Part ① تركيب معلومات

لو سألني شو العلاقة بين مركبين:

① نفس الذرات وأنواعها ↰ مختلفين ← المركبين مختلفين

↳ نفس الاشي ← نروح على خطوة ②

② Connectivity ↰ مختلفة ← المركبين structural / substitutional

- skeletal
- Positional
- Functional

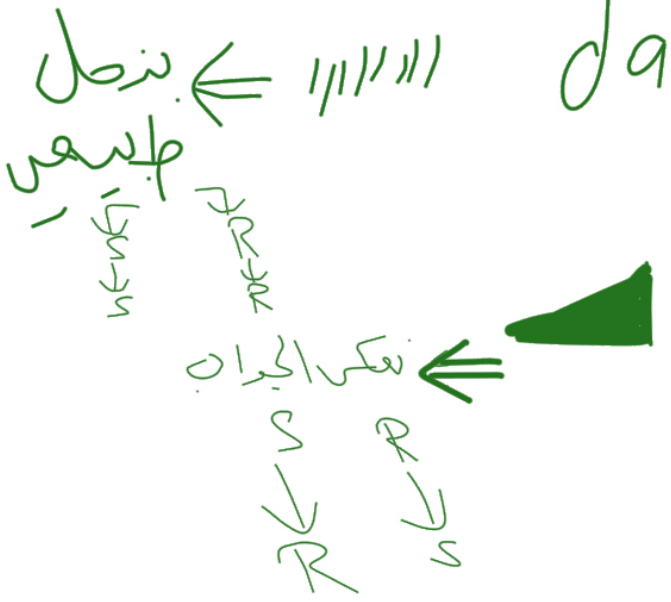
↳ نفس ال connectivity ← نروح ل خطوة ③

③ Stereoisomers ↰

- cis / trans , = or حلقة → Geometrical
- Newman, ring flip → Conformational
- chiral → R S → واحد و التاني enantiomers, لكن اذا كانوا R, R أو S, S ← Same compound
- no chiral → Same compound

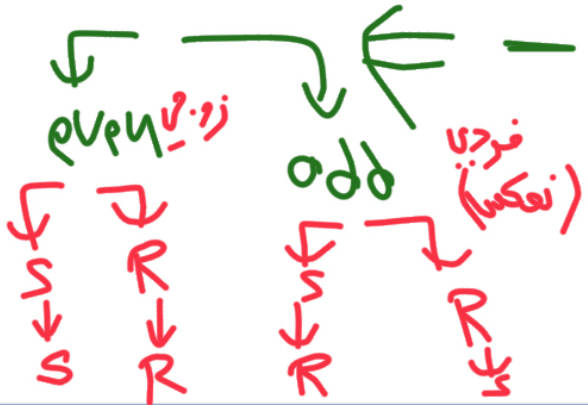
3 حالات

1- يكرر رقمها أربعة على الـ dash

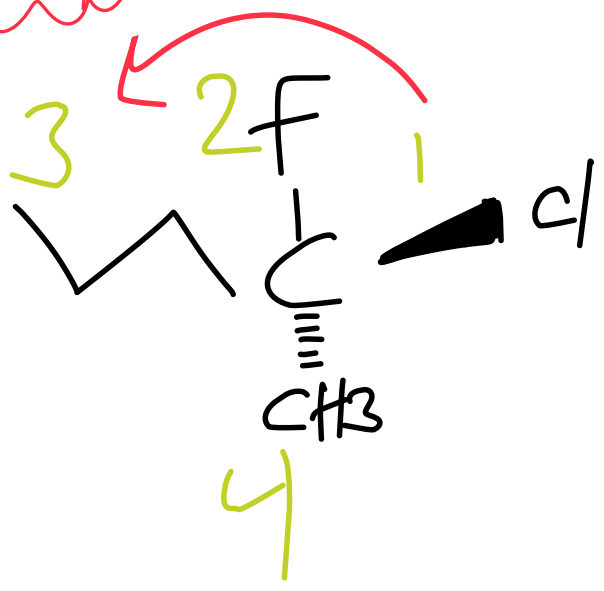


2- يكرر رقمها أربعة على الـ solid

3- يكرر رقمها أربعة على الـ continuous



example



C→chiral

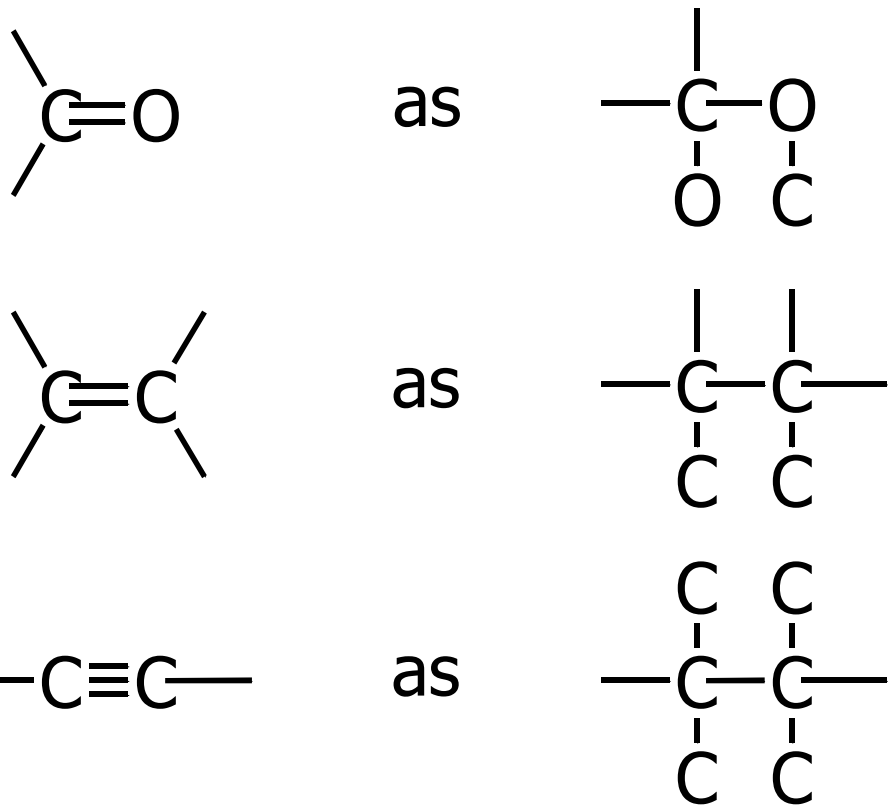
Cl > F > C–C > CH

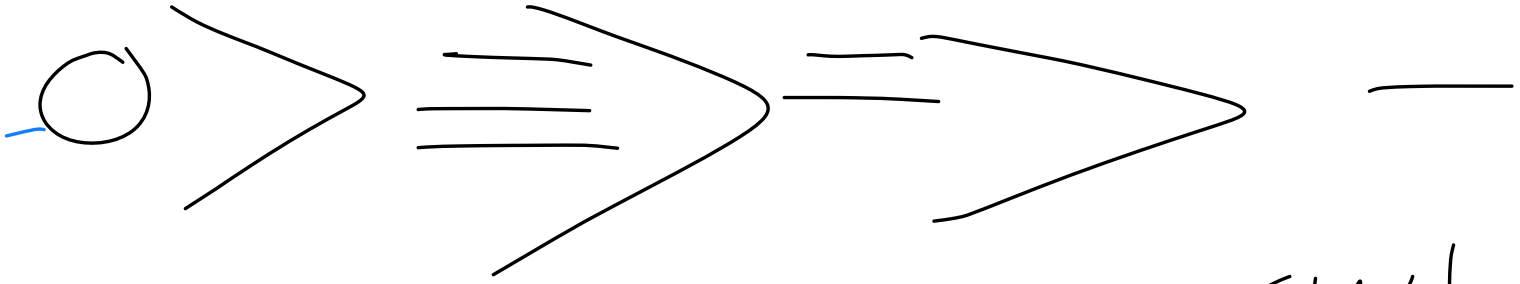
1 2 3 4

dashed

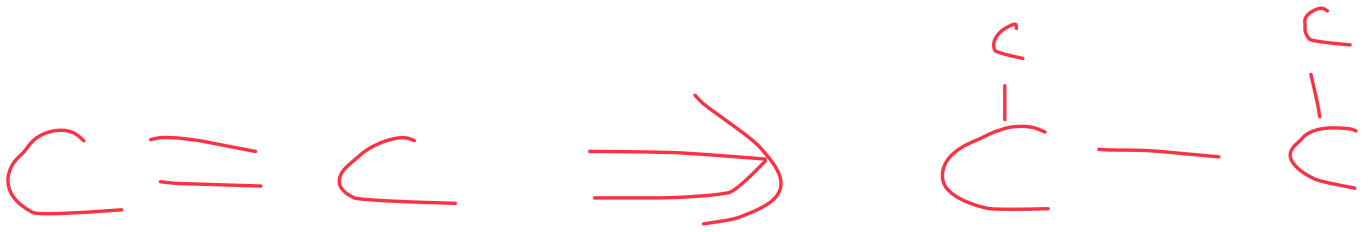
S

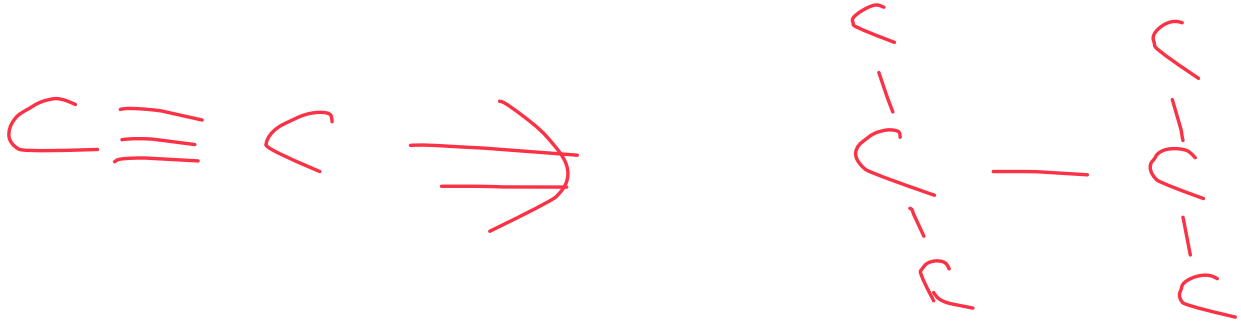
- Rule 4
  - For groups containing double or triple bonds, assign priorities as if both atoms were duplicated or triplicated

e.g. 

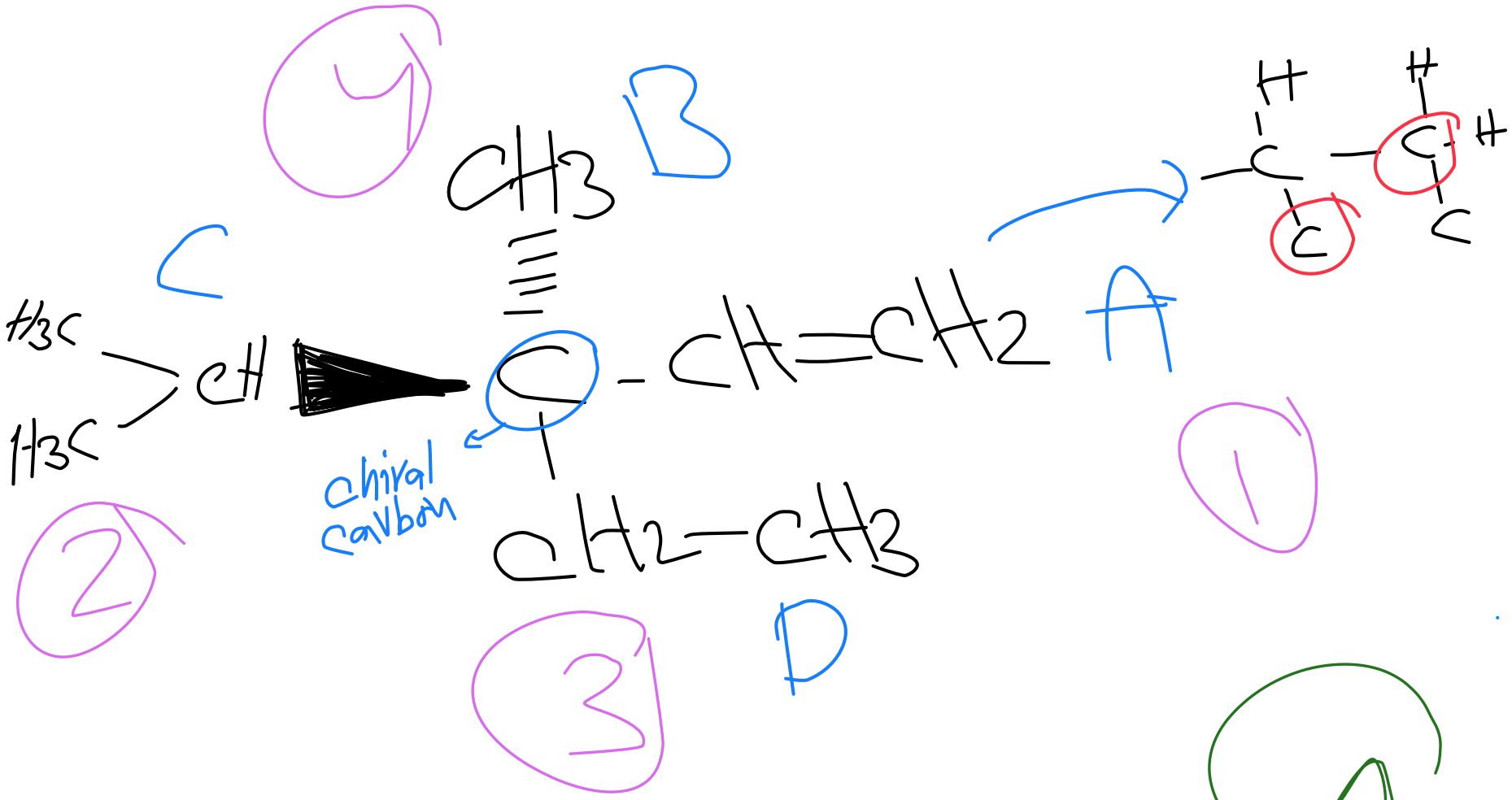


الأعمدة بالترقيم





example ①


CH3
H3C
H3C
CH
C
C
CH=CH2
chiral carbon
CH2—CH3
C
C
H
H
H
C
C
A
B
C
D
1
2
3
S

A (1)	B (4) dash	C (2)	D (3)
C	C	C	C
C	H	C	C
C		C	H
H		H	
C		H	

→ متصل مع chiral carbon

→ أعلى اشي متصل مع اللي متصل بأعلى اشي مع chiral

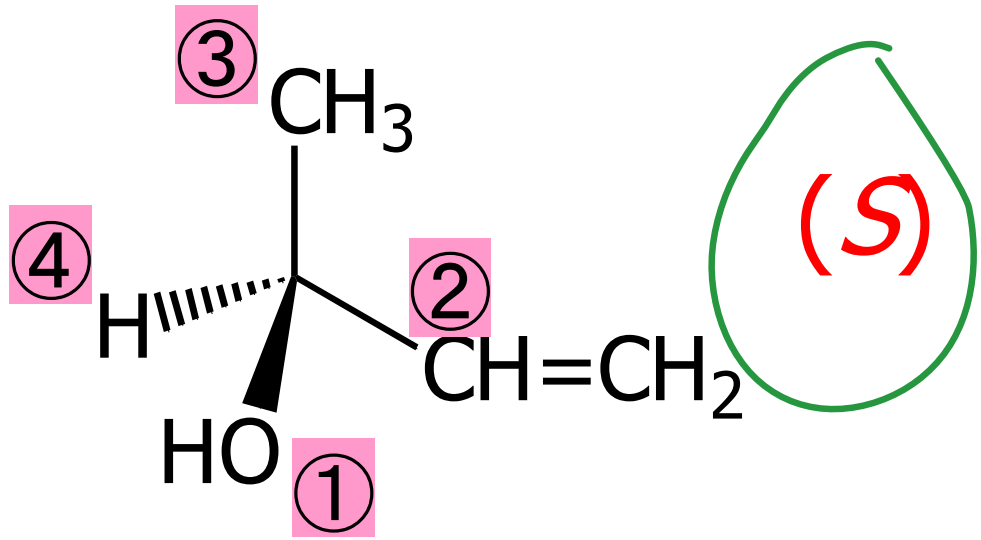
→ ثاني أعلى اشي متصل مع اللي متصل بأعلى اشي مع chiral

→ ثالث أعلى اشي متصل مع اللي متصل بأعلى اشي مع ال chiral

في حالة تساوي أربع مرات نروح على أول ذرة متصلة بالذرة الملتصقة بال Chiral ونشوفها من أعلى:

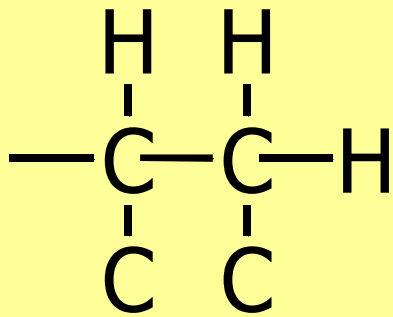
B → A →

❖ Example



Compare —CH_3 & —$CH=CH_2$:

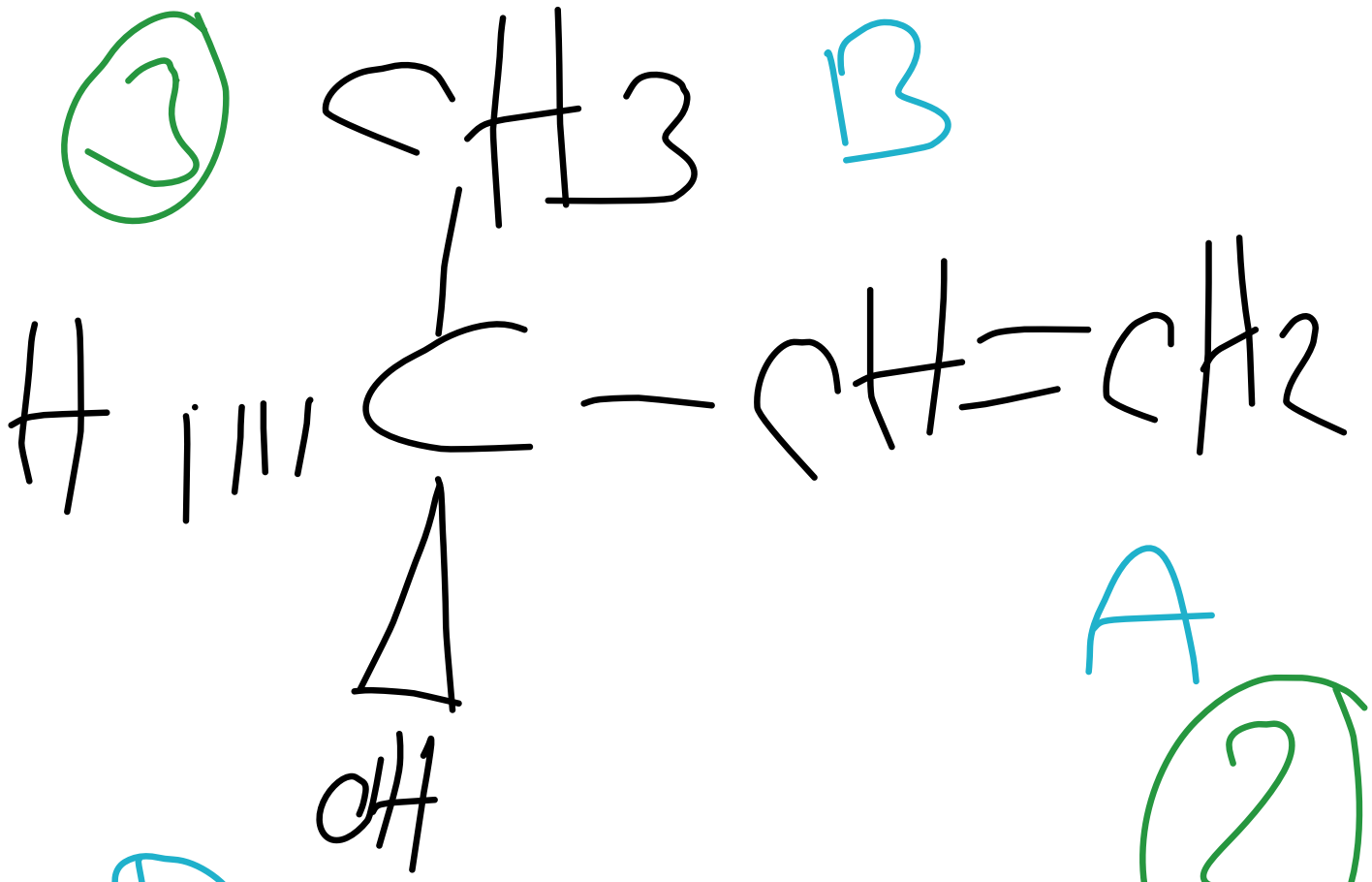
—$CH=CH_2$ equivalent to

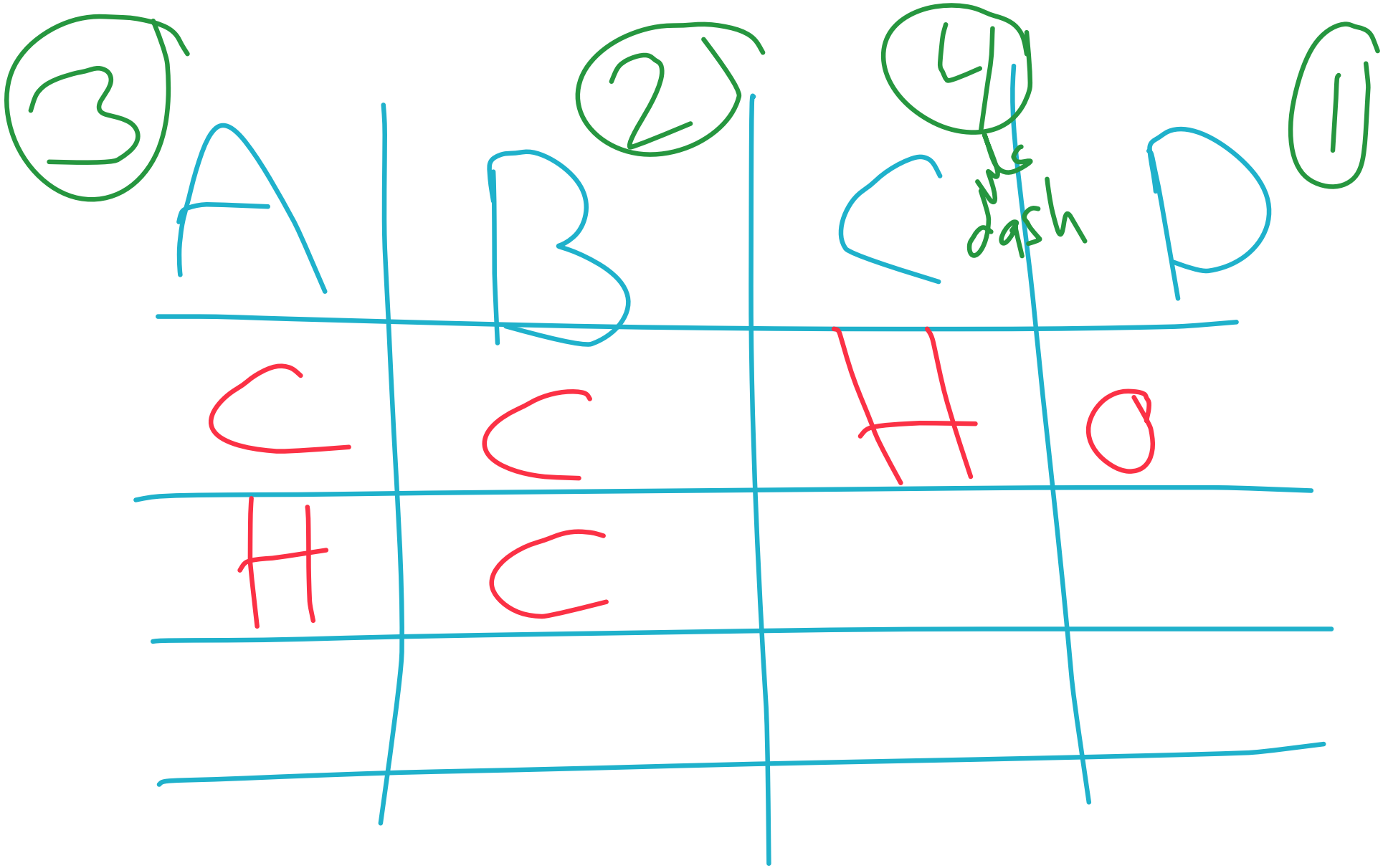


Thus, —CH_3 ⇒ (H, H, H)

