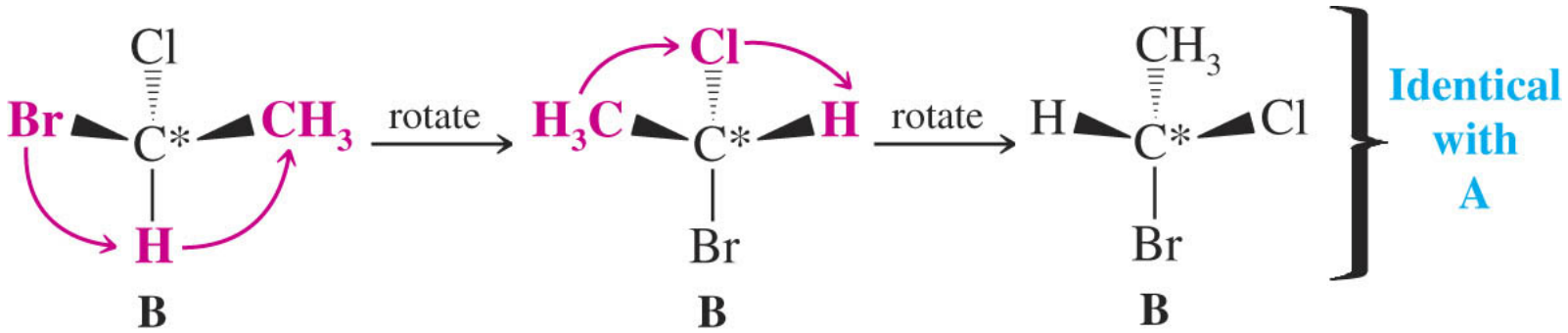
≡

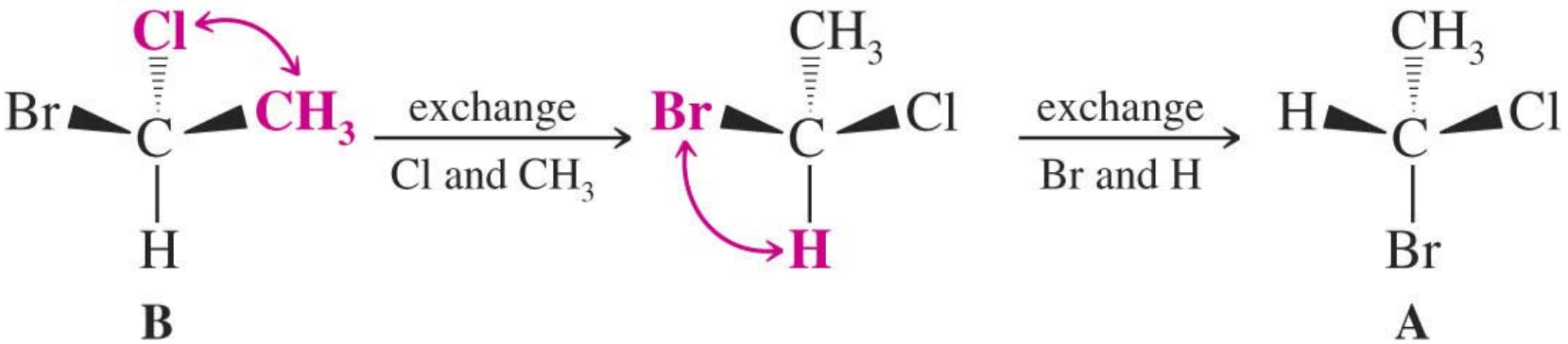


(*S*)

Problem: Are A and B identical or enantiomers (two approaches)?



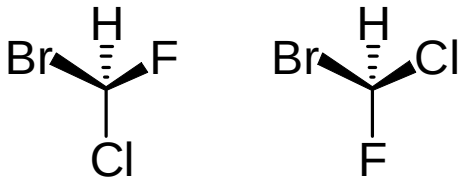




經過兩次官能基團的互換後重合：為同一化合物

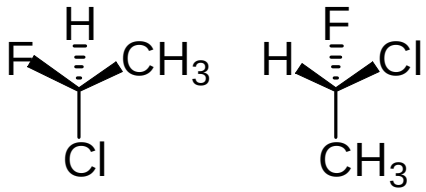
Exercise on page 208: Tell whether the two structure represent enantiomers or same compound:

a)



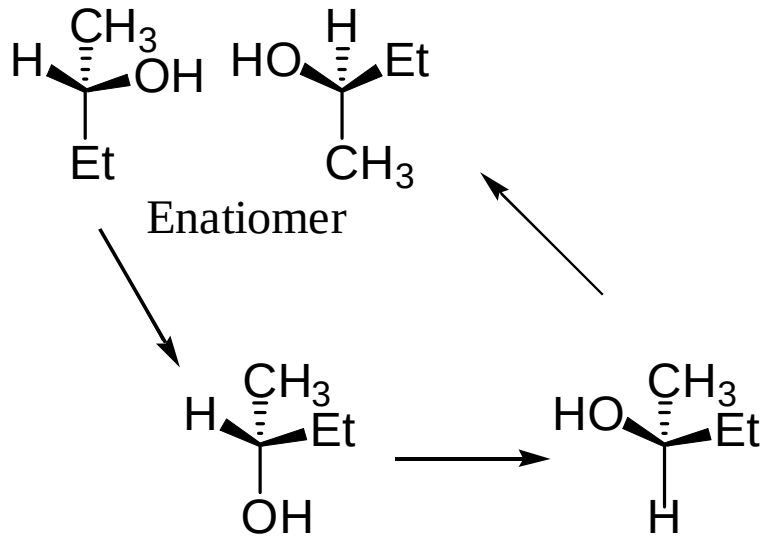
Enatiomers

b)



Same compounds

c)



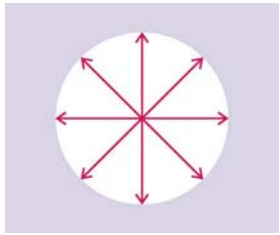
Enatiomer

b) Physical Properties of Enantiomers

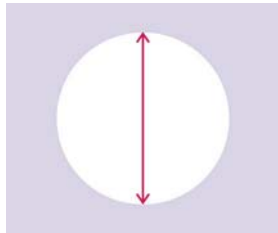
Unlike the constitutional isomers and diastereomers, enantiomers have almost all identical physical properties (melting point, boiling point, density, IR) See the table on page 208

**** Enatiomers show different rates of reaction toward other chiral molecules***

**** Enantiomers rotate the plane of polarized light(偏振光) in equal but opposite directions, For this reason, seperated enantiomers are said to be optically active compounds***

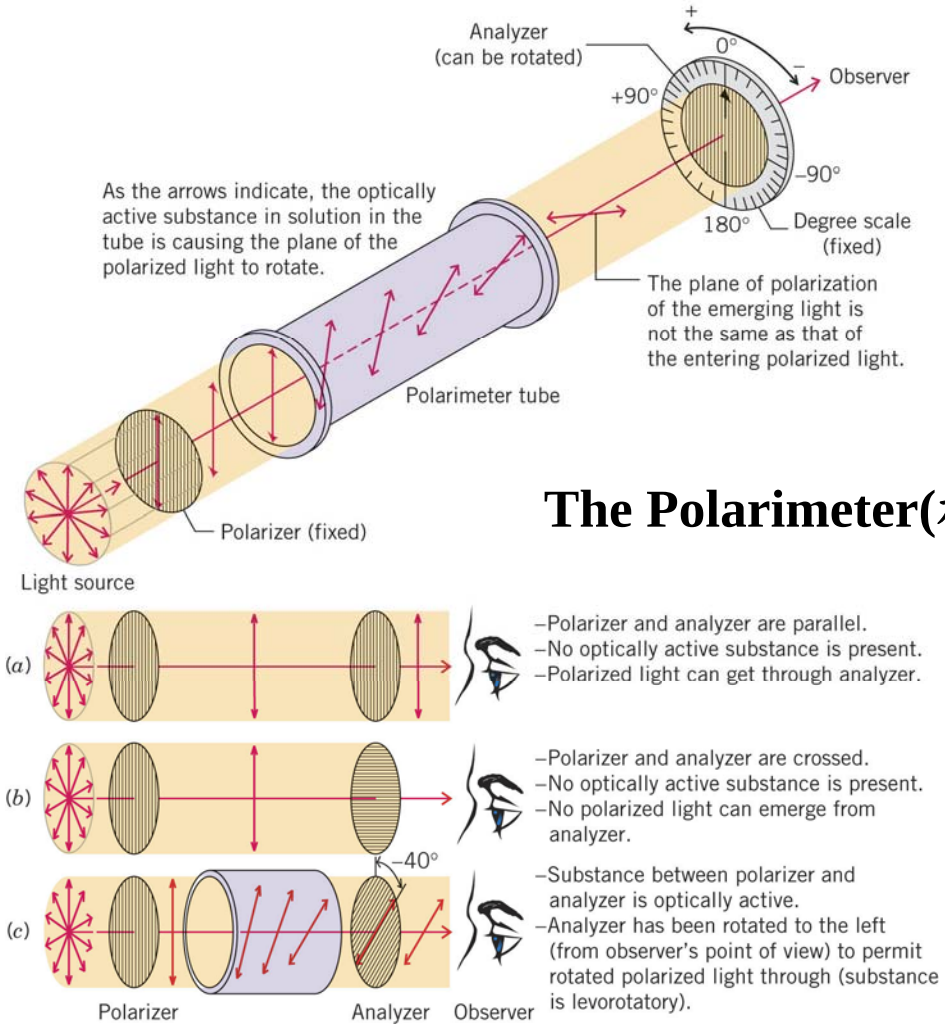


Oscillation of the electric field of ordinary light occurs in all possible planes perpendicular to the direction of propagation



