

Pharmaceutical Organic Chemistry-1

Chapter-5: Stereoisomerism

8 مواضيع (تتعلق على)

- to spark curiosity

- big picture

- chirality & stereochemistry

- Isomerism: Constitutional isomers & stereoisomers

- Enantiomers & Diastereomers

- geometrical isomers (A type of diastereomers) cis/trans isomers

- enantiomers and chiral molecules

- A single chirality center (causes a molecule to be chiral)

- Tetrahedral vs trigonal Stereogenic centers

4- more about the biological importance of chirality (Thalidomide)

5- how to test chirality (planes of symmetry)

6- Naming enantiomers: R/S system

- how to assign R and S configuration 4 rules

7- properties of enantiomers (optical activity)

- Optical activity A- plane polarized light B- the polarimeter C- specific rotation

- the origin of optical activity

A- Racemic Forms

B- Racemic Forms and enantiomers excess

- the synthesis of chiral molecules

A- Racemic Forms

B- Stereoselective syntheses

- molecules with more than one chirality center

A- meso compound

B- How to name compounds with more than one chirality center

- how to draw and use fisher projection

- stereoisomerism of cyclic compounds

A- cyclohexane derivatives

- chiral molecules that don't possess a chirality center

Chirality & Stereochemistry

متطابق

An object is **achiral** (not chiral) if the object and its mirror image are identical

← نقی A chiral



A **chiral** object is one that cannot be superposed on its mirror image

Asymmetric

غير متماثل

ما يتطابقا على بعضه



1. Isomerism: Constitutional Isomers & Stereoisomers

- same molecular formula

- different connectivity

↳ same atoms connected to each other but (different positions)

1A. Constitutional Isomers

Isomers: different compounds that have the same molecular formula

Constitutional isomers: isomers that have the same molecular formula but different connectivity — their atoms are connected in a different order
(positions)

Do the compounds have the same molecular formulae?

NO

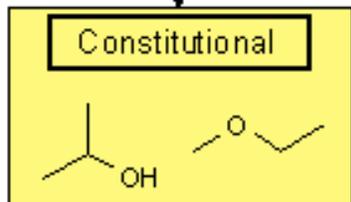
Not isomers

YES

Isomers

Do the compounds have the same connectivity?

NO



same molecular formula
different connectivity

YES

Stereoisomers

same molecular formula ✓
same connectivity ✓
different arrangement in space

Can the compounds be interconverted by rotation about single bonds?

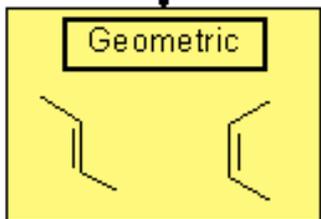
NO

Configurational

ترکیبی

Is the isomerism at a double bond?

YES



(cis/trans) isomers

Alkene
cyclo alkane

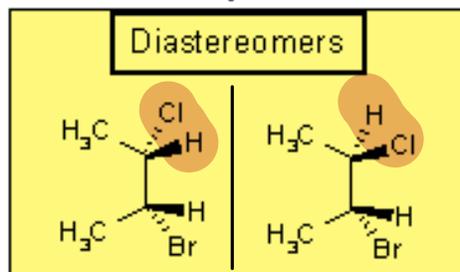
NO

Optical

بجری

Are the compounds non-superimposable mirror images?

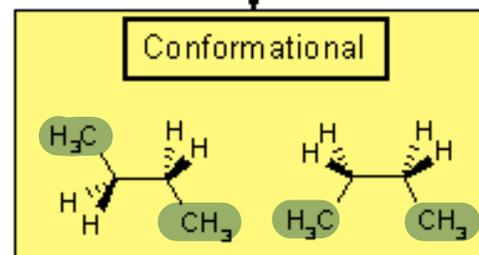
NO



not mirror images

YES

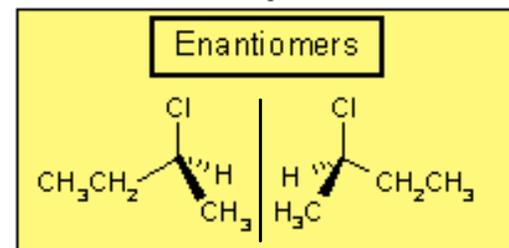
Conformational



different spatial arrangements of the same molecule

YES

Enantiomers



mirror images

Examples

Molecular
Formula

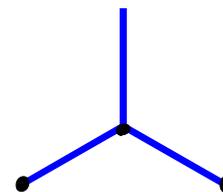
Constitutional
Isomers

C₄H₁₀



Butane

and



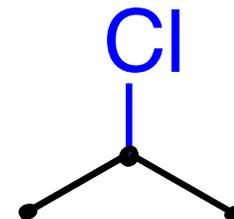
2-Methylpropane

C₃H₇Cl



1-Chloropropane

and



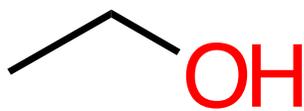
2-Chloropropane

Examples

Molecular Formula

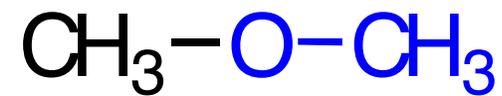


- Alcohol
- ether



Ethanol

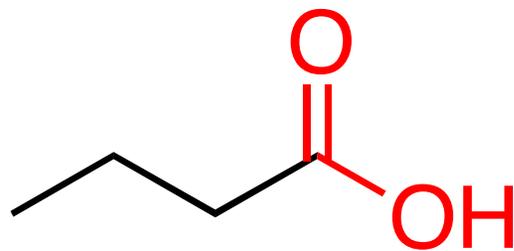
and



Methoxymethane

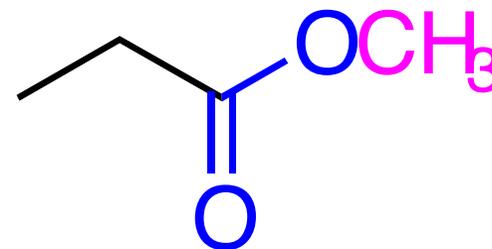


- carboxylic acid
- Ester



Butanoic acid

and



Methyl propanoate

1B. Stereoisomers

<https://youtu.be/XftlUcLWTEE?si=yzV0BystyS9KIQzh>

easy
explanation
3:0 دقيقة

Stereoisomers are **NOT** constitutional isomers

same connectivity

Stereoisomers have their atoms connected in the same sequence but they differ in the arrangement of their atoms in space. The consideration of such spatial aspects of molecular structure is called stereochemistry

فضائيات



Q9:

The given molecules are _____.

- (a) constitutional isomers
- (b) conformers
- (c) stereoisomers
- (d) identical
- (e) None of these

Answer: (c) stereoisomers

Q1: Compounds with different atomic configurations in space but the same atoms bonded to each other are said to as having.

- a) stereoisomerism
- b) functional group isomerism
- c) chain isomerism
- d) position isomerism

Answer: a) stereoisomerism

Explanation: Stereoisomer varies from structural isomers, which have the same molecular formula but differ in their bond connections or order. Molecules that are stereoisomers of one other have the same structural isomer by definition.

1C. Enantiomers & Diastereomers

Stereoisomers can be subdivided into two general categories:

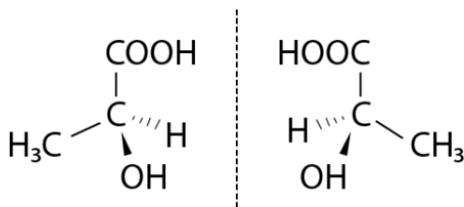
enantiomers & *diastereomers*

غير مطابق

Enantiomers – stereoisomers whose molecules are nonsuperposable mirror images of each other

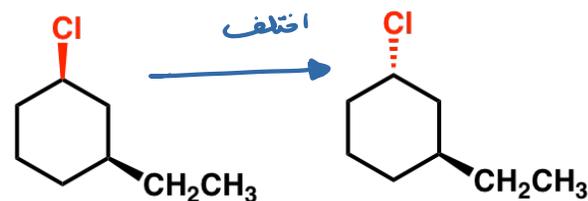
Diastereomers – stereoisomers whose molecules are not mirror images of each other

Enantiomers



- mirror images of each other
- غير مطابق

Diastereomers



- Are not mirror images

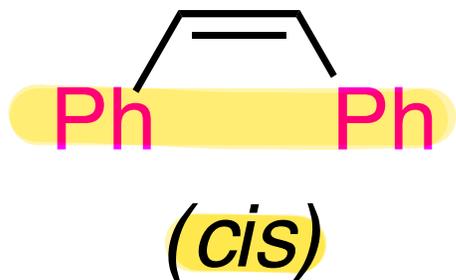
Geometrical isomers (*cis* & *trans* isomers) are:

Diastereomers

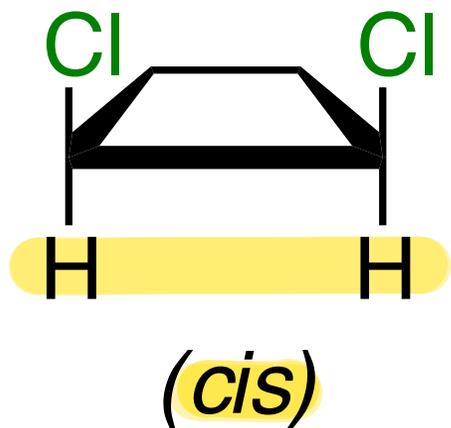
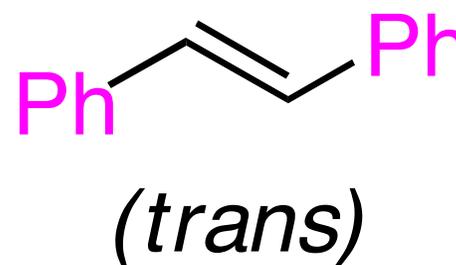
cis : same side
trans : opposite side

e.g.

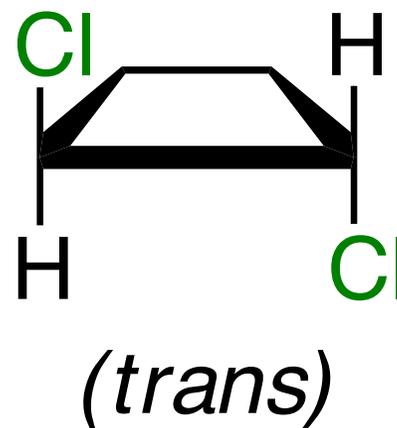
same
side



and



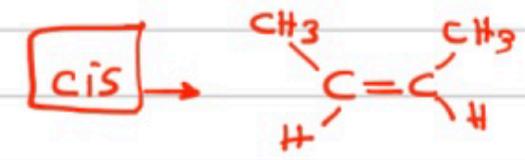
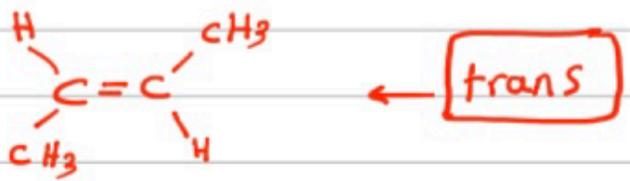
and



القيمت هذا التصيغ بسيط

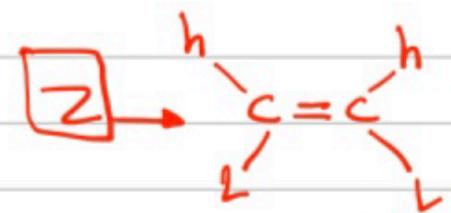
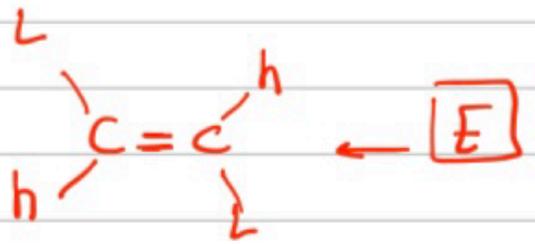
شروط عشوائية أعدد trans / cis !!

- ① ما يكونان المجموعتين ياب على C زي بعض .
 - ② وجود H على ال C .
- يكون على الكربون الواحدة H وتفرع



إذا كانت الكربونات ما عليهم H وتفرع ثاني ما عليهم بنظام (E/Z)

بمعارنة المجموعات الي على نفس C اعدد الأولوية (E/Z) ما النظام يشتغل زي نظام (R/S) لترتيب الأولويات .



$I > Br > Cl > S > F > O > N > C > H$

التفرع إلى أعلى أولوية
same side Z

Q2: Which of the following terms best describes the following pair of molecules?

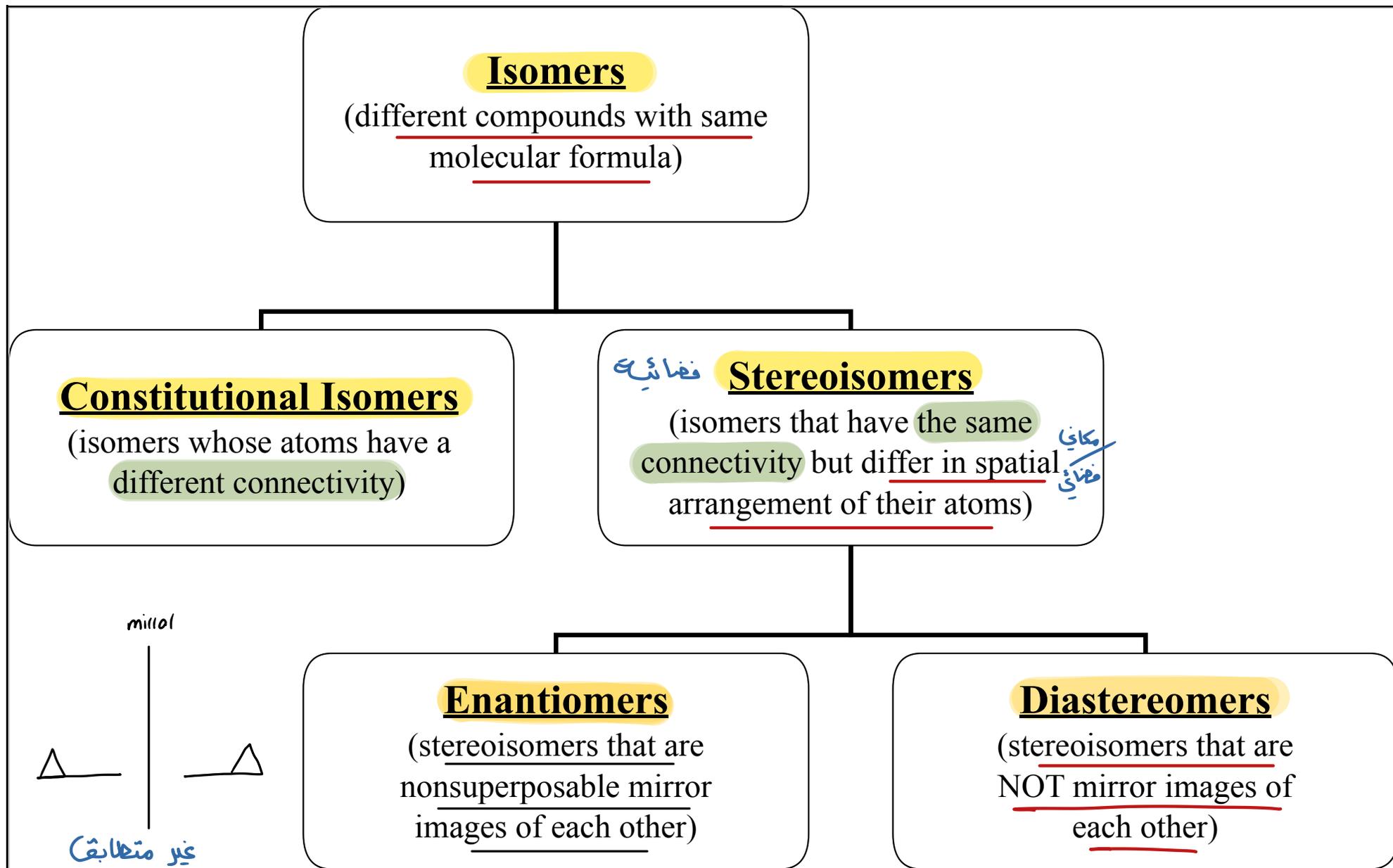


- a) Isomers
- b) Geometrical isomers
- c) Configurational isomers
- d) Constitutional isomers

Answer: b) Geometrical isomers

Explanation: These molecules are isomers since they have the same chemical formula (C_7H_{14}). However, due to a double bond, the molecules' spatial orientations differ. And hence, the molecules can best be characterised as geometric isomers.

Subdivision of Isomers





Q9:

The given molecules are _____.

- (a) constitutional isomers
- (b) conformers
- (c) stereoisomers
- (d) identical
- (e) None of these

Answer: (c) stereoisomers

2. Enantiomers and Chiral Molecules

Asymmetric غير متماثل

Enantiomers occur only with compounds whose molecules are **chiral**

A chiral molecule is one that is NOT superposable on its mirror image

The relationship between a chiral molecule and its mirror image is one that is *enantiomeric*. A chiral molecule and its mirror image are said to be enantiomers of each other

17

* ?Which of the following is the definition of chiral
(ābhāi 1)

- The non-superposability of molecules on its mirror image
- A molecule that has a carbon atom with four different substituents
- The superposability of molecules on its mirror image
- A molecule that has a carbon atom with two different substituents
- None of the above

18

* ?Which among the following does not exhibit geometric isomerism
(ābhāi 1)

2

Type here to search

Taskbar with icons for Start, File Explorer, Edge, Mail, and Chrome. System tray on the right shows AR, Desktop, and network/Bluetooth icons.

DELL

5.2. Chiral molecules that have nonsuperimposable mirror images are called:

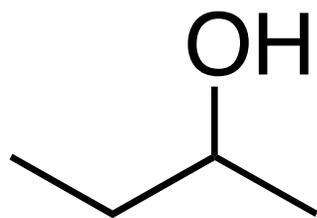
***a.** enantiomers

b. diastereomers

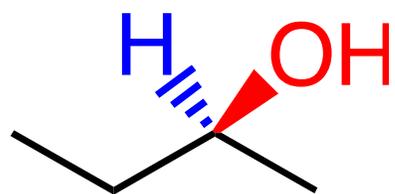
c. *meso* compounds

d. stereogenic

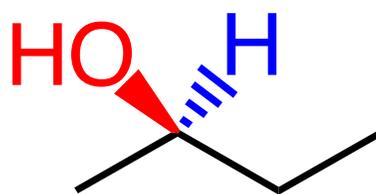
e. symmetrical



(2-Butanol)



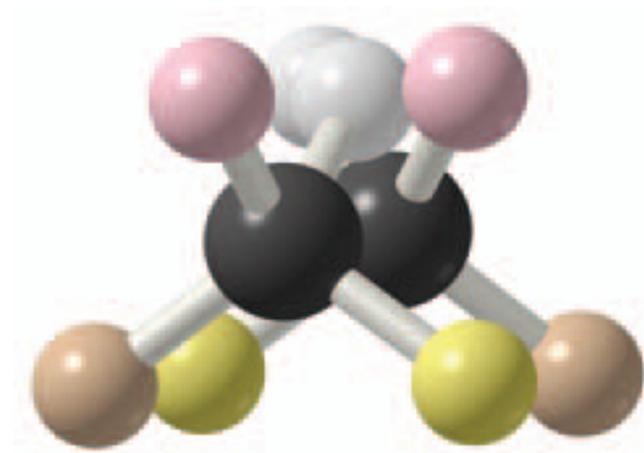
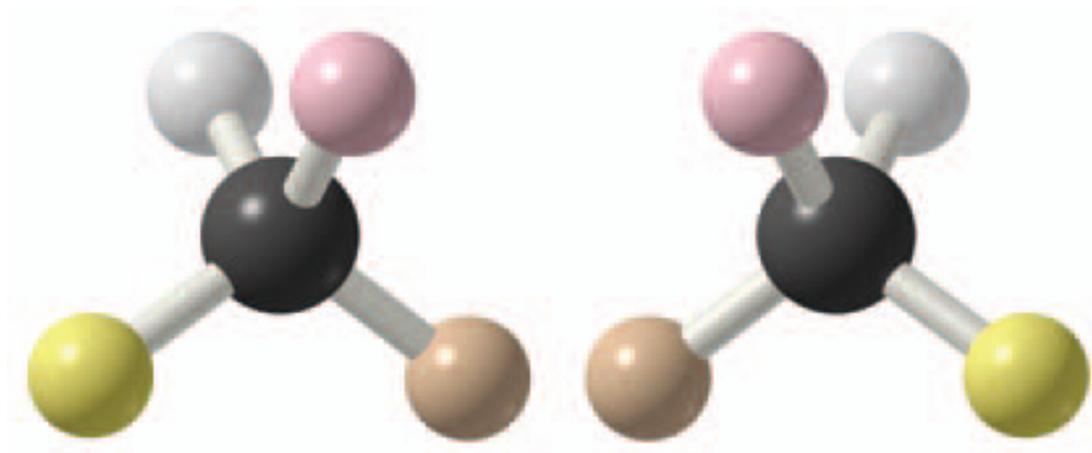
(I)



(II)

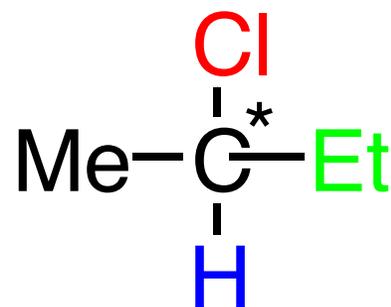
(I) and (II) are nonsuperposable mirror images of each other

- enantiomers -

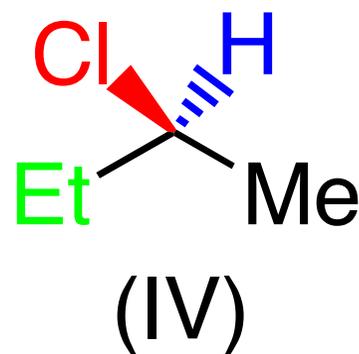
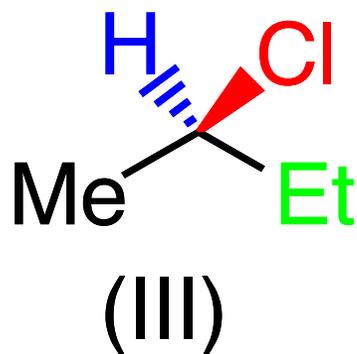


3. A Single Chirality Center Causes a Molecule to Be Chiral

The most common type of chiral compounds that we encounter are molecules that contain a carbon atom bonded to *four different groups*. Such a carbon atom is called an *asymmetric carbon* or a *chiral center* and is usually designated with an asterisk (*)



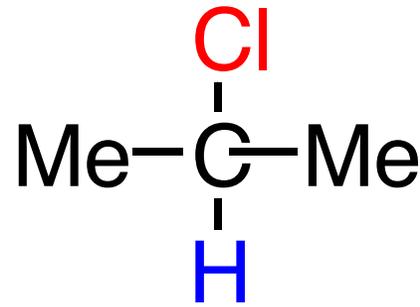
Four different groups
chiral ✓



mirror

Enantiomers

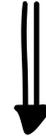
(III) and (IV) are nonsuperposable mirror images of each other



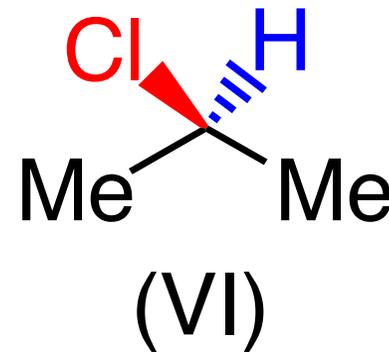
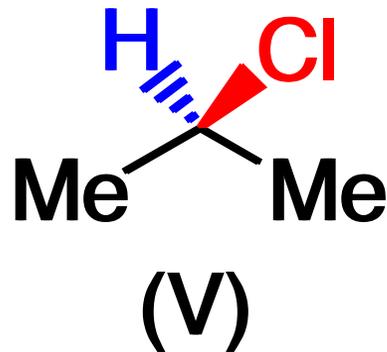
Are not Four different
groups

Achiral

Not chiral



Not enantiomers



mirror

متكافئ

(V) and (VI) are superposable

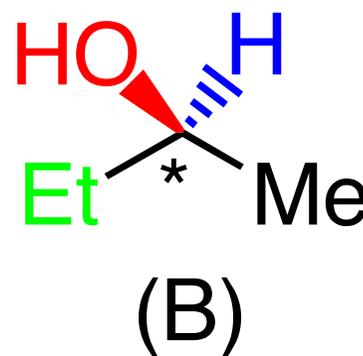
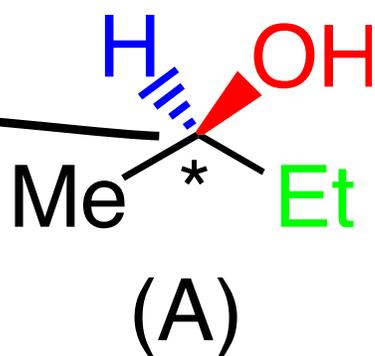
⇒ not enantiomers ⇒ achiral

3A. Tetrahedral vs. Trigonal Stereogenic Centers ⇒

1 First: what is a stereogenic center?

A stereogenic center is any atom where swapping two attached groups creates a different stereoisomer.