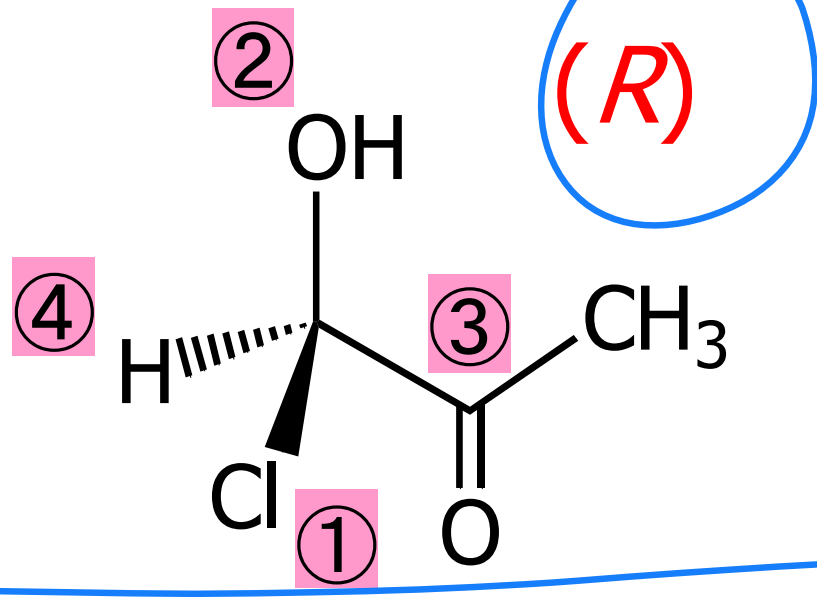
—$CH=CH_2$ ⇒ (C, C, H)

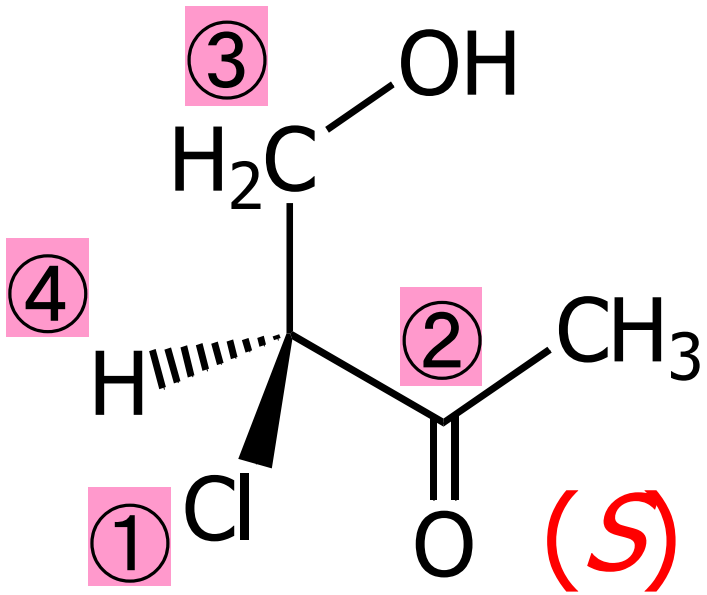
Example (2)




3
2
4
1
A
B
C
D
we dash
C
C
H
O
H
C

❖ Other examples

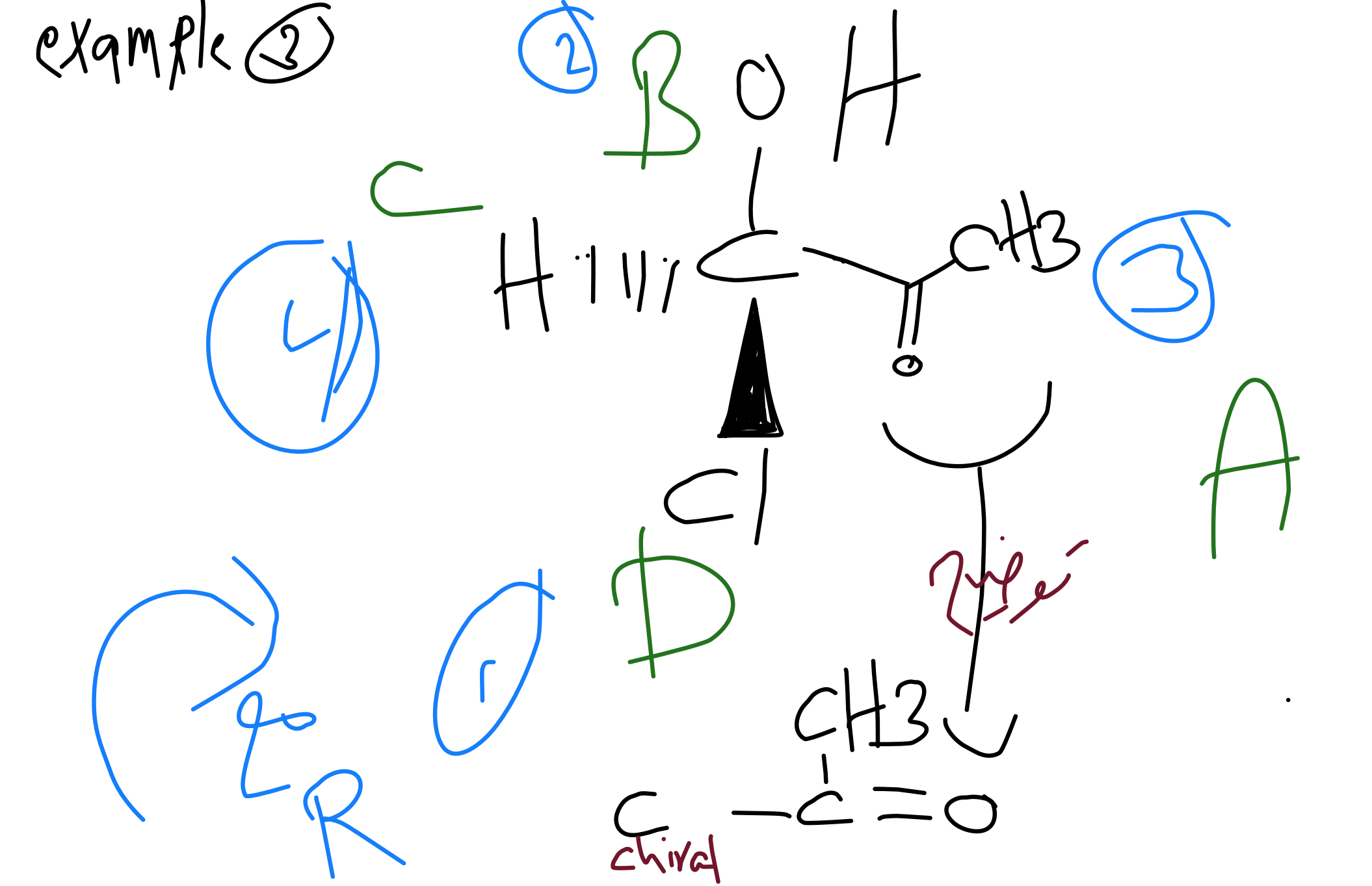


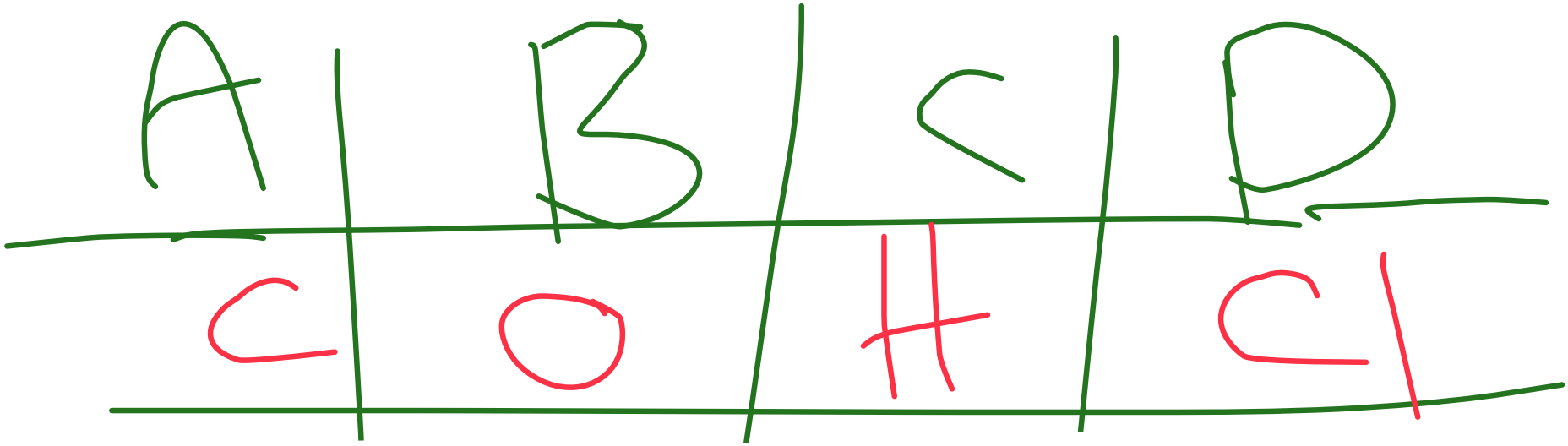


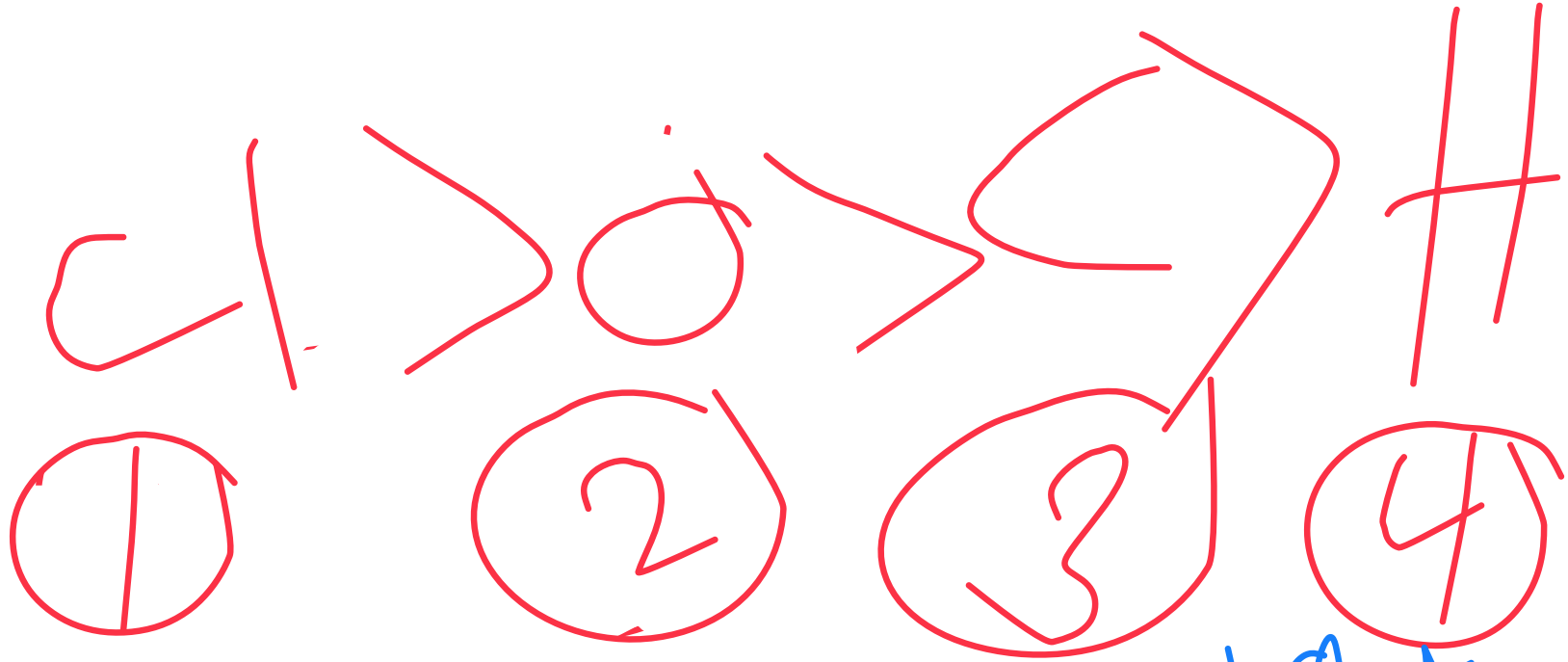
② C ⇒ (O, O, C)

③ C ⇒ (O, H, H)