If the light is passed through a polarizer(偏振光器), only one plane emerges

The Polarimeter(旋光儀)



Specific Rotation [a]

***An empty sample tube or one containing an achiral molecule will not rotate the plane-polarized ligh**

***An optically active substance (*e.g.* one pure enantiomer) will rotate the plane-polarized light**

- **The degree the analyzer needs to be turned to permit light through is called the observed rotation α**
- **The standard value specific rotation [α] can be calculated**
- **If the analyzer is rotated clockwise the rotation is (+) and the molecule is dextrorotatory (D)**
- **If the analyzer is rotated counterclockwise the rotation is (-) and the molecule is levorotatory (L)**

$$[\alpha] = \frac{\alpha}{c \cdot l}$$ **Specific rotation:(比旋光) 僅與溫度和波長有關**

where $[\alpha]$ = the specific rotation

α = the observed rotation

c = the concentration of the solution in grams per milliliter of solution (or density in g mL^{-1} for neat liquids)

l = the length of the tube in decimeters (1 dm = 10 cm)

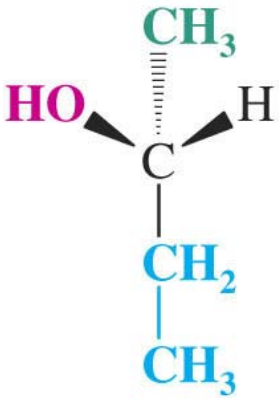
$25^{o}C$

Sample containing 1.00gmL-1 of optically active substance in 1-dm tube, produce a rotation of 3.12^{o} in clockwise direction.

$$[\alpha]_{D}^{25} = +3.12^{o}$$

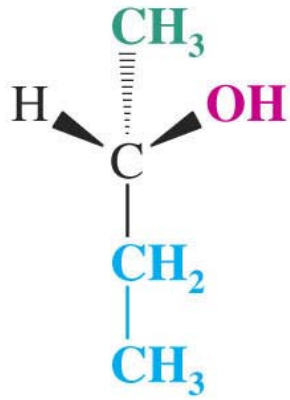
D line of a sodium lamp

– **The specific rotation of the two pure enantiomers of 2-butanol are equal but opposite**



(*R*)-2-Butanol

$[\alpha]_D^{25} = -13.52°$



(*S*)-2-Butanol

$[\alpha]_D^{25} = +13.52°$

– **There is no straightforward correlation between the *R,S* designation of an enantiomer and the direction [(+) or (-)]in which it rotates plane polarized light**

i) Enatiomerically pure: a sample consist of a single entiomer. (enantiomeric excess is 100%)

ii) Racemic mixture(外消旋物): A 1:1 mixture of enantiomers. No net optical rotation . Often designated as (±)

(±)-2-butanol or as (±)-$CH_3CH_2CHOHCH_3$

iii) enantiomeric excess (ee) < 1:

$$\%\ \text{Enantiomeric excess} = \frac{\text{moles of one enantiomer} - \text{moles of other enantiomer}}{\text{total moles of both enantiomers}} \times 100$$

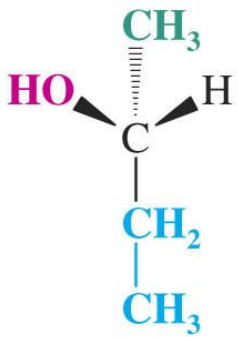
$$\%\ \text{Enantiomeric excess*} = \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}} \times 100$$

The optical rotation of a sample of 2-butanol is +6.76°. What is the enantiomeric excess?

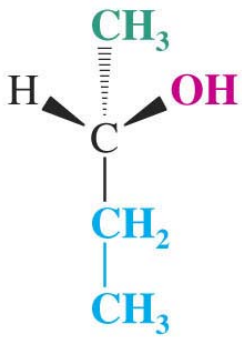
$$\text{Enantiomeric excess} = \frac{+6.76^\circ}{+13.52^\circ} \times 100 = 50\%$$

50% is (+) enantiomer; 50% is racemic form

Exercise on page 215: a sample of 2-methyl-1-butanol has a specific rotation equal to + 1.151°, a) what is the enantiomeric excess b) (R) or (S) c) what is the compositions of the mixture?



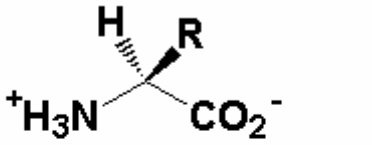
(*R*)-2-Butanol
$[\alpha]_D^{25} = -13.52^\circ$

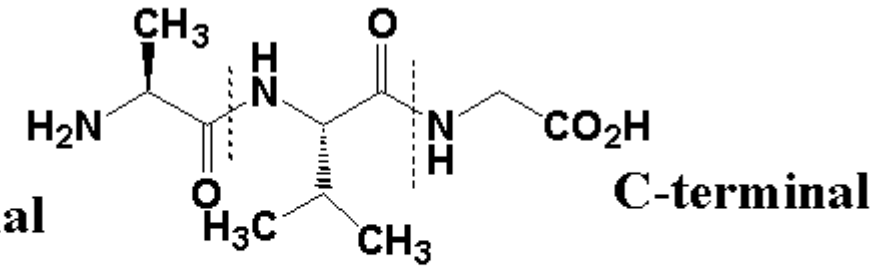


(*S*)-2-Butanol
$[\alpha]_D^{25} = +13.52^\circ$

三）*Chiraty in Biology and Chemistry*

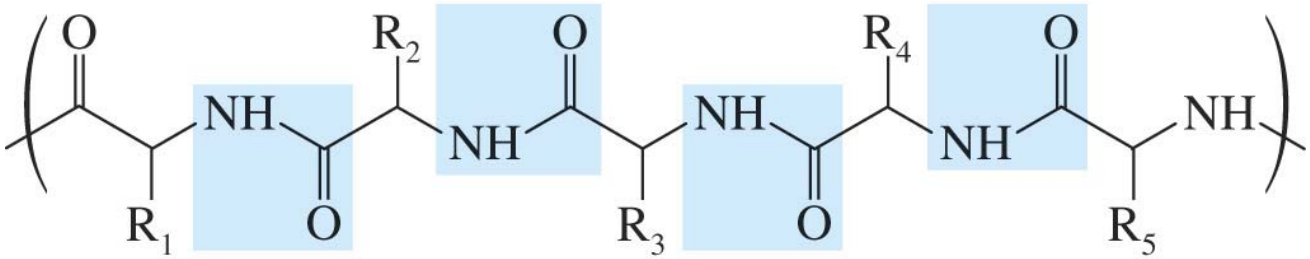
a) The biological molecul





L- Amino acids

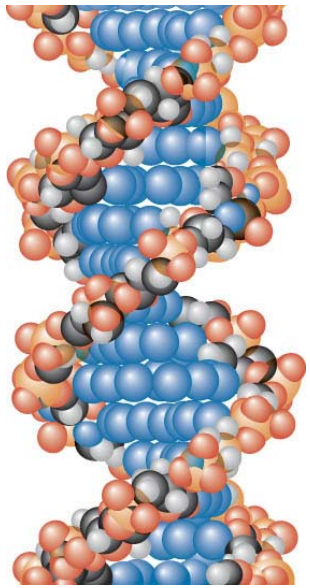
Ala-Val-Gly



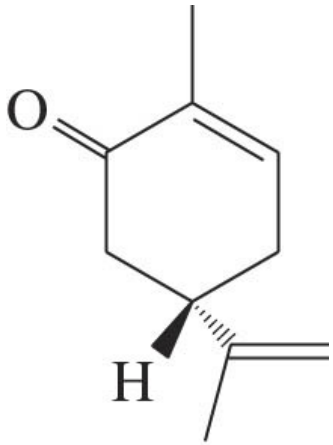
A portion of a protein molecule

Amide (peptide) linkages are shaded.