Chirality centers are tetrahedral stereogenic centers



mirror

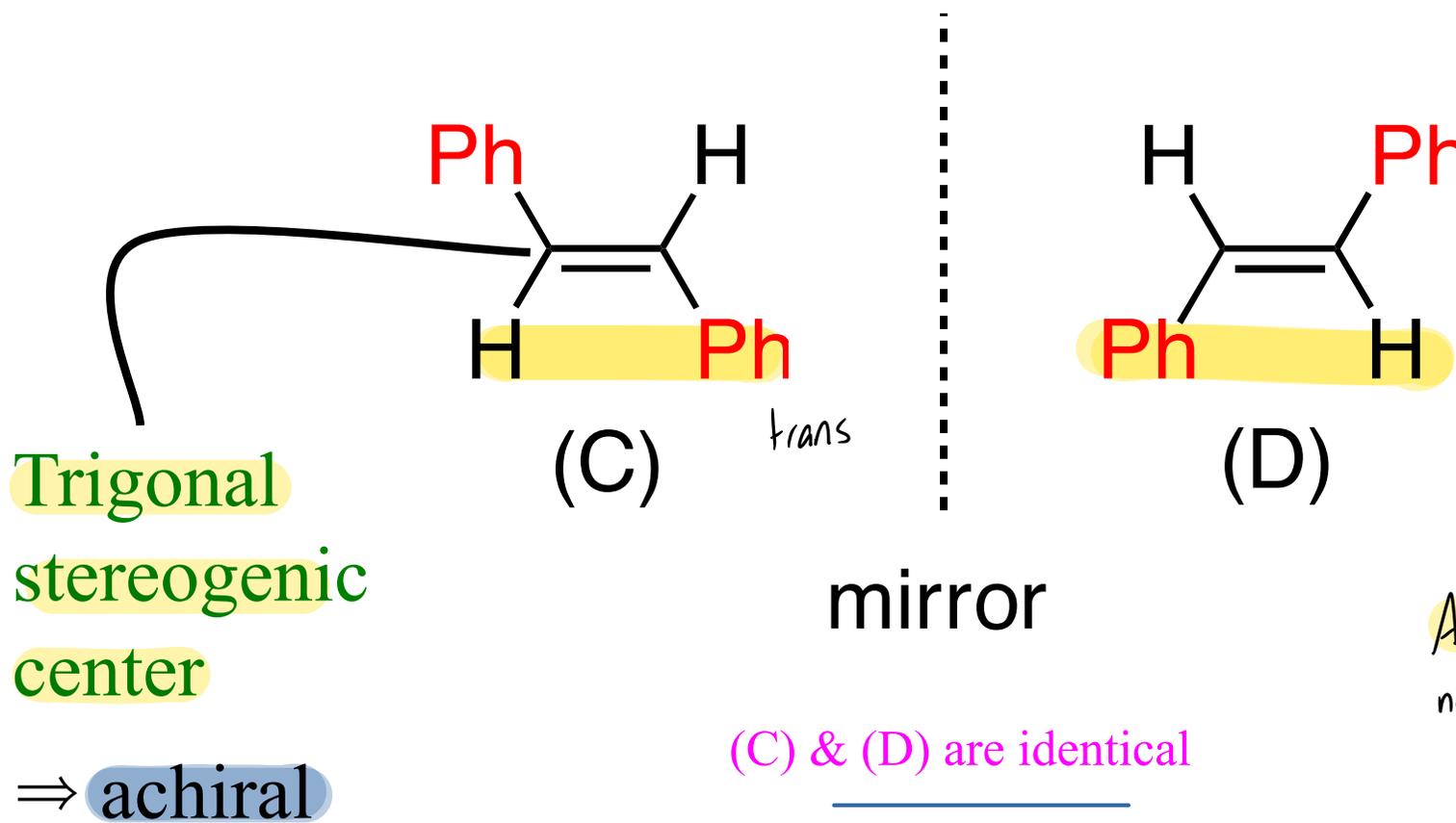
(A) & (B) are
enantiomers

Tetrahedral
stereogenic
center

⇒ chiral

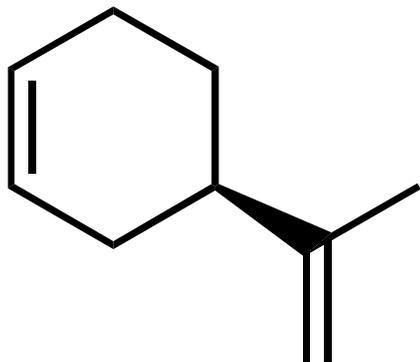
- Four different groups (chiral) ✓
- non superposable mirror images ✓

Cis and trans alkene isomers contain trigonal stereogenic centers



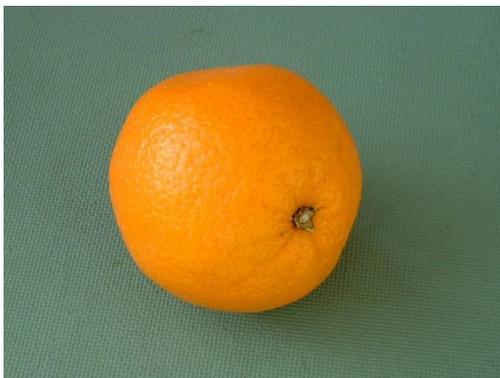
Symmetrical
Are not four different groups
not chiral (Achiral) symmetrical

4. More about the Biological Importance of Chirality (Asymmetrical)

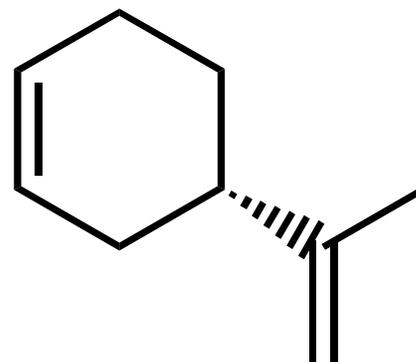


(+)-Limonene

(limonene enantiomer found in oranges)



contain one tetrahedral chiral carbon



(-)-Limonene

(limonene enantiomer found in lemons)



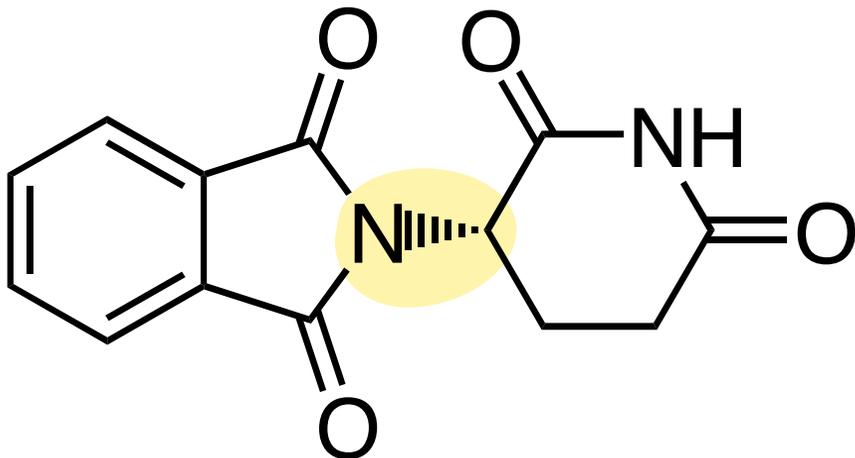
two enantiomers

Thalidomide

The activity of drugs containing chirality centers can vary between enantiomers, sometimes with serious or even tragic consequences

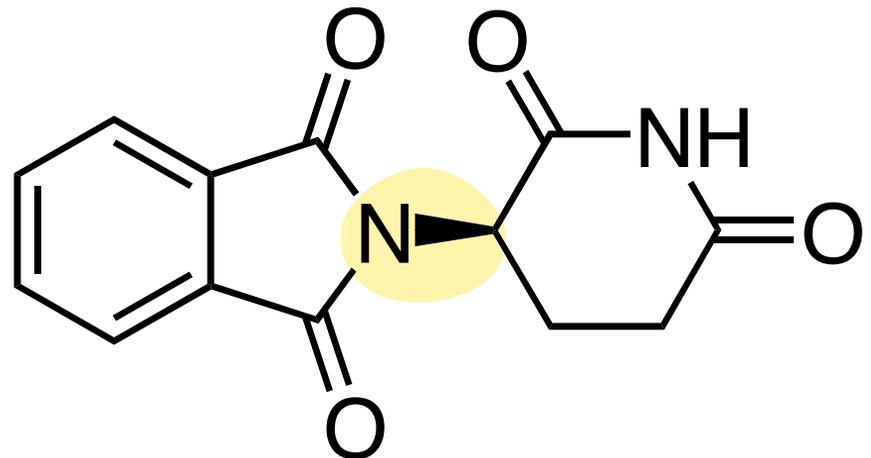
For several years before 1963 thalidomide was used to alleviate the symptoms of morning sickness in pregnant women

In 1963 it was discovered that thalidomide (sold as a mixture of both enantiomers) was the cause of horrible birth defects in many children born subsequent to the use of the drug



Thalidomide

(cures morning sickness)



enantiomer of

Thalidomide

(causes birth defects)

5. How to Test for Chirality:

Planes of Symmetry

A molecule will not be chiral if it possesses a plane of symmetry

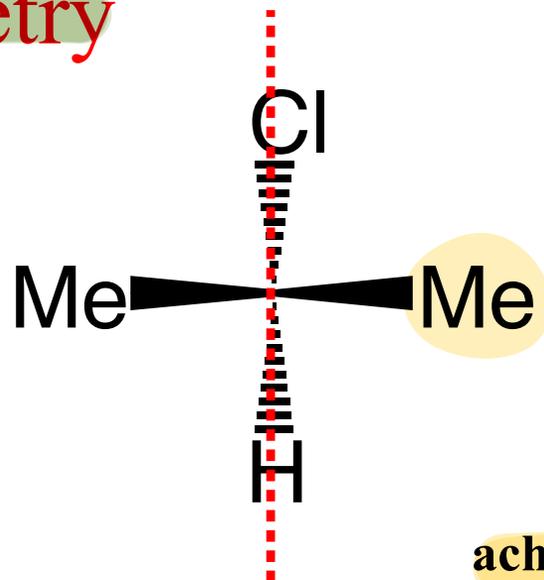
A **plane of symmetry** (mirror plane) is an imaginary plane that bisects a molecule such that the two halves of the molecule are mirror images of each other

All molecules with a plane of symmetry in their most symmetric conformation are *achiral*

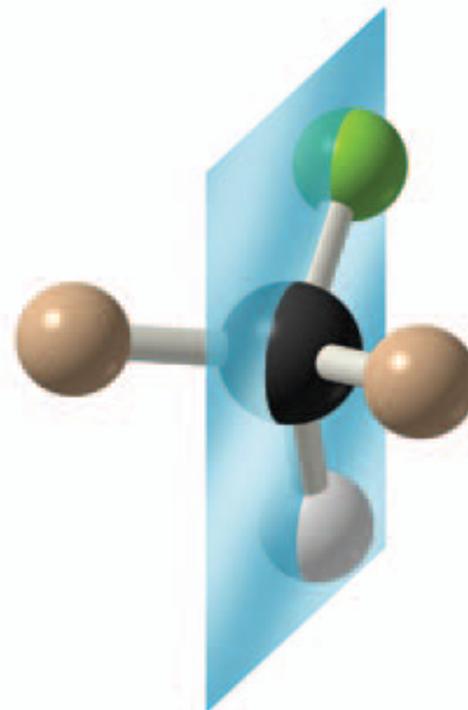
Plane of symmetry

Not four different groups
not chiral

Achiral

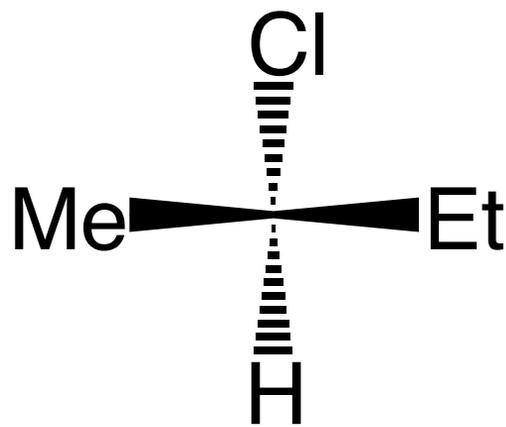


achiral

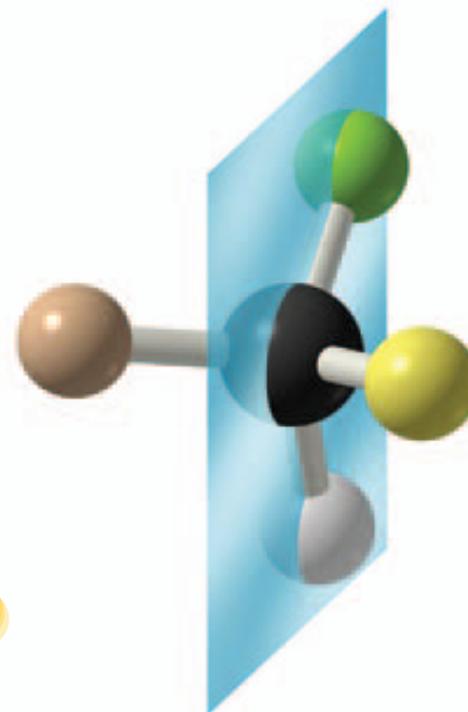


Four different groups

chiral

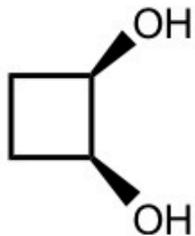


chiral



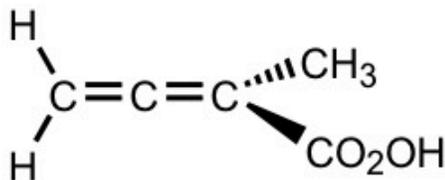
No plane of symmetry

1) Is the molecule shown below chiral or achiral?



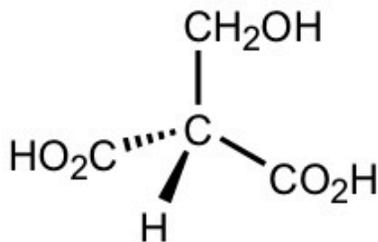
has a plane of symmetry

2) Is the molecule shown below chiral or achiral?



Not 4 different groups

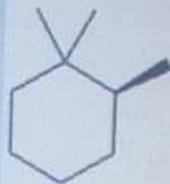
3) Is the molecule shown below chiral or achiral?



Not 4 different groups

all Achiral

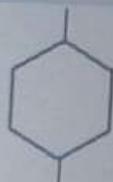
3



A



B



C

Which of the following compound(s) is/are chiral? * 

(1 Point)

- A and B
- Only B
- B and C
- Only A
- None of these

4

Which of the following molecules has a C-C-H bond angle of approximately 120° ? *

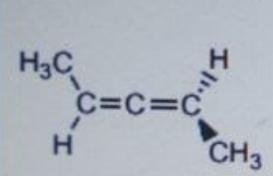
(1 Point)

Question 9

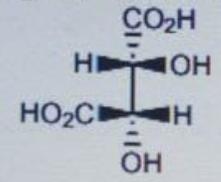
Not yet answered

Marked out of 1.00

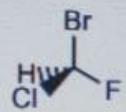
Which of the following molecules is achiral?



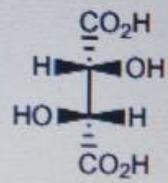
I



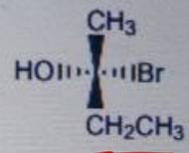
II



III



IV

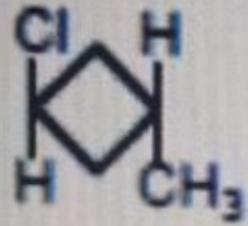


V

- A) I
- B) II
- C) III
- D) IV
- E) V

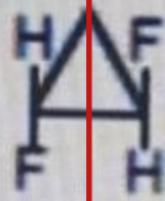
- A
- B
- C
- D
- E

40 * ? Which of the following substances is achiral (1 نقطة)



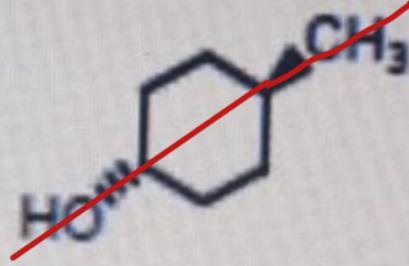
I

chiral



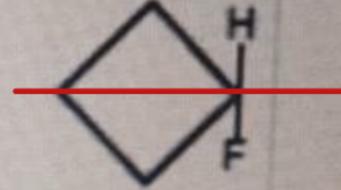
II

chiral



III

Achiral



IV

Achiral

I & II

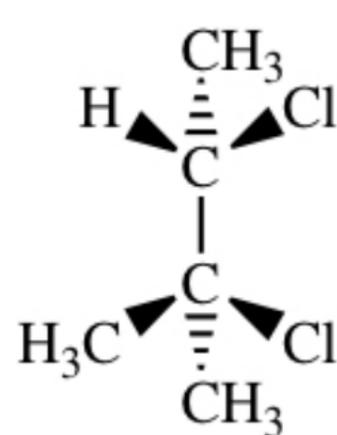
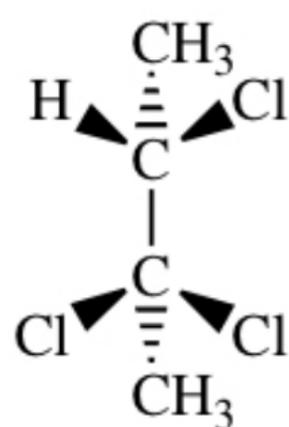
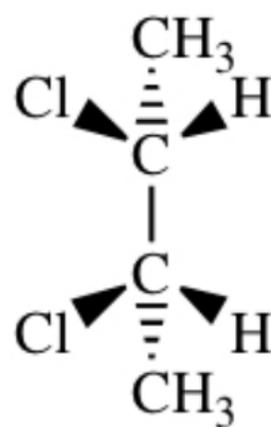
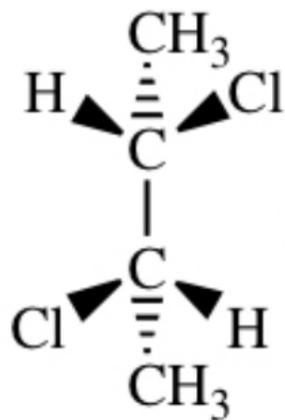
II & III

III & IV

IV & I

More than two of these

5.3. Which of the following molecules has a mirror plane of symmetry?



a. 1

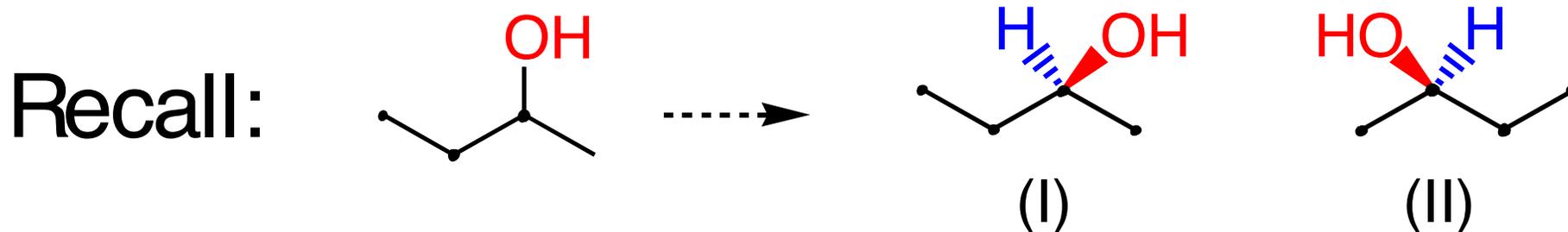
*b. 2

c. 3

d. 4

e. all of them

6. Naming Enantiomers: *R,S*-System



Using only the IUPAC naming that we have learned so far, these two enantiomers will have the same name:

2-Butanol

This is undesirable because each compound must have its own distinct name

6A. How to Assign (R) and (S) Configurations

Rule 1

Assign priorities to the four different groups on the stereocenter from highest to lowest (priority bases on atomic number, the higher the atomic number, the higher the priority)

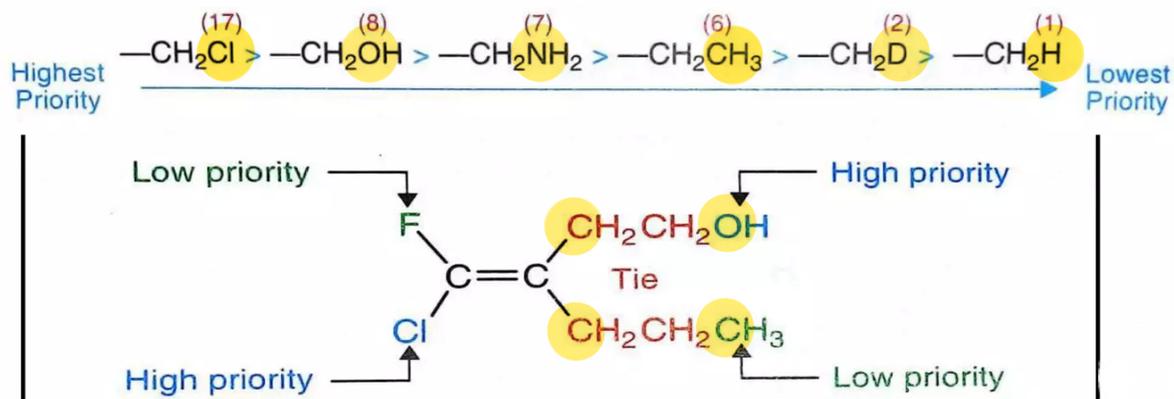
Higher Atomic number



Lower Atomic number

Rule 2

When a priority cannot be assigned on the basis of the atomic number of the atoms that are directly attached to the chirality center, then the next set of atoms in the unassigned groups is examined. This process is continued until a decision can be made.