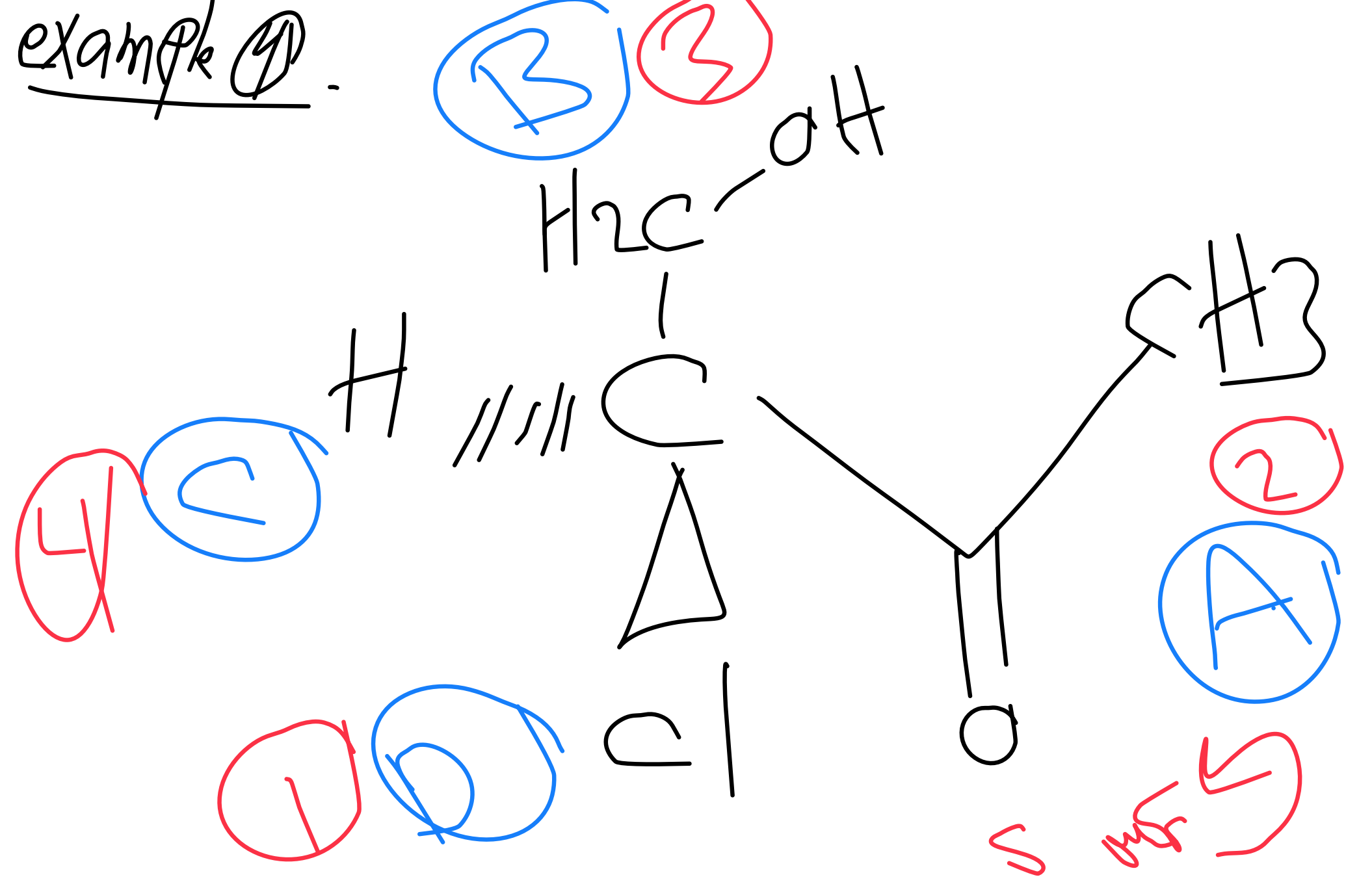
example ②

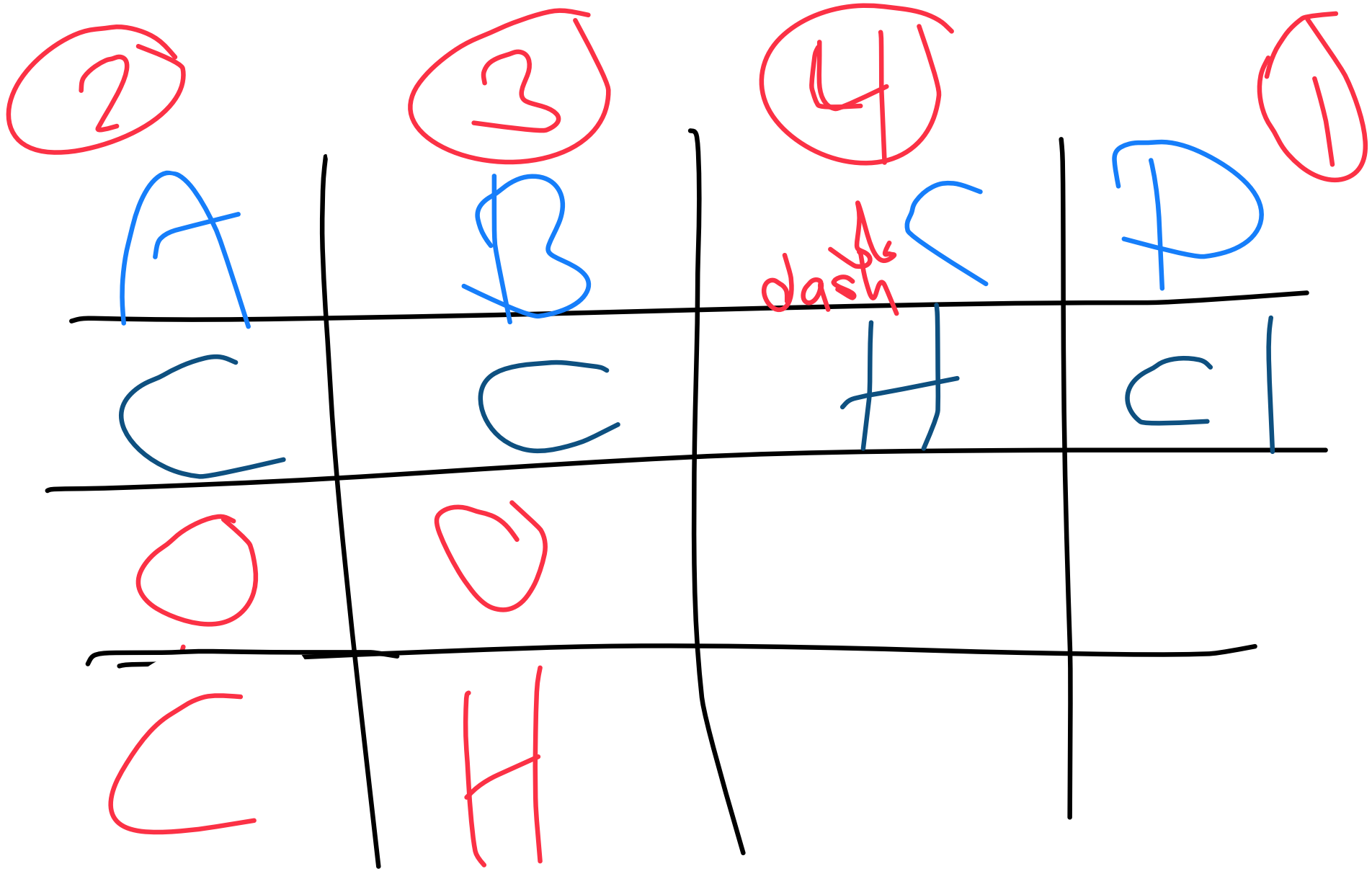



A
B
C
D
C
O
H
Cl

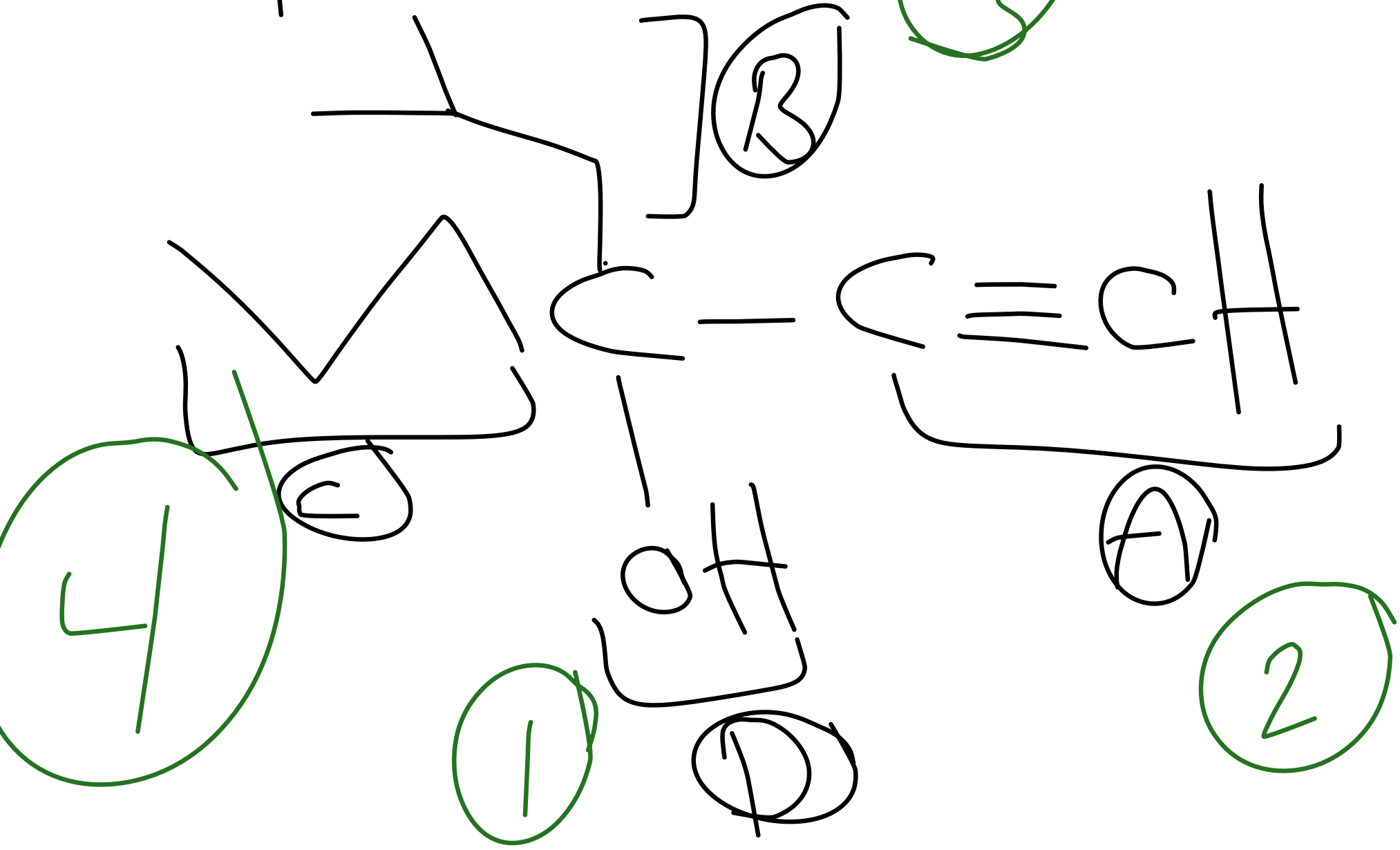

Cl
O
C
H
1
2
3
4

example (1).




2
3
4
1
A
B
dash
C
D
C
C
H
Cl
O
O
C
H

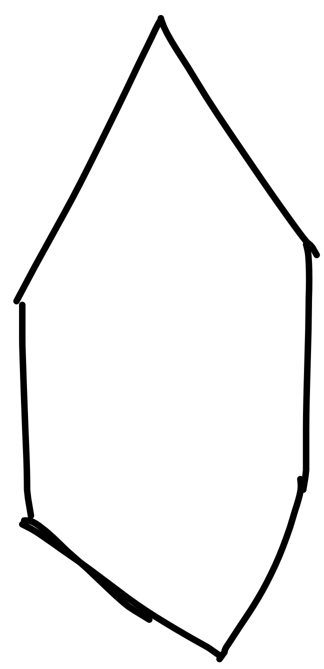
example (5).



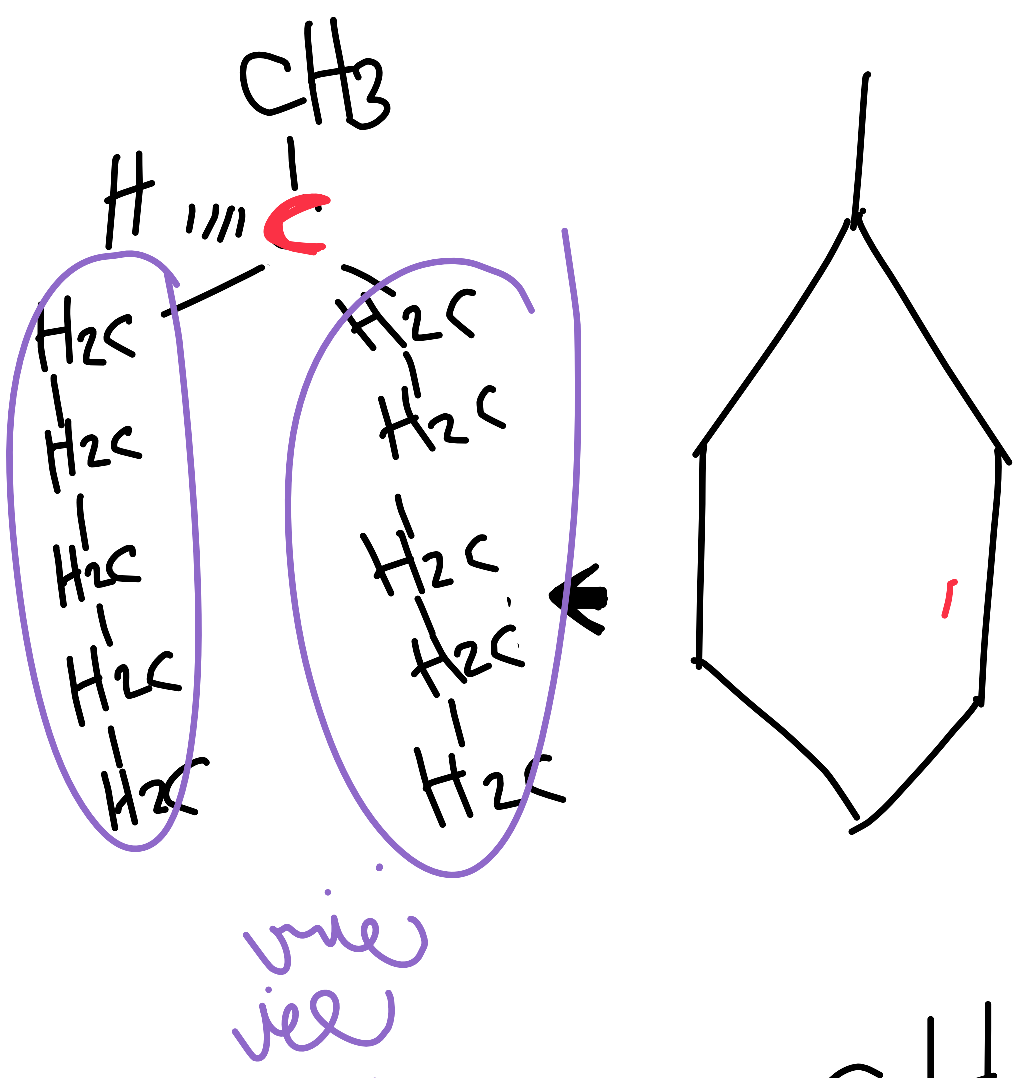
A	B	C	D
C	C	C	O
C	C	C	
C	H	H	
	H	H	
C	C		
C	C		
C	H		

تشابهوا Br
بإزاحة نزولاً على الذرة
المتصلة بالذرة المتصلة بـ
Chiral

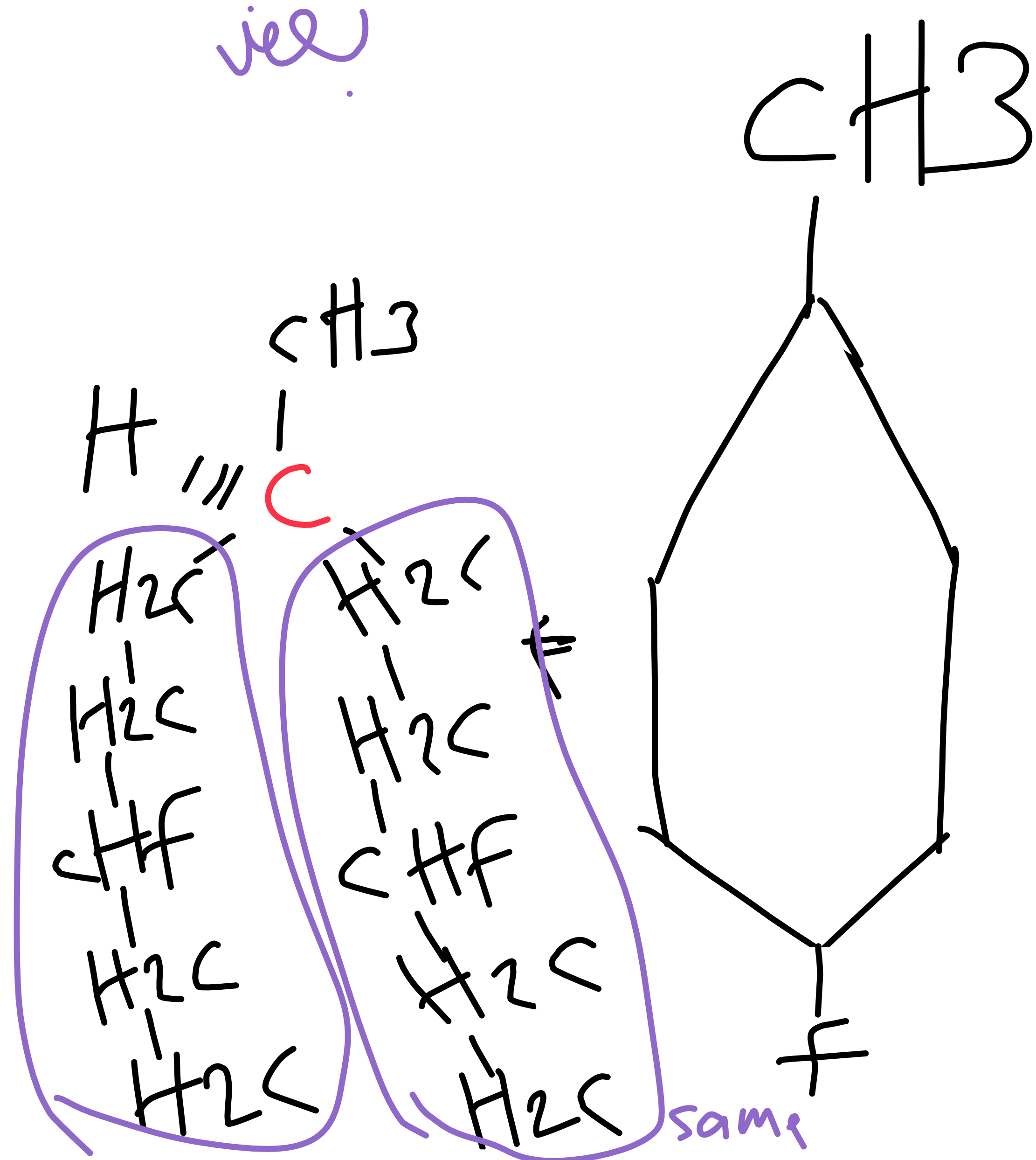
example



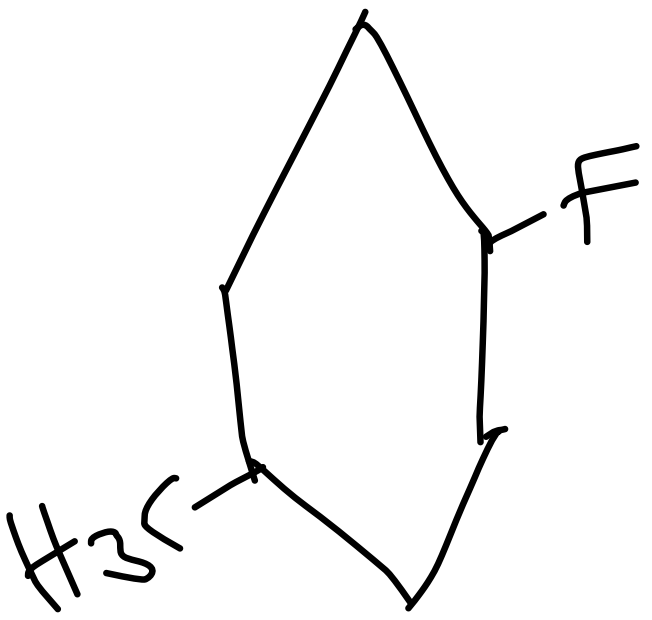
⇒ كل الكربونات يلي هون مش chiral



⟶ كل الكربونات يلي هون achiral مش chiral



⟶ كل الكربونات يلي هون achiral



→ chiral

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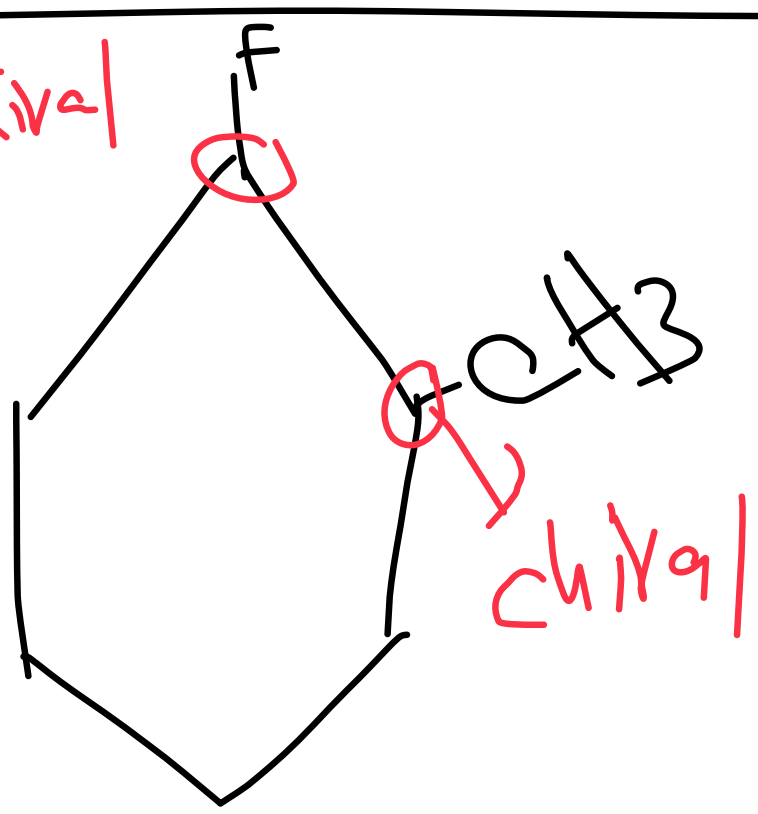
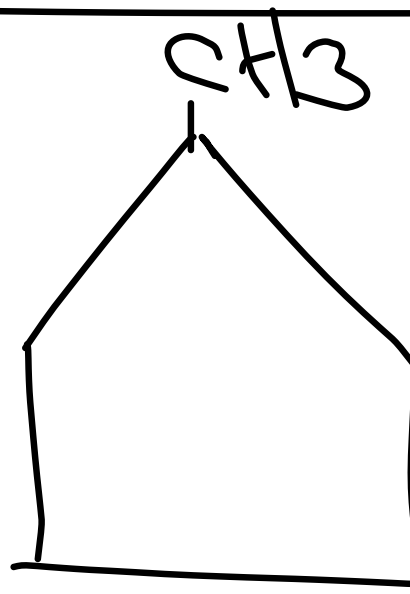
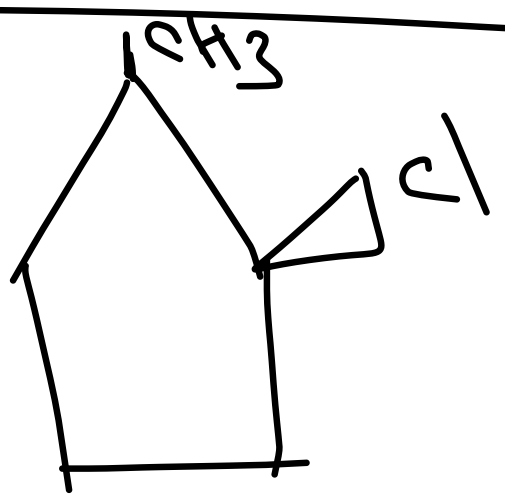
chiral



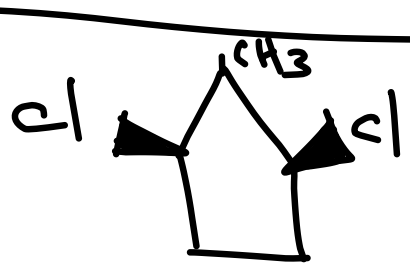
→ chiral



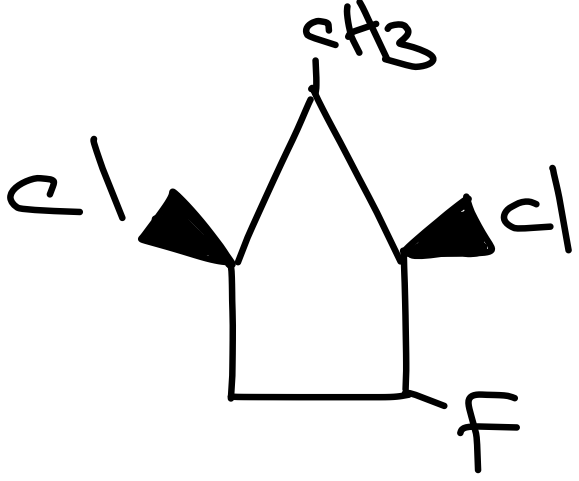
→ chiral



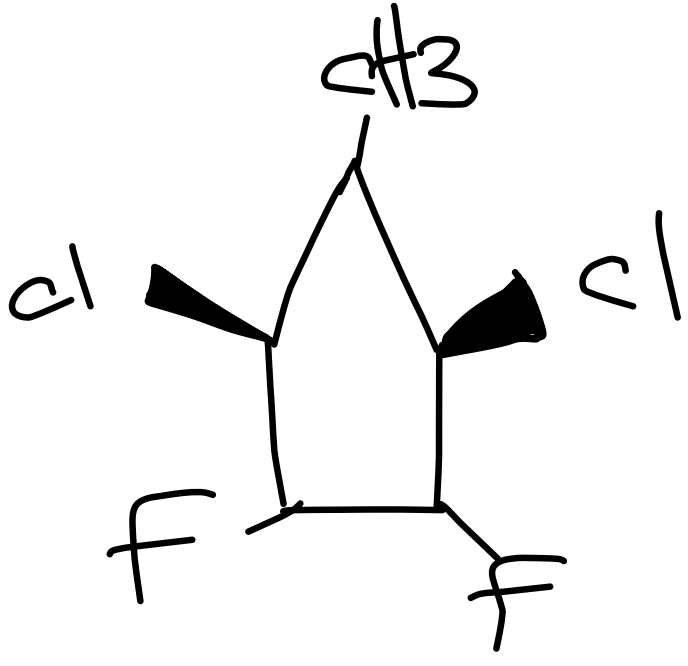
→ chiral



→ chiral



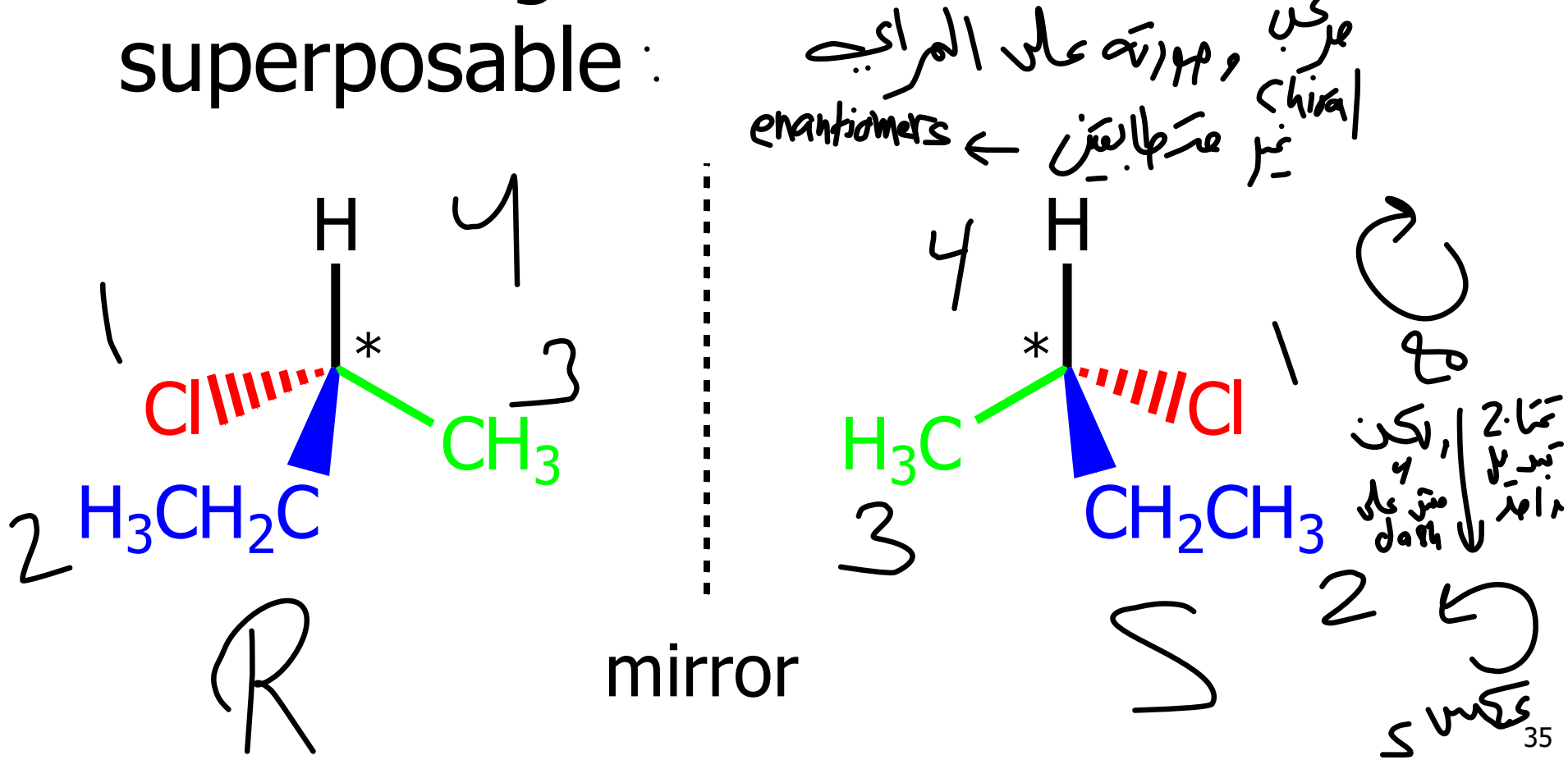
⇏ Chiral



→ Chiral

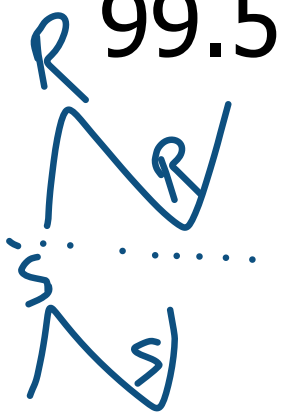
7. Properties of Enantiomers: Optical Activity

- Enantiomers
  - Mirror images that are not superposable :



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

Compound	bp (°C)	mp (°C)
(*R*)-2-Butanol	99.5	
(*S*)-2-Butanol	99.5	
(+)-(*R*,*R*)-Tartaric Acid		168 – 170
(–)-(*S*,*S*)-Tartaric Acid		168 – 170
(+/–)-Tartaric Acid		210 – 212



- Enantiomers
  - 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

اذا الـ R حرك الضوء إلى اليمين الـ S بحركة لليسار.
اذا الـ S حرك الضوء إلى اليمين الـ R بحركة لليسار.