R_1–R_5 may be any of the possible side chains.



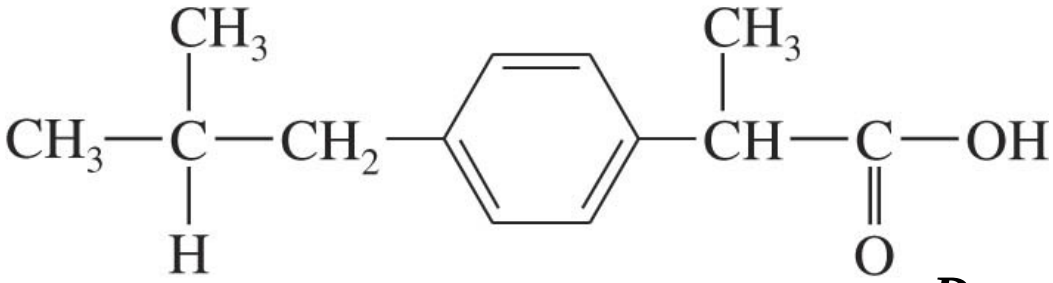
b) The Natural product



(+)-Carvone

Analyzing the configuration

c) The Drugs



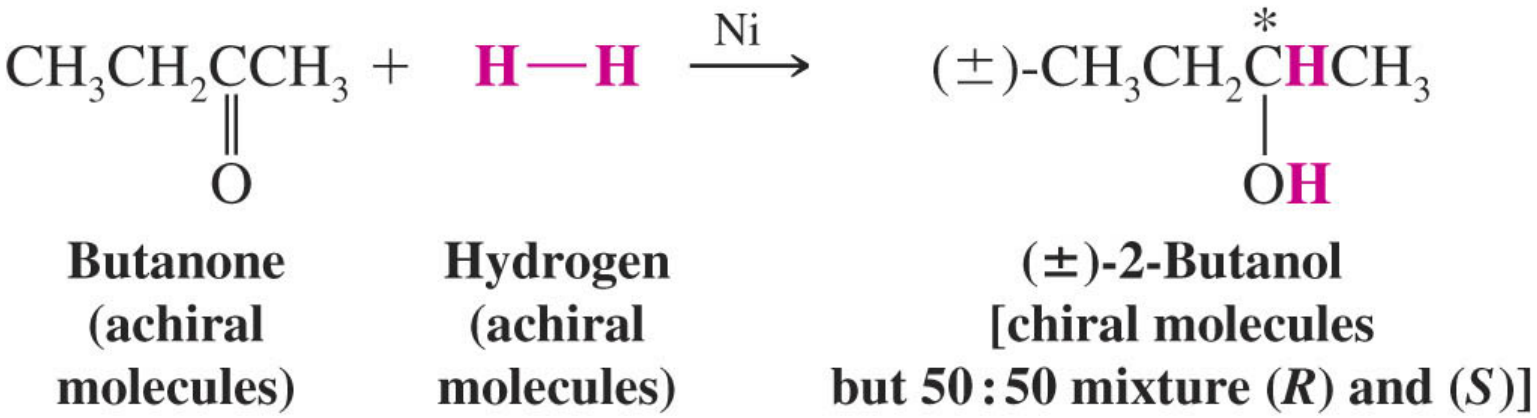
Ibuprofen

Drawing the Active configuration

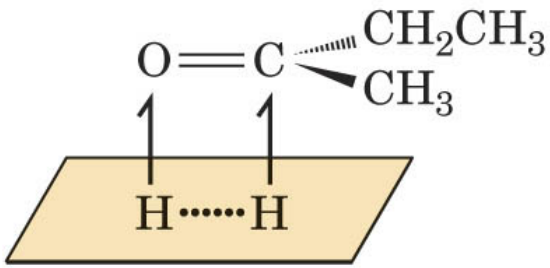
Anti-inflammatory drug: (S) active; (R) non-active

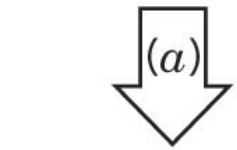
Exercise on page 217

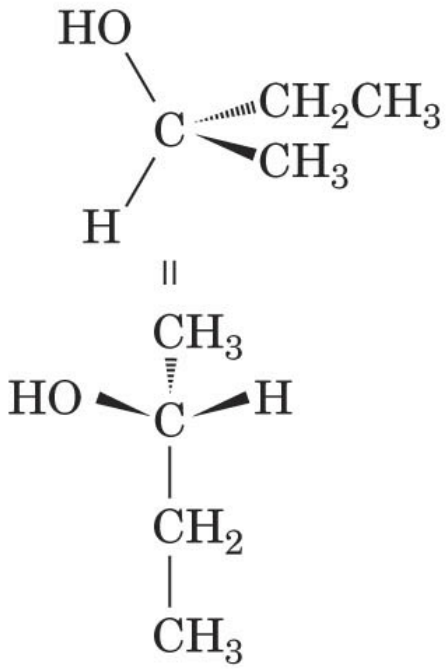
d) The Non-stereoselective Organic Reaction



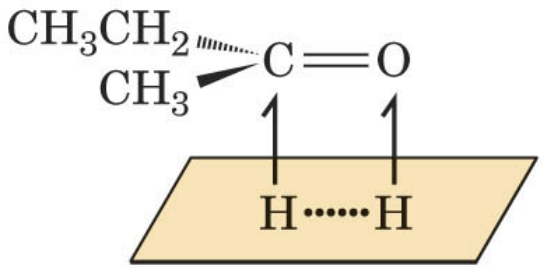
Reactions carried out with achiral reactants can often lead to achrial (mistake in page 215) products, that is, in racemic forms.