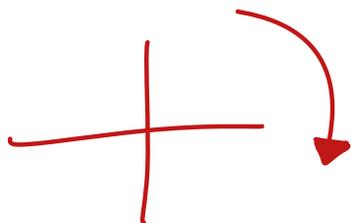
Rule 3

Visualize the molecule so that the lowest priority group is directed away from you, then trace a path from highest to lowest priority. If the path is a clockwise motion, then the configuration at the asymmetric carbon is (R). If the path is a counter-clockwise motion, then the configuration is (S)

clockwise

R configuration

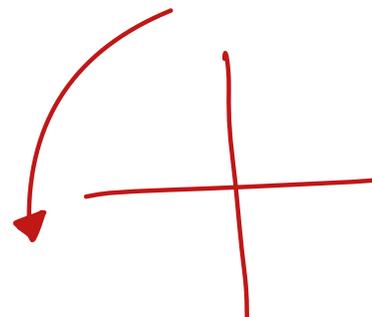
Right



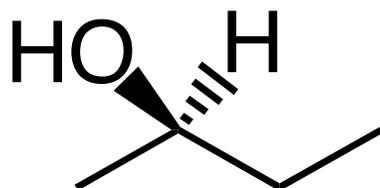
counterclockwise

S configuration

Left

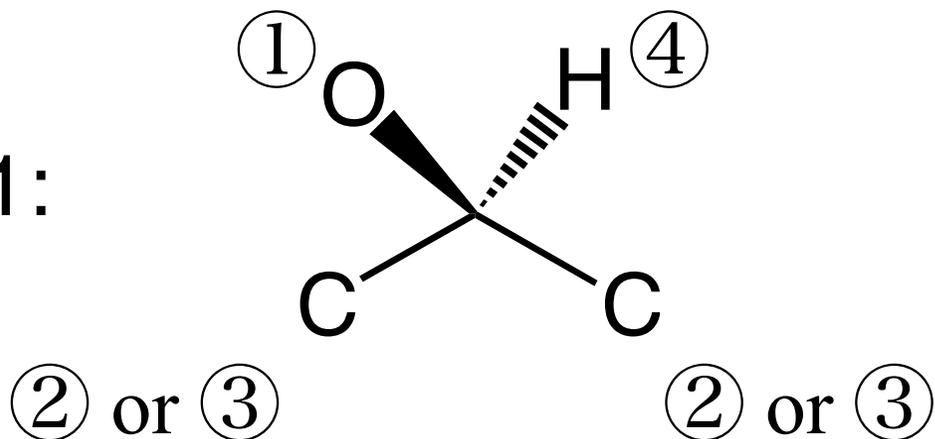


Example

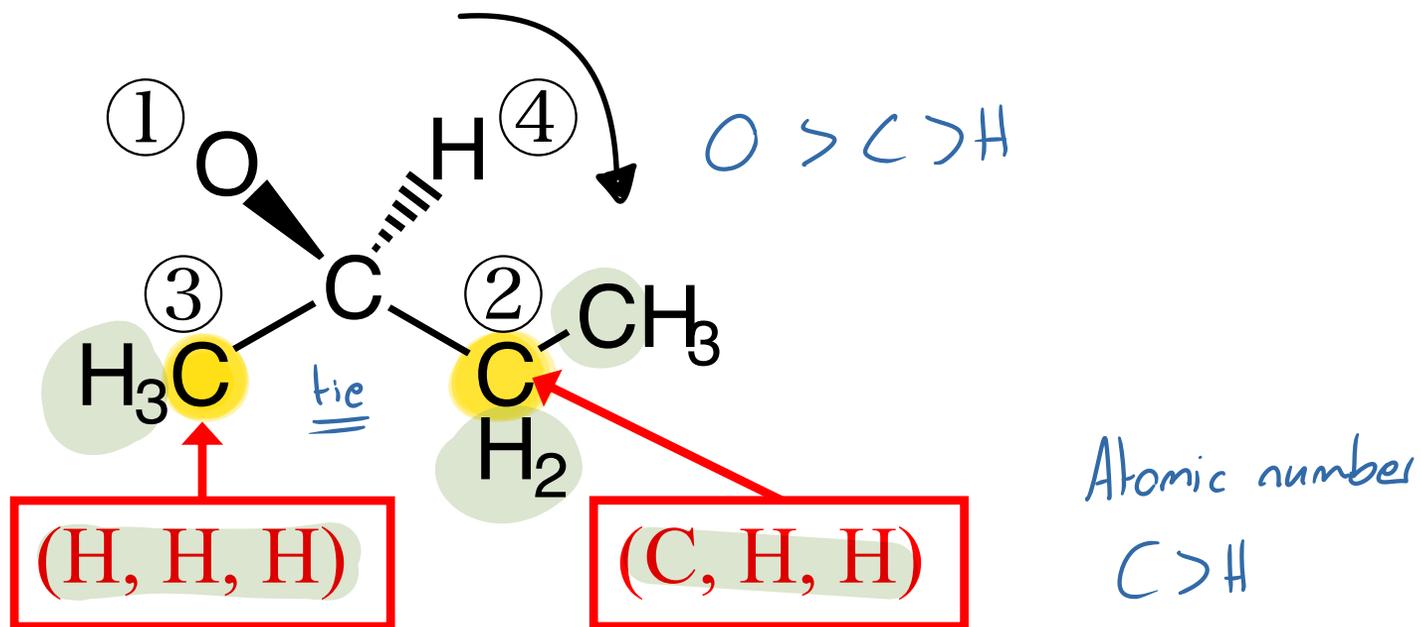


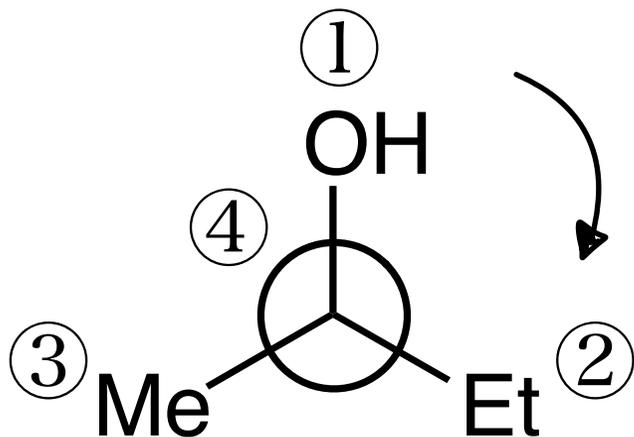
(2-Butanol)

Step 1:

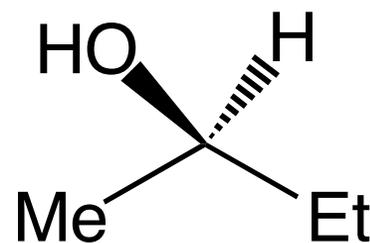
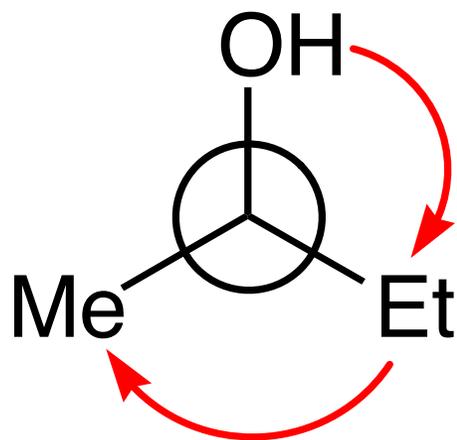
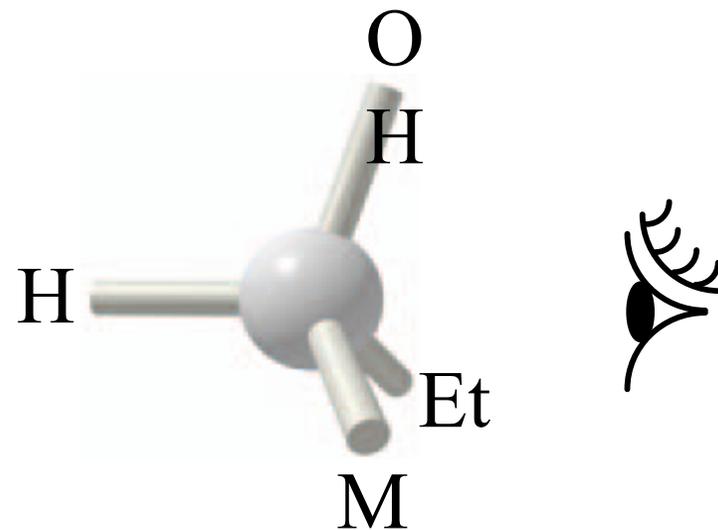


Step 2:

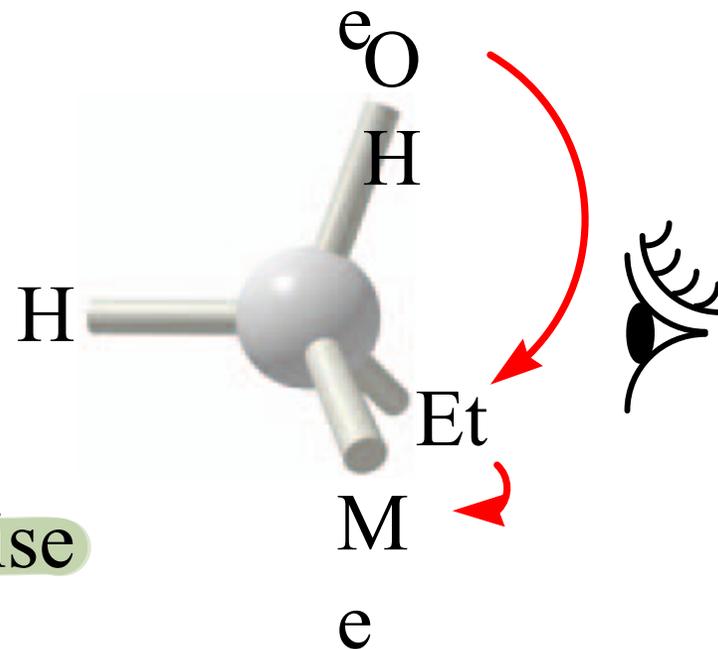




Right
clockwise



Arrows are clockwise

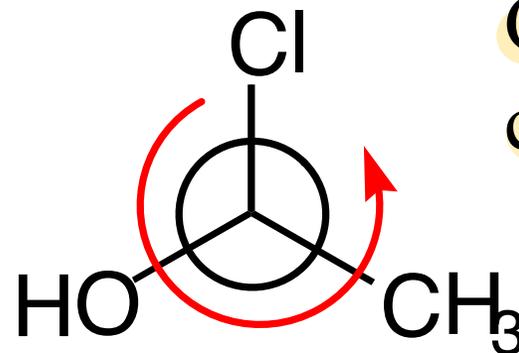
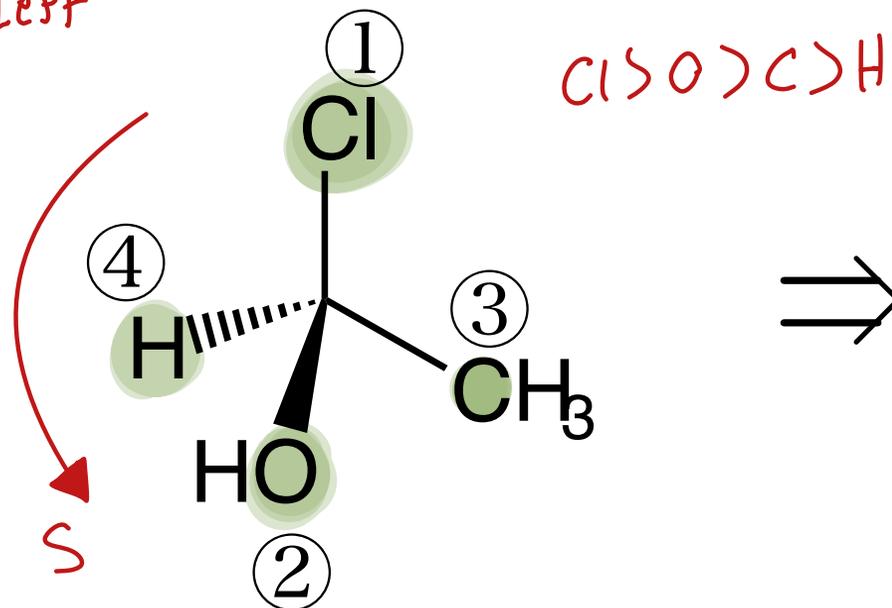


(R)-2-Butanol

Other examples

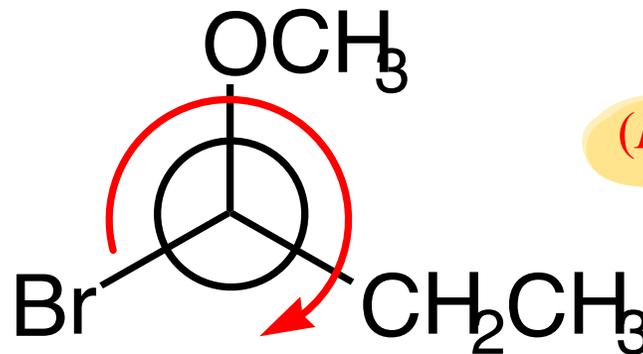
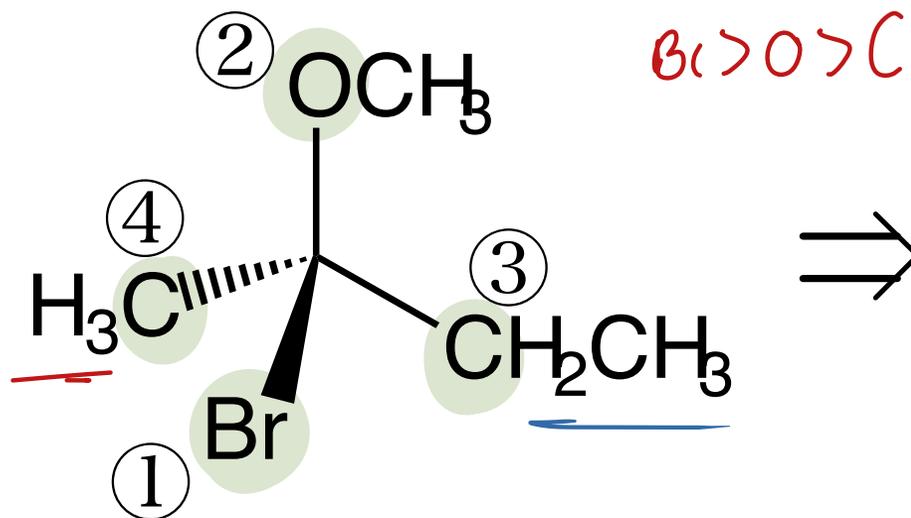
4 on dash ✓
...))

Left



Left
Counter-clockwise

(S)



Right
Clockwise

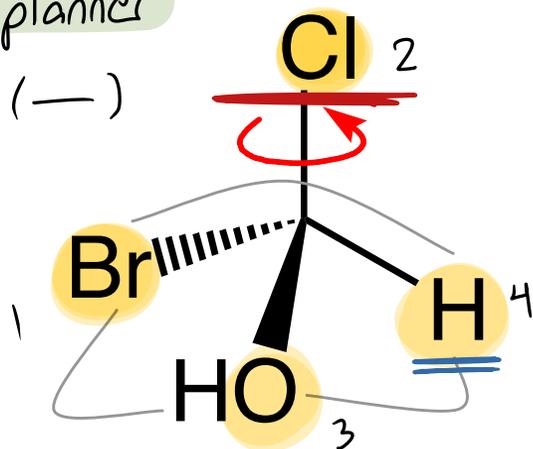
(R)

Other examples

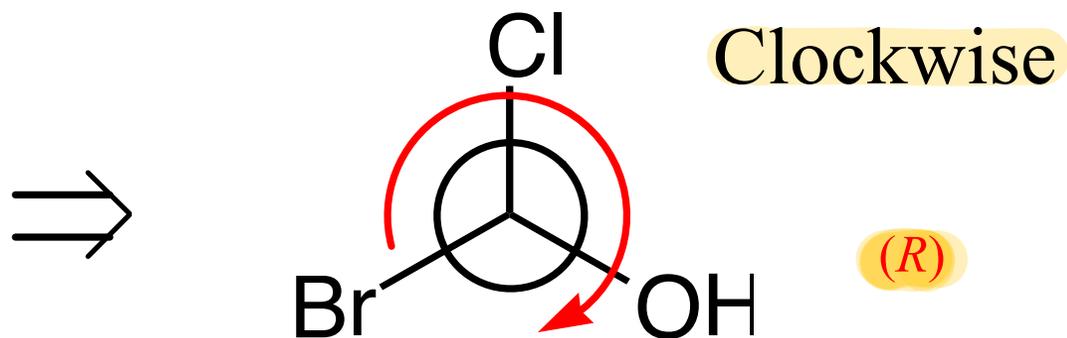
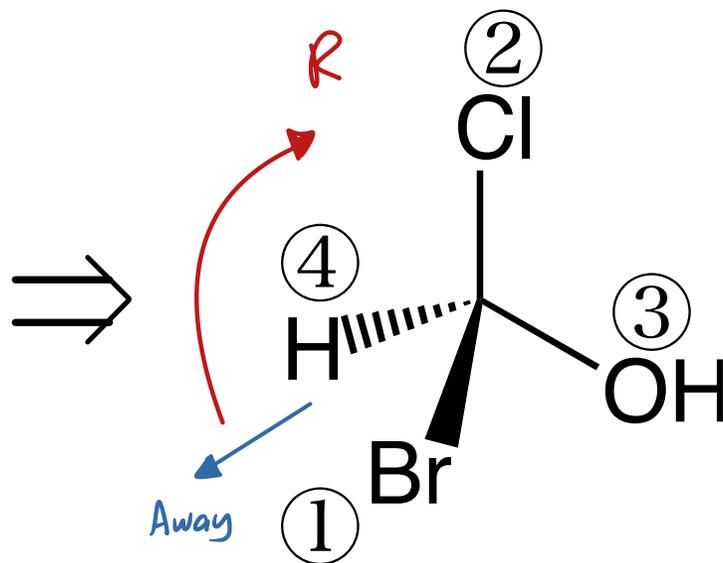
the rule says the lowest priority group must be pointed away of you.

Rotate C-Cl bond such that H is pointed to the back

group 4 on a planner

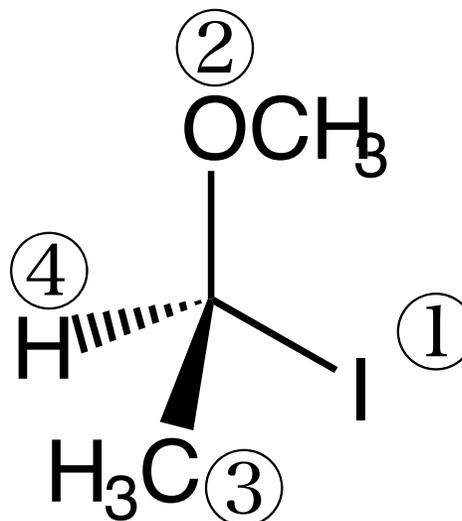
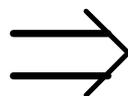
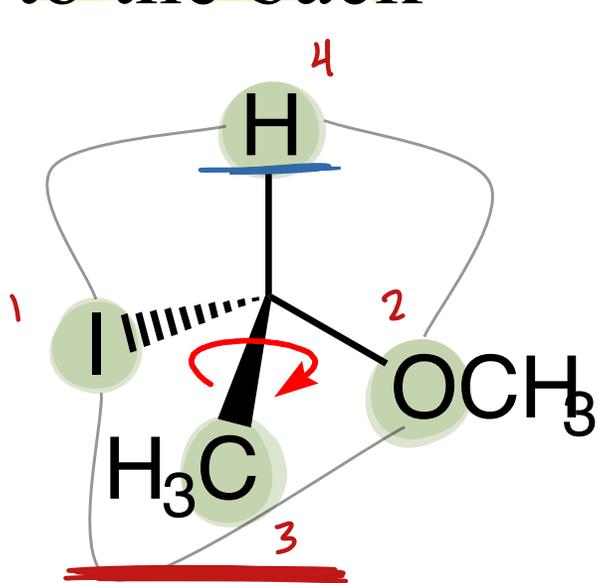


Br > Cl > O > H
Atomic number



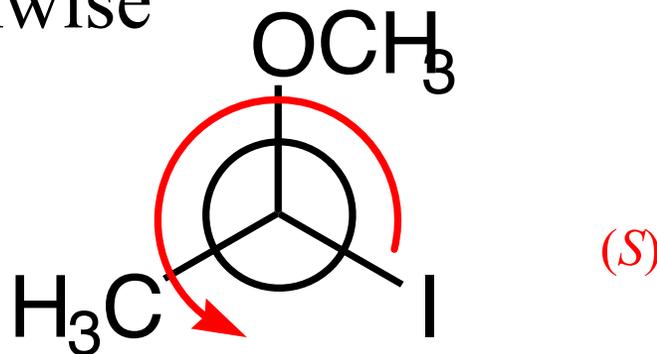
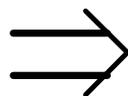
Other examples

Rotate C-CH₃ bond such that H is pointed to the back



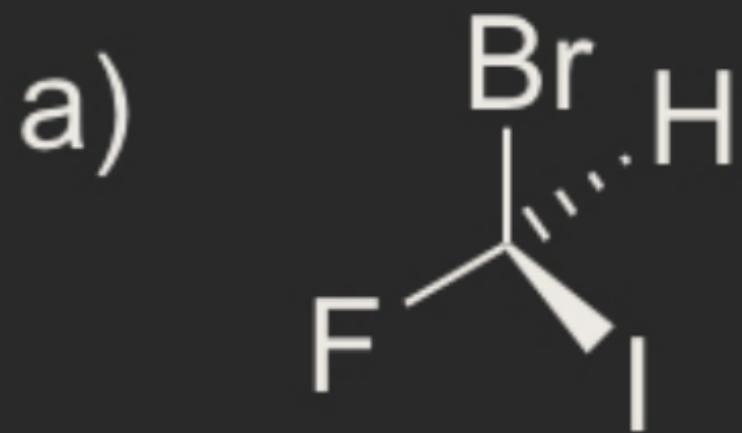
$I > O > C > H$

Counter-clockwise

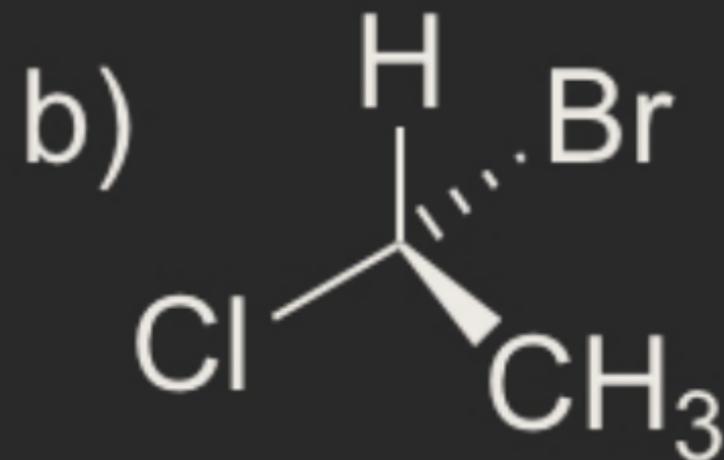


(S)

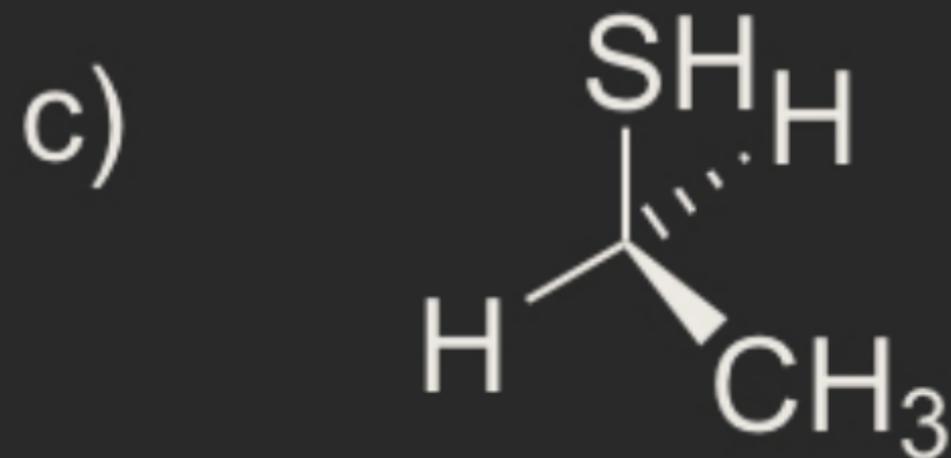
Assign the following chiral centers as (*R*) or (*S*).



S



R



None

Rule 4

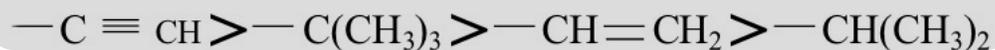
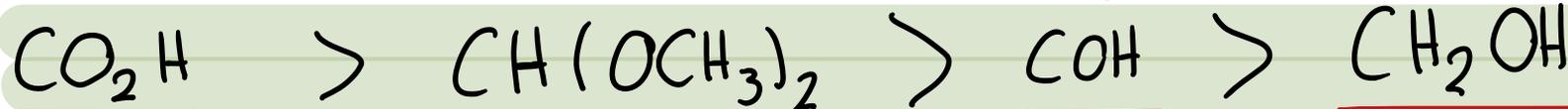
أولوية كس tie

For groups containing double or triple bonds, assign priorities as if both atoms were duplicated or triplicated

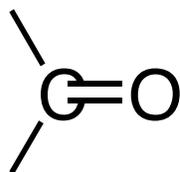
carboxylic group

Aldehyde

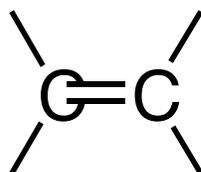
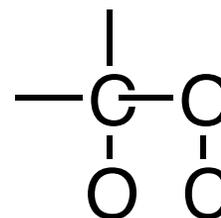
Alcohol



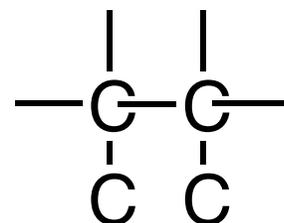
e.g.