❖ Optical activity

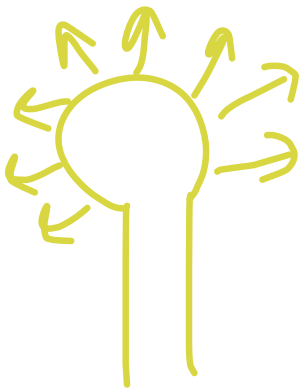
- The property possessed by chiral substances of rotating the plane of polarization of plane-polarized light

optical activity
⇓
خاصية عند مرور الضوء
R chiral بمركب
أو S لحزء الضوء
بزاوية.

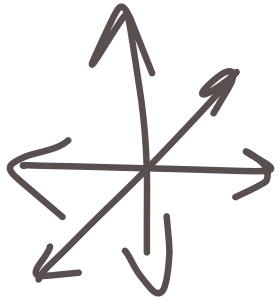
R and S
same → physical properties
↳ chemical properties

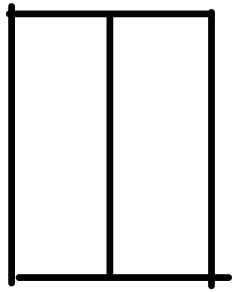
different → rxn with chiral substances.
↳ plan-polarized light rotation.

Polarization of plane polarized light



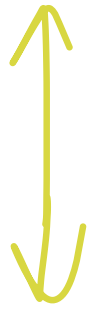
ضوء



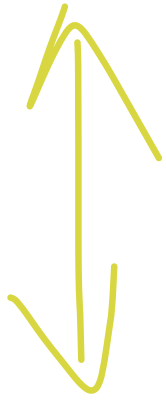


Polarizer device

عبارة عن لوح لونه
أسود ما يمرر الضوء
داله فتحة، فلما أمرر
الضوء منه يخرج أجبره يتحرك
باتجاه واحد.



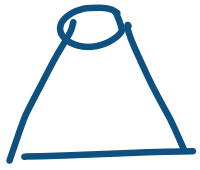
(plan-polarized light)



(Plan-Polarized light)

(PPL)

optically active



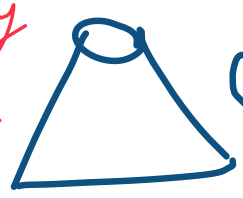
(1) R

الزاوية اليسار أو الزاوية اليمين

يؤثر على (2)

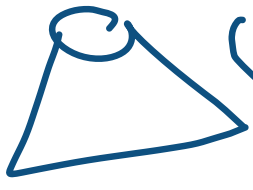
4 solutions

optically active



(2) S

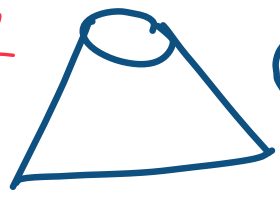
not optically active



(3) achiral

Same

not optically active

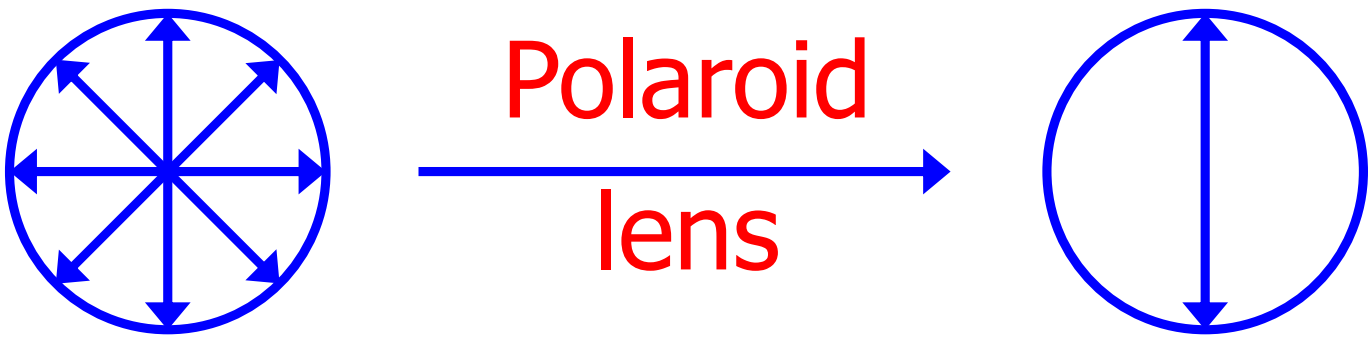


(4) Racul S

Same

7A. Plane-Polarized Light

- 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 (Polaroid lens)

- A device for measuring the optical activity of a chiral compound

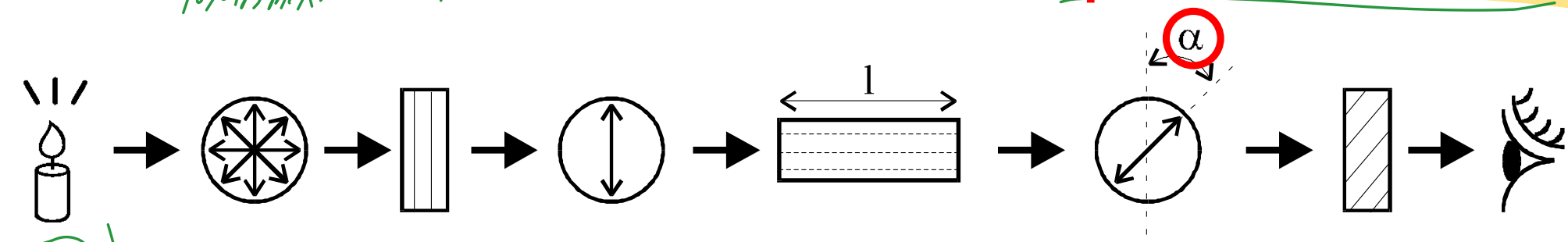
optical activity

جهاز يقيس قدرة المركب على خاصية

صرفا الضوء بزاوية

عند تمريره من Polarimeter

α = observed optical rotation



يلف بكل الاتجاهات

جهاز لا يمرر الضوء إلا من فتحة واحدة

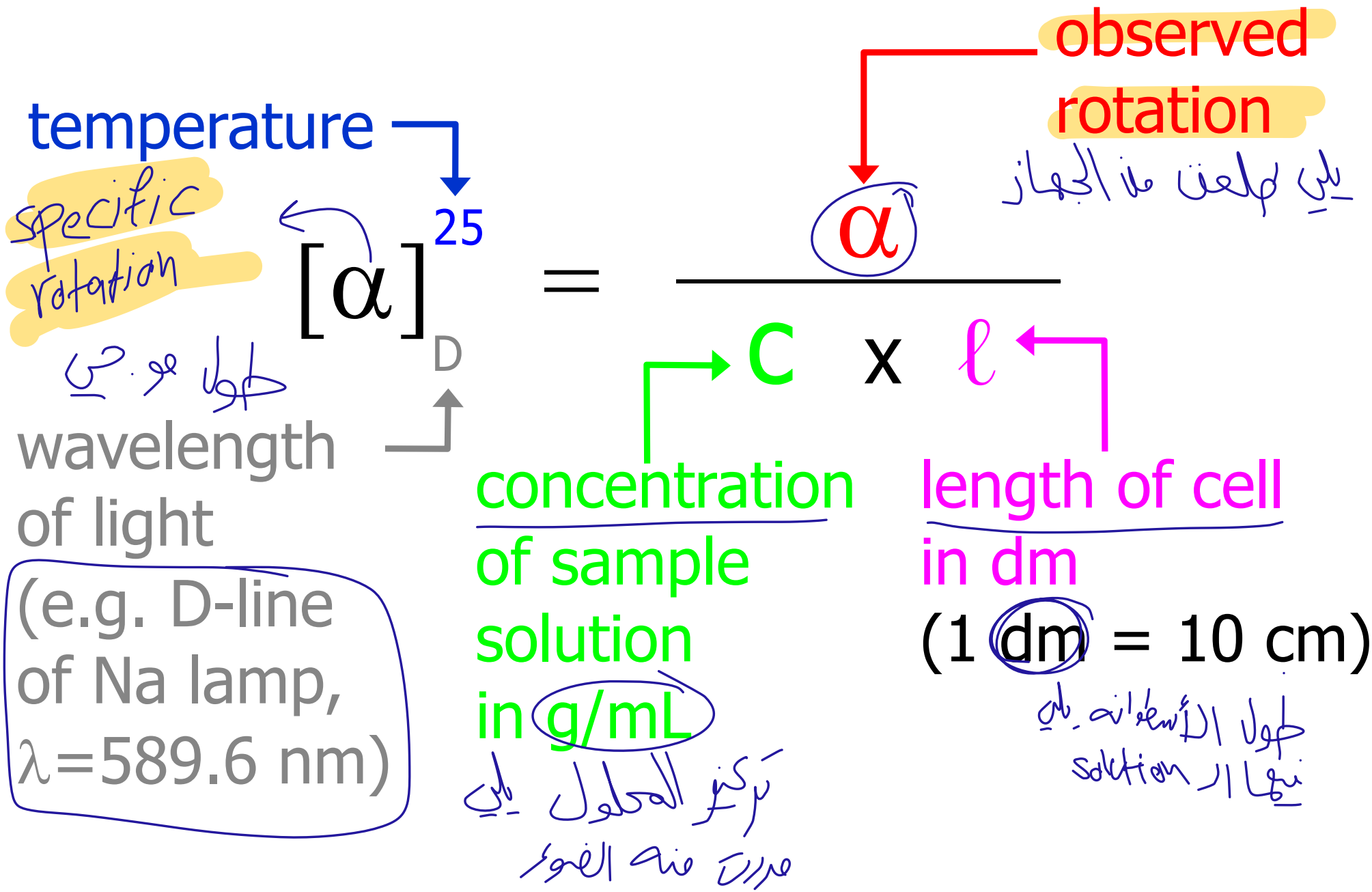
أجبرنا الضوء على المرور بـ Just one plane

محلول المركب الكايرال سواء R أو S

أدار الضوء بزاوية (Optical active)

جهاز تقليل عشان نتحكم كم يا الضبط

7C. Specific Rotation



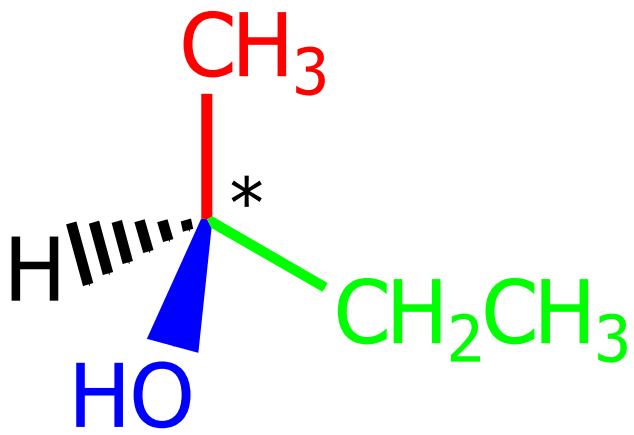
observed rotation

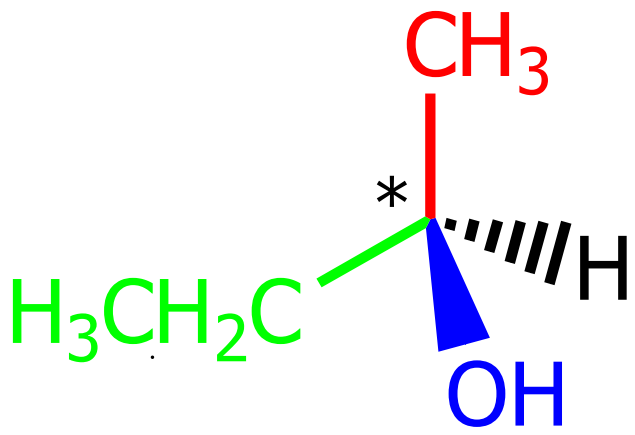
- The value of α depends on the particular experiment (since there are different concentrations with each run)
  - But specific rotation $[\alpha]$ should be the same regardless of the concentration

α : observed rotation ⇒ - Depend on the Particular exp.
- Change with different concentrations.

$[\alpha]$: specific rotation ⇒ - doesn't change with different concentrations.

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



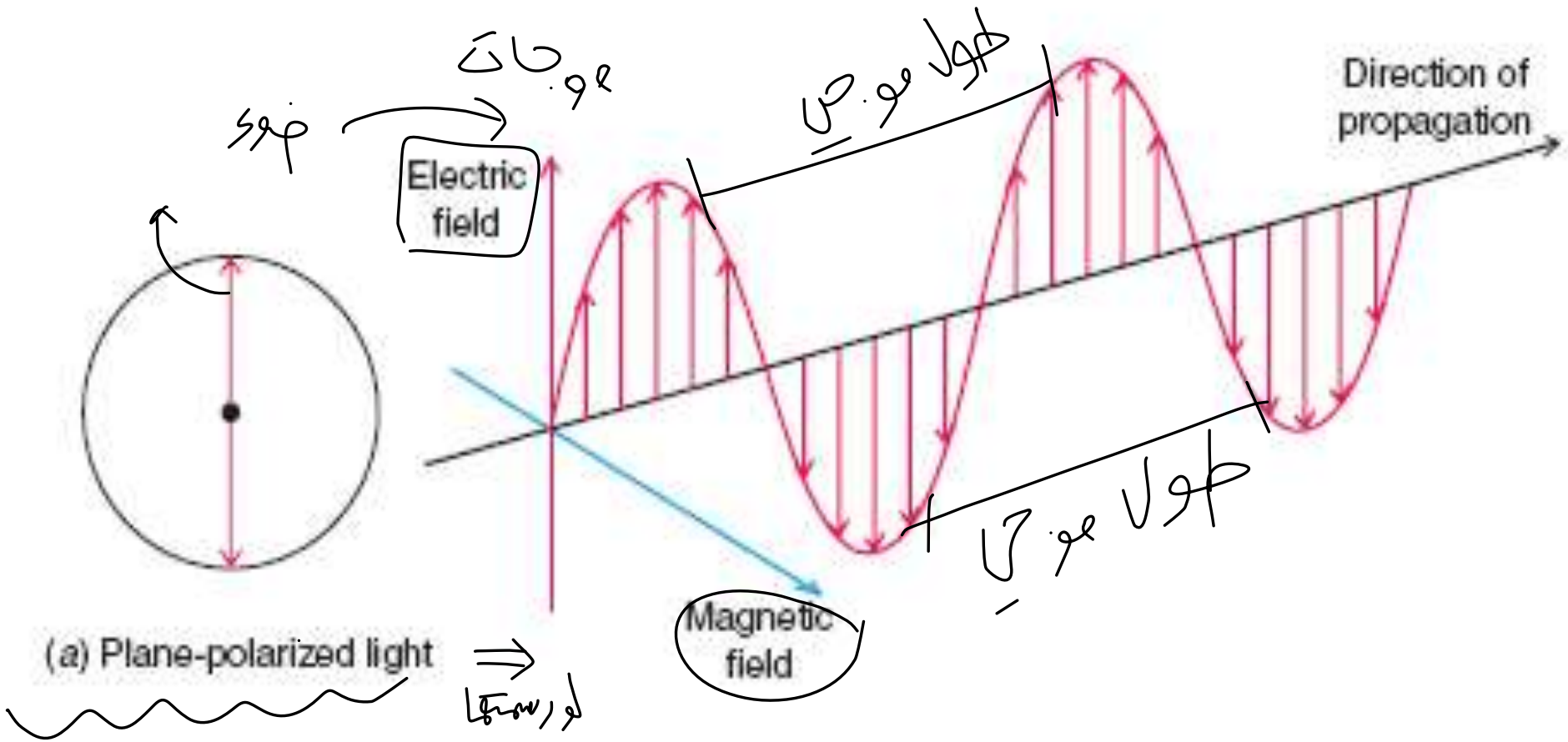


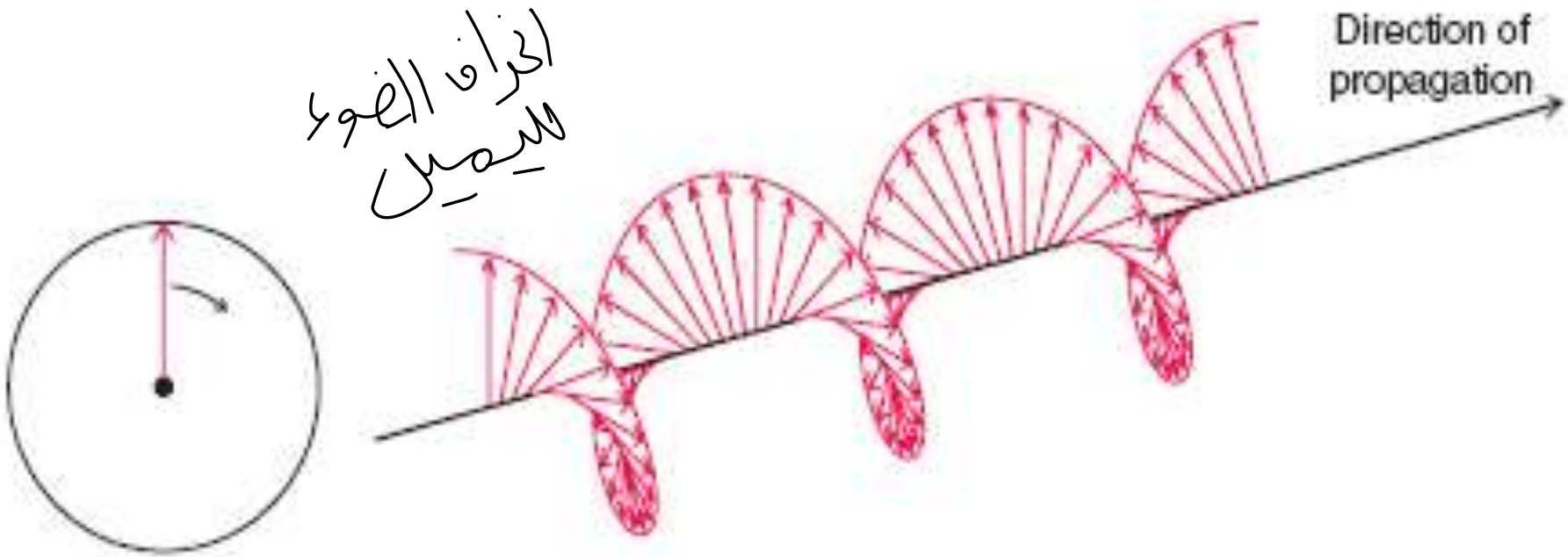
$[\alpha]_D^{25} = +13.5^o$ mirror $[\alpha]_D^{25} = -13.5^o$

enantiomers ↱ same ↳ different

$[\alpha]_D^{25}$ → ...