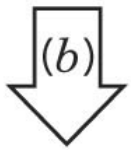


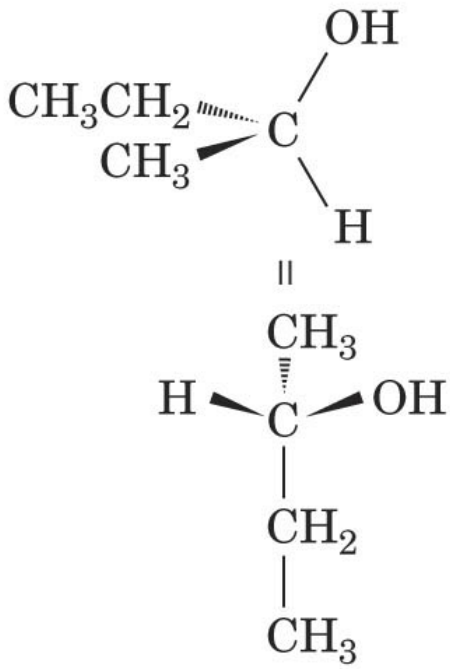




(*R*)-(–)-(2)-Butanol

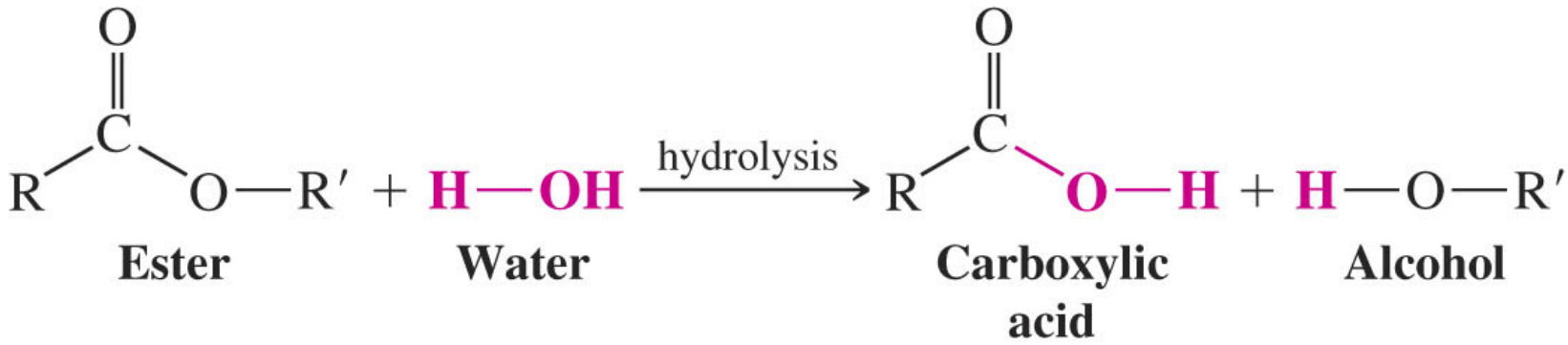


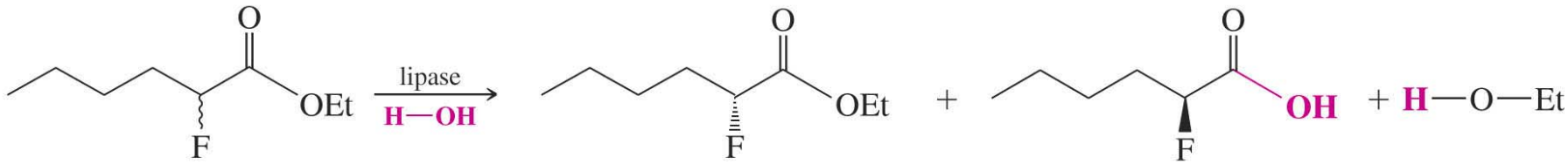




(*S*)-(+)-(2)-Butanol

***e) The Stereoselective Organic Reaction*:可使得某一個立體異構物的生成佔優勢的有機反應 (*enantioselective and diastereoselective*).**



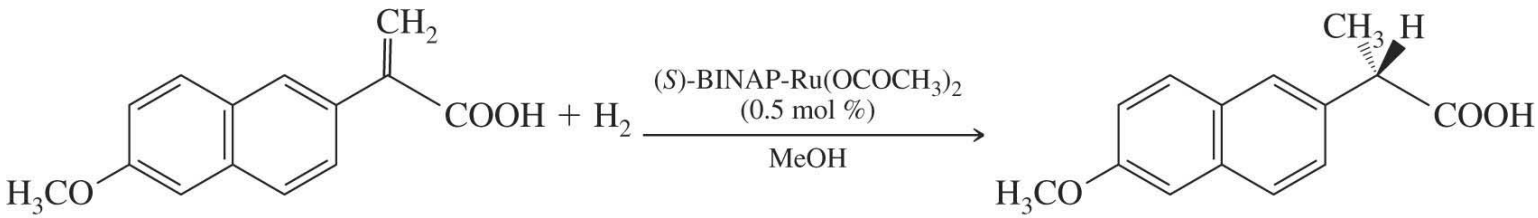


Ethyl (±)-2-fluorohexanoate [an ester that is a racemate of (*R*) and (*S*) forms]

Ethyl (*R*)-(+)-2-fluorohexanoate (>99% enantiomeric excess)

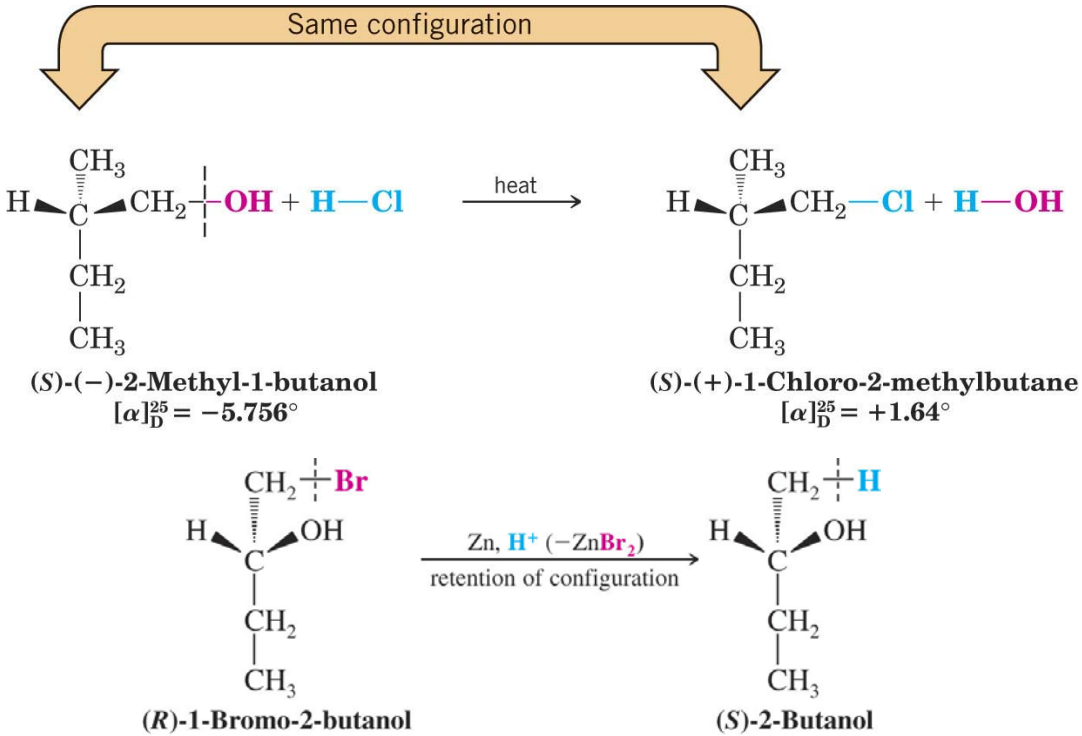
(*S*)-(−)-2-Fluorohexanoic acid (>69% enantiomeric excess)

Kinetic resolution: the resulting mixture consists predominantly of one stereoisomer of reactant and one stereoisomer of product

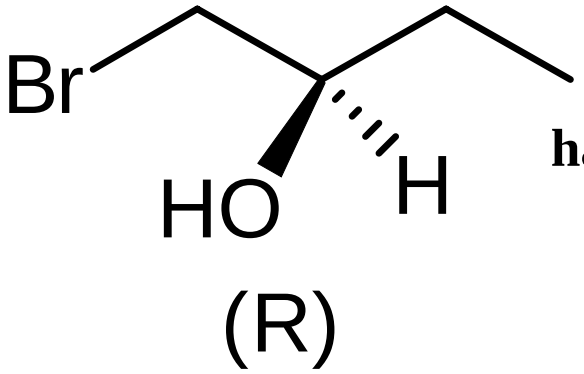


(*S*)-Naproxen
(an anti-inflammatory agent)
(92% yield, 97% ee)

如果掌性的化合物的化學反應不涉及到掌性中心化學鍵的斷裂，那麼生成物亦保留掌性 **(retention of configuration),** 即反應物與生成物有相同的 **relative configuration.**

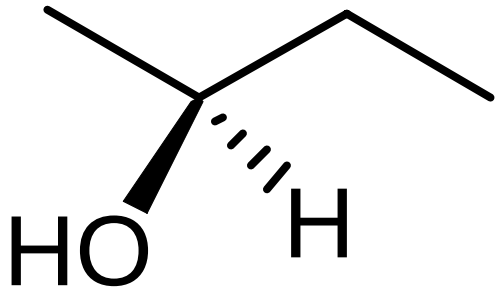


***Relative configuration*: the relationship between comparable stereogenic centers in two different molecules:**

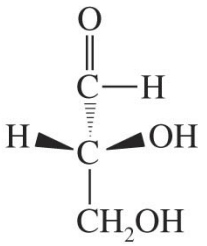


(R)

has the same *relative configuration* with

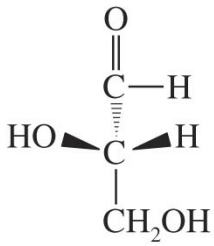


(S)