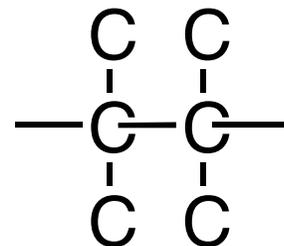
as



as

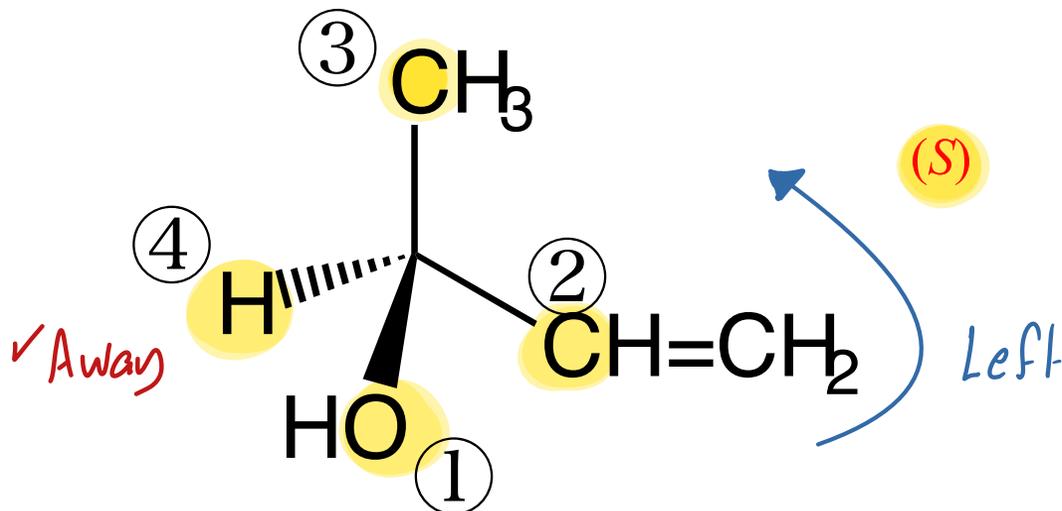


as



Example

$O > C > H$



Compare $-\text{CH}_3$ & $-\text{CH}=\text{CH}_2$:

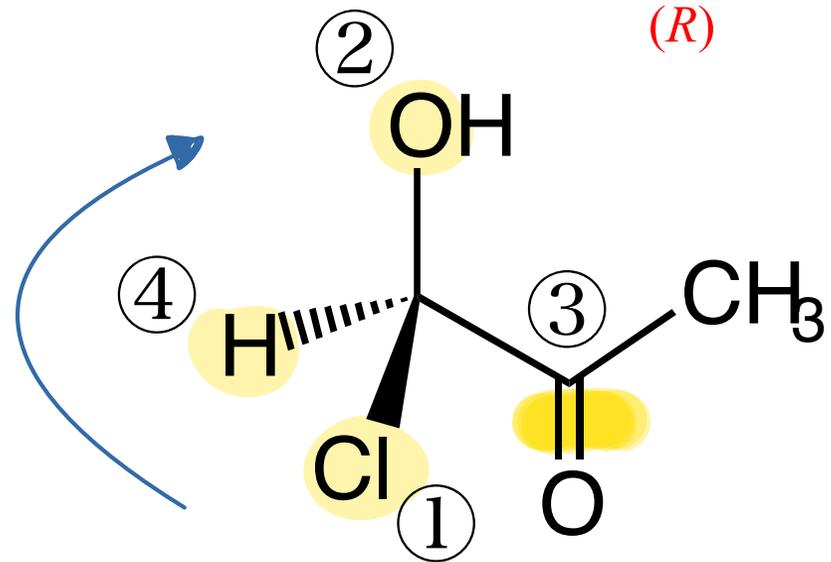


Thus, $-\text{CH}_3 \Rightarrow (\text{H}, \text{H}, \text{H})$

$-\text{CH}=\text{CH}_2 \Rightarrow (\text{C}, \text{C}, \text{H})$

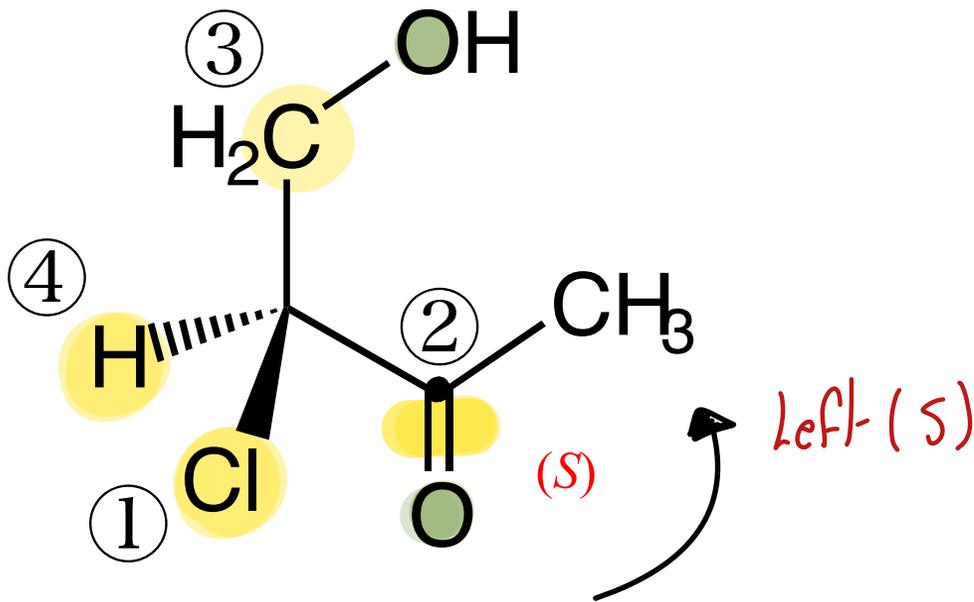
Other examples

Right
clockwise

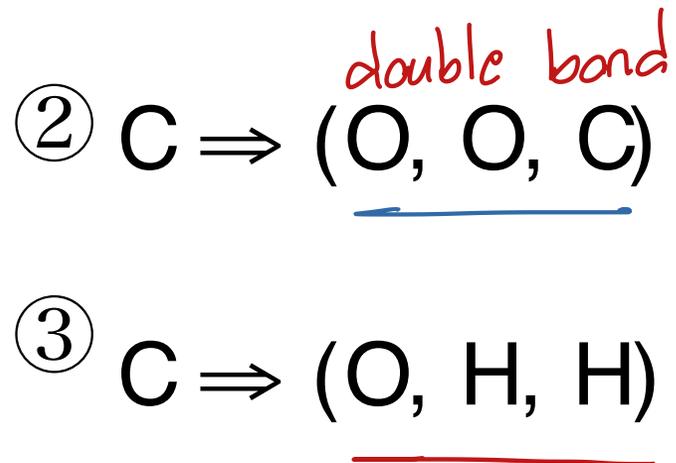


$Cl > O > \text{double bond} > H$
bond

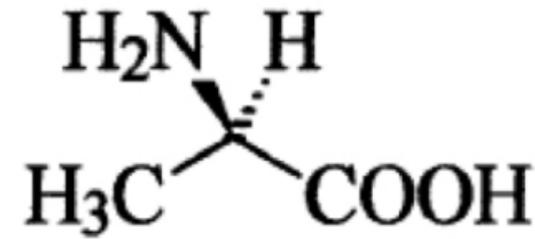
counter clockwise



$Cl > \text{double bond} > C > H$



Q19) Determine the configuration of the isomer of the amino acid alanine shown below.



A19) R- configuration

N, COOH, CH₃,

Which of the following groups has the lowest priority according to the Cahn-Ingold-Prelog sequence rules?

- a. $-\text{CH}_2\text{CH}_2\text{OH}$
- b. $-\text{C}\equiv\text{CH}$
- c. $-\text{CH}=\text{CH}_2$
- d. $-\text{CH}(\text{OH})\text{CH}_3$

q

7. Properties of Enantiomers:

Optical Activity

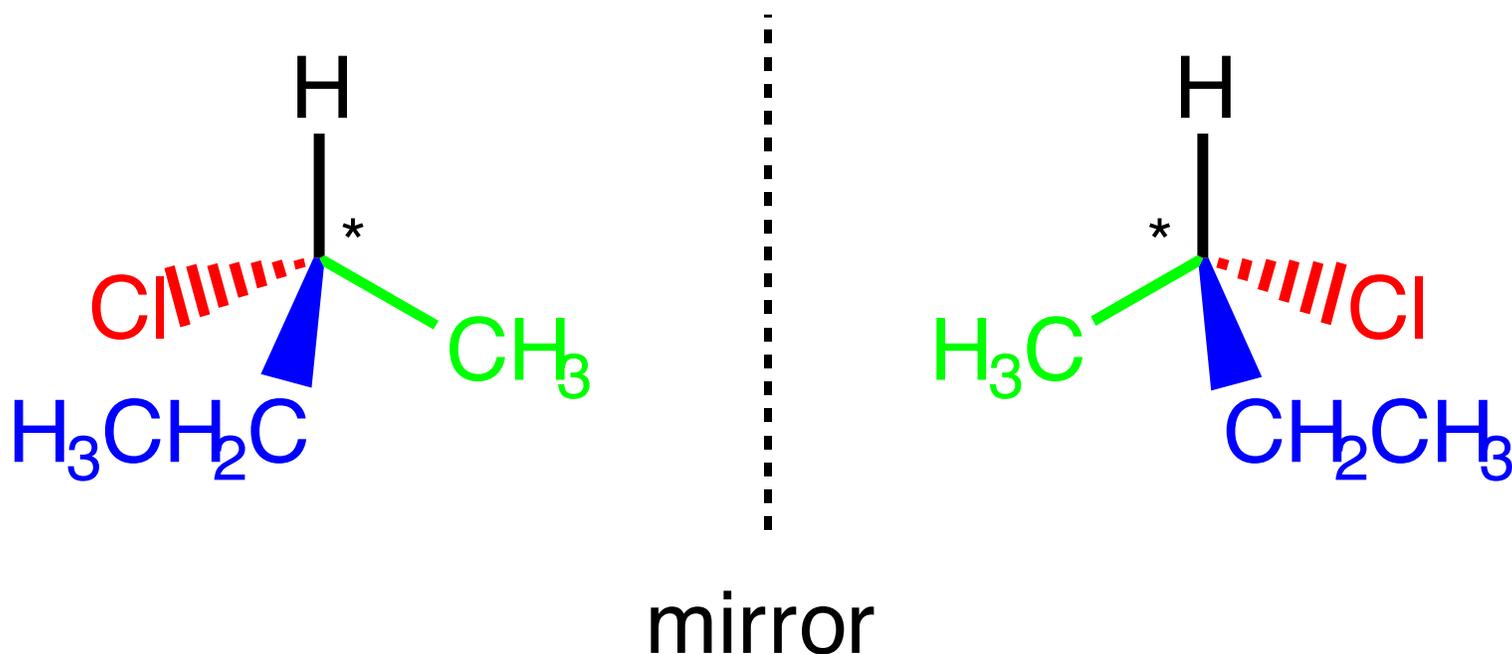
=
chiral

نشطاً
مضوئياً
= جبرئياً

Enantiomers

Mirror images that are not superposable

Four different groups (chiral)



Enantiomers have identical physical properties (e.g. melting point, boiling point, refractive index, solubility etc.)

Compound	bp (oC)	mp (oC)
<i>(R)</i> -2-Butanol	99.5	
<i>(S)</i> -2-Butanol	99.5	
<i>(+)</i> - <i>(R,R)</i> -Tartaric Acid		168 – 170
<i>(-)</i> - <i>(S,S)</i> -Tartaric Acid		168 – 170
<i>(+/-)</i> -Tartaric Acid		210 – 212

Enantiomers (*chiral*)

Have the same chemical properties (except reaction/interactions with chiral substances)

- Show different behavior only when they interact with other chiral substances

Turn plane-polarized light on opposite direction

5.51. Enantiomers may differ in the following property:

- *a.** the rate at which they react with a chiral reagent
- b.** boiling point
- c.** melting point
- d.** number of degrees they rotate plane polarized light
- e.** solubility in water

Optical activity

The property possessed by chiral substances of rotating the plane of polarization of plane-polarized light



1 First: what is plane-polarized light?

- Ordinary light vibrates in all directions perpendicular to its path.
- When it passes through a polarizer, only one plane of vibration remains.
- This is called plane-polarized light.

So now we have light vibrating in one fixed plane.

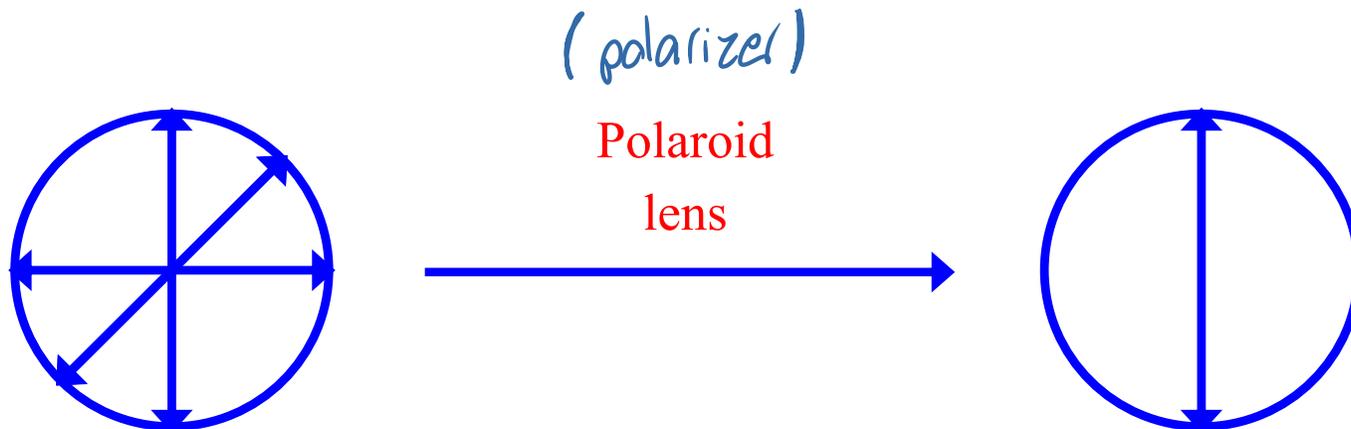
https://youtu.be/duGxp_XZzvw?si=6uiviuncdq2QOKio

easy explanation

7A. Plane-Polarized Light

مکثذب

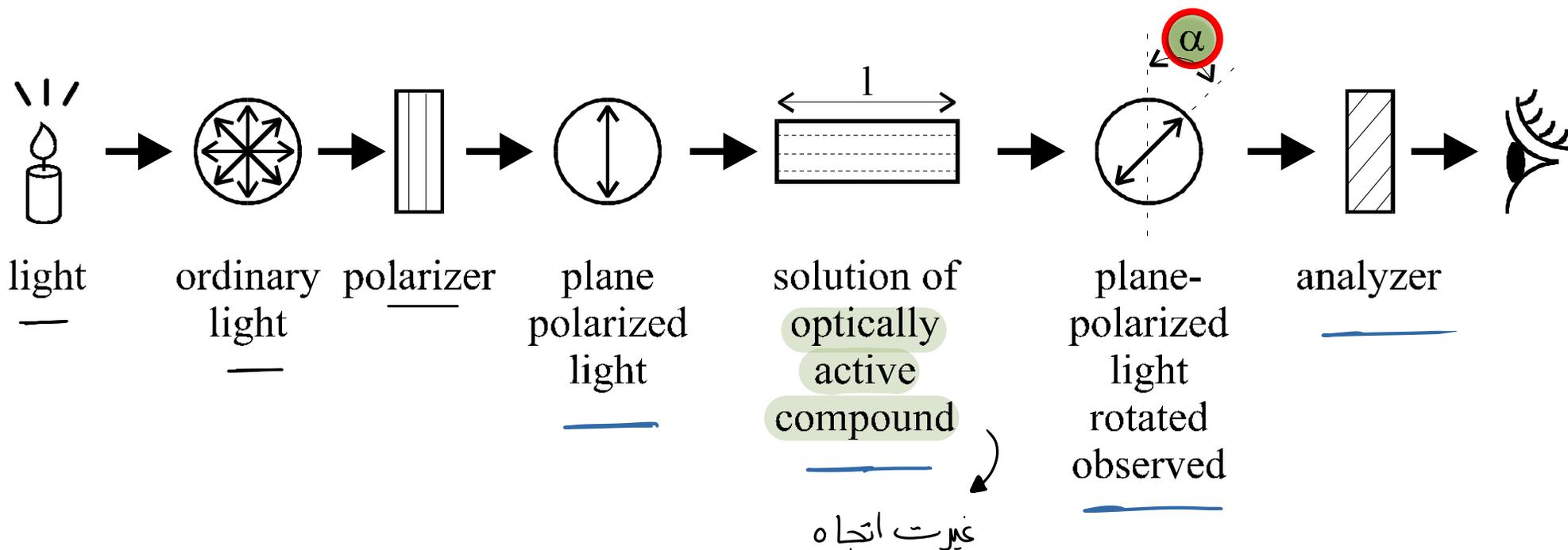
The electric field (like the magnetic field) of light is oscillating in all possible planes
When this light passes through a polarizer (Polaroid lens), we get plane-polarized light
(oscillating in only one plane)



7B. The Polarimeter

A device for measuring the optical activity of a chiral compound

$$a = \frac{\text{observed}}{\text{optical rotation}}$$



7C. Specific Rotation

- α -

temperature

$[\alpha]_{\text{D}}^{25} = \frac{\alpha}{C \times \ell}$

observed rotation
degrees

wavelength of light
(e.g. D-line of Na lamp,
 $\lambda = 589.6 \text{ nm}$)

concentration of sample solution
in g/mL

length of cell in dm
(1 dm = 10 cm)
(1 cm = 10 mm)

5.20. The observed rotation for 100 mL of an aqueous solution containing 1 g of sucrose, placed in a 2-decimeter sample tube, is $+1.33^\circ$ at 25°C . What is the specific rotation of sucrose?

***a.** $+66.5^\circ$

b. $+266^\circ$

c. $+41.5$

d. $+133^\circ$

e. 108°

$$\cdot \quad C = \frac{1}{100} \text{ g/ml} \quad l = 2 \text{ dm} \quad a = +1.33$$

$$[\alpha]^{25} = \frac{1.33}{2 \cdot \frac{1}{100}} = 0.665 \times 100 = +66.5^\circ$$

α

A 1.00 g sample of a chiral drug dissolved in 5.00 ml of solvent and placed in a sample tube having a path length of 1 dm has an observed rotation $\alpha = -16^\circ$. Calculate the specific rotation $[\alpha]_D$

$$C = \frac{1}{5} \text{ g/ml} \quad l = 1 \text{ dm} \quad \alpha = -16$$

$$[\alpha] = \frac{-16}{\frac{1}{5}} = -80$$

:Select one



a. 16°



b. -16°



c. 80°



d. -80°

observed optical rotation

The value of **a** depends on the particular experiment (since there are different concentrations with each run)

But specific rotation [a] should be the same regardless of the concentration

دورانِ نوری

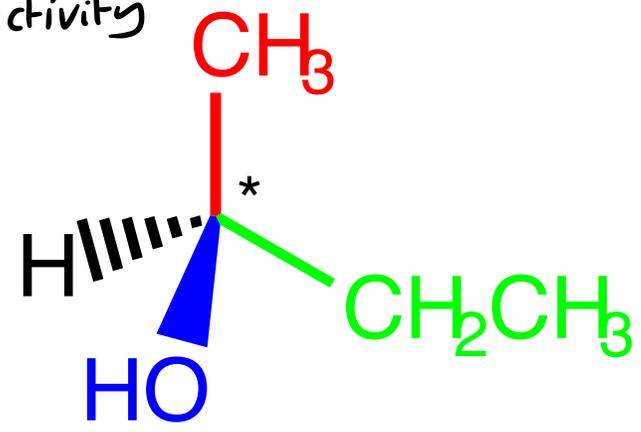
[α]

Two enantiomers should have the same value of specific rotation, but the signs are opposite

(- +)
↙ ↘
rotate light to the left rotate light to the right

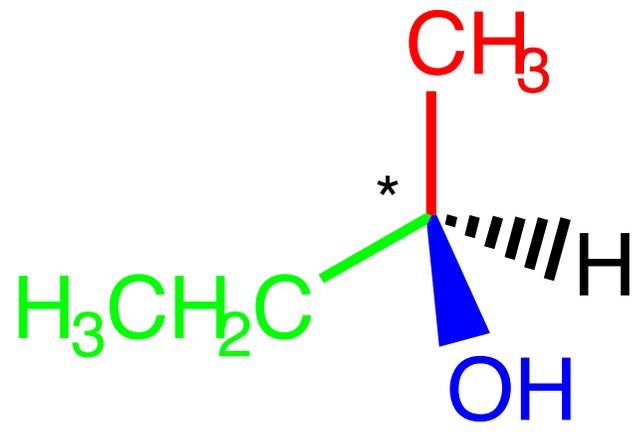
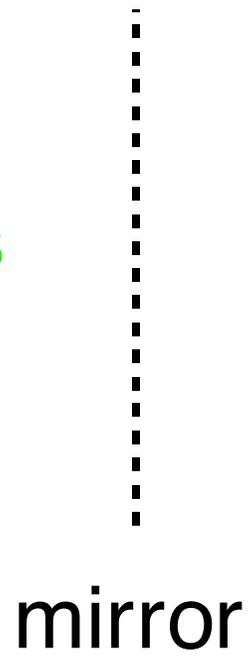
مما يلاحظه تجريباً R/S ≠ - +