8. The Origin of Optical Activity



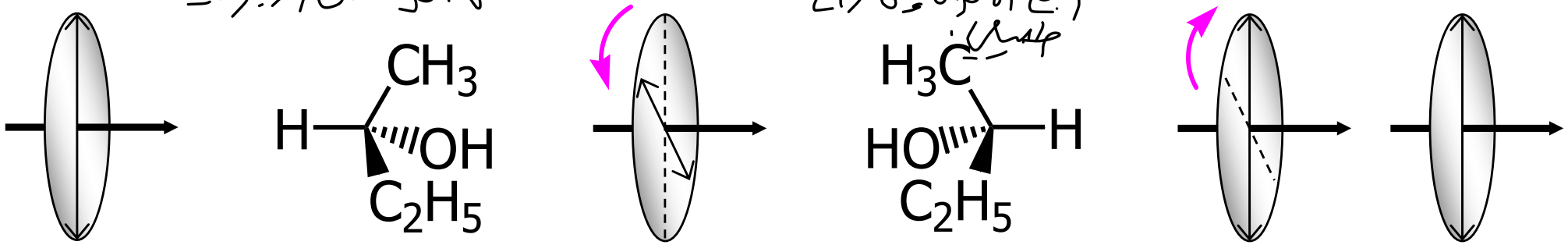

انكسار الضوء
بالسيمبل
Direction of
propagation

8A. Racemic Forms

(50% R + 50% S) racemic or racemate

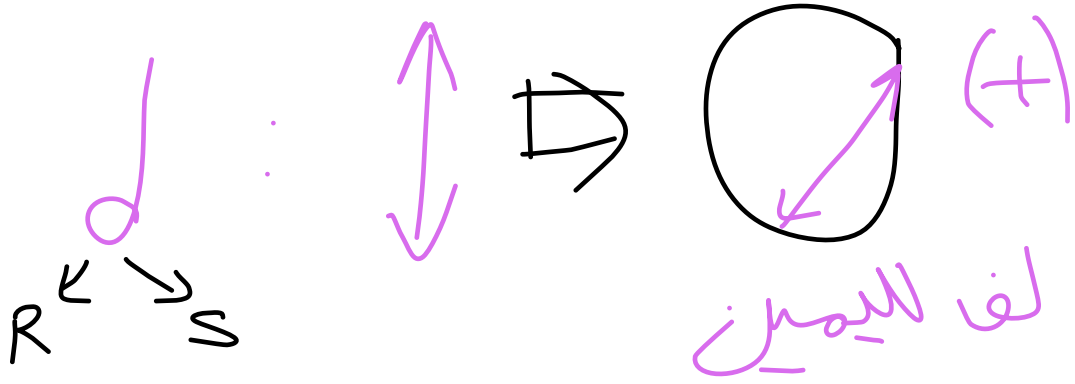
- An equimolar mixture of two enantiomers is called a racemic mixture (or *racemate* or *racemic form*)
- A racemic mixture causes no net rotation of plane-polarized light

(الانزياح بالضوء not optically active)

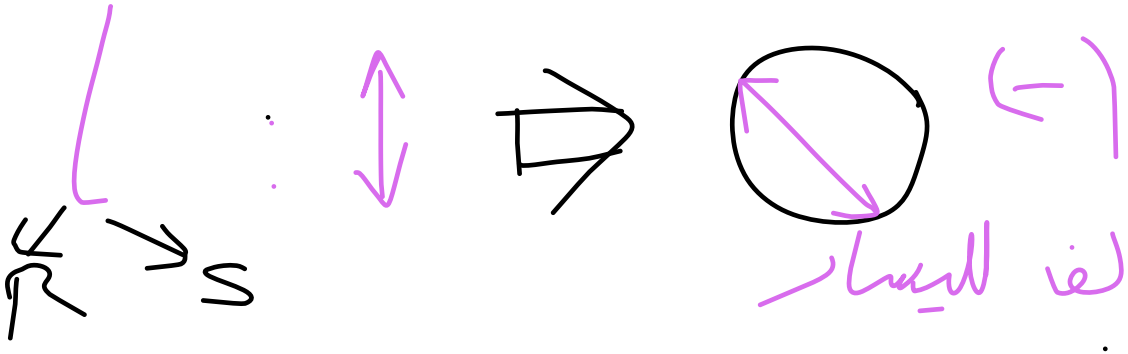


(R)-2-Butanol

(S)-2-Butanol (if present)



d (dextro) : لليمين
(+)



l (levo) : لليسار
(−)

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

$$[\alpha]_D^{25} = +13.52$$

- 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 $0 < [\alpha]_D^{25} < +13.52$
- Such a sample is said to have an *enantiomeric excess* less than 100%

الحالة الأولى

Sample

%100 S

$[\alpha]_D^{25} = +13.52$

نضيف R تشويه لل Sample

⇓

%90 S (+)

%10 R (−)

$0 < [\alpha]_D^{25} < +13.5$

2) يقل

لأنه نضيف سالب

لحد ال zero

الحالة الثانية

Sample

%100 R

رقم افتراضي

$[\alpha]_D^{25} = -13.52$

نضيف تشويه S

⇓

%90 R (−)

%10 S (+)

2) تكبر $[\alpha]_D^{25}$ تزداد لحد ال zero

الحالة الثالثة

Sample

%50 R

%50 S

عند ال

zero

❖ Enantiomeric excess (ee)

- Also known as the optical purity

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

- Can be calculated from optical rotations

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

❖ Example

$[\alpha]_D^{25}$ of S-(+)-2-butanol = +13.52

- A mixture of the 2-butanol enantiomers showed a specific rotation of +6.76. The enantiomeric excess of the (S)-(+)-2-butanol is 50%

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

example ①

Mix → 2-butanol (S) + 2-butanol (R) →

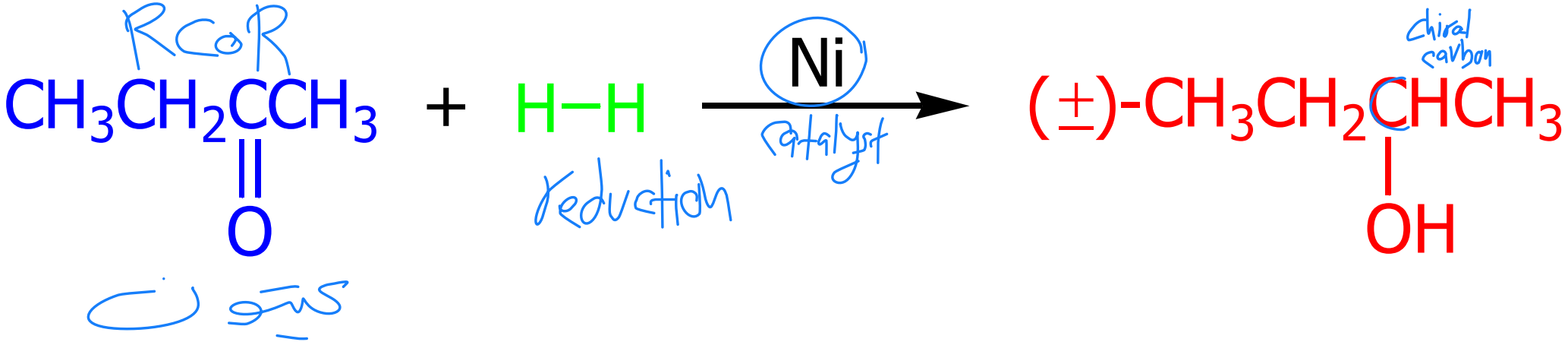
Specific rotation = +6.76

% enantiomeric excess * = $\frac{\text{Specific rotation}}{\text{specific rotation of pure enantiomers}} * 100\%$

$= \frac{6.76}{13.52} * 100\% = 50\%$

9. The Synthesis of Chiral Molecules

9A. Racemic Forms



Butanone (achiral molecules)

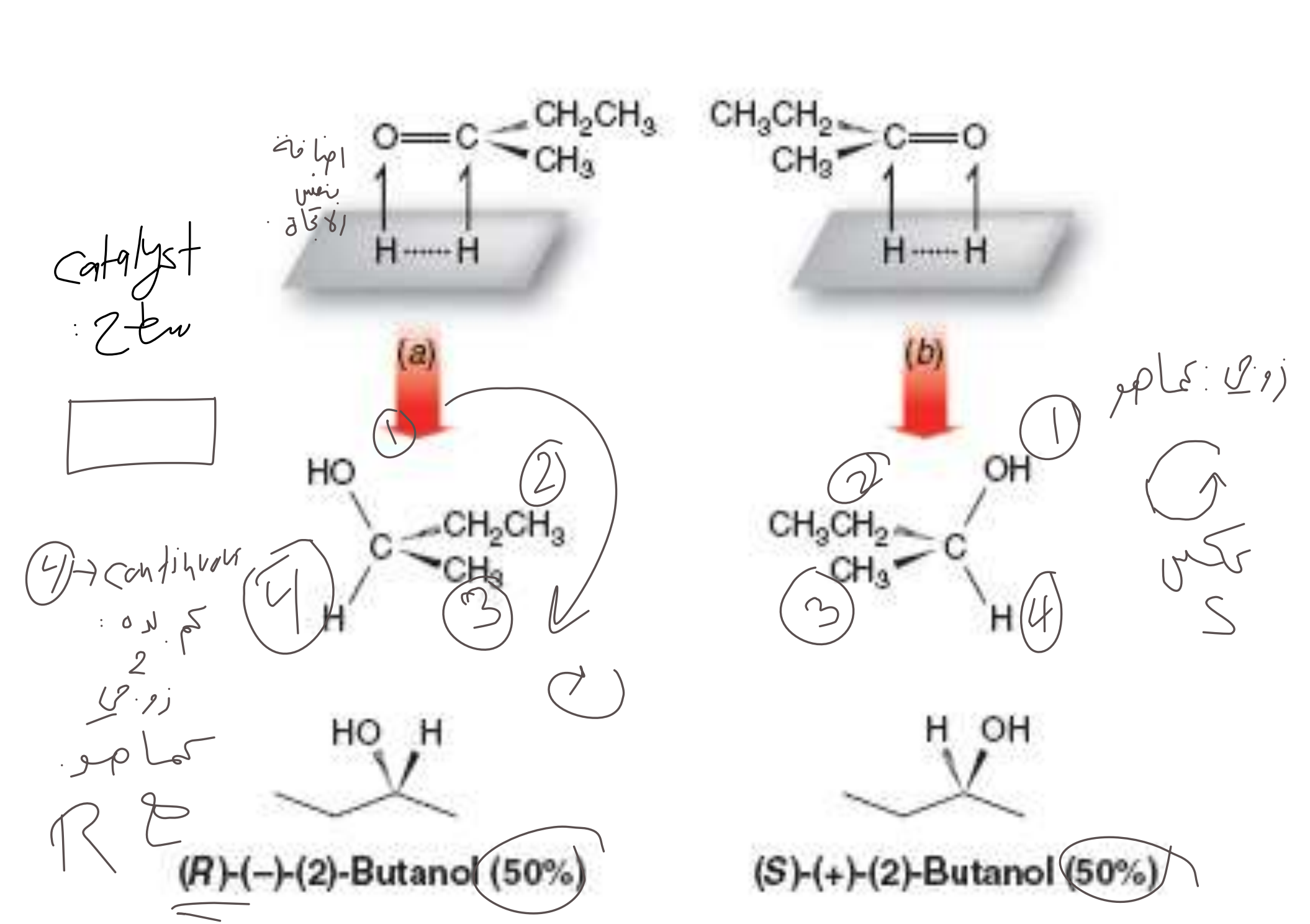
Hydrogen (achiral molecules)

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

achiral molecule + achiral molecule → chiral molecule mix (R+S) (not optically active)

polymer

(Racemix) (Racemate)


catalyst
(a)
(b)
(R)-(−)-(2)-Butanol (50%)
(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

(Stereoselective)

$$A \longrightarrow \underset{\%90}{B} + \underset{\%10}{C}$$

$$\underset{\%100}{B} + \underset{\%0}{C}$$

① أول شرط: المركب يعطيني ناتجين بأي كمية

(enantio selective) أكبر من الثانية

② ثاني شرط: ومكونات

steroisomers بينهم relation

(diastereoselective)

Example

مثال

Stereoselective

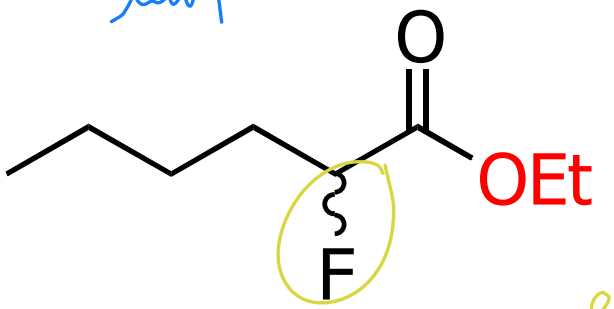
لا يعد

حمض كربوكسيلي

٥٠٪

كحول

٥٠٪



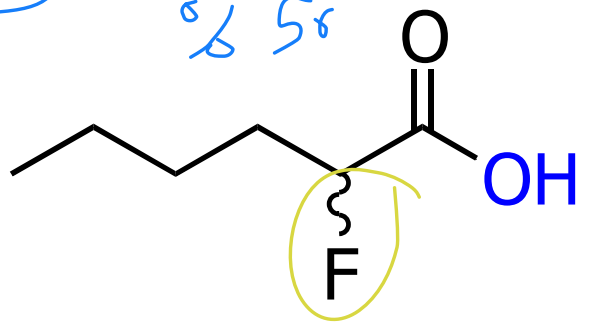
racemate (±)

٥٠٪ R : ٥٠٪ S

H^+, H_2O

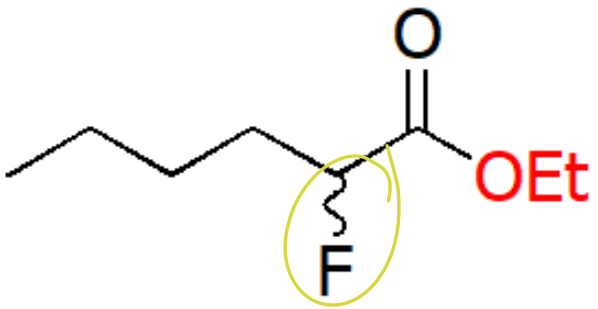
heat

ما تغيرت ال chiral carbon



+ EtOH

racemate (±)



racemate (±)

٥٠٪ R

٥٠٪ S

H_2O

lipase

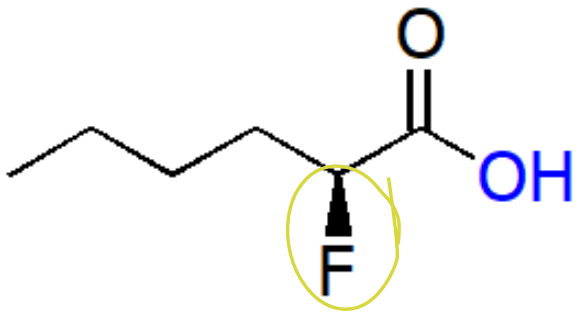
enantiomer يحب يشتغل على أكثر من الثاني

لهذا

Stereoselective

لأن

chiral ال تغيرت carbon



+ EtOH

(–)

(> 69% ee)

(–) > (+)

٦٩٪ ٣١٪

10. Molecules with More than One Chirality Center

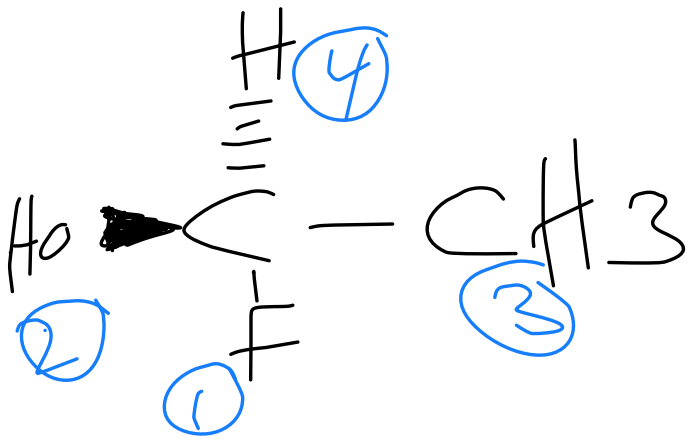
Diastereomers

- Stereoisomers that are not enantiomers
- Unlike enantiomers, diastereomers usually have substantially different chemical and physical properties

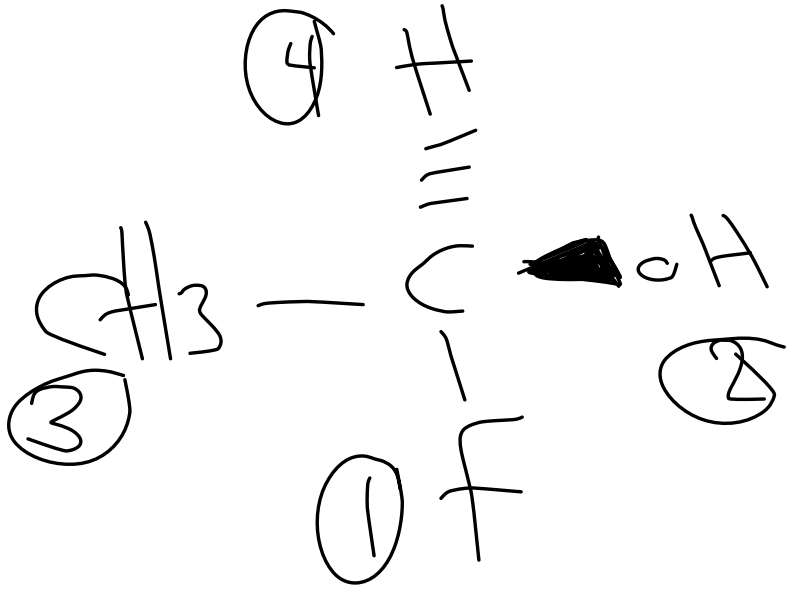
* نلاحظ لما يكون عندنا مركب فيه two chiral centers أو أكثر، أو ضد الـ mirror image ما يكسم كلهم ⇐ enantiomers

لما يكون عندنا مركب فيه two chiral centers أو أكثر، أو ضد الـ mirror image ما يكسم الكل ⇐ diastereomers

example ①



mirror



to

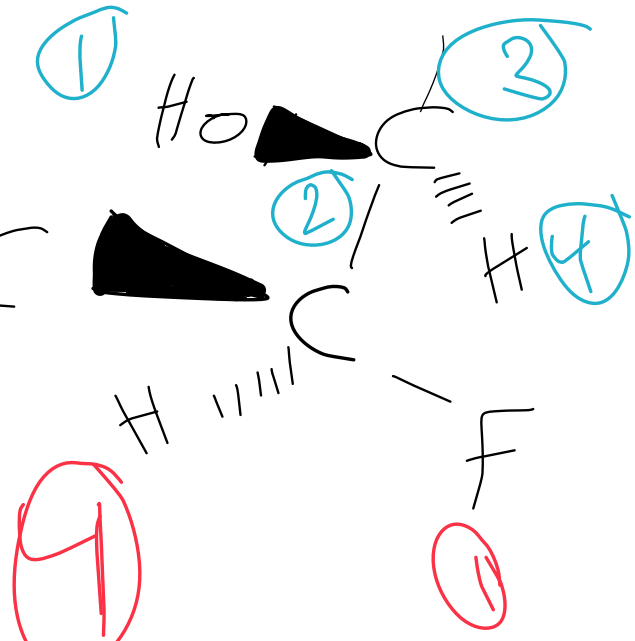
R

enantiomers

S

example (2)

(A)



(B)