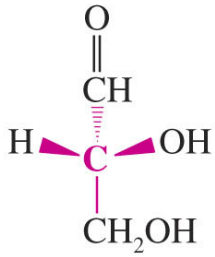


(*R*)-Glyceraldehyde

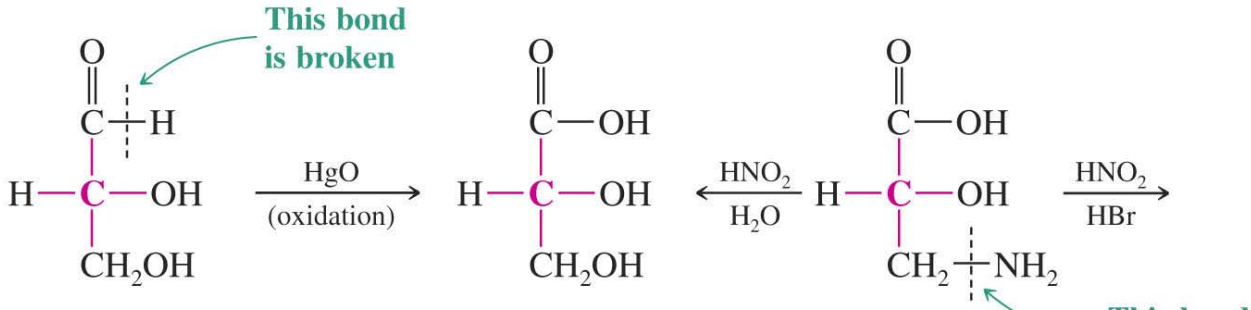
and



(*S*)-Glyceraldehyde



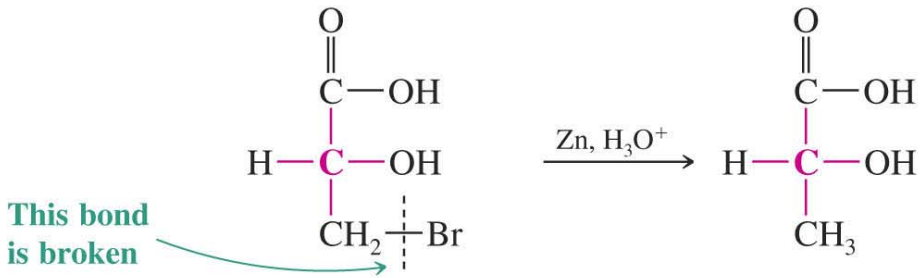
(*R*)-(+)-Glyceraldehyde



(+)-Glyceraldehyde

(−)-Glyceric acid

(+)-Isoserine

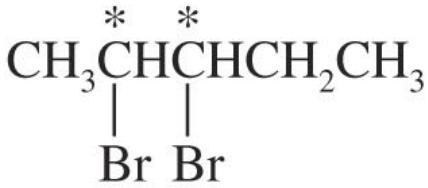


(−)-3-Bromo-2-hydroxy-propanoic acid

(−)-Lactic acid

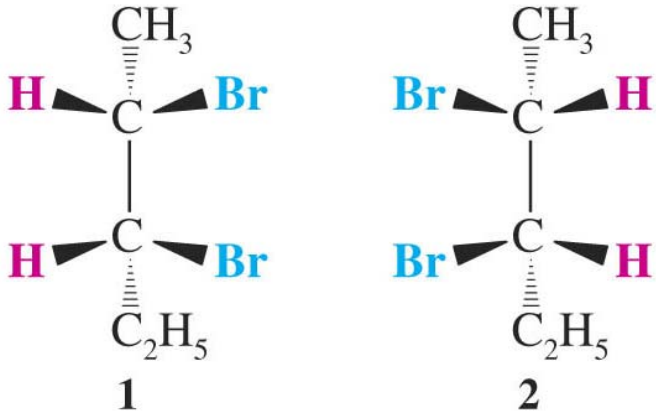
Absolute configuration: the actual 3-dimensional orientation of the atoms in a chiral molecule

四）化合物含兩個以上 **stereogenic centers**



2,3-Dibromopentane

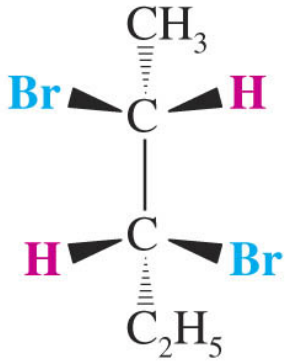
對於含有sp^3 stereogenic centers的化合物，它們立體異構物的數目不會超過2^n個



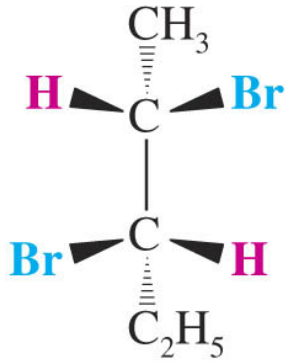
1 **2**

i) We usually write our structures in eclipsed conformation, they make it easy for us to recognize planes of symmetry

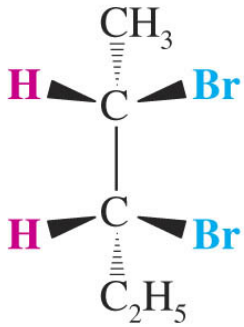
ii) we also write the longest carbon chain in a generally vertical orientation, this make the structure directly comparable.



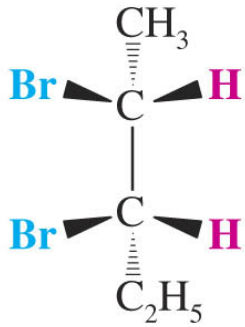
3



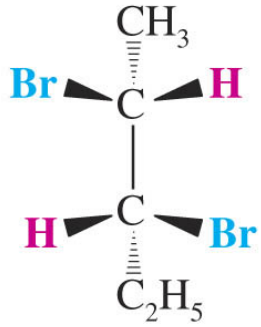
4



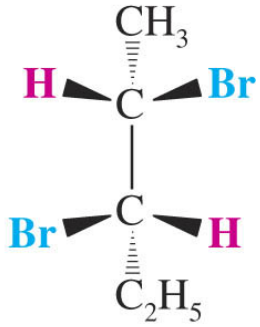
1



2



3

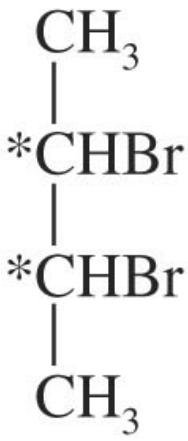


4

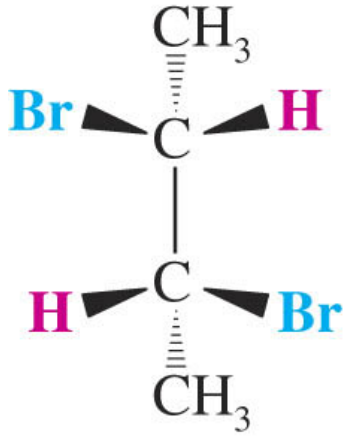
1) There are two pairs of enantiomers (1, 2) and (3,4), Enantiomers are not easily separable so 1 and 2 cannot be separated from each other

2) Diastereomers: stereoisomers which are not mirror images of each other(1 and 3; 2 and 3, etc.). <u>They have the different physical properties.</u>

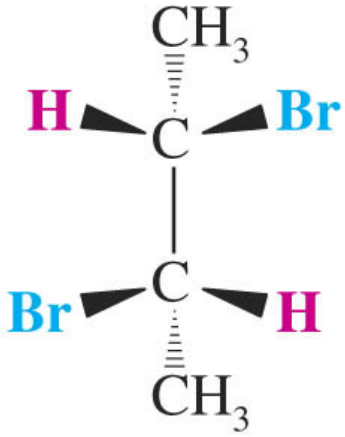
對於含有兩個 **stereogenic centers** 的化合物， 它們立體異構物的數目不一定為 $2^n(4)$個：



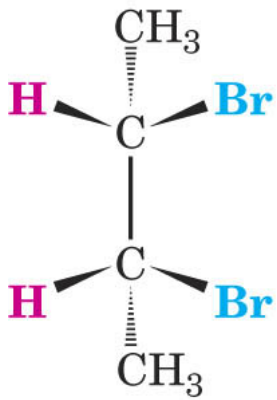
2,3-Dibromobutane



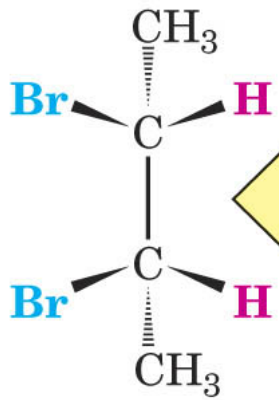
A



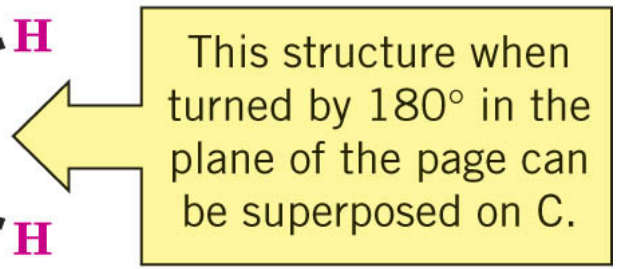
B



C

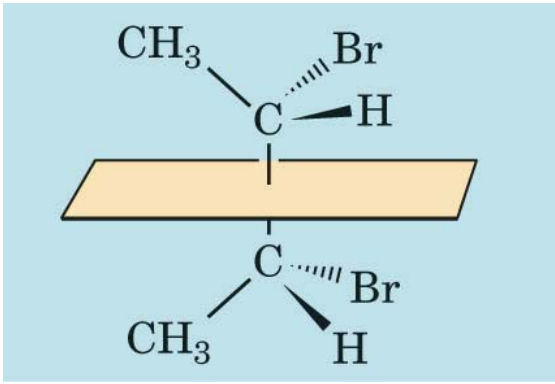


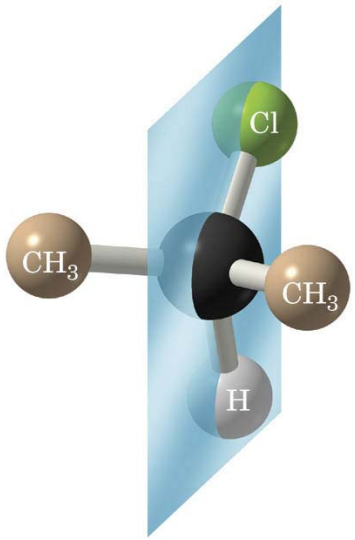
D



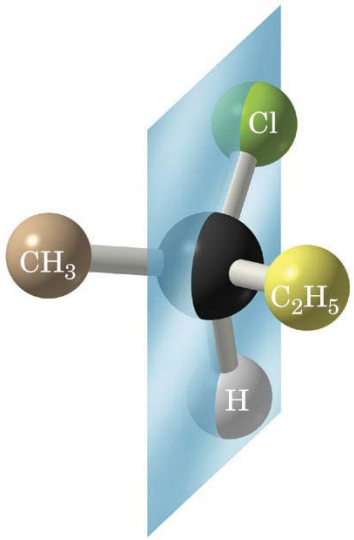
C (or D) is called meso compound (內消旋物), because they are achiral, the meso compounds are not optical active