- chiral
- enantiomer
- optical activity



$$[\alpha]_D^{25} = + 13.5^\circ$$

dextrorotatory



$$[\alpha]_D^{25} = - 13.5^\circ$$

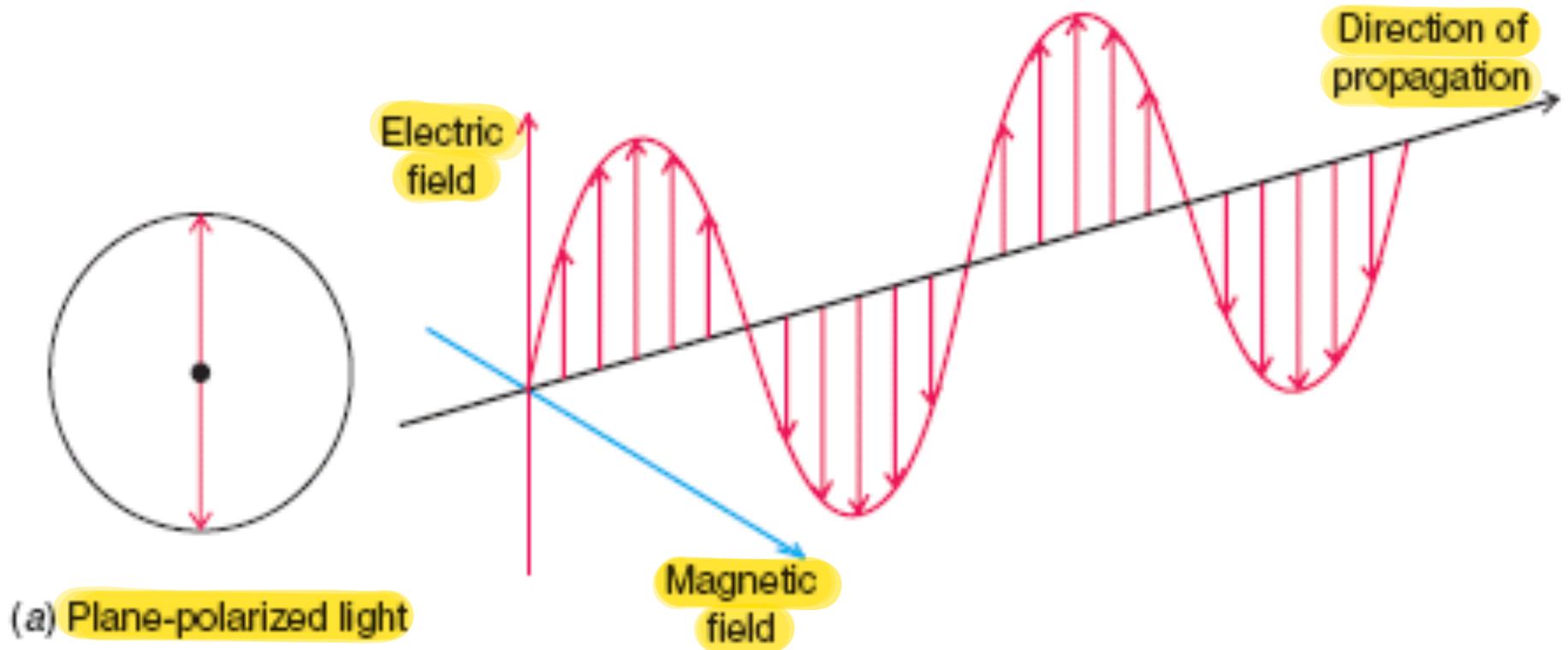
levorotatory

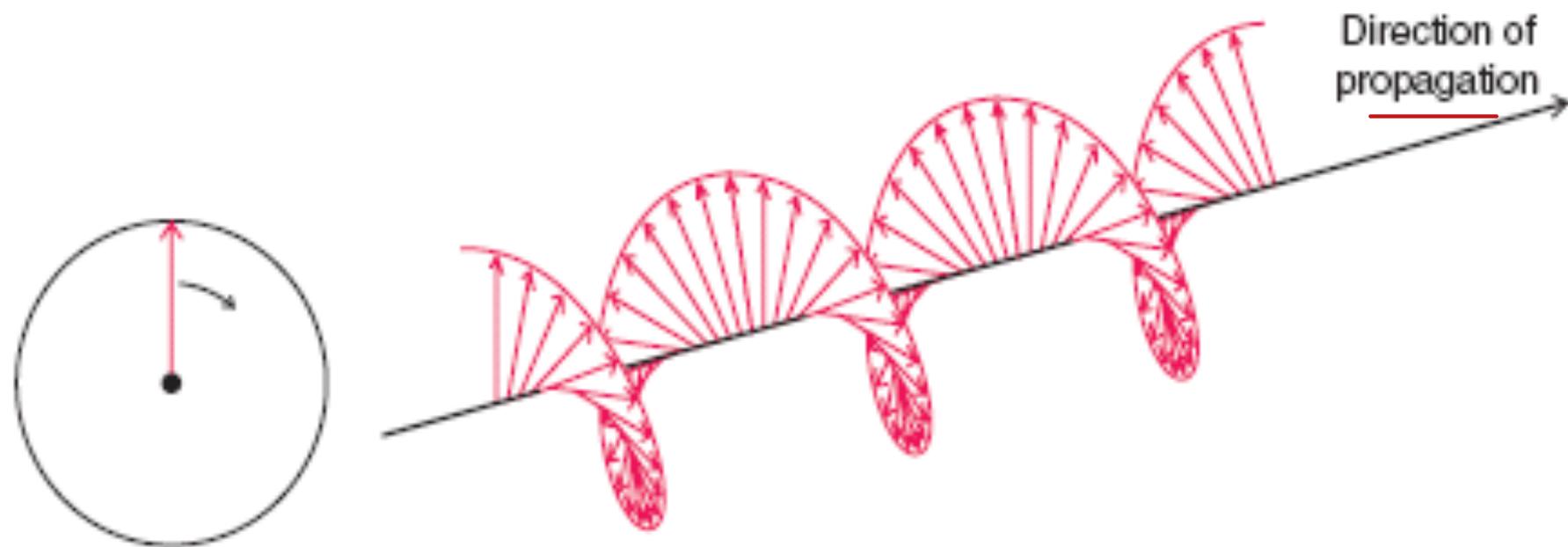
8

The molecule is chiral and has an absolute configuration of (-), which direction does it rotate light? * 
(1 Point)

- Clockwise R
- Counter-clockwise S
- It does not rotate the plane of polarized light
- Can't be determined from the information given
- None of the above

8. The Origin of Optical Activity





8A. Racemic Forms

optically inactive

An equimolar mixture of two enantiomers is called a **racemic mixture** (or racemate or racemic form)

A **racemic mixture** causes **no net rotation of plane-polarized light**

$$\text{net rotation} = 0$$

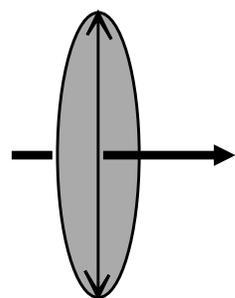
1 First, what does racemic mean?

A racemic form (or racemic mixture) is a mixture that contains equal amounts of two enantiomers of a chiral compound.

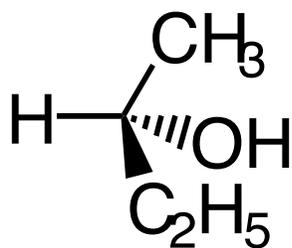
Enantiomers = non-superimposable mirror images (like left and right hands).

So a racemic mixture is:

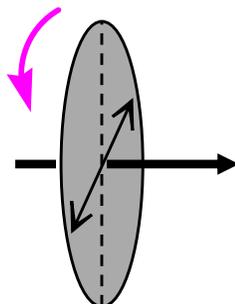
- 50% one enantiomer
- 50% its mirror image



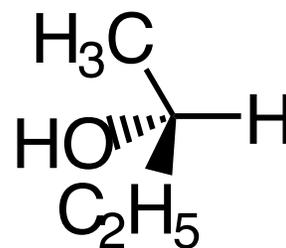
(R)-2-Butanol



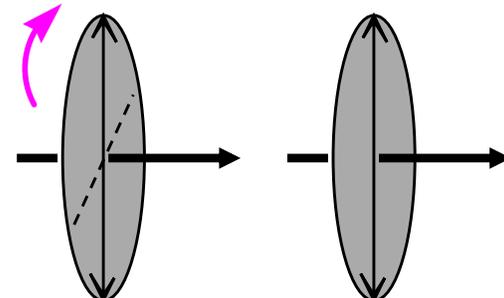
rotation



(S)-2-Butanol
(if present)



equal & opposite
rotation by the
enantiomer



net rotation = 0

بلا دوران

5.5. A 50:50 mixture of enantiomers

a. is a *meso* form.

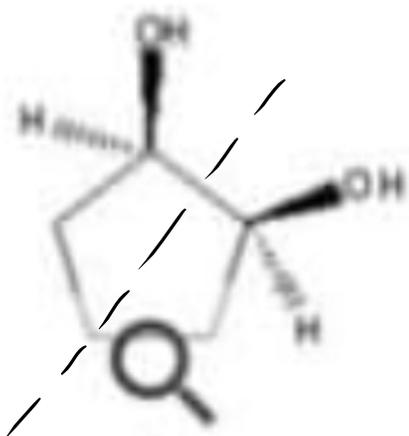
***c.** is a racemic mixture.

e. is a pair of conformers.

b. is a pair of diastereomers.

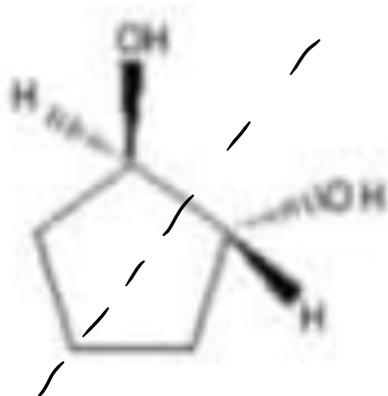
d. rotates plane polarized light.

Which of the following compounds is optically inactive?



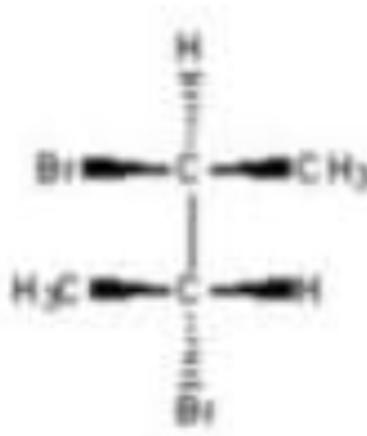
I

inactive
Achiral



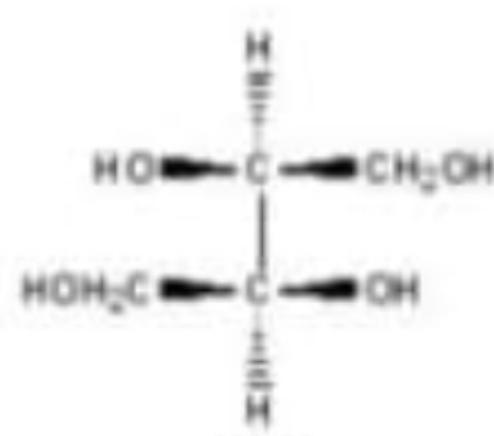
II

Active
chiral



III

Active
chiral



IV

Active
chiral

:Select one



a. IV



b. III

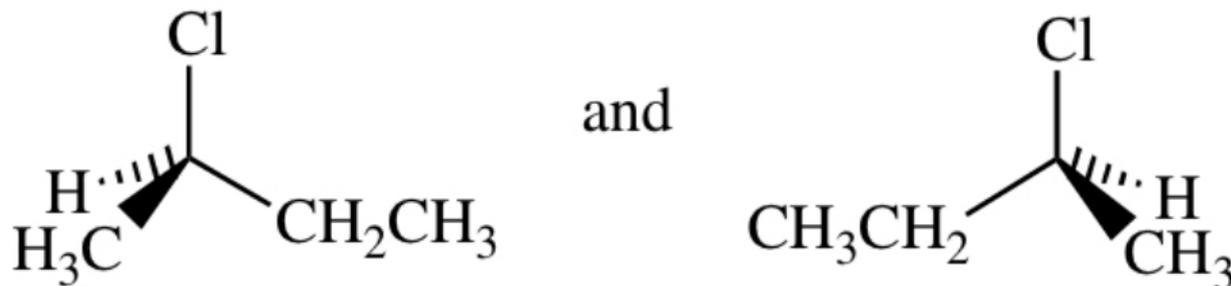


c. I



d. II

5.28. Which of the following statements about the pair of molecules shown below is *not* true?



- a. They have the same boiling point.
- b. One rotates plane polarized light in the opposite direction from the other.
- c. They have the same density.
- *d. One rotates plane polarized light a different number of degrees than the other.
- e. They are mirror images of each other.

8B. Racemic Forms and Enantiomeric Excess

A sample of an optically active substance that consists of a single enantiomer is said to be **enantiomerically pure** or to have an **enantiomeric excess** of 100%

An **enantiomerically pure sample** of (S)-(+)-2-butanol shows a specific rotation of +13.52

$$[\alpha]_{\text{D}}^{25} = +13.52$$

A sample of (S)-(+)-2-butanol that contains less than an **equimolar** amount of (R)-(-)-2-butanol will show a specific rotation that is less **than 13.52 but greater than zero**

Such a sample is said to have an *enantiomeric excess* less than 100%

Enantiomeric excess (ee)

Also known as the optical purity

$$\% \text{ enantiomeric excess} = \frac{\left(\text{mole of one enantiomer} \right) - \left(\text{moles of other enantiomer} \right)}{\text{total moles of both enantiomers}} \times 100$$

Can be calculated from optical rotations

$$\% \text{ enantiomeric excess}^* = \frac{\overset{a}{\text{observed specific rotation}}}{\text{specific rotation of the pure enantiomers}} \times 100$$

Example

A mixture of the 2-butanol enantiomers showed a specific rotation of +6.76.

The enantiomeric excess of the (S)-(+)-2-butanol is 50%

$$\underline{a = +6.76} \quad ee = 50\%$$

$$50\% = \frac{+6.76}{X} \times 100\% \quad \underline{X = +13.52}$$

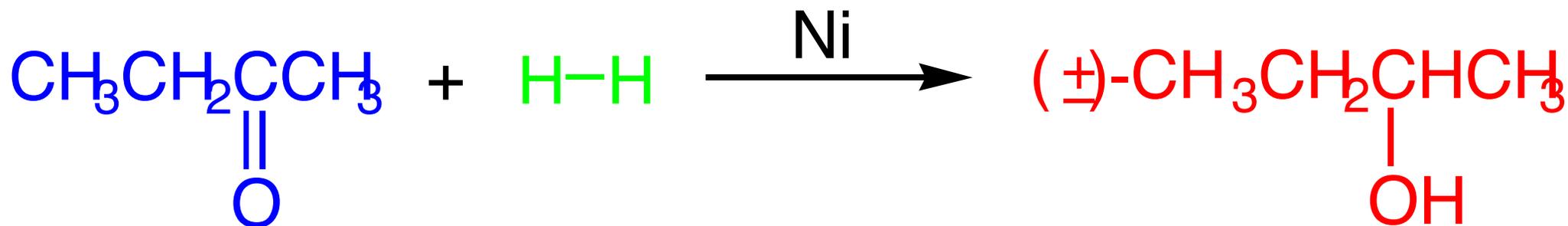
$$\% \text{ enantiomeric excess}^* = \frac{+6.76}{+13.52} \times 100 = 50\%$$

9. The Synthesis of Chiral Molecules

9A. Racemic Forms

Ketone reduction

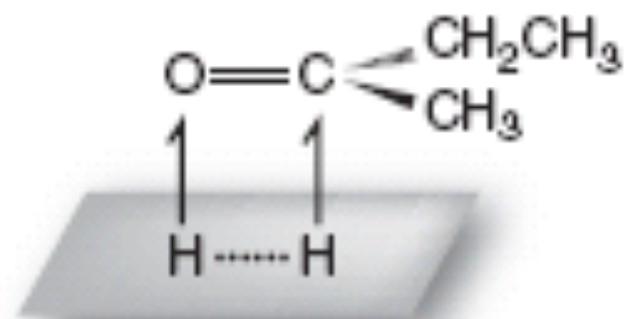
secondary Alcohol



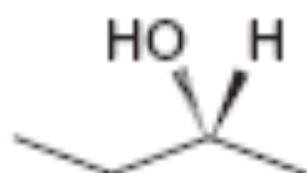
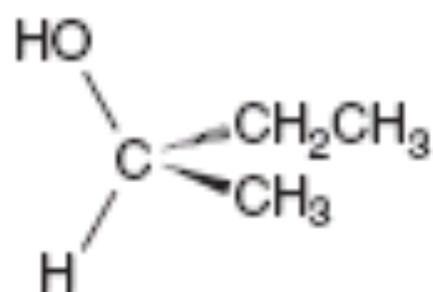
Butanone
(achiral
molecules)

Hydrogen
(achiral
molecules)

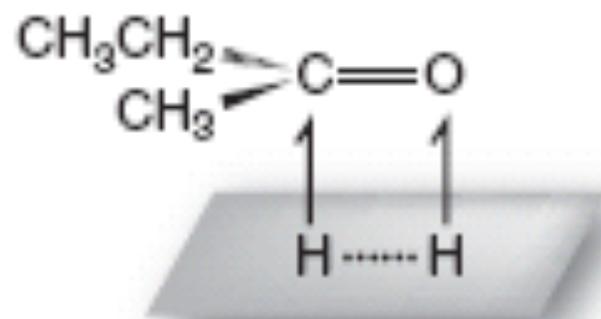
(±)-2-Butanol
(chiral
molecules; but
50:50 mixture
(R) & (S))



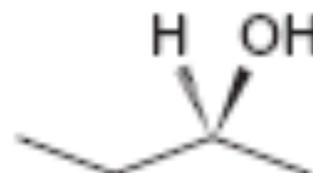
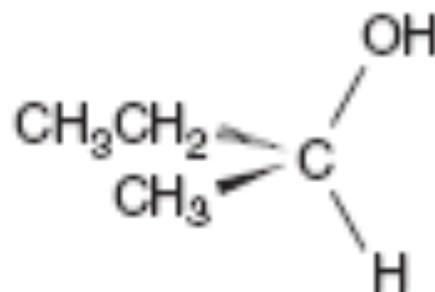
(a)



(R)-(-)-2-Butanol (50%)



(b)



(S)-(+)-2-Butanol (50%)

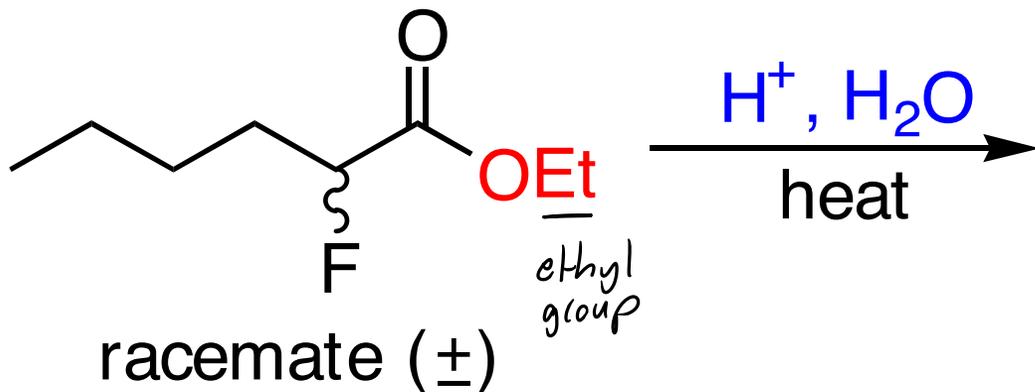
9B. Stereoselective Syntheses

Stereoselective reactions are reactions that lead to a preferential formation of one stereoisomer over other stereoisomers that could possibly be formed

enantioselective – if a reaction produces preferentially one enantiomer over its mirror image

diastereoselective – if a reaction leads preferentially to one diastereomer over others that are possible

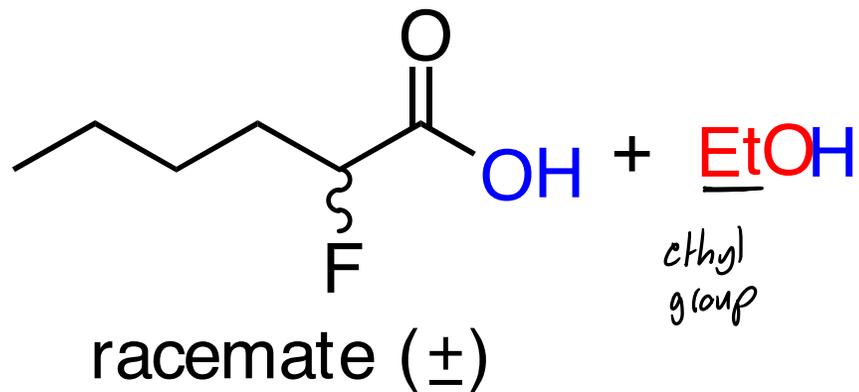
ester



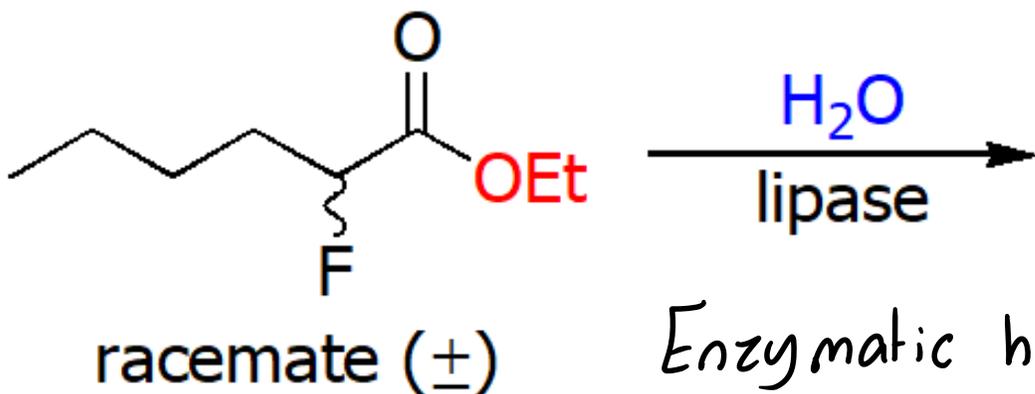
equal amounts of both enantiomers

carboxylic acid

Alcohol



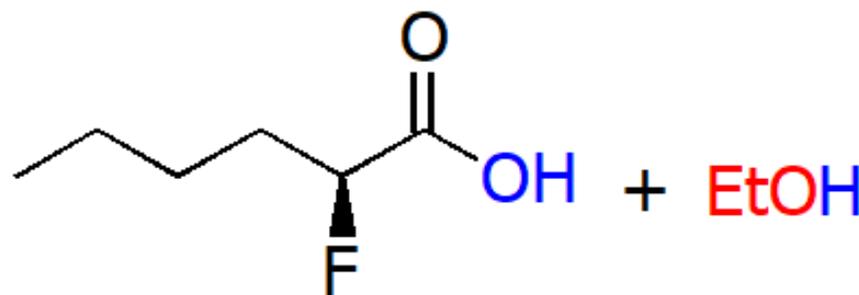
Not enantioselective



Enzymatic hydrolysis

(-)

(> 69% ee)



product mostly one enantiomers

enantioselective

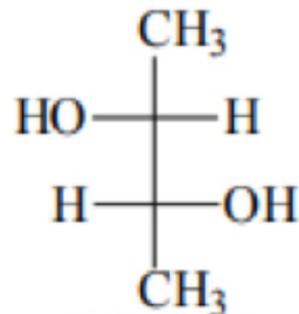
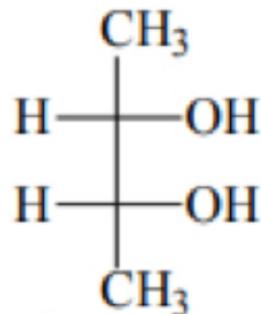
10. Molecules with More than One Chirality Center

Diastereomers

Stereoisomers that are not **enantiomers**

Unlike **enantiomers**, **diastereomers** usually have substantially different
chemical and physical properties

Q7) The relationship between the following two structures is:



(A) enantiomers

(B) diastereomers

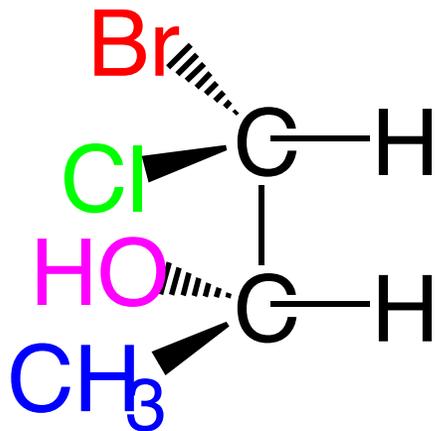
(C) structural isomers

(D) identical

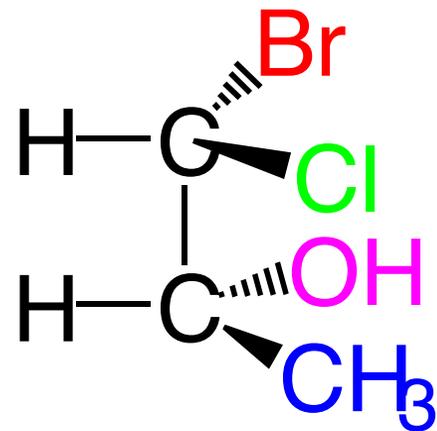
(E) none of the above

A7) The answer is (B) (by definition)

(I)



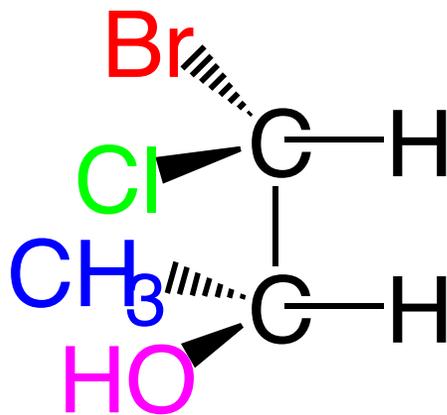
(II)



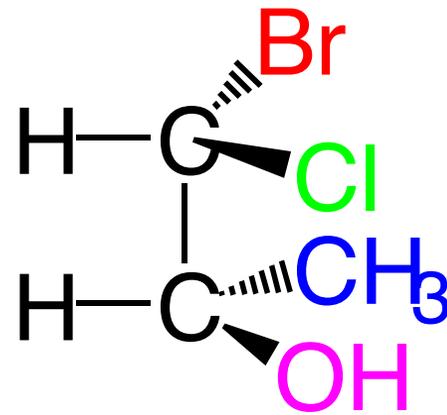
enantiomers

non superimposable mirror images

(III)



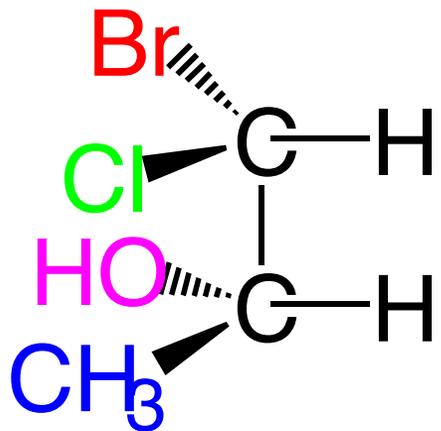
(IV)



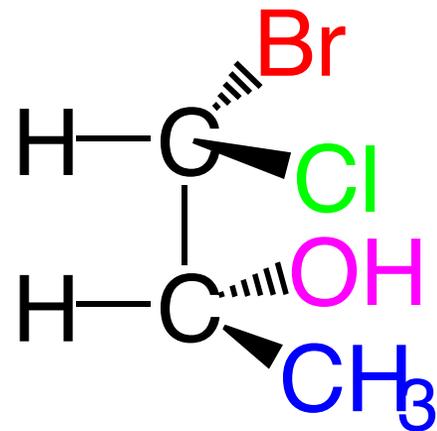
enantiomers

Note: In compounds with n tetrahedral stereocenters, the maximum number of stereoisomers is $2n$.