(2S,3R)- 3-floro - 2 - butanol

(2R,3S)-3-floro-2-butanol

A, B ⟹ diastoroisomers


S
R
R
S
S
R
A
enantiomers
B

Compound

two Chiral centers

یک‌توی

S,S → | R,R — enantiomers

R,R → | S,S — enantiomers

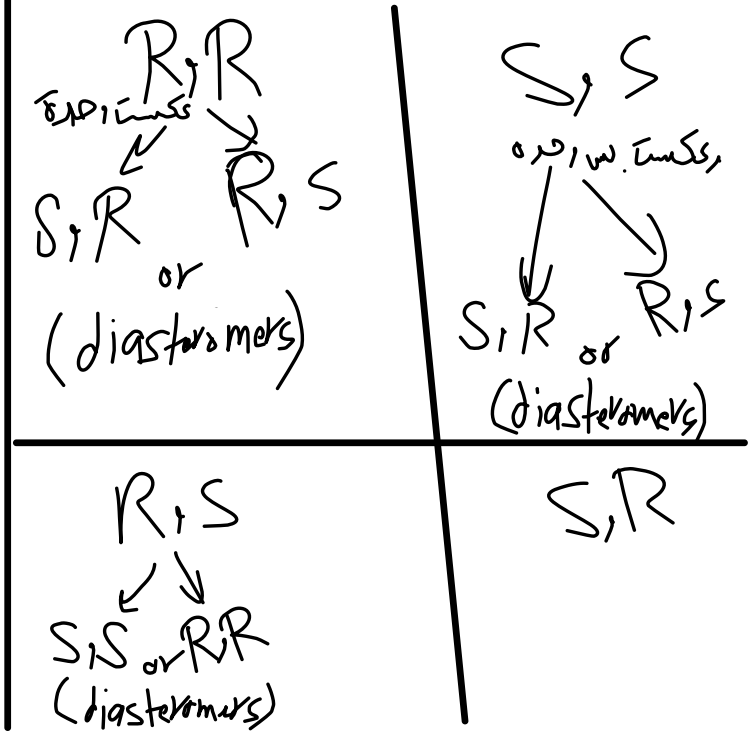
S,R → | R,S — enantiomers

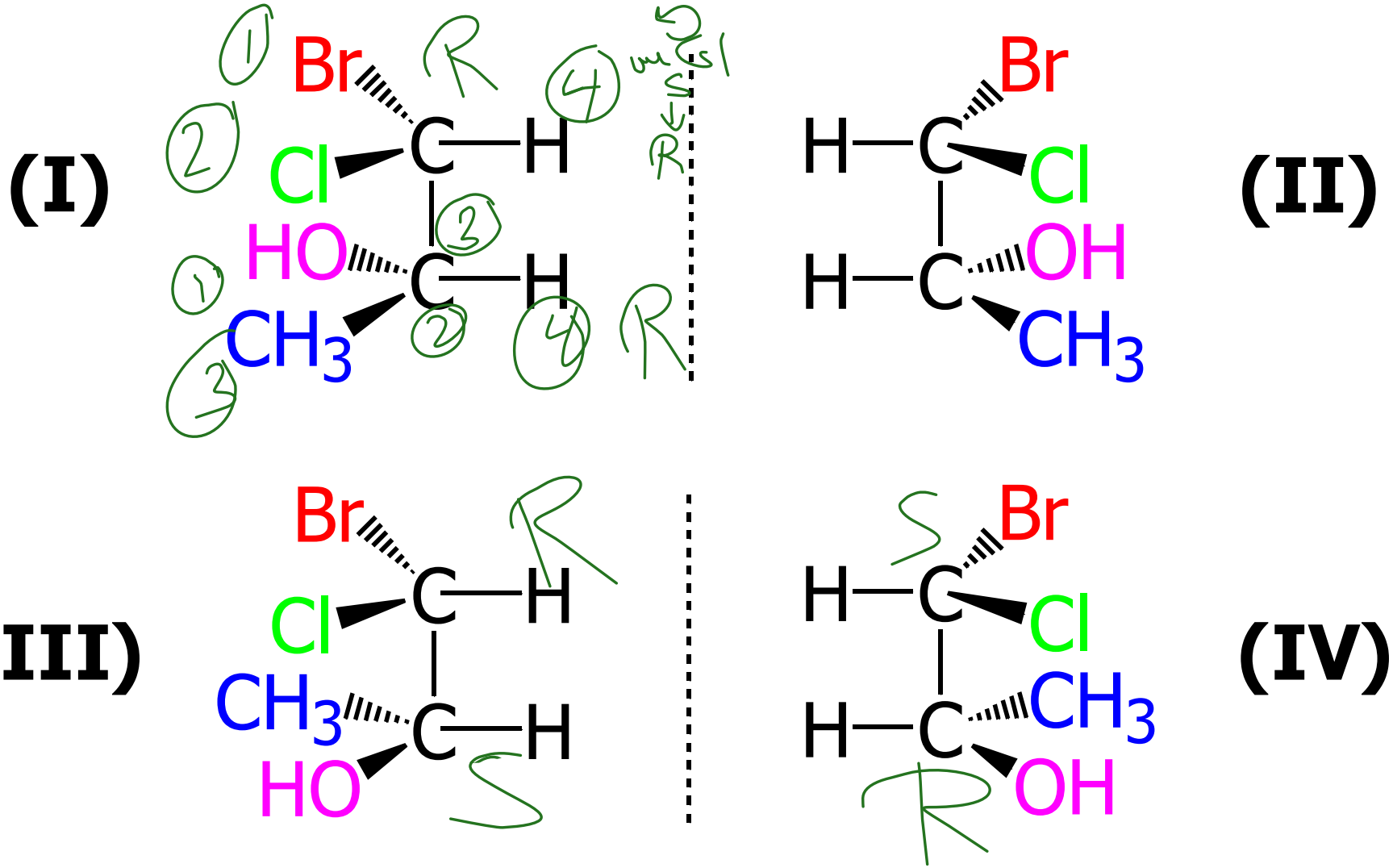
R,S → | S,R — enantiomer

Compound

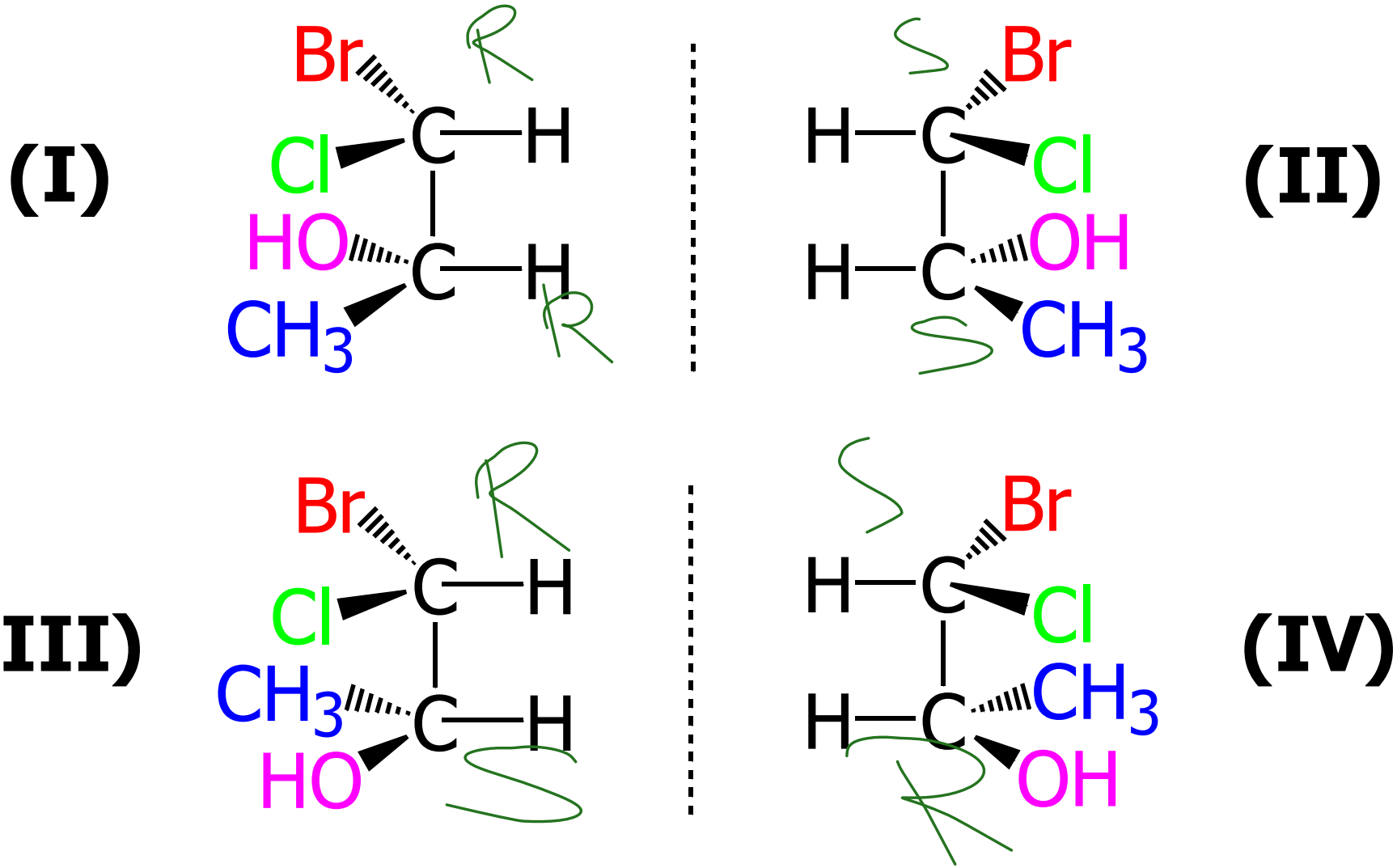
two Chiral centers

یک‌توی



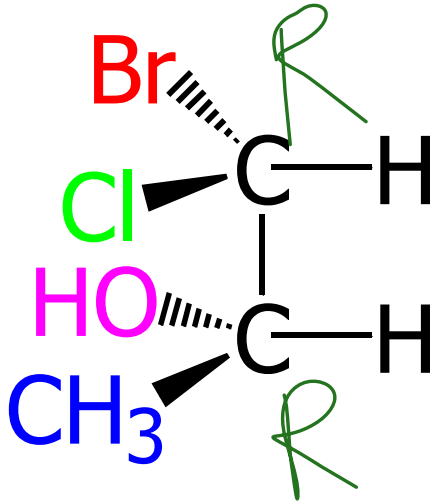


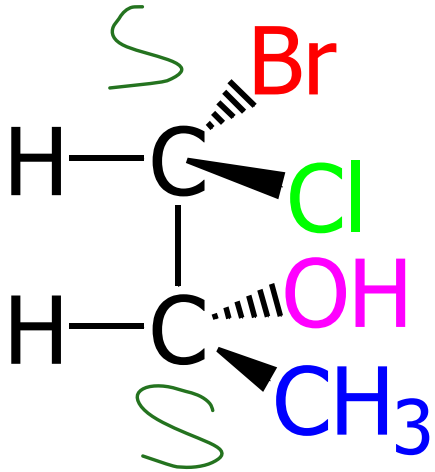
Note: In compounds with *n* tetrahedral stereocenters, the maximum number of stereoisomers is 2^n.



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

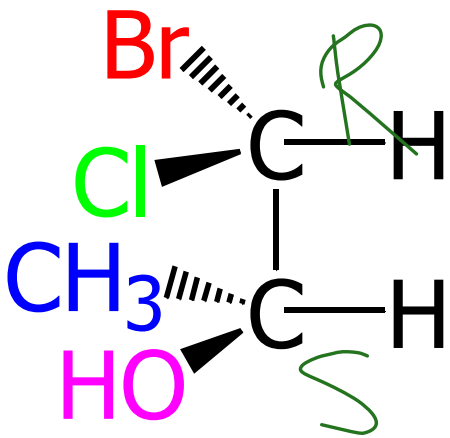
(I)

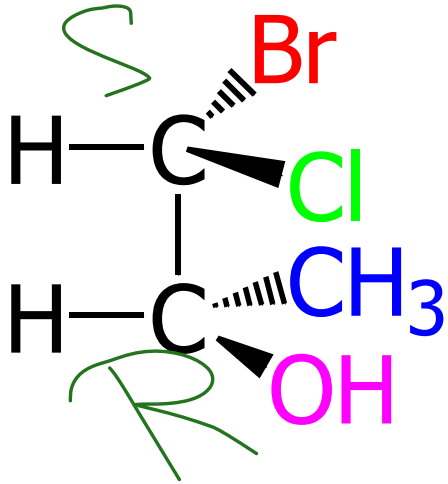




(II)

(III)



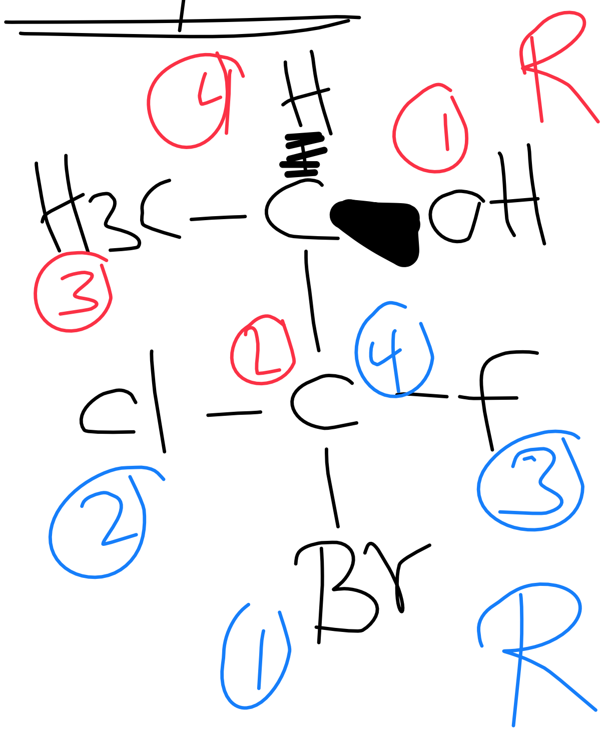


(IV)

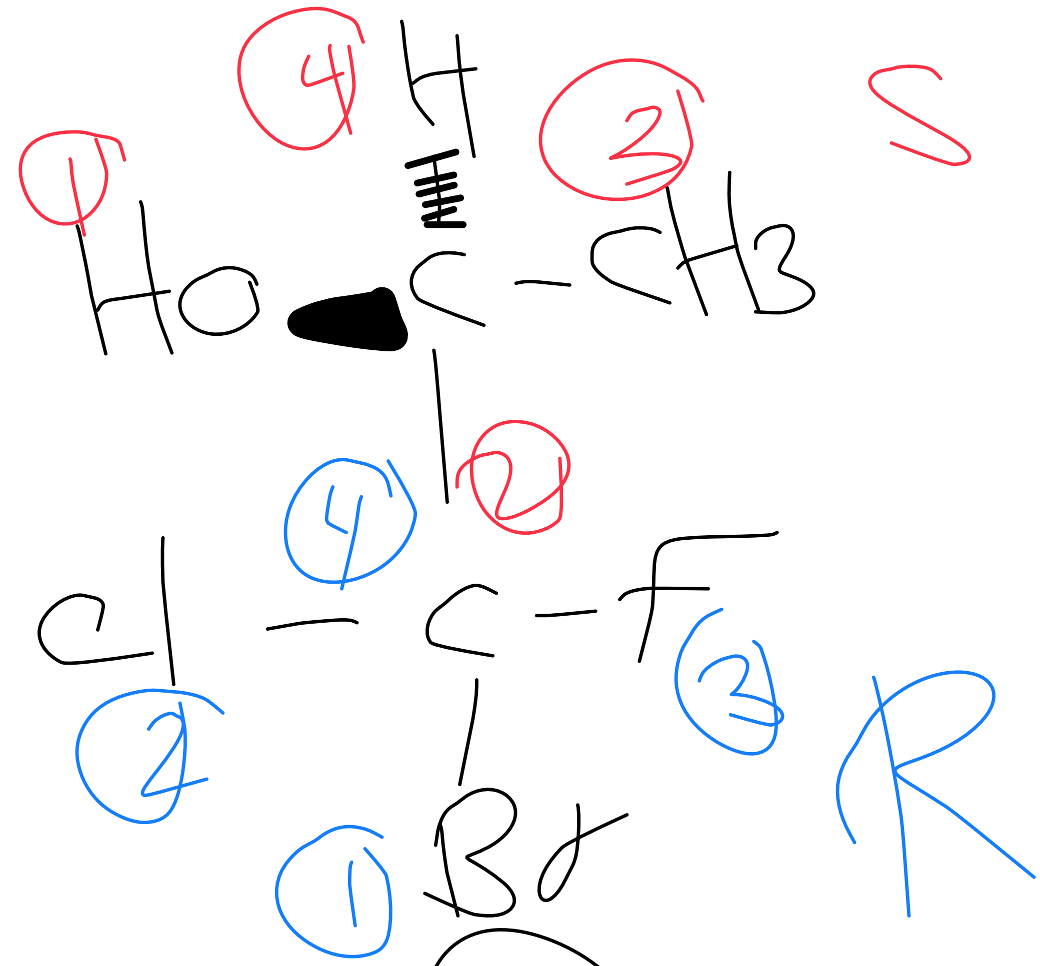
❖ Diastereomers to each other:

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

examples



A



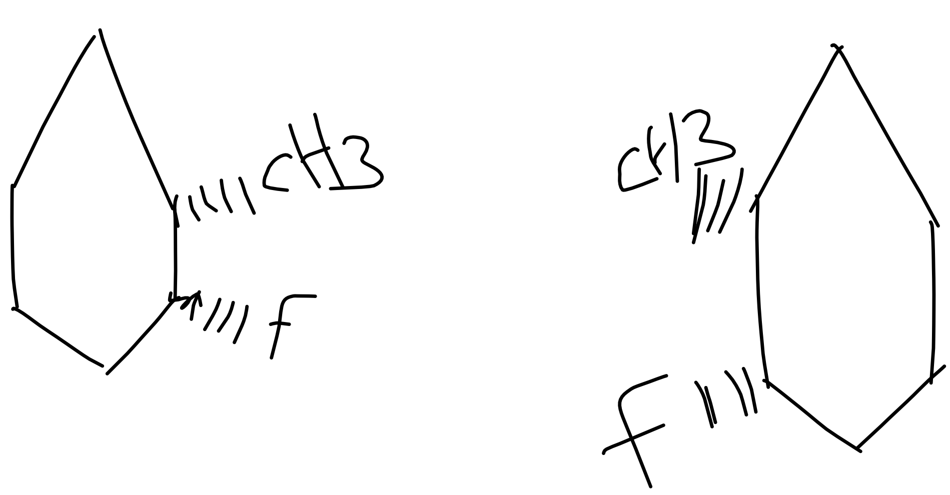
B

شو العلاقة بين A and B :

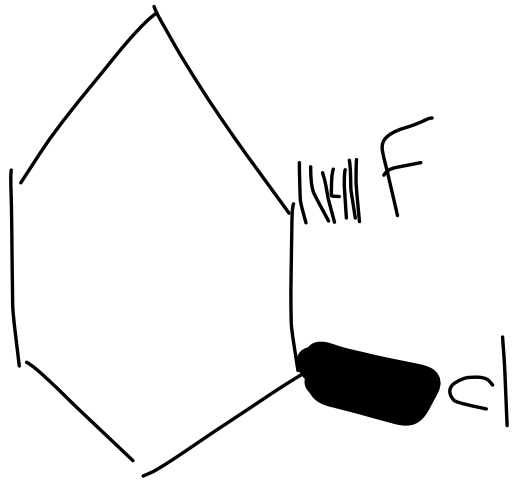
R , R
↓
S , R → diastereoisomers

---

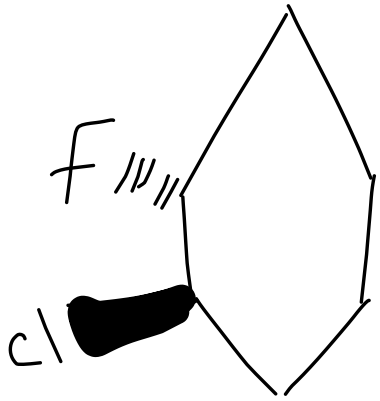
example



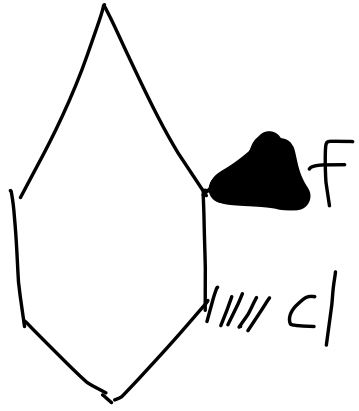
enantiomers ← مجسمين صورة مرآة



A



B



C

A + B → enantiomers

A + C → enantiomers

B , C
Same
Compound
بس مقلوب

10A. Meso Compounds

- 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)

$2^n - 1 = 2^2 - 1 = 3$

[meso R,S
و
meso S,R
نفس المركب]

Meso compound

- → 2 chiral centers
- → عالطرفين نفس التفرعات
- → واحد R والثاني S

→ meso:

فيه chiral centers على الأقل 2، ولكنه يعتبر achiral

وهو not optically active

achiral ... —

enantiomers ... chiral ... achiral ...

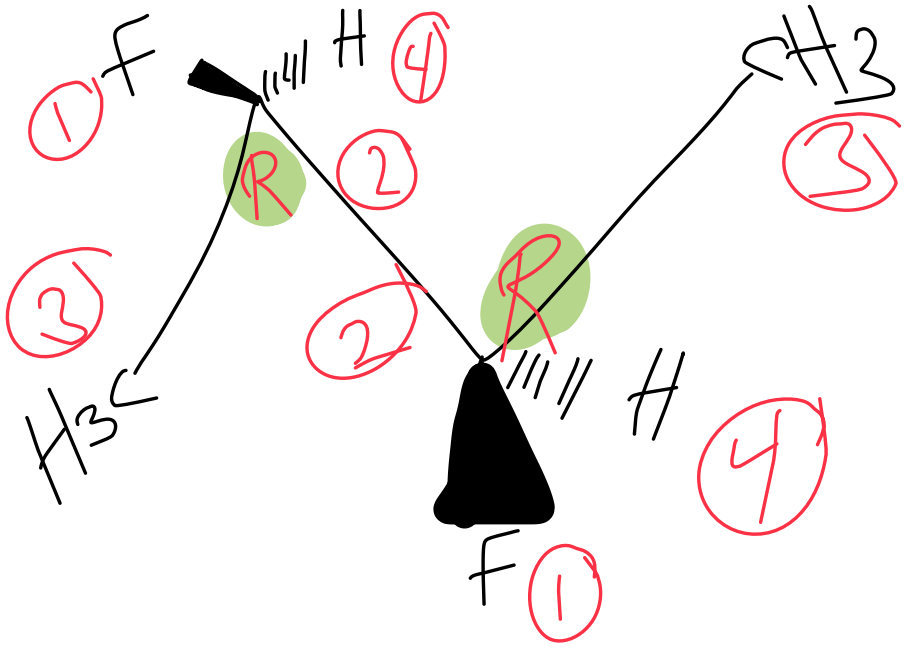
$2^n - 1$ ← ... same compound [meso S,R = meso R,S] —

diastereoisomers ← [R,R ... meso R,S] ...

diastereoisomers ← [R,R ... meso S,R] ...

diastereoisomers ← [S,S ... meso R,S] ...

diastereoisomers ← [S,S ... meso S,R] ...