判斷內消旋物的依據：*has a plane of symmetry*





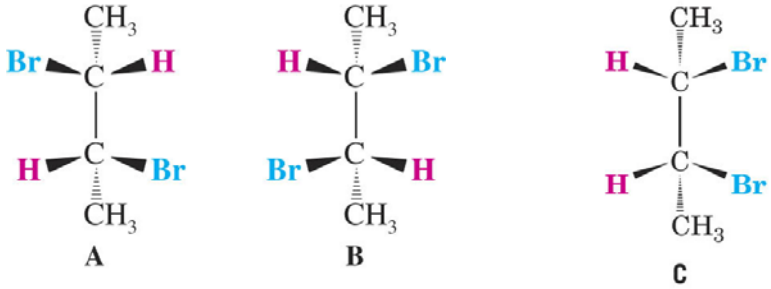
(*a*)



(*b*)

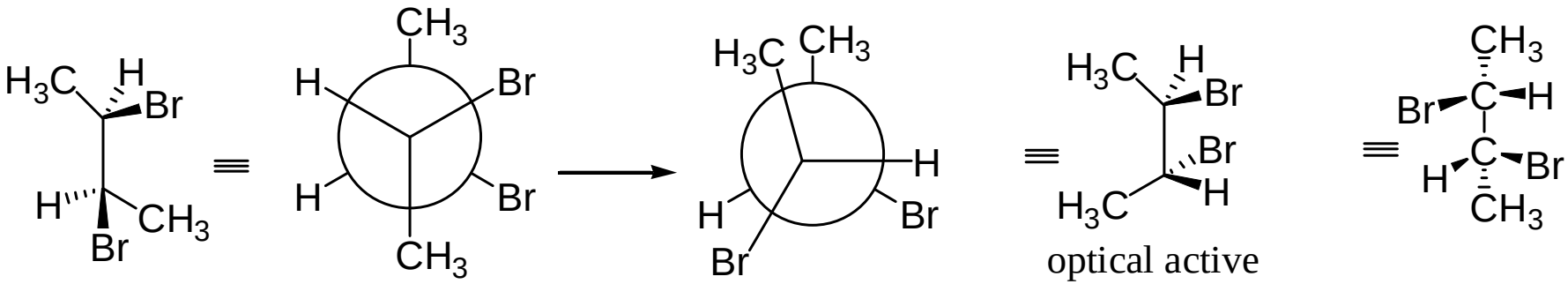
***Exercise on page 221*:**

a) Which of following would be optically active? i) pure A; ii) pure B; iii) pure C iv) An equimolar mixture of A and B



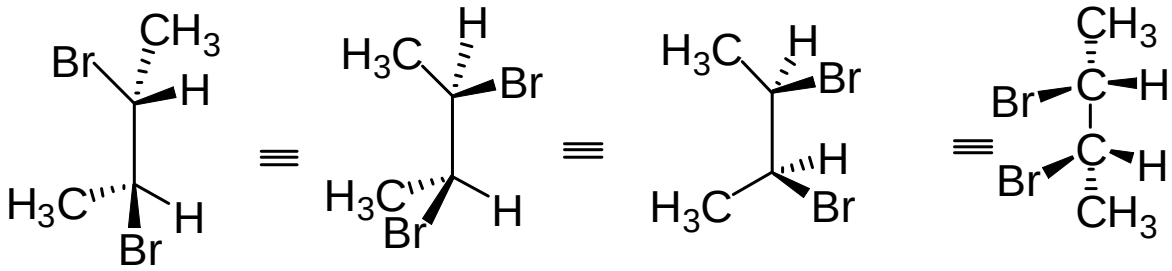
b) Write the eclipsed (mistake) conformations, and tell which compound each formular represents?

a)

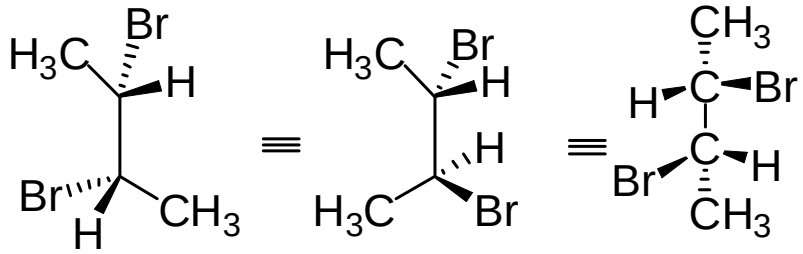


optical active

b)

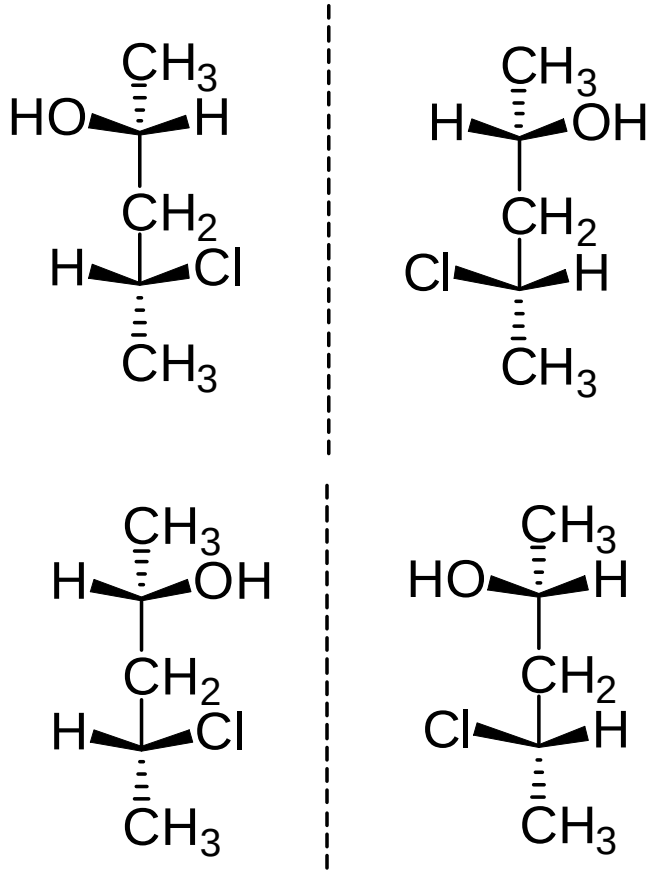


c)

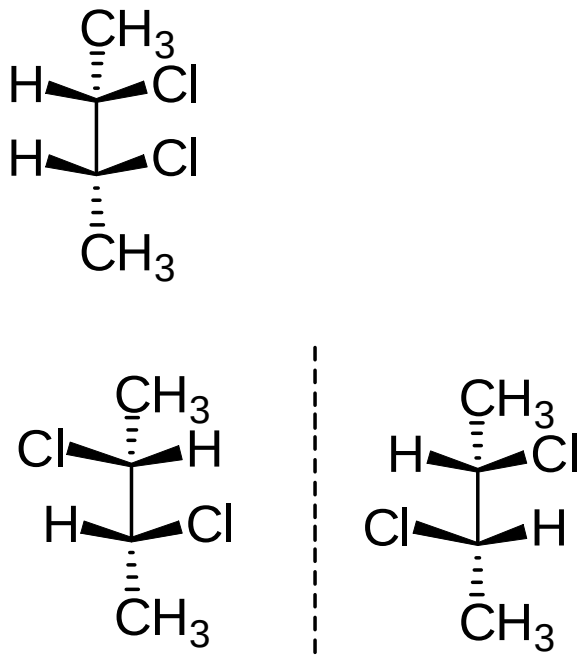


c) Write the three-dimensional formulas. Label pair of enantiomers and meso compound.