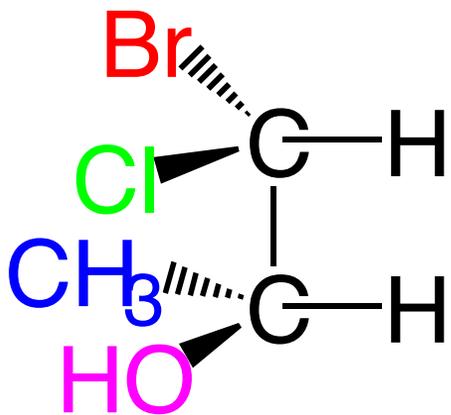
(I)



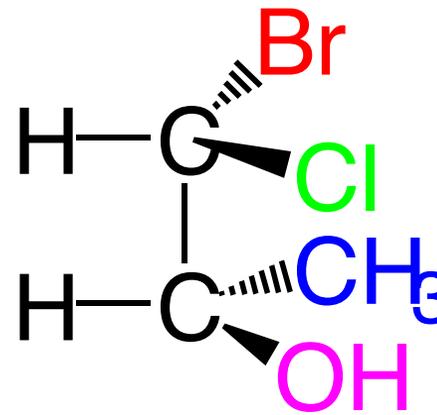
(II)



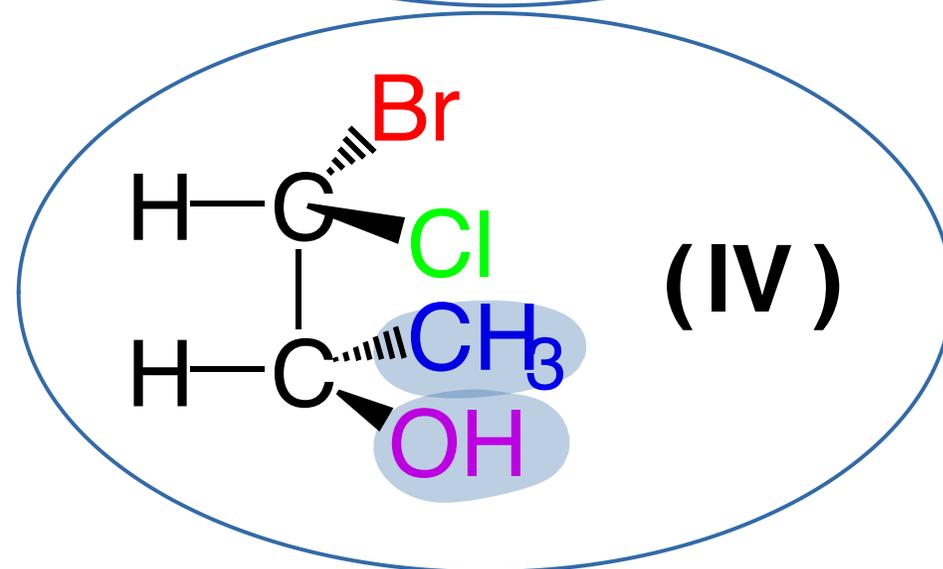
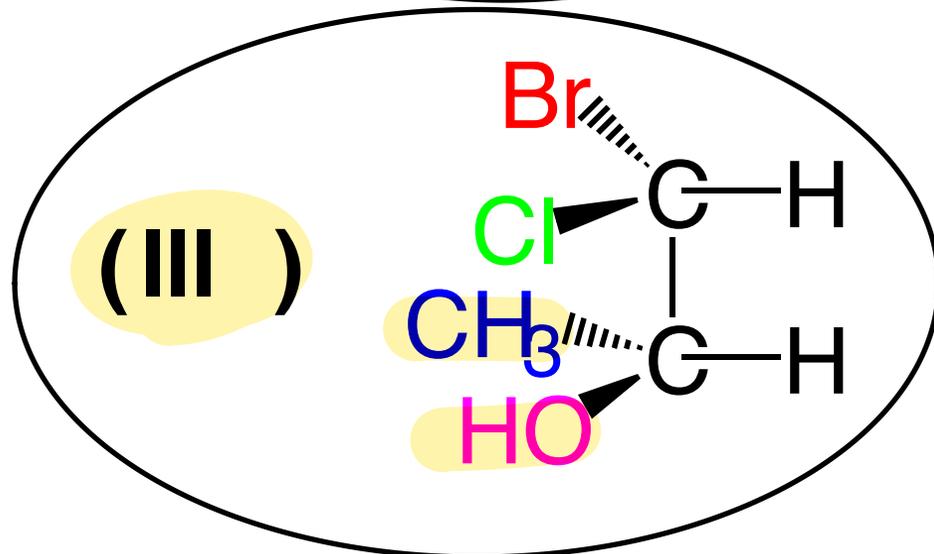
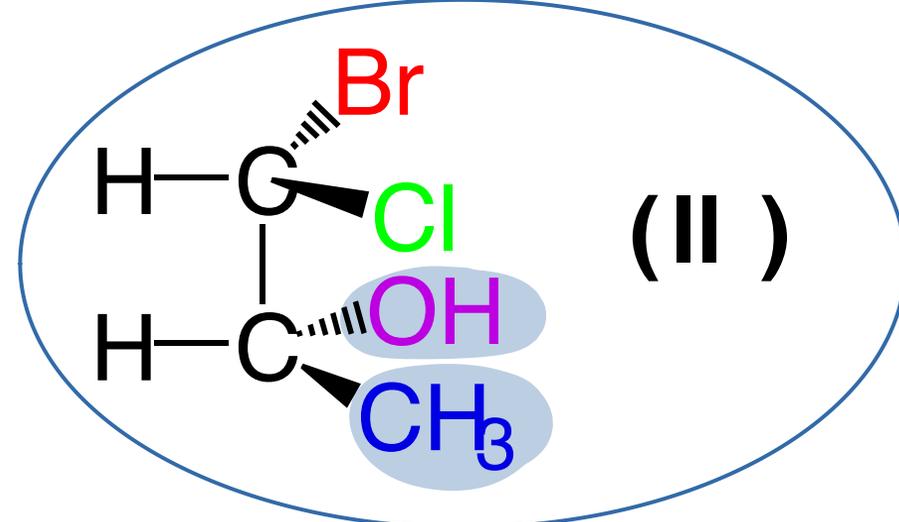
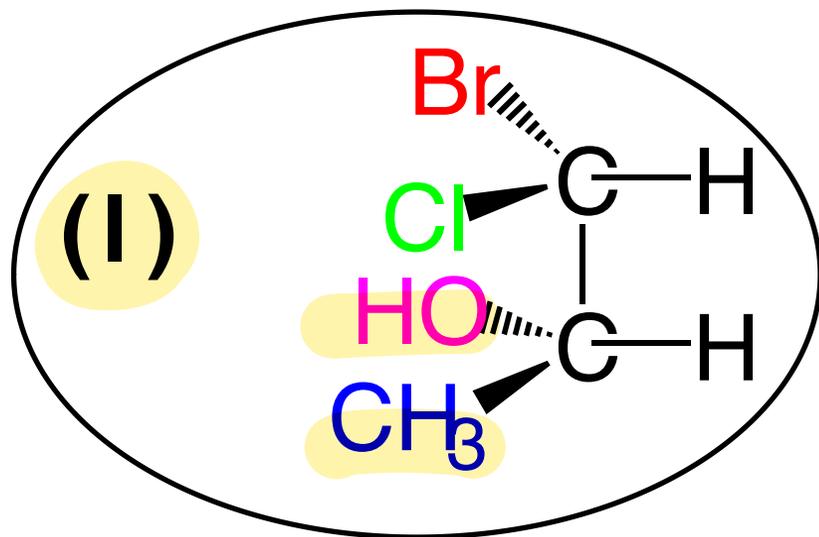
(III)



(IV)



(I) & (II) are enantiomers to each other
(III) & (IV) are enantiomers to each other

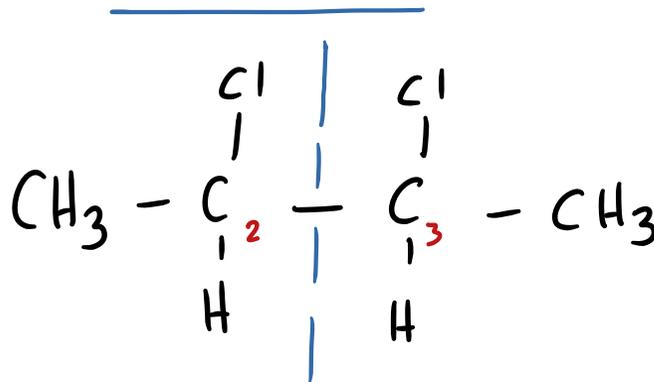
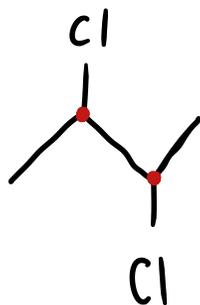


Diastereomers to each other:

(I) & (III), (I) & (IV), (II) & (III), (II) & (IV)

10A. Meso Compounds (Achiral compound)

Compounds with two stereocenters do not always have four stereoisomers ($2^2 = 4$) since some molecules are achiral (not chiral), even though they contain stereocenters. For example, 2,3-dichlorobutane has two stereocenters, but only has 3 stereoisomers (not 4)

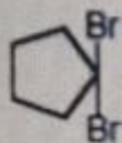


carbon 2/3 stereocenters

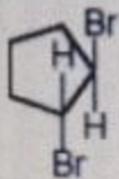
- plane of symmetry

↳ - Achiral -

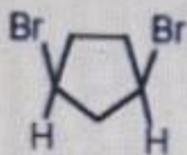
* Which of the following is (are) meso
(1 نقطة)



(I)



(II)



(III)

2,3-dichlorobutan

(IV)

2,3-dibromopentane

(V)

I & II

II & V

III & II

III & IV

None of the above

Q2. Which property is characteristic of meso compounds?

- They are optically active and rotate plane-polarized light
- They are optically inactive despite having stereocenters
- They always exist as racemic mixtures
- They never contain stereocenters

Correct Answer: **They are optically inactive despite having stereocenters**

Q7. Which statement is correct about meso compounds and enantiomers?

- Meso compounds exist as a pair of enantiomers
- Meso compounds are identical to their mirror images and are not enantiomers
- Meso compounds are always racemic mixtures
- Meso compounds cannot have stereocenters

Correct Answer: **Meso compounds are identical to their mirror images and are not enantiomers**

Q8. For a molecule with two stereocenters, which configuration pair commonly gives a meso form?

- R,R
- S,S
- R,S or S,R with internal symmetry
- No combination can give meso

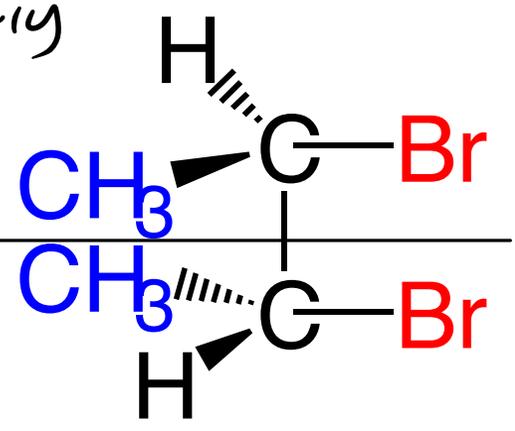
Correct Answer: R,S or S,R with internal symmetry

Q4. How many stereocenters are present minimally in a meso compound?

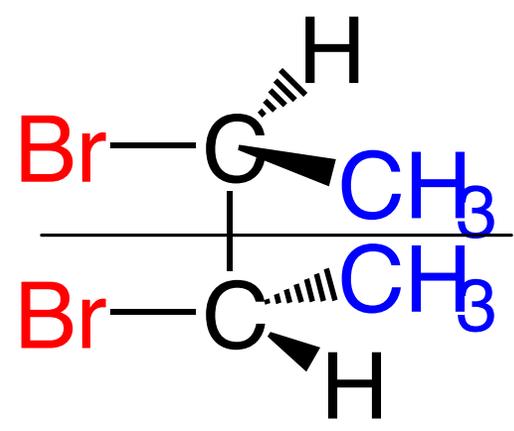
- One stereocenter
- At least two stereocenters
- No stereocenters
- At least three stereocenters

plane of symmetry
(Achiral)

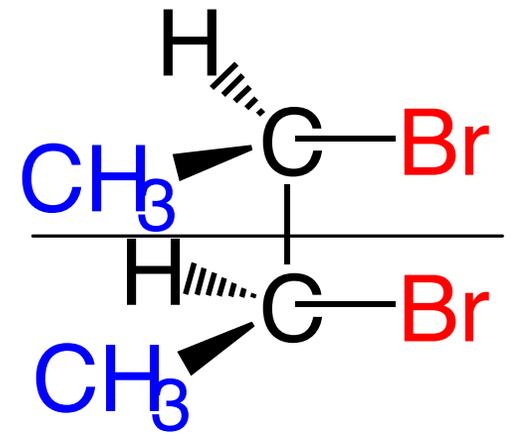
(I)



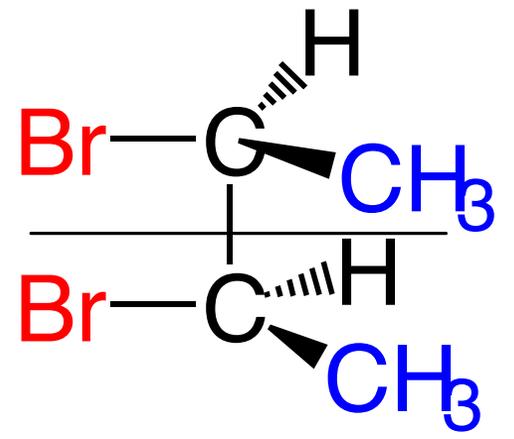
(II)



(III)



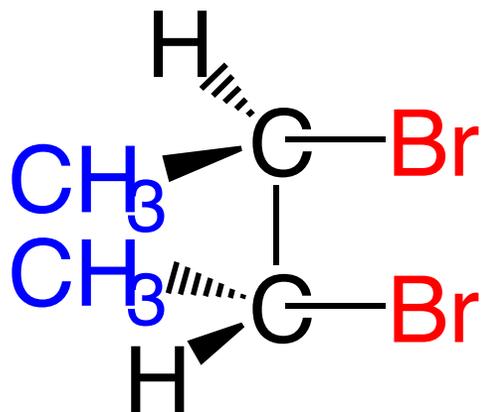
(IV)



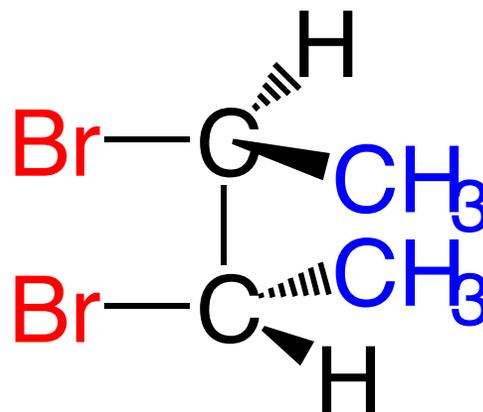
Note: (III) contains a plane of symmetry, is a meso compound, and is achiral ($[\alpha] = 0$).

2 stereocenters

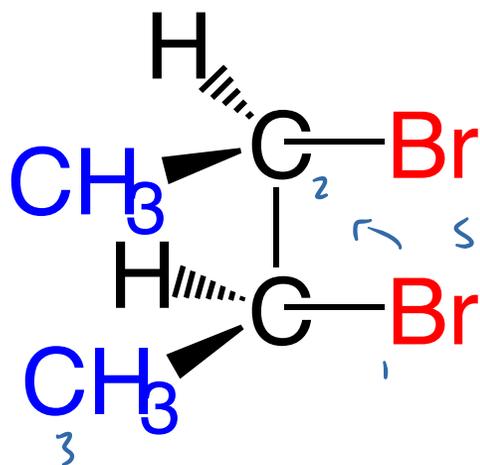
(I)



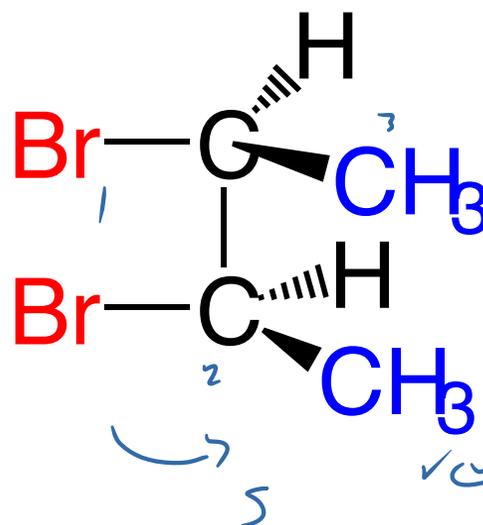
(II)



(III)



(IV)



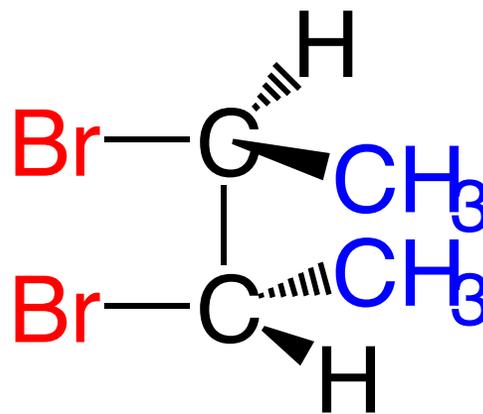
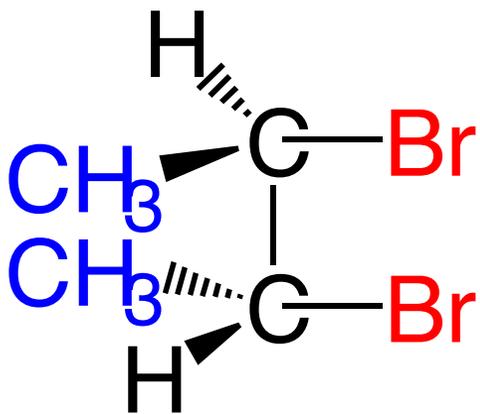
- نفس عدد ونوع الذرات ✓
- نفس الدوران S

(I) & (II) are enantiomers to each other and chiral

(III) & (IV) are identical and achiral

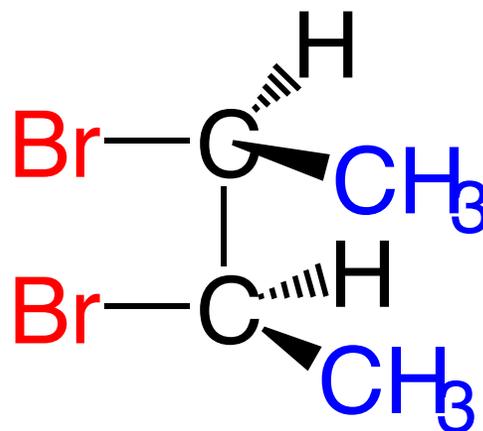
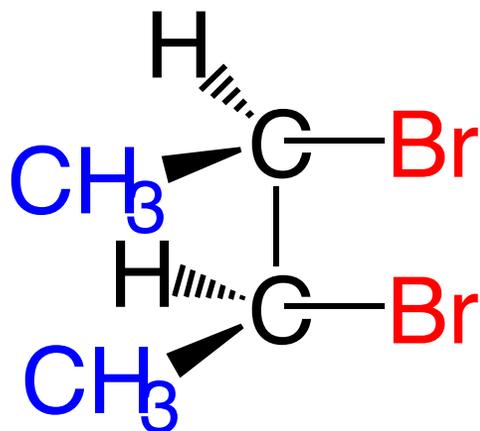
Identical ✓

(I)



(II)

(III)



(IV)

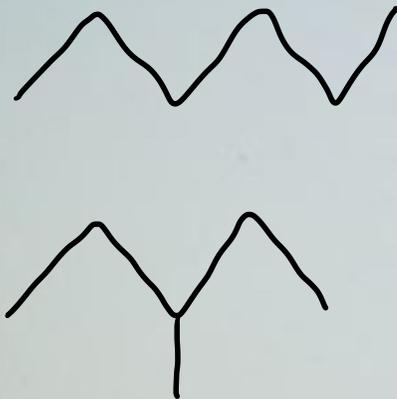
(I) & (III), (II) & (III) are diastereomers

Only 3 stereoisomers:

(I) & (II) {enantiomers}, (III) {meso} - 2 stereocenters
- Achiral

Hexane and 3-methylpentane are examples of:

- A) enantiomers. ~~x~~
- B) stereoisomers. ~~x~~
- C) diastereomers. ~~x~~
- D) constitutional isomers.
- E) None of these

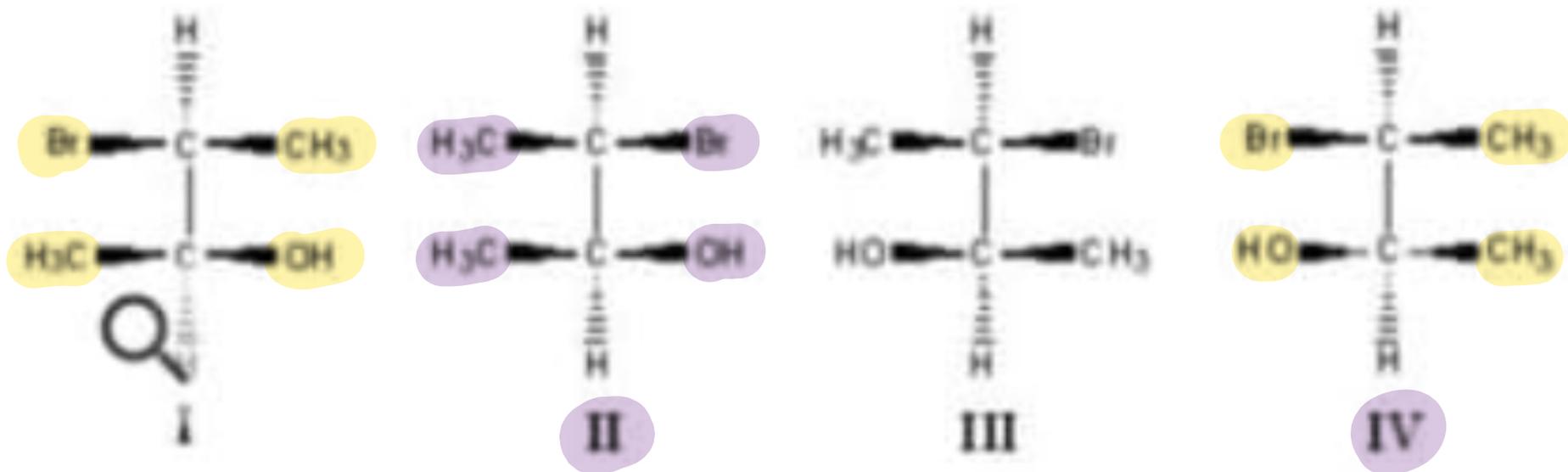


same MF
different connectivity

- A
- B
- C
- D
- E

D

Which of the following compound pairs are non superimposable mirror image of each other ? enantiomers