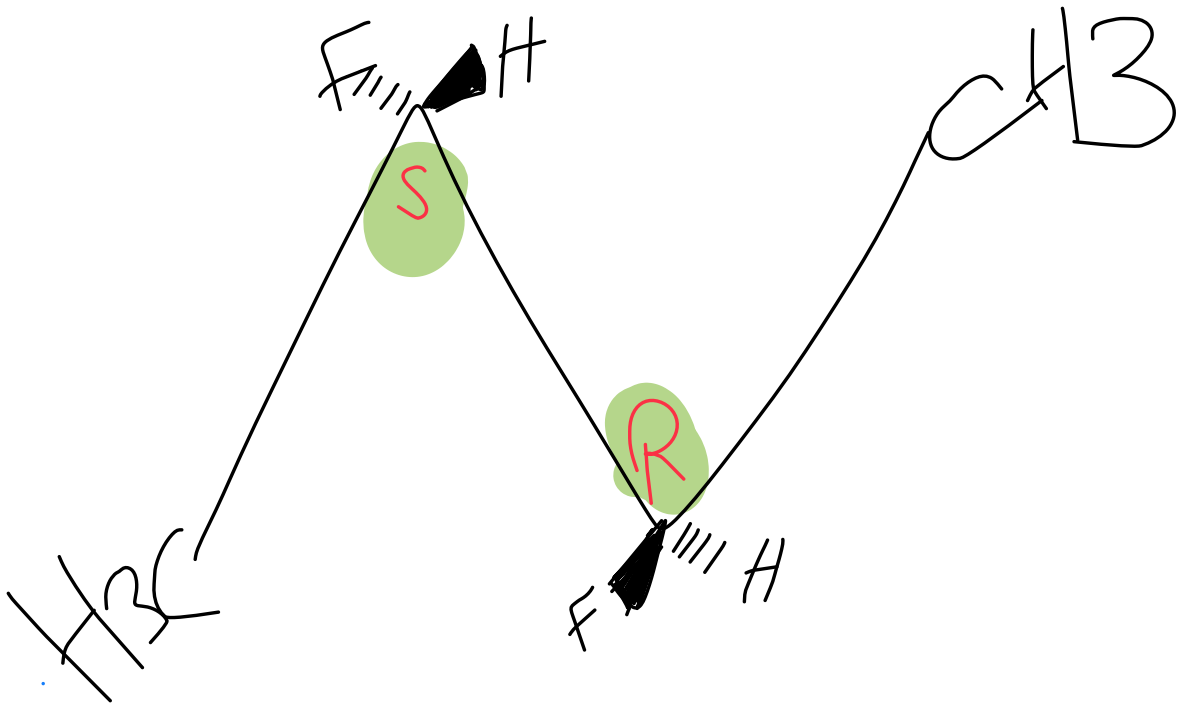


2 chiral

نفس التبديلات

R,R

not meso compound



meso R,S & S,R

same compound

stereoisomers $> 2^n - 1$

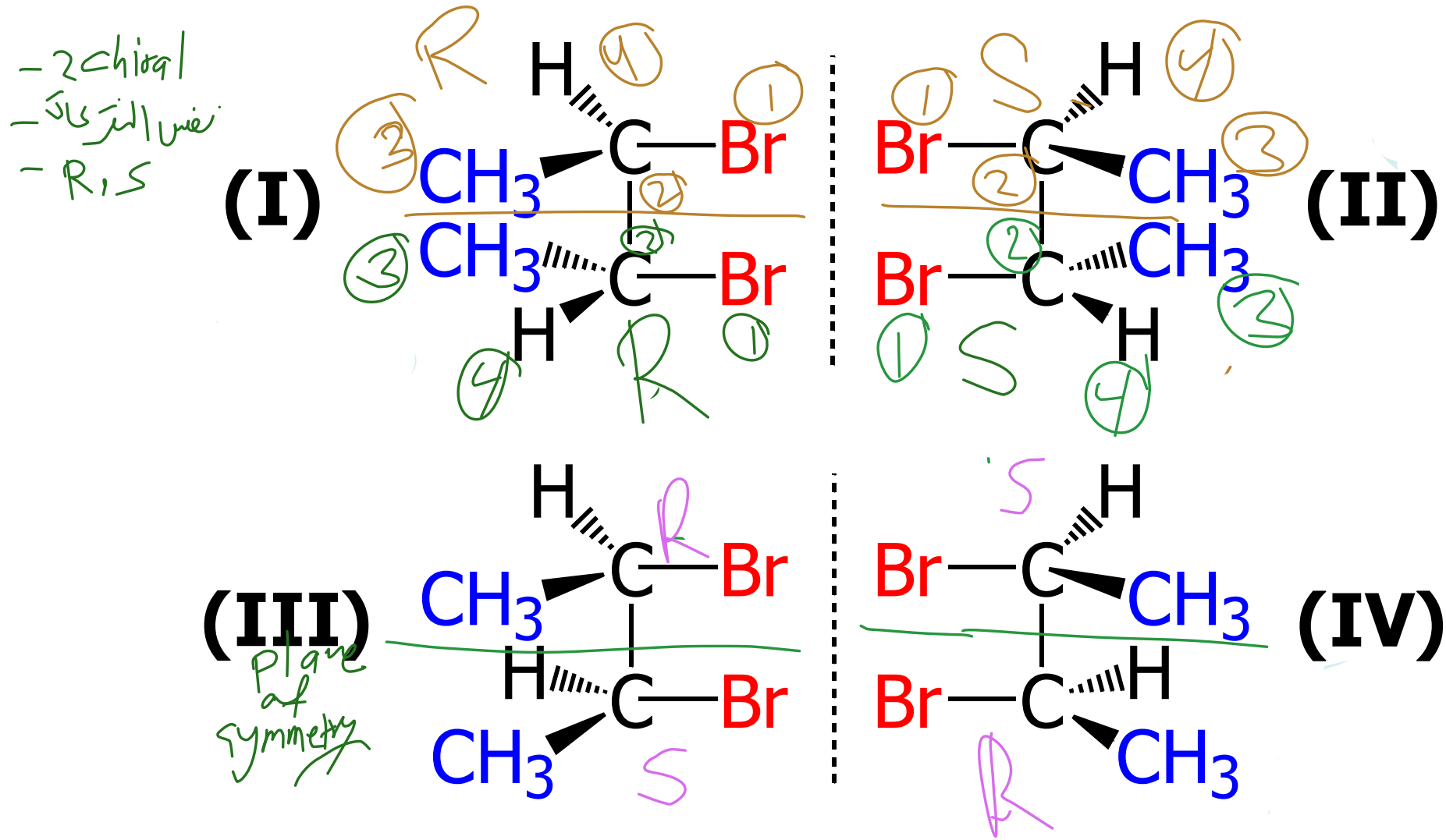
meso

① 2 chiral

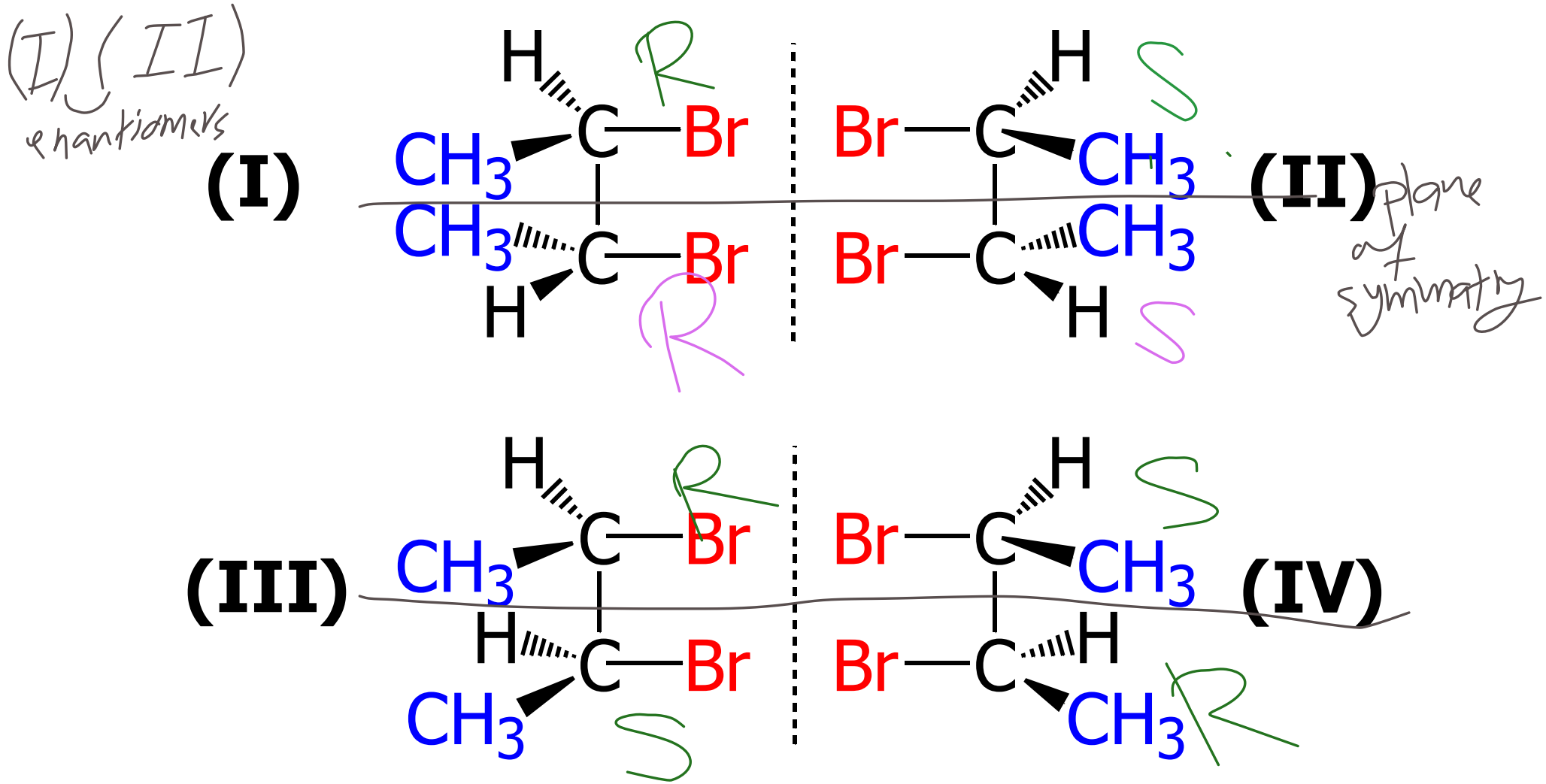
② same substituents

③ R, S

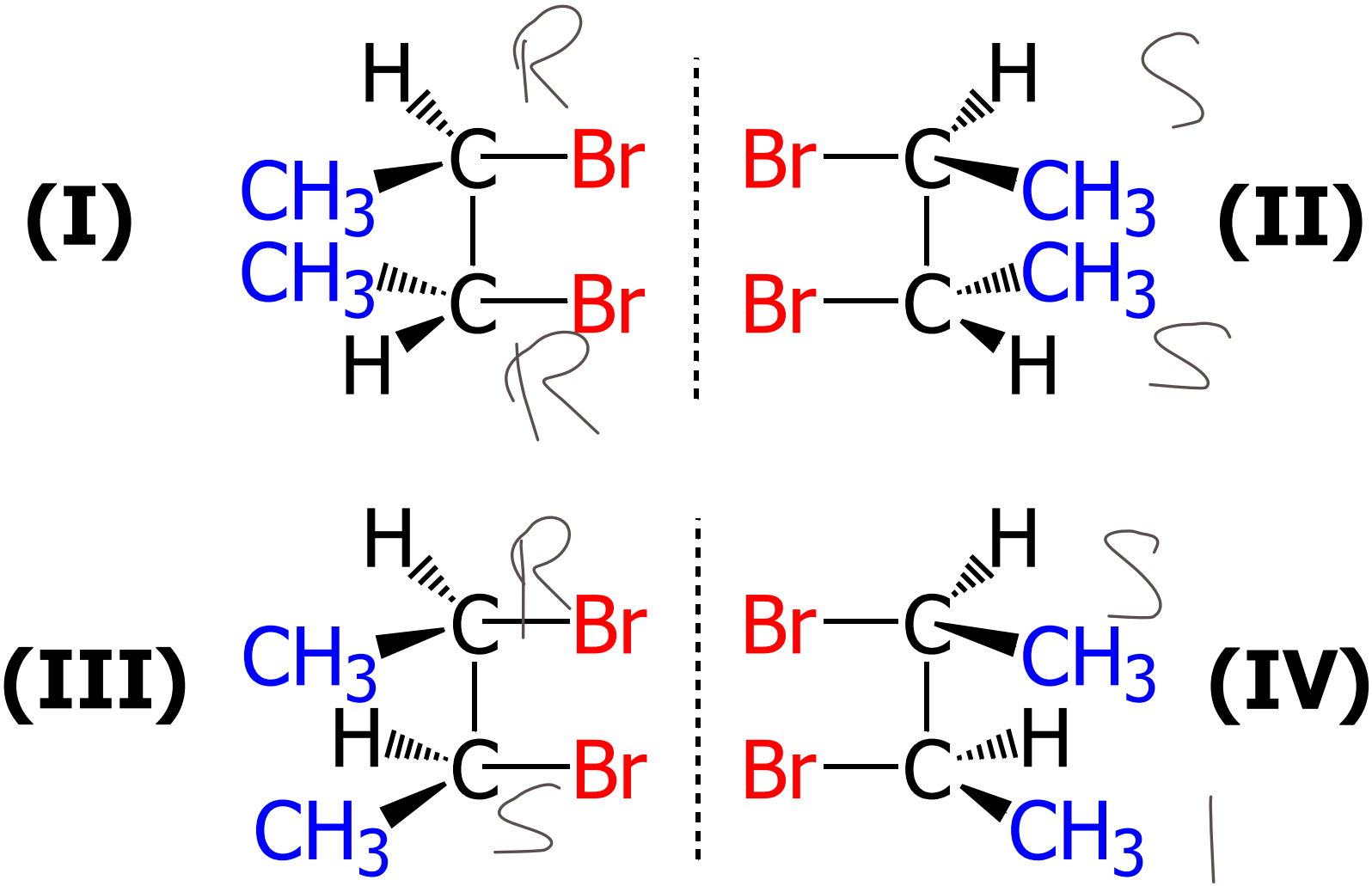
$\Rightarrow$ meso compound



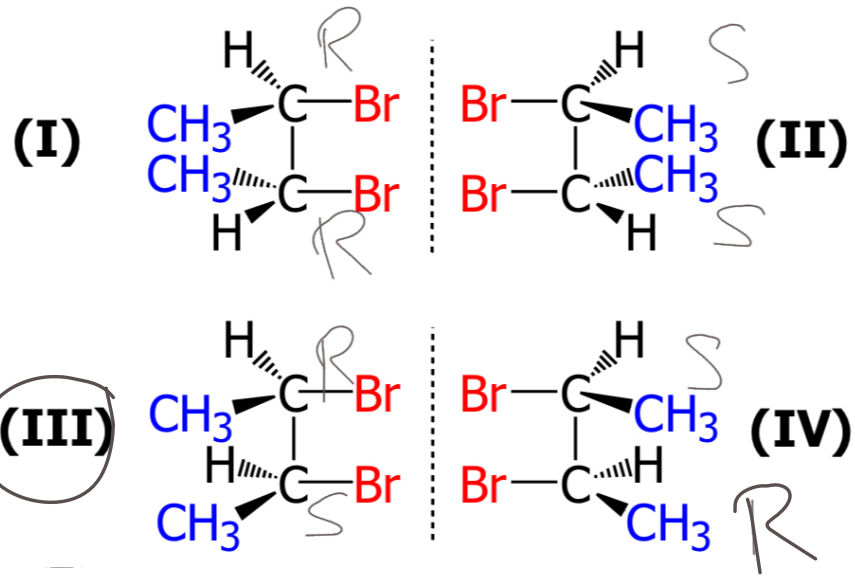
Note: (III) contains a plane of symmetry, is a meso compound, and is achiral ([α] = 0°).



- (I) & (II) are enantiomers to each other and chiral
- (III) & (IV) are identical and achiral

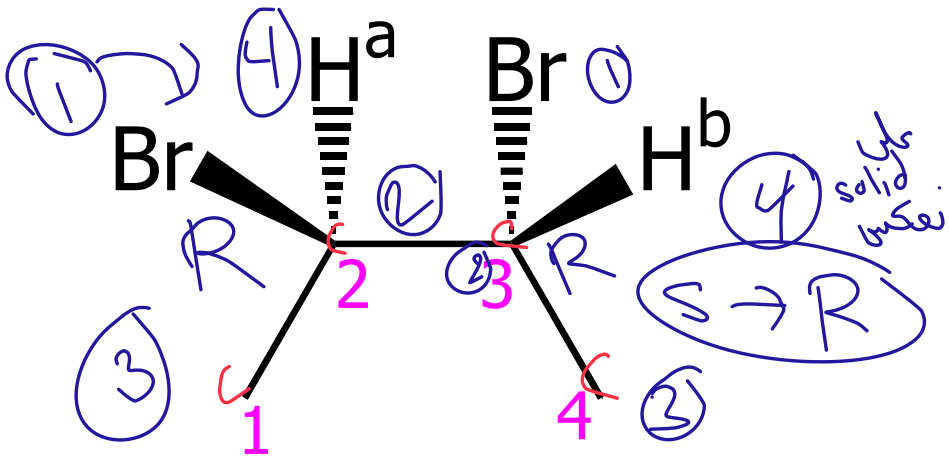


- (I) & (III), (II) & (III) are diastereomers
- Only 3 stereoisomers:
  - (I) & (II) {enantiomers}, (III) {meso}


(I)
(II)
(III)
(IV)
R
S
meso
achiral
(I) with (II) → enantiomers
(III) with (IV) → same compound
meso
(III) with (I) → diastereoisomers
(III) with (II) → diastereoisomers
(IV) with (I) → diastereoisomers
(IV) with (II) → diastereoisomers
number of stereoisomers
chiral center
= 2^n
= 2^2 − 1 = 3
R,R
S,S
R,S / S,R
meso
same

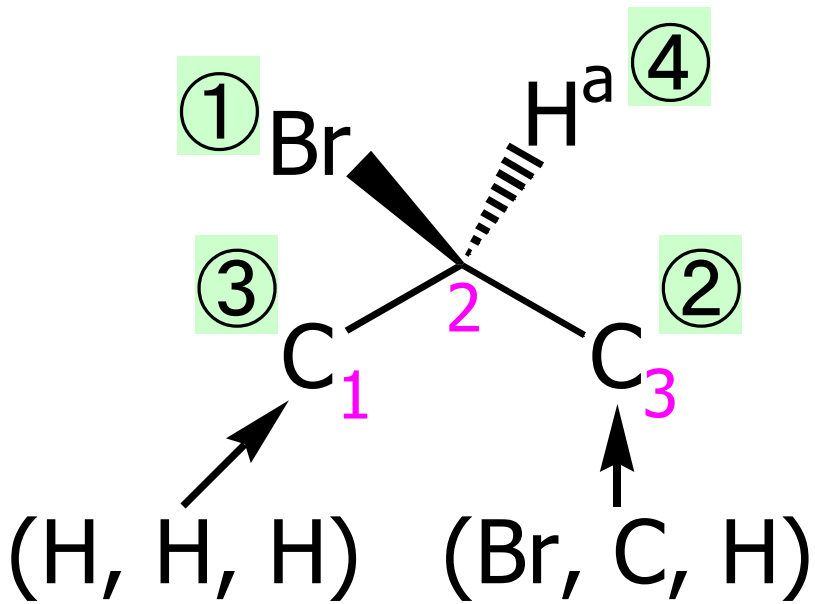
10B. How to Name Compounds with More than One Chirality Center

- 2,3-Dibromobutane



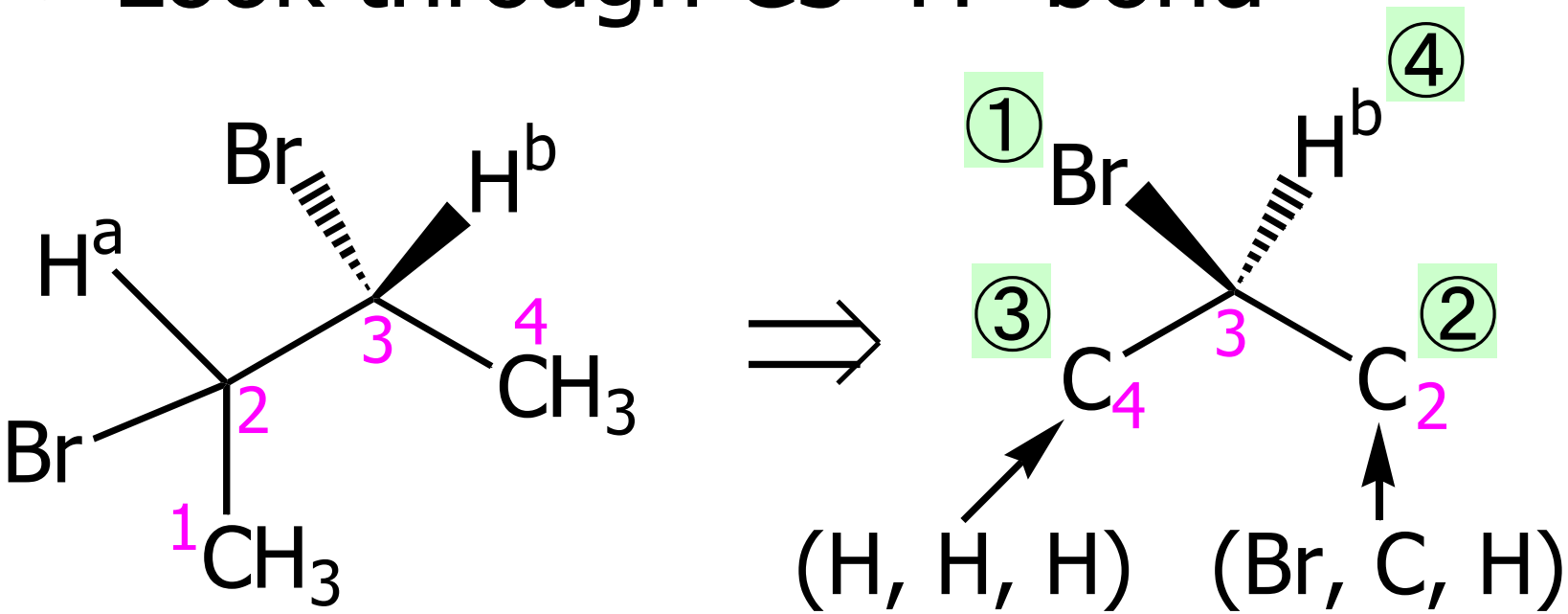
(2R,3R)-2,3-dibromobutane

  - Look through C2–H^a bond



C2: *(R)* configuration

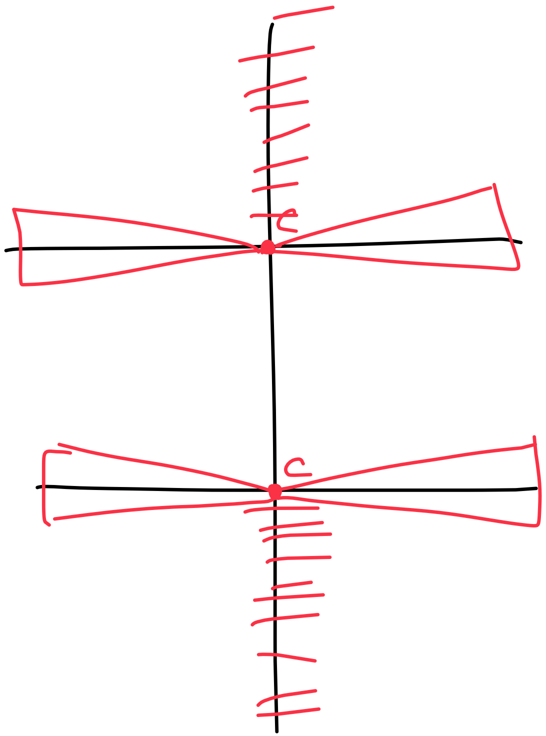
- Look through C3–H^b bond



C3: *(R)* configuration

- Full name:
  - ♦ *(2R, 3R)*-2,3-Dibromobutane

Fischer Projection



نقطة تقاطع
الخطوط ⇐ كربونة
C

خط عمودي ⇐ solid

خط أفقي ← dash

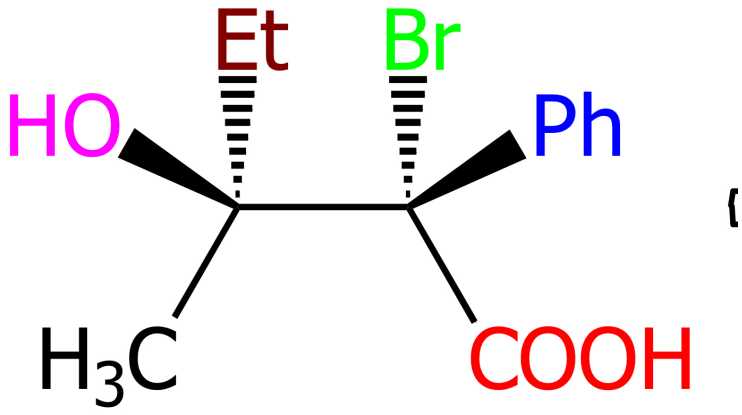
3 معلومات للتحويل :