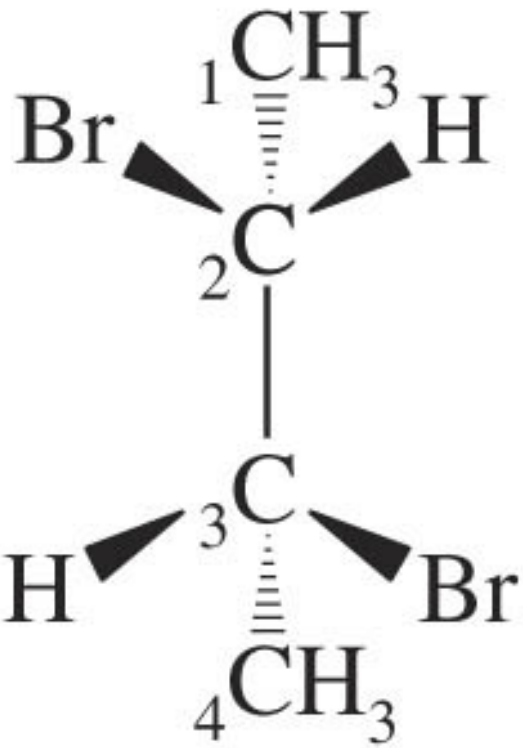
d) $CH_3CHOHCH_2CHClCH_3$



a) $CH_3CHClCHClCH_3$

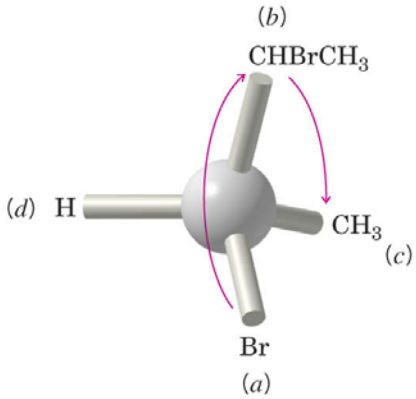


Naming Compounds with More than One Stereogenic Center



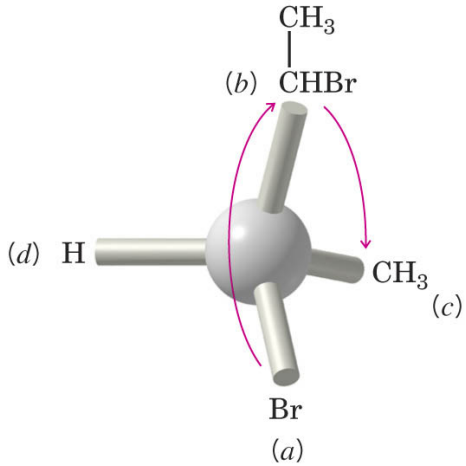
A

2,3-Dibromobutane



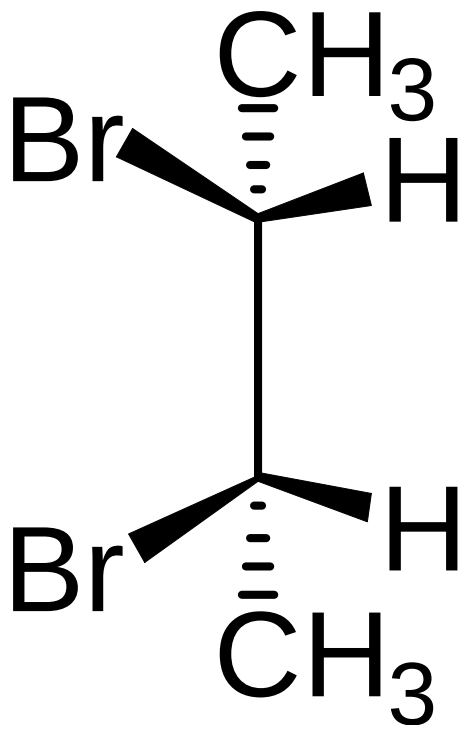
(*R*) Configuration

Viewer



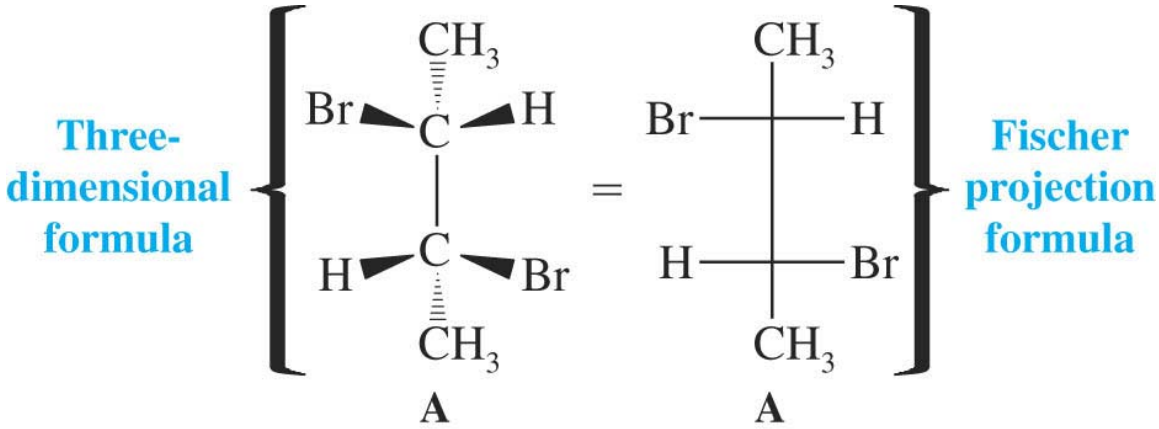
(*R*) Configuration

Viewer



Give the configuration at C2 and C3

立體異構物另一种表示方法：**Fisher Projection formulars:**



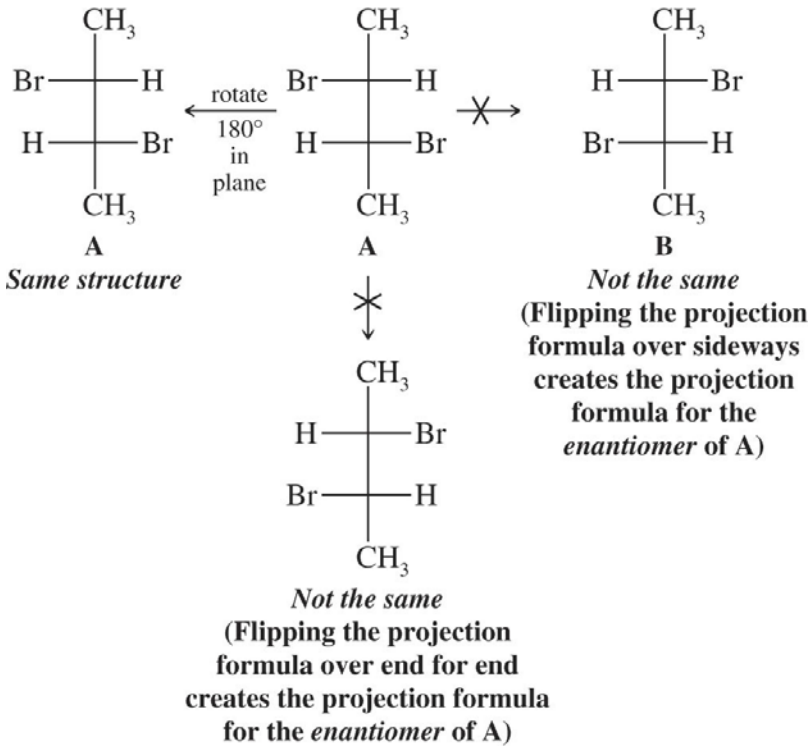
i) Written with main carbon chain extending from top to bottom.All groups are eclipsed

ii) Vertical lines represent bonds that project behind the plane of the paper.

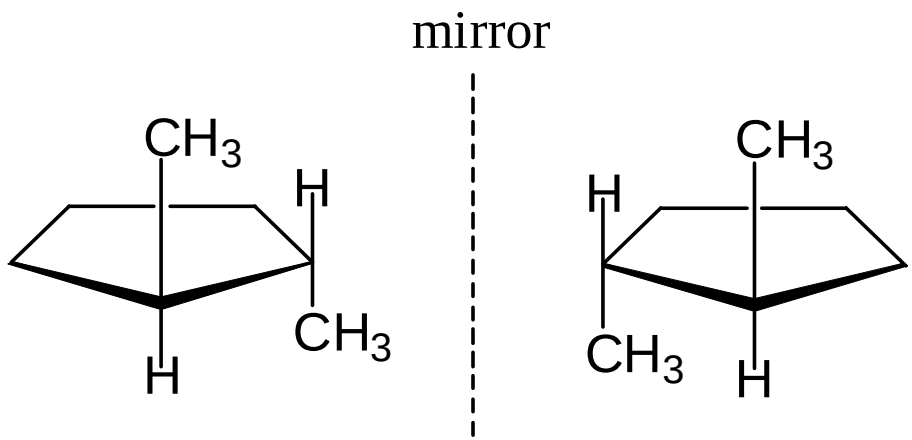
iii) Horizontal lines represent bonds that project out of the plane of the paper

iv) Intersection represent the carbon of stereogenic center.