:Select one



diastereomers



a. I & IV



diastereomers



b. I & II



c. II & IV



diastereomers

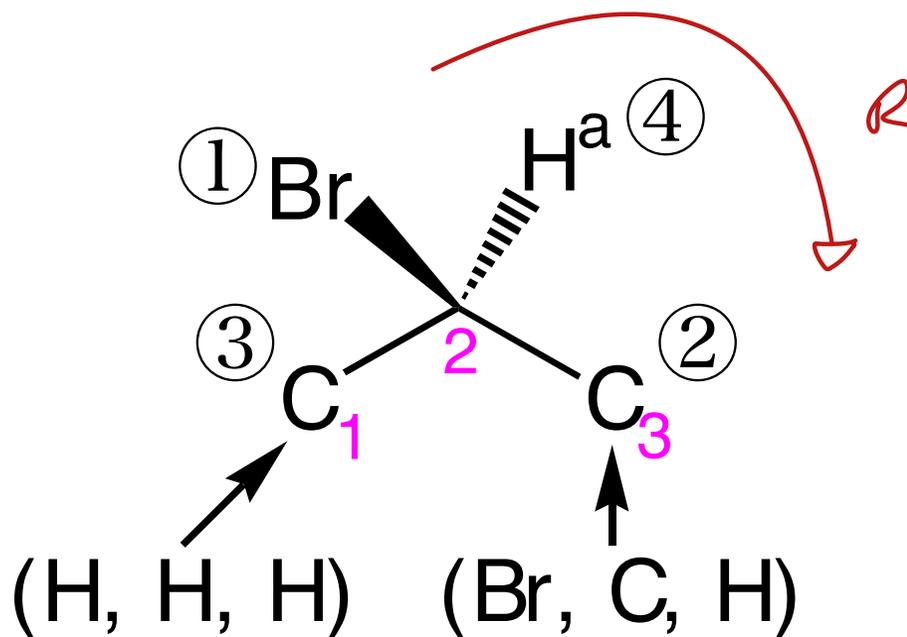
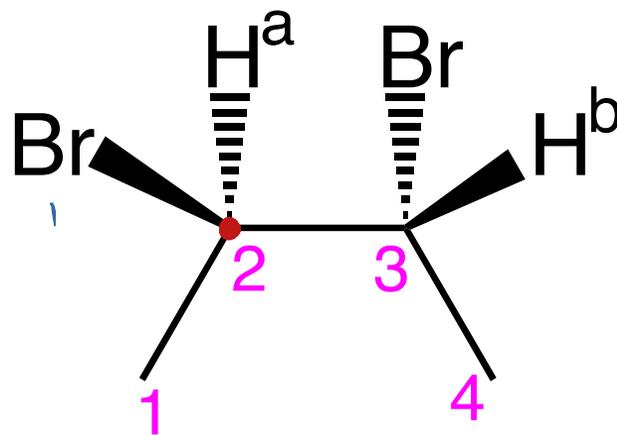


d. III & IV

10B. How to Name Compounds with More than One Chirality Center

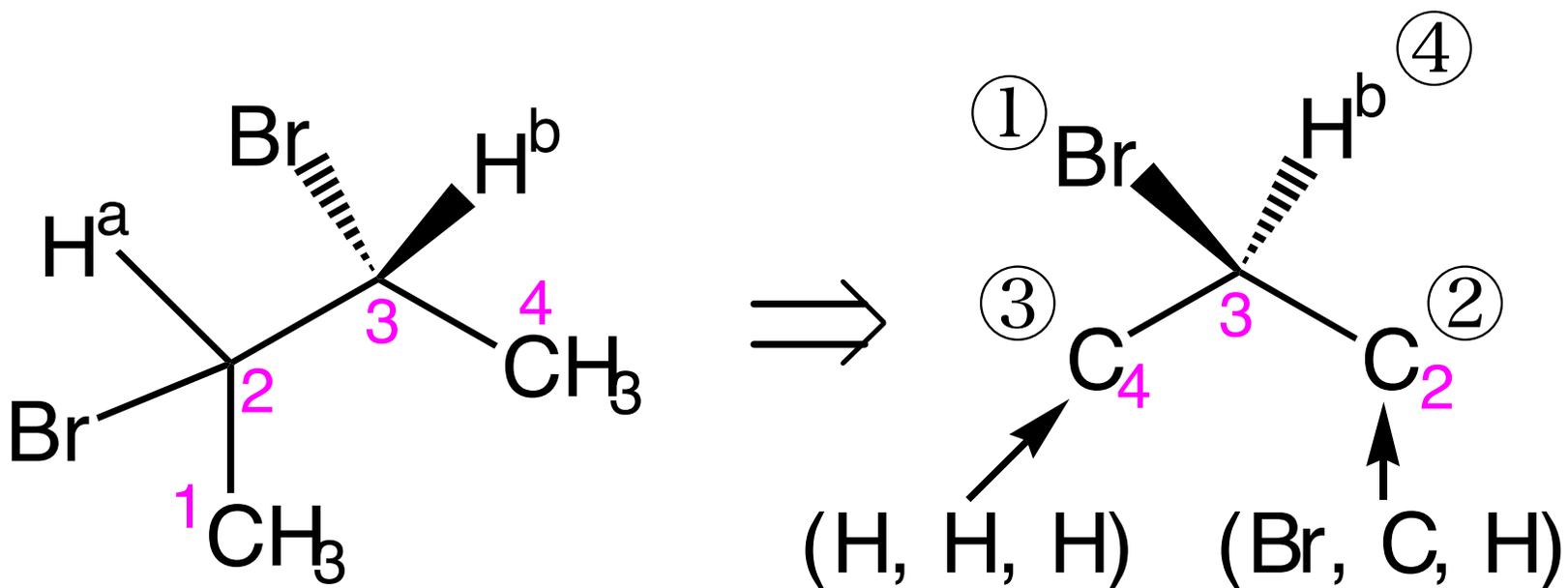
✓ 2,3-Dibromobutane

Look through C2–H^a bond



C2: *(R)* configuration

Look through C3–H^b bond

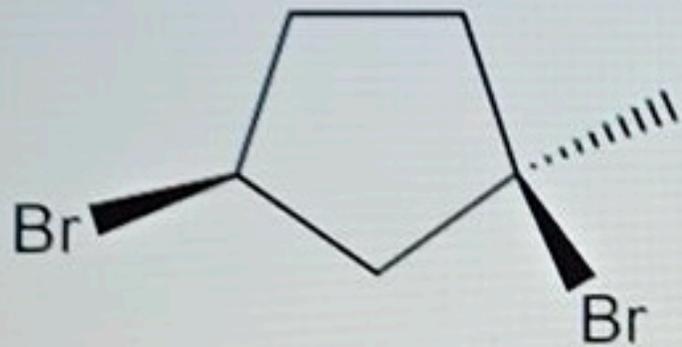


C3: (*R*) configuration

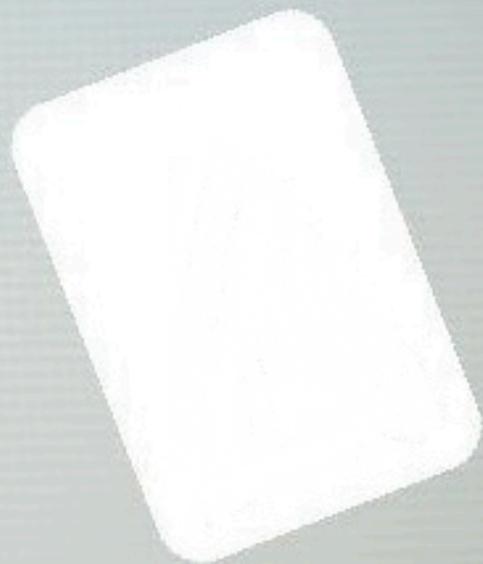
Full name:

(2*R*, 3*R*)-2,3-Dibromobutane

What is the complete IUPAC name of the following substance?

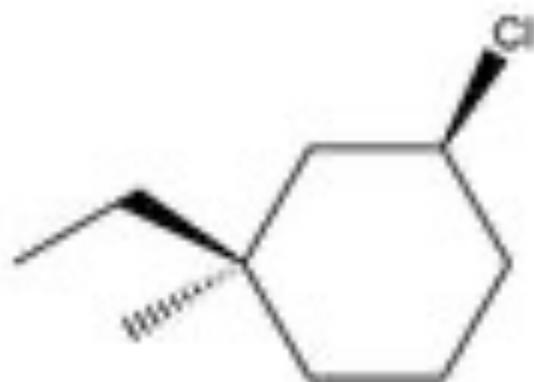


- a. (1S,3S)-1,3-dibromo-1-methylcyclopentane
- b. (1R,3S)-1,3-dibromo-1-methylcyclopentane
- c. (1R,3R)-1,3-dibromo-1-methylcyclopentane
- d. (1S,3R)-1,3-dibromo-1-methylcyclopentane



B

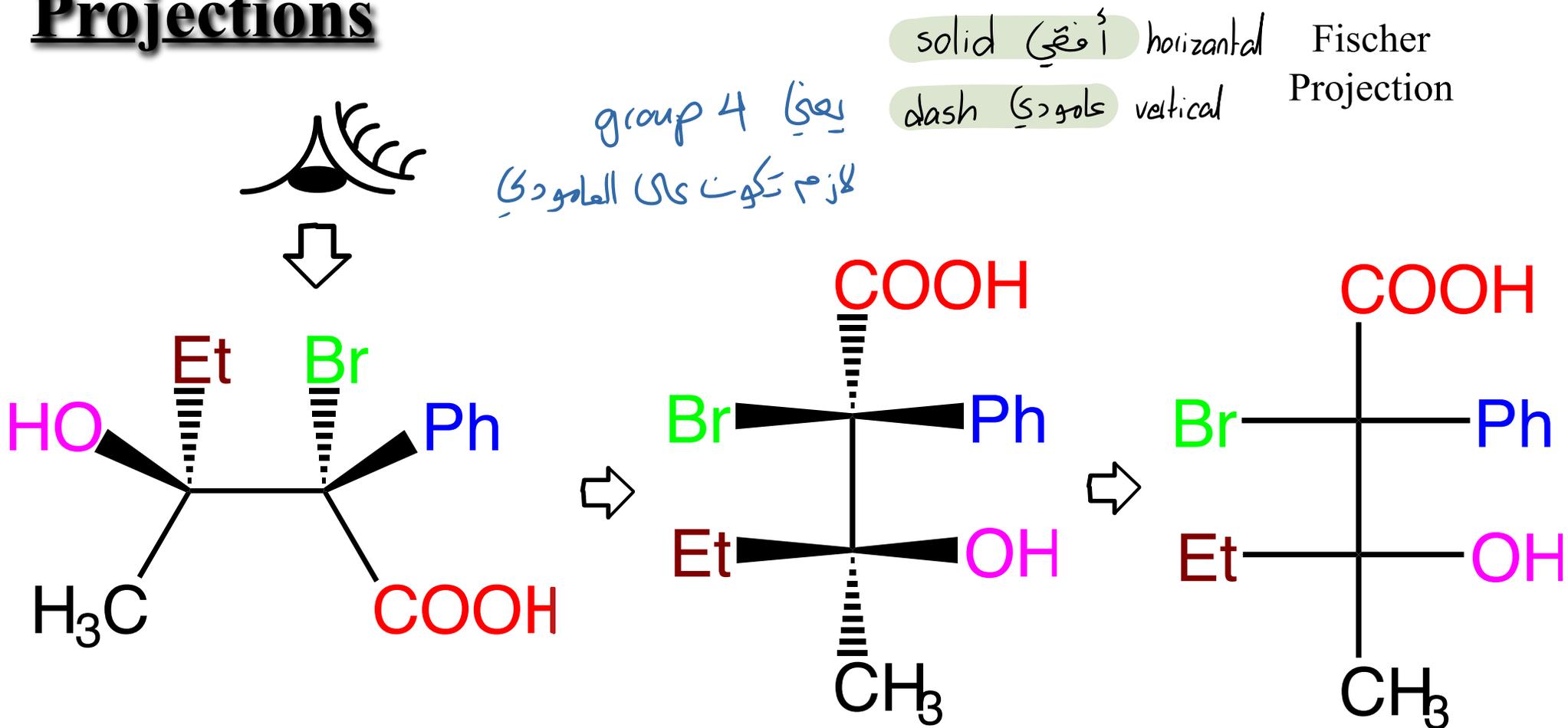
What is the correct IUPAC name of the following structure?

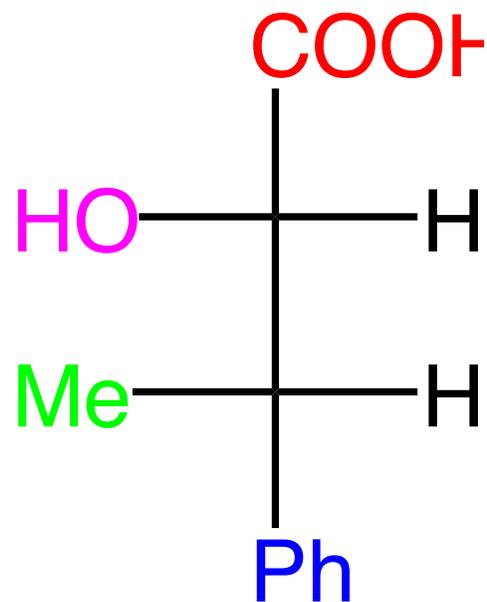
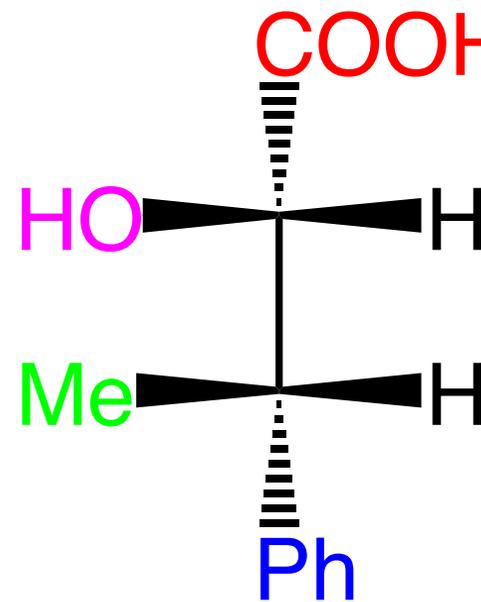
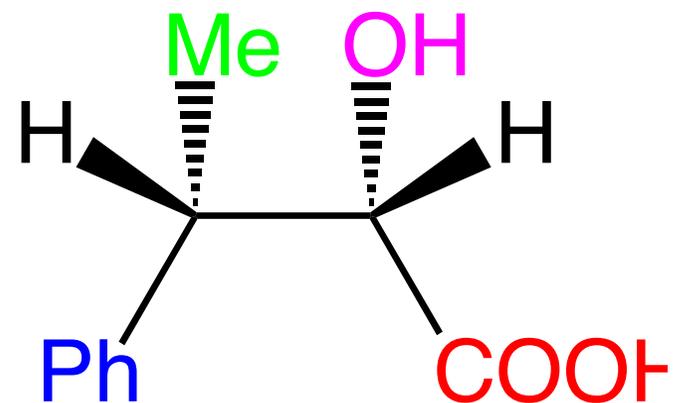
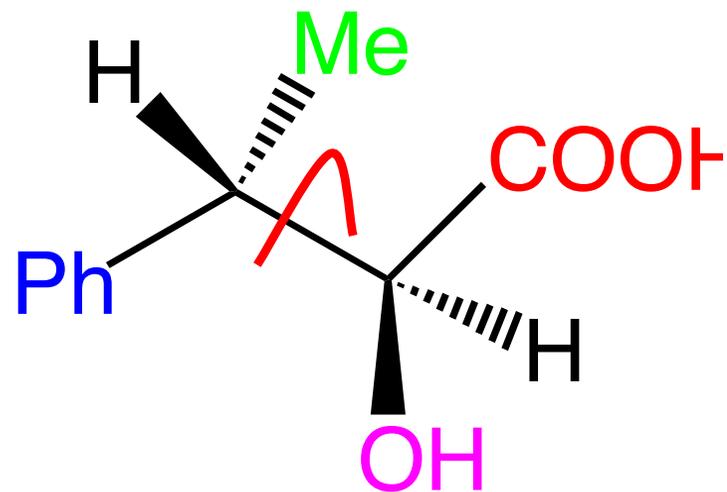


- (1R, 3S)-1-chloro-3-ethyl-3-methylcyclohexane
- (1S, 3R)-1-chloro-3-ethyl-3-methylcyclohexane
- (1S, 3R)-3-chloro-1-ethyl-1-methylcyclohexane
- (1R, 3S)-3-chloro-1-ethyl-1-methylcyclohexane

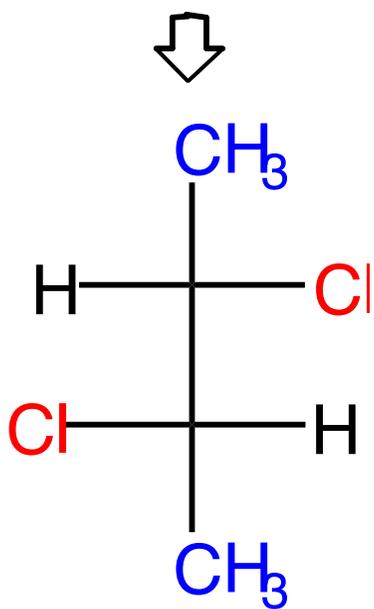
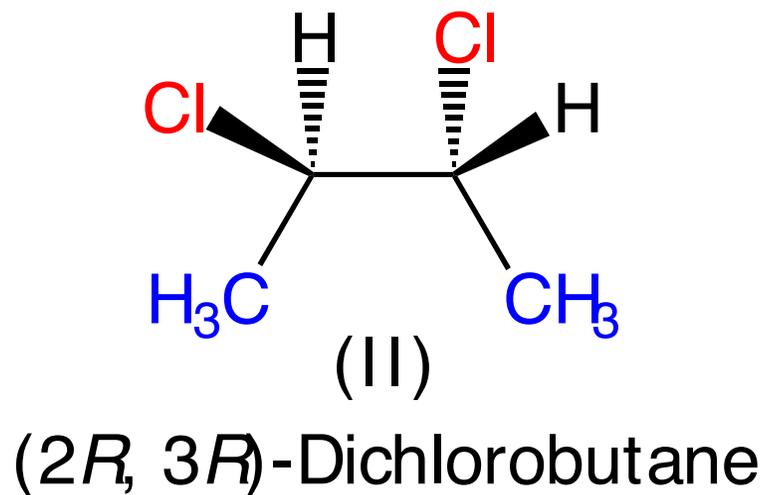
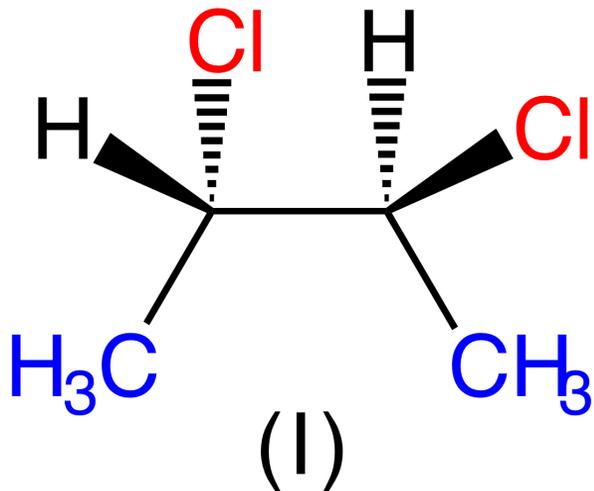
11. Fischer Projection Formulas

11A. How To Draw and Use Fischer Projections



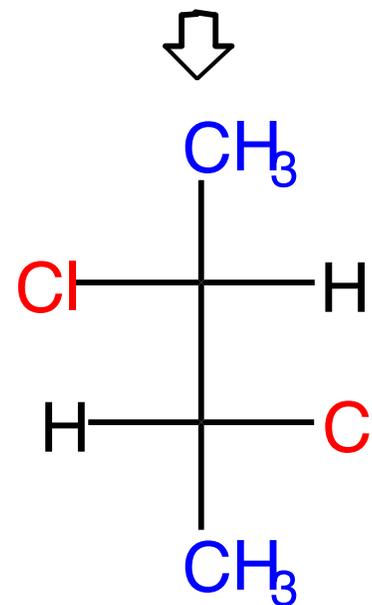


Fischer
Projection

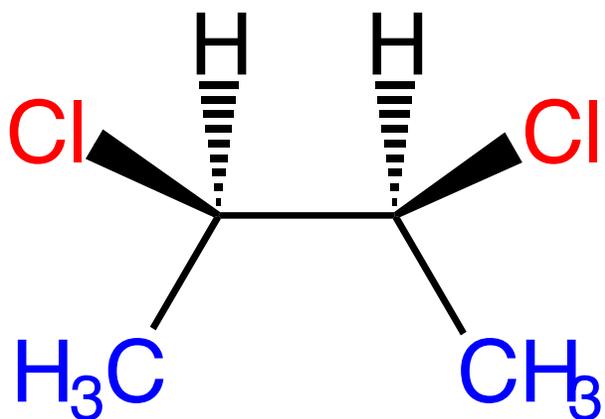


enantiomers

mirror

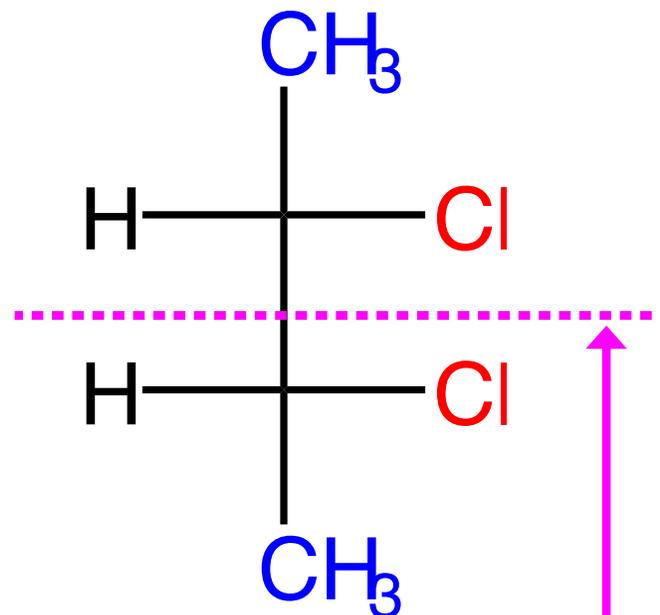
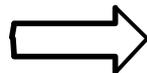


(I) and (II) are both chiral and they are enantiomers with each other



(III)

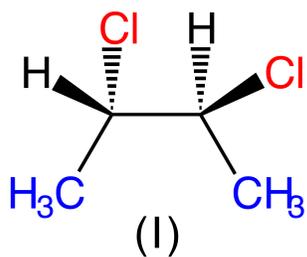
(2*S*, 3*R*)-Dichlorobutane



Plane of symmetry

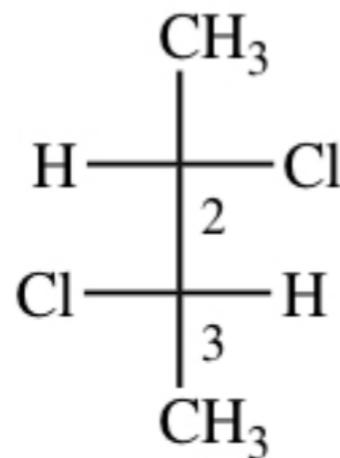
(III) is achiral (a meso compound)

(III) and (I) are diastereomers to each other ✓



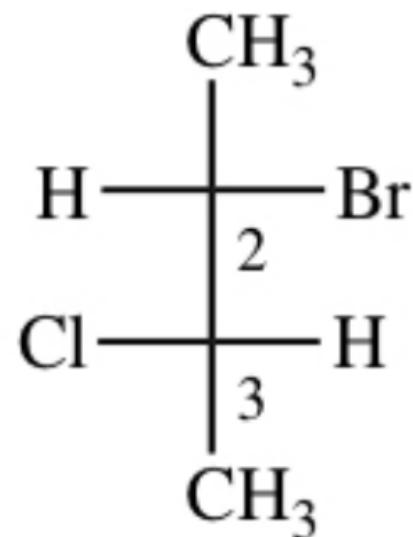
(I)

5.40. What is correct name for the following structure?



- a. (*R,S*)-2,3-dichlorobutane b. (*2R,3S*)-2,3-dichlorobutane
*c. (*2S,3S*)-2,3-dichlorobutane d. (*2R,3R*)-2,3-dichlorobutane
e. none of these