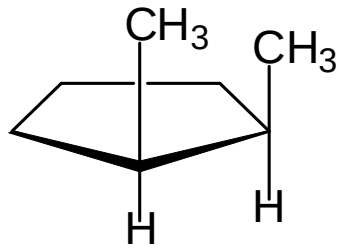
v) In using Fisher projections to test the superposability for two structures:



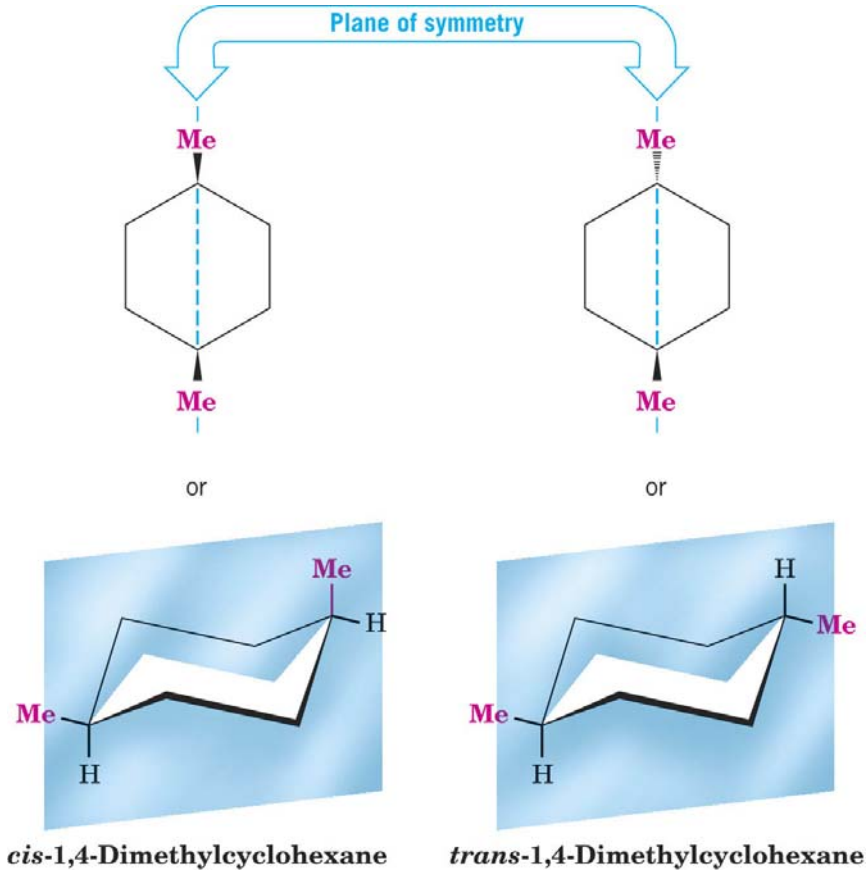
五 ）環狀化合物的掌性



Enantiomers



Meso compound, with a plane of symmetry, superposable with its mirror image, nonchiral molecule, no optical activity, diastereoisomeric with trans isomers

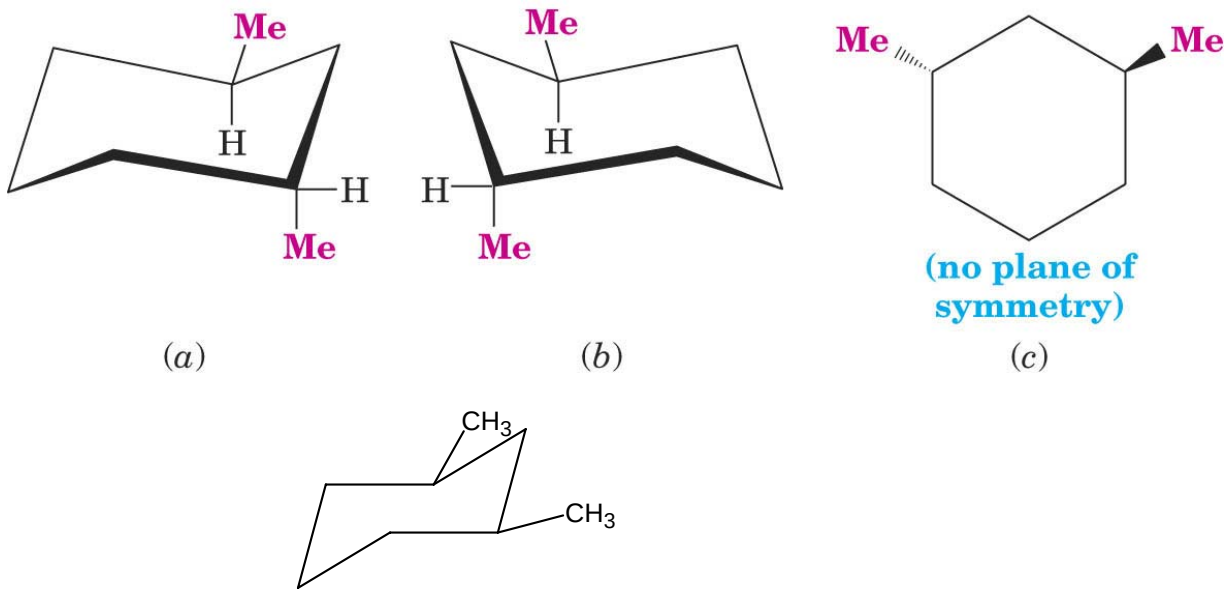


i) cis and trans forms are diastereomers to each other

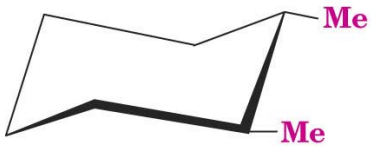
ii) do not contain a tetrahedral atoms with four diffeent groups

iii) Neither compounds is chiral and optically active

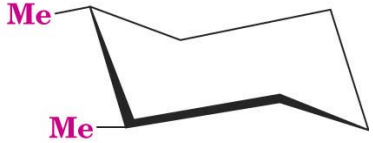
iv) Both have a plane of symmetry



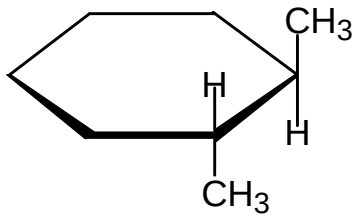
i) The trans and cis compounds each have two stereogenic centers
ii) The cis compound has a plane of symmetry and is meso
iii) The trans compound exists as a pair of enantiomers

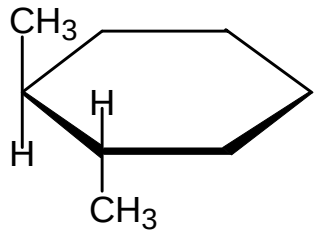


(*a*)

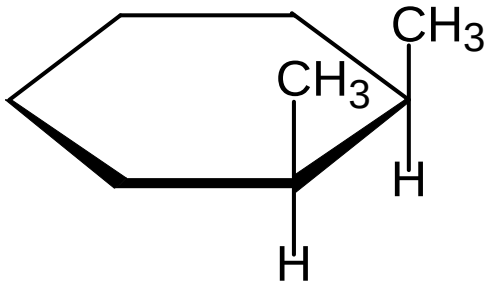


(*b*)

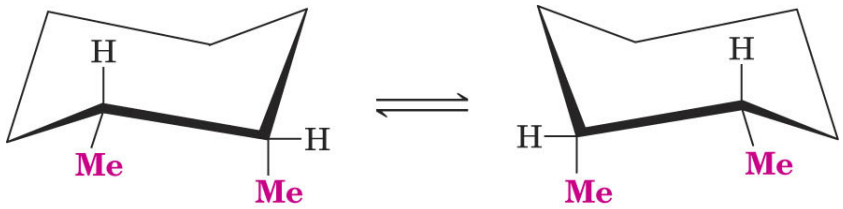




Trans isomers represents a pair of enantiomers



With plane of symmetry



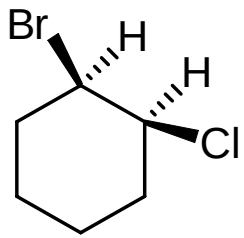
(*c*) (*d*)

Interconvertible, different conformations of the same compound

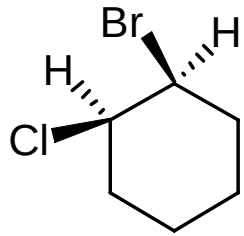
***Exercise on page 227*:**
5.26

a) 1-bromo-2-chlorocyclohexane: 4 isomers
b) 1-bromo-3-chlorocyclohexane: 4 isomers
c) 1-Bromo-4-chlorocyclohexane: 2 isomers

5.27



(R,S)-1-bromo-2-chlorocyclohexane



(S,R)-1-bromo-2-chlorocyclohexane