5.41. What is the absolute configuration around C-2 and C-3?



a. *R, R*

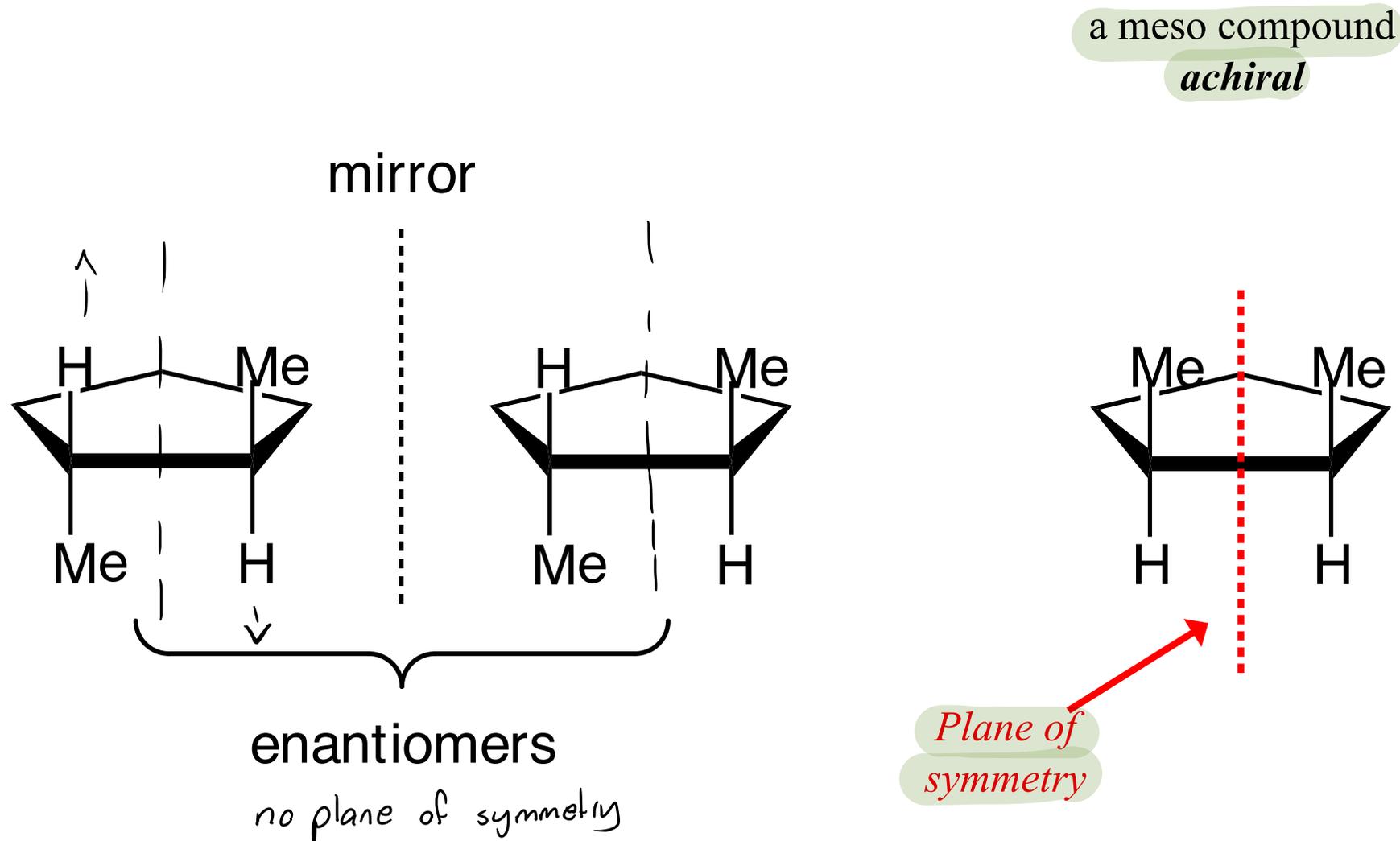
*b. *S, S*

c. *R, S*

d. *S, R*

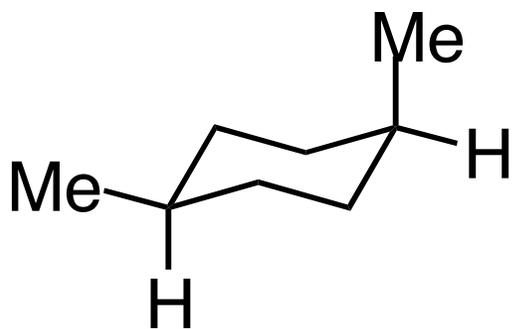
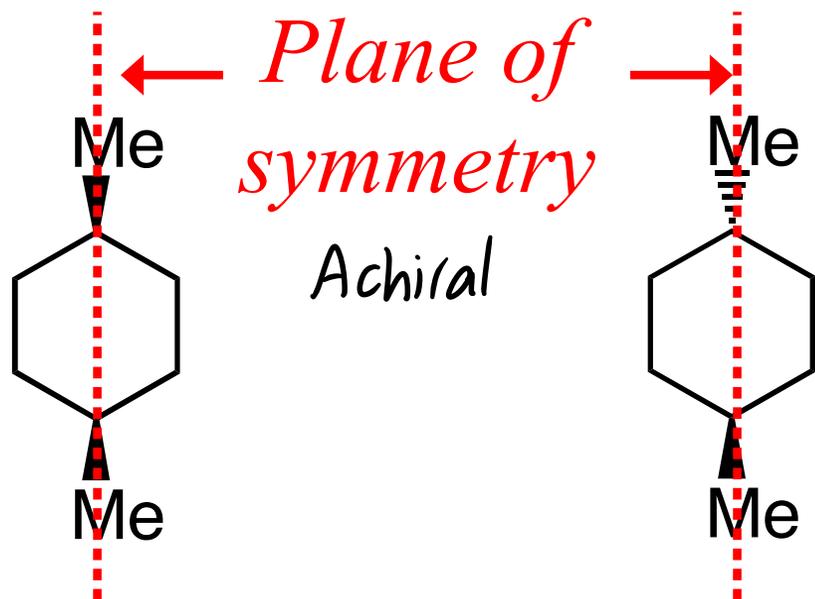
e. *E, Z*

12. Stereoisomerism of Cyclic Compounds

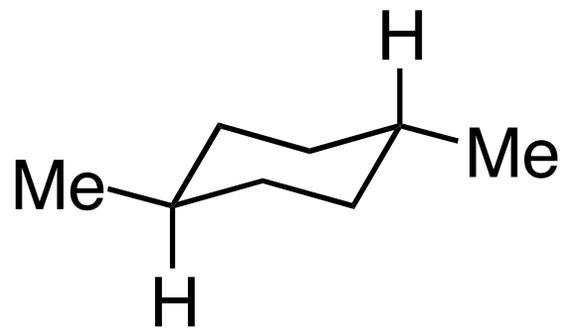


12A. Cyclohexane Derivatives

1,4-Dimethylcyclohexane



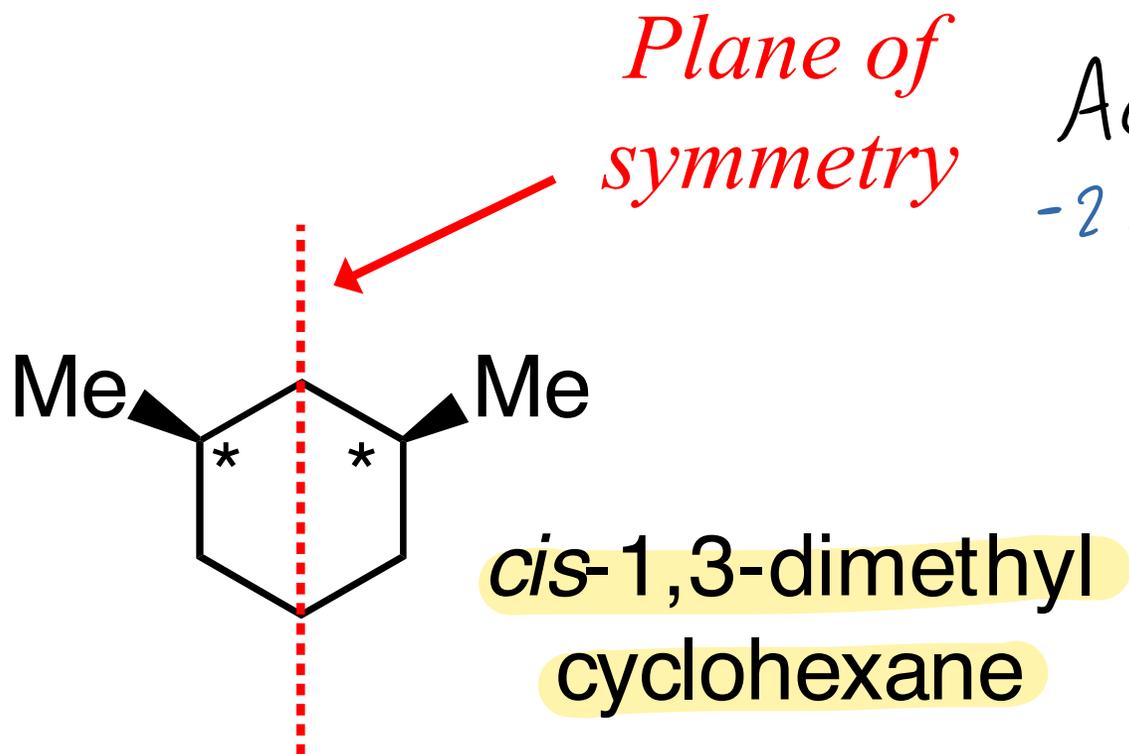
cis-1,4-dimethyl
cyclohexane



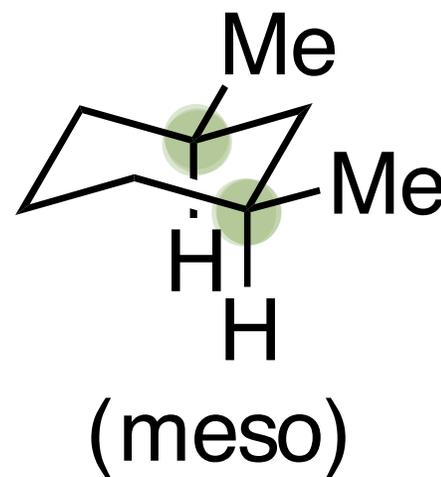
trans-1,4-dimethyl
cyclohexane

- Both *cis*- & *trans*-1,4-dimethylcyclohexanes are *achiral* and *optically inactive*

1,3-Dimethylcyclohexane



Achiral
- 2 stereocenter

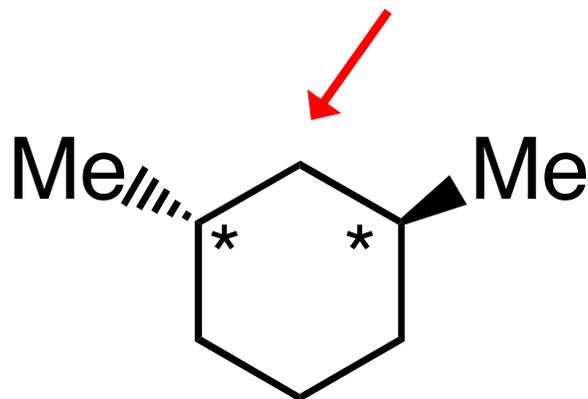


cis-1,3-Dimethylcyclohexane has a plane of symmetry and is a meso compound

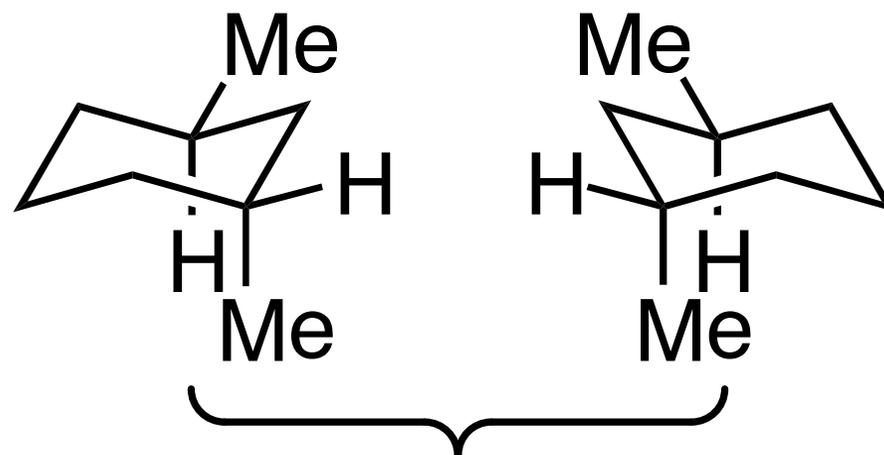
1,3-Dimethylcyclohexane

(chiral)

NO plane of symmetry



trans-1,3-dimethyl
cyclohexane



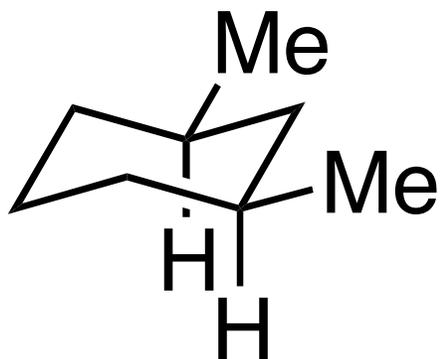
enantiomers

trans-1,3-Dimethylcyclohexane exists as a pair of enantiomers

1,3-Dimethylcyclohexane

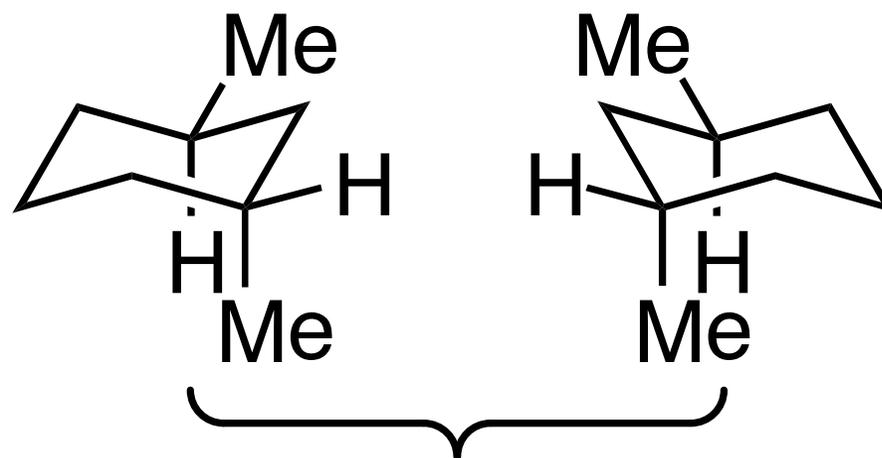
Has two chirality centers but only *three* stereoisomers

cis-1,3-dimethyl
cyclohexane



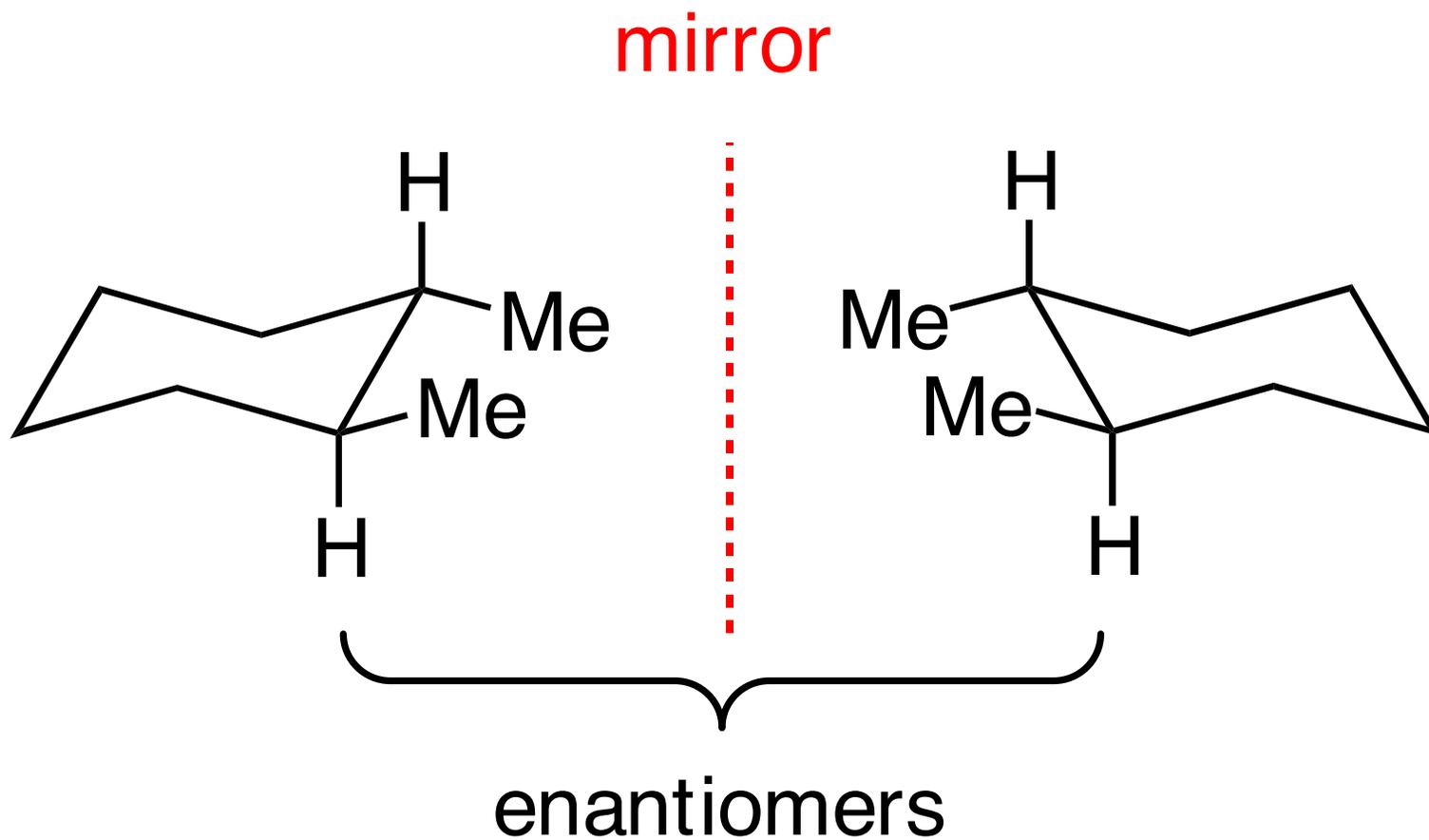
(meso)

trans-1,3-dimethyl
cyclohexane



enantiomers

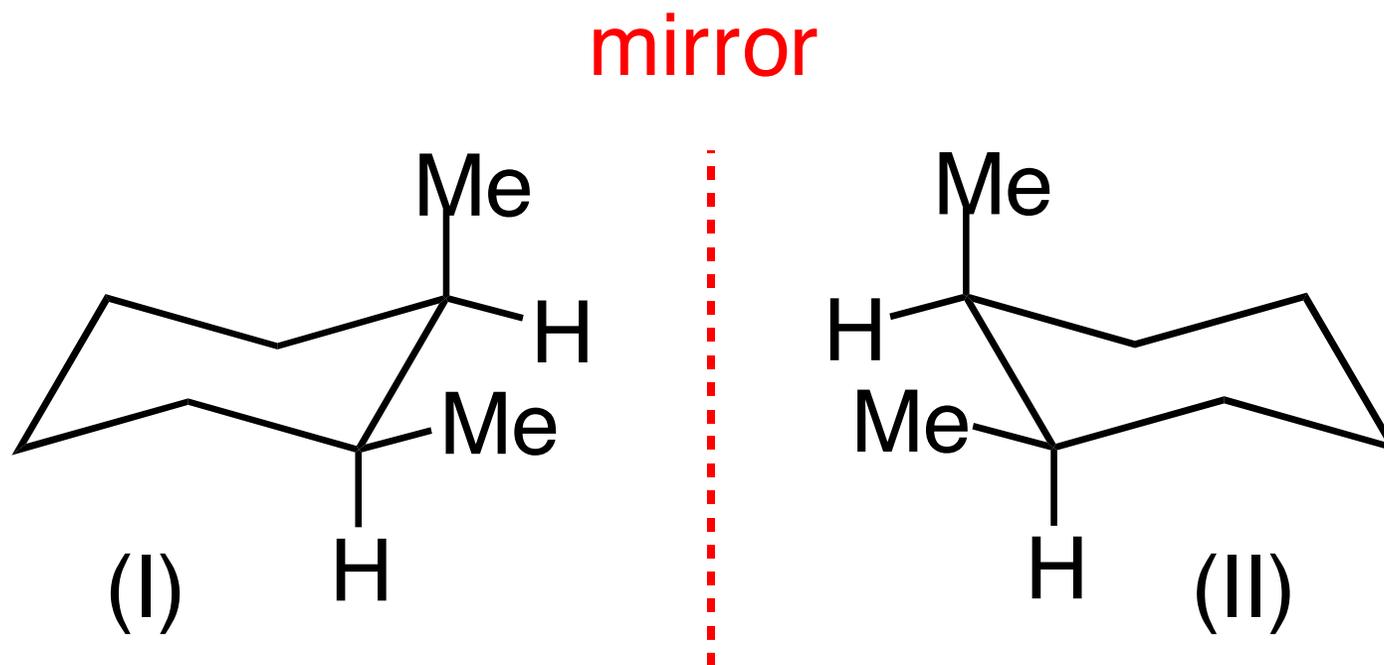
1,2-Dimethylcyclohexane



trans-1,2-Dimethylcyclohexane exists as a pair of enantiomers

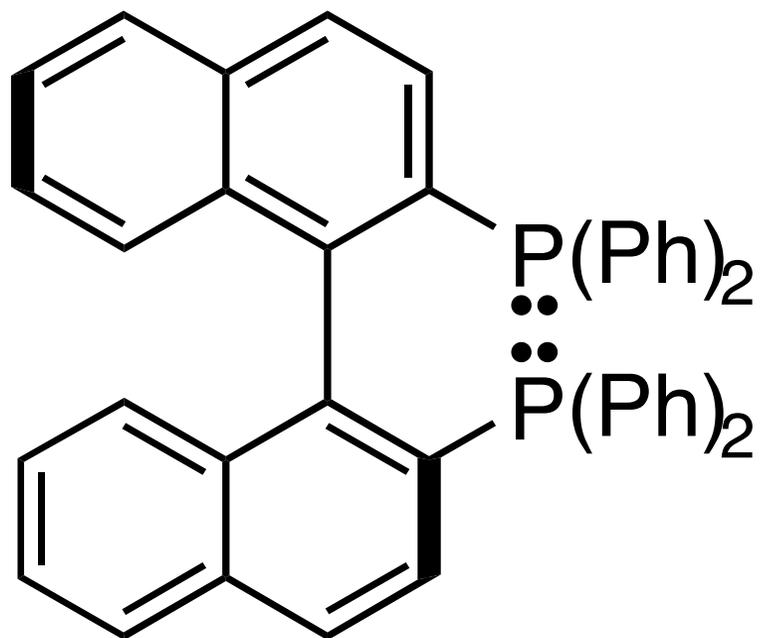
1,2-Dimethylcyclohexane

With *cis*-1,2-dimethylcyclohexane the situation is quite complicated

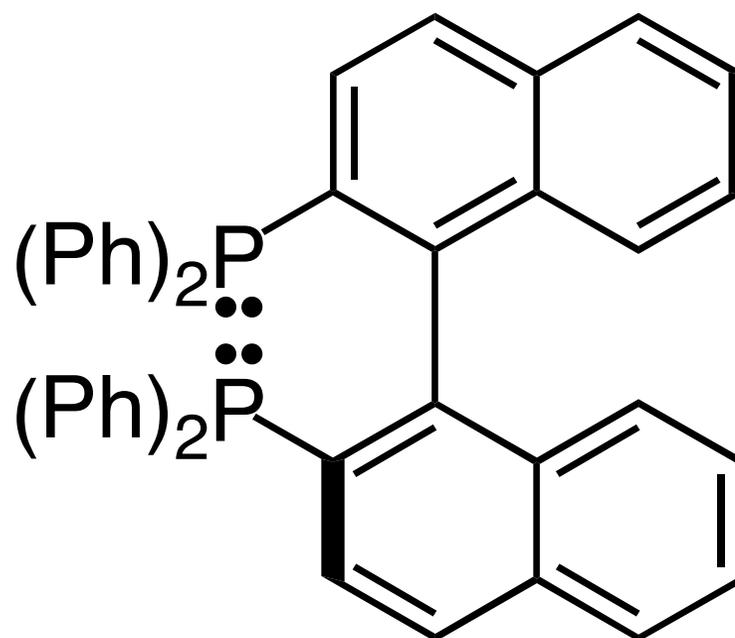


(I) and (II) are enantiomers to each other

13. Chiral Molecules That Do Not Possess a Chirality Center



(S)-BINAP



(R)-BINAP

bi

enantiomers