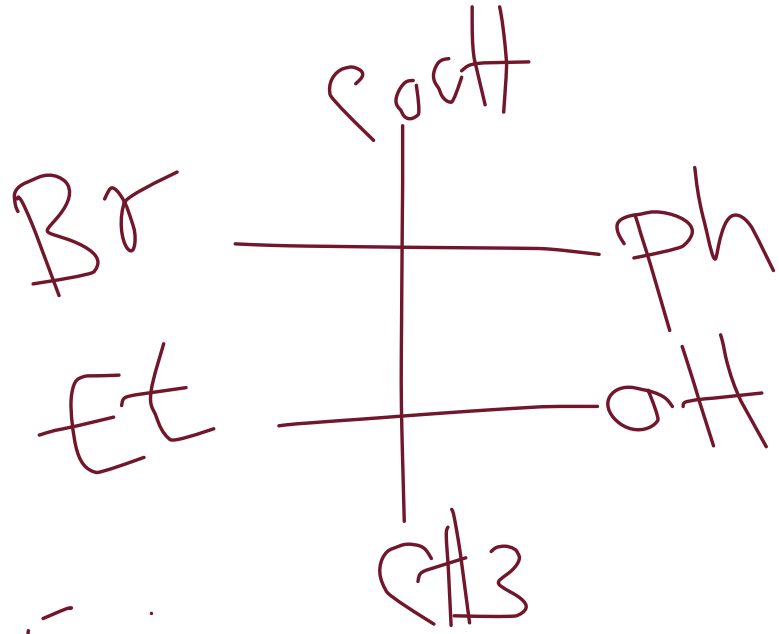
بال Candihvas ← فوق وتحت

بال solid ← يمين

بال dash ← يسار

example ⟹ Fischer Projection حول المركب الآتي إلى الرسم





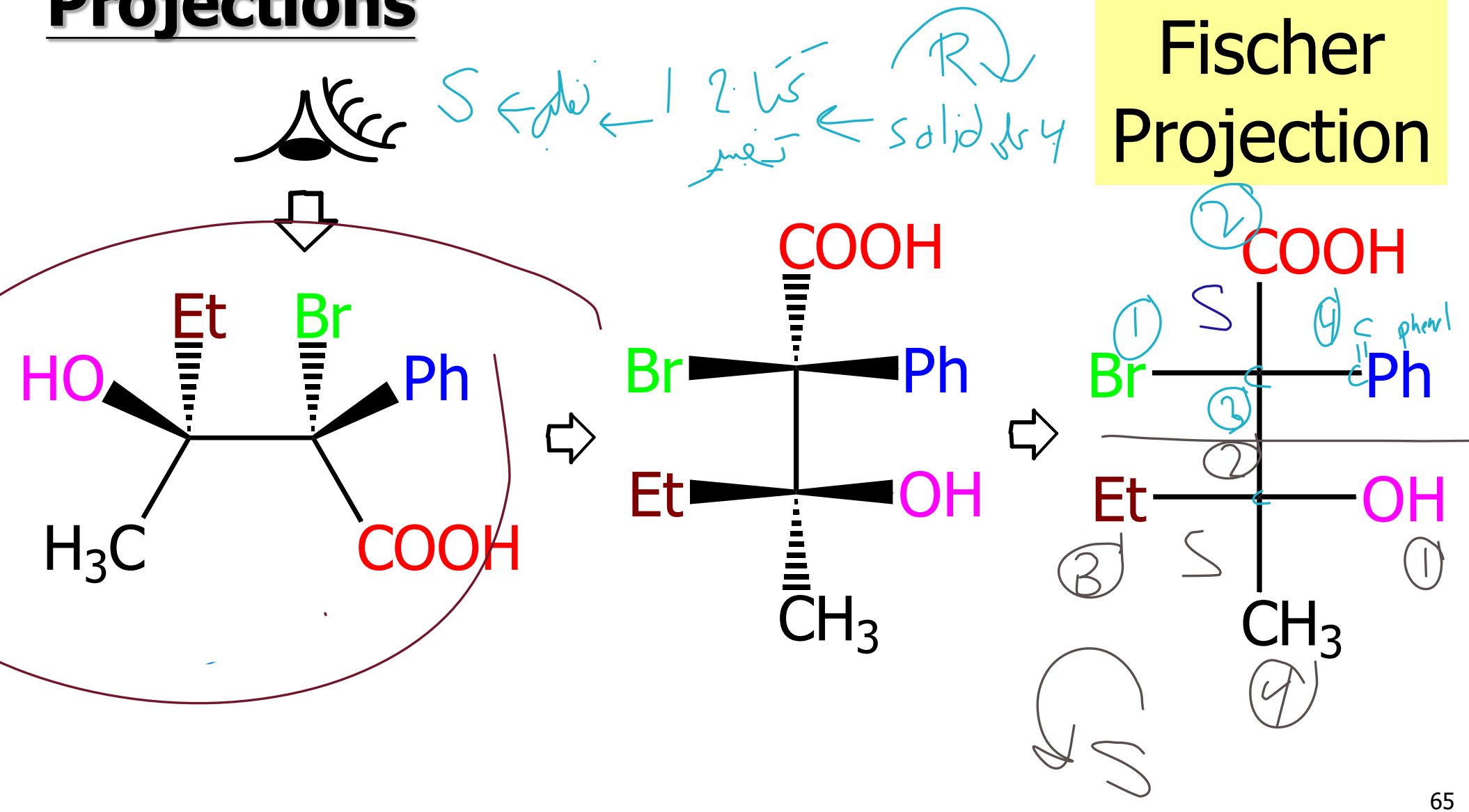
Continuous (——) ⟹ فوق وتحت

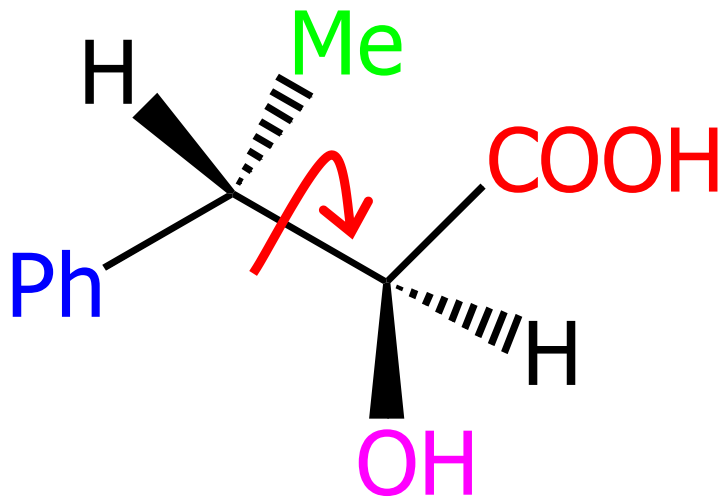
dash (IIIII) ⟹ يسار

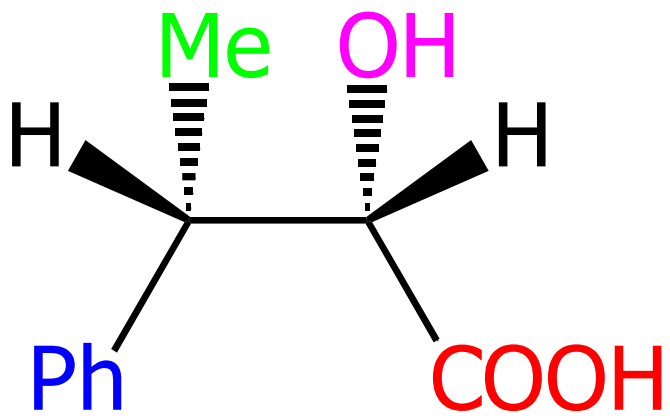
Solid (▬) ⟹ يمين

11. Fischer Projection Formulas

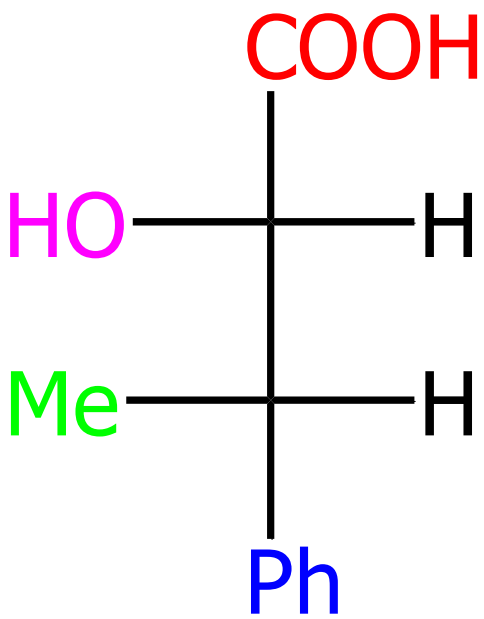
11A. How To Draw and Use Fischer Projections

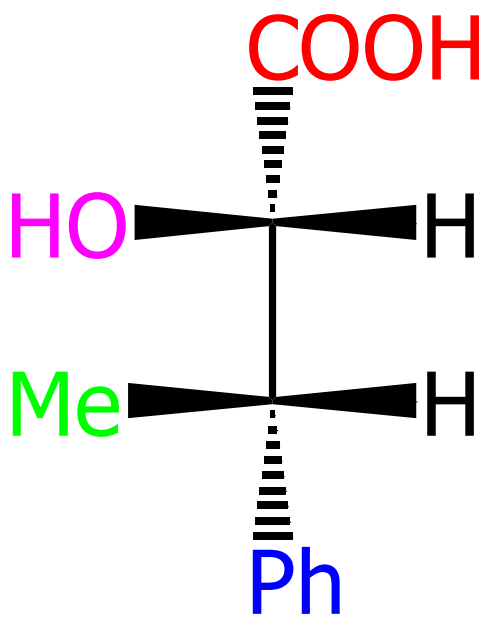


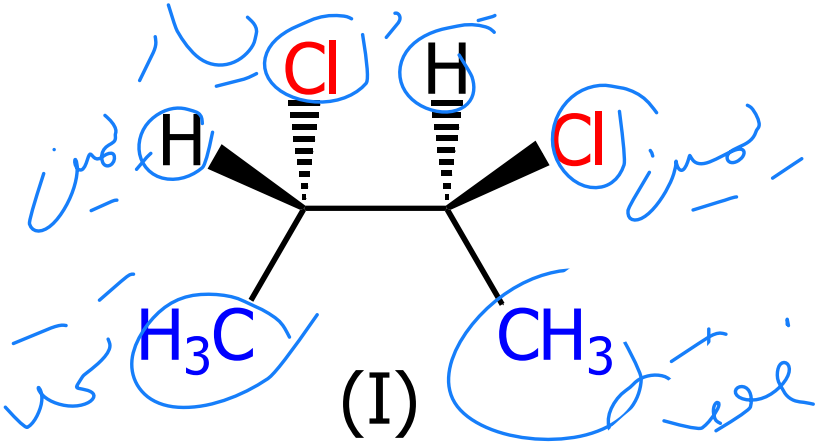




Fischer Projection

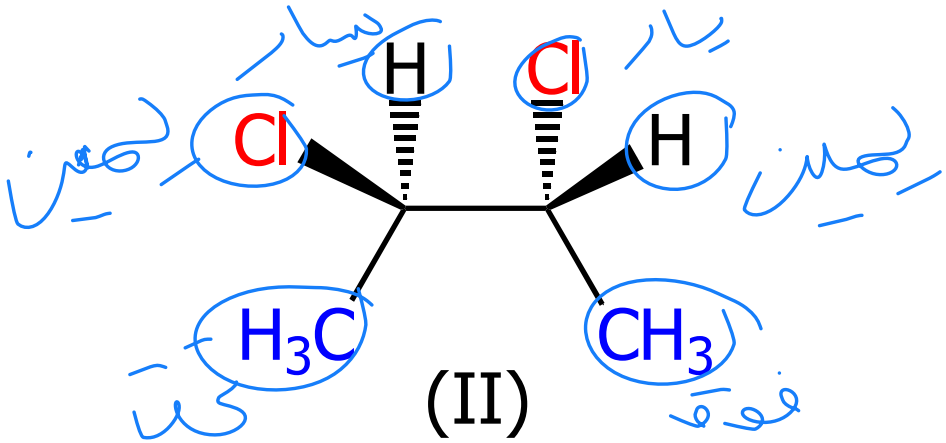






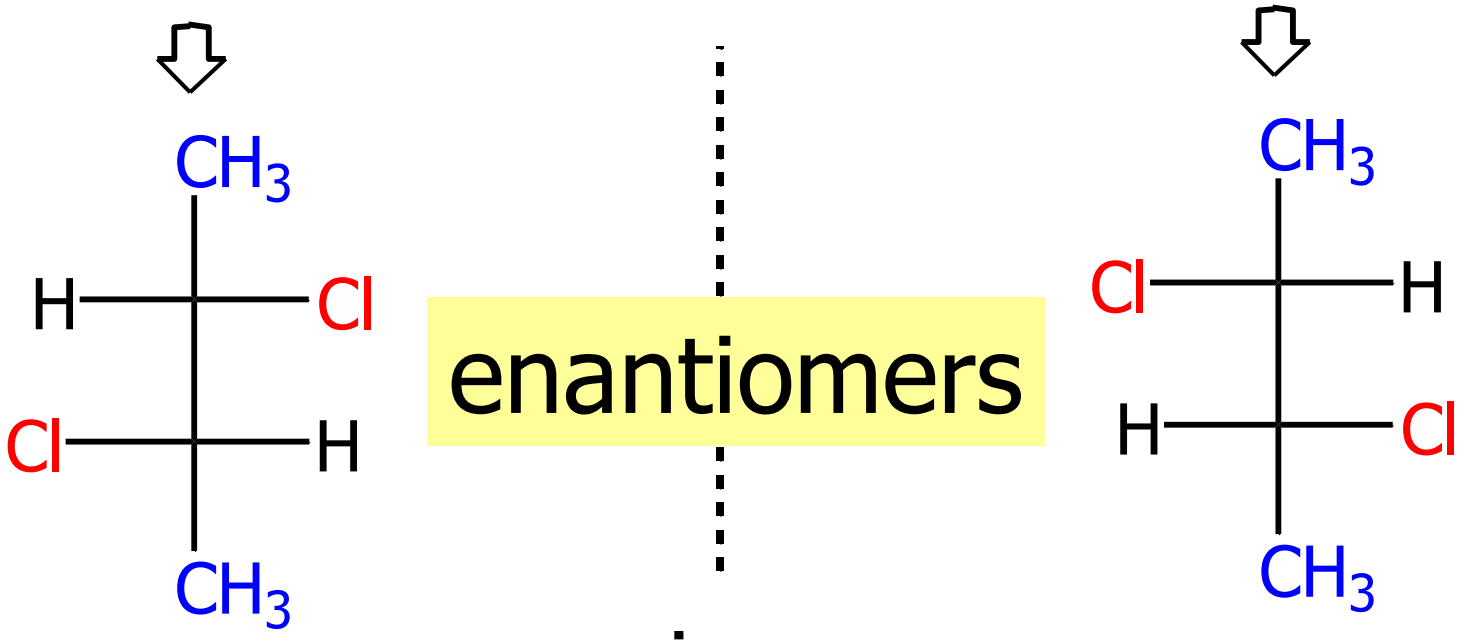
(I)

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

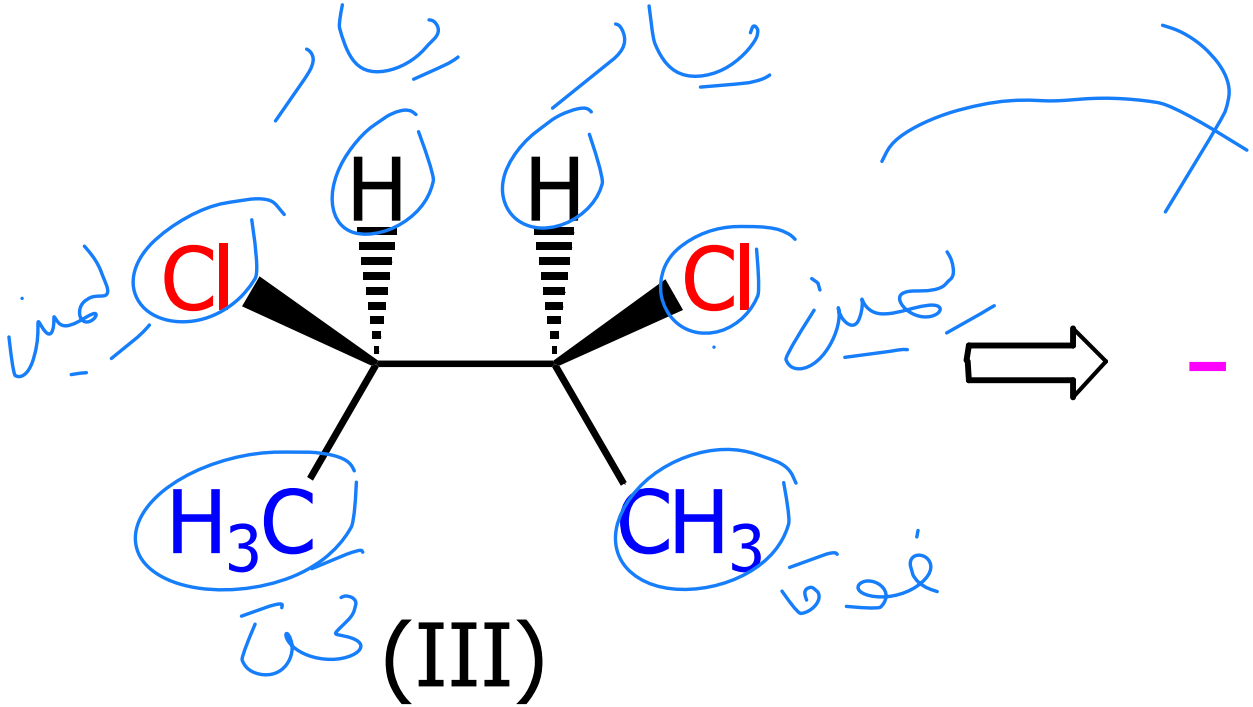


(II)

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

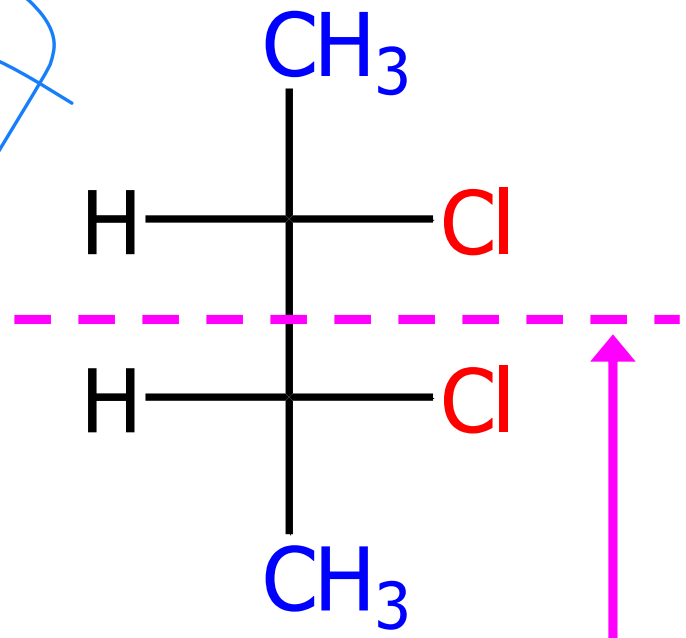


- (I) and (II) are both chiral and they are enantiomers with each other



(III)

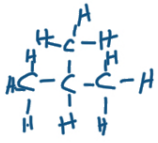
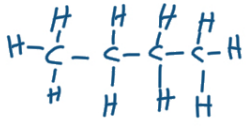
(2*S*, 3*R*)-Dichlorobutane

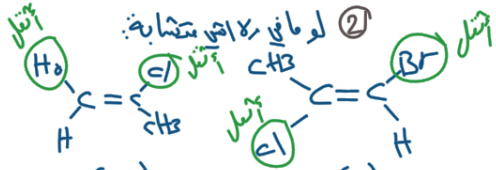
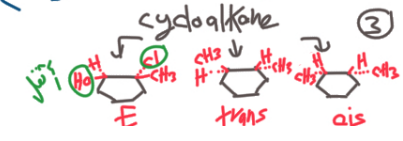


Plane of symmetry

- (III) is achiral (a meso compound)
- (III) and (I) are diastereomers to each other

Isomers :molecular formula مركبات لها نفس ال

- Constitutional
  - نفس الصيغة العامة ولكن تختلف بالرفع النراني
  - (Example)
  - C_4H_{10}
  - 
  - 
- Stereoisomer
  - Conformational
    - - أيثان -
    - ① (open chain)
    - 

    - ② ring
      - boat
      - chair
      - half-chair
      - twist
    - newman projection
  - Configuration
    - geomatrical ①
      - Cis ← على الأقل مجموعتين متشابهات → trans
      - 
      - ② لو مافي مجموعات متشابهة:
      - 
      - (Z) (E)
      - cycloalkane ③
      - 

    - Optical / enantiomeres

الوسائل شو العلاقة بين مركبين :

① نفس الذرات وأنواعها ← مختلفين ← المركبين مختلفين .

↳ نفس الاشي ← نروح على خطوة ② .

② connectivity ← مختلفة ← المركبين ← structural / constitutional
- skeletal
- Positional
- Functional

↳ نفس ال connectivity ← نروح على خطوة ③ .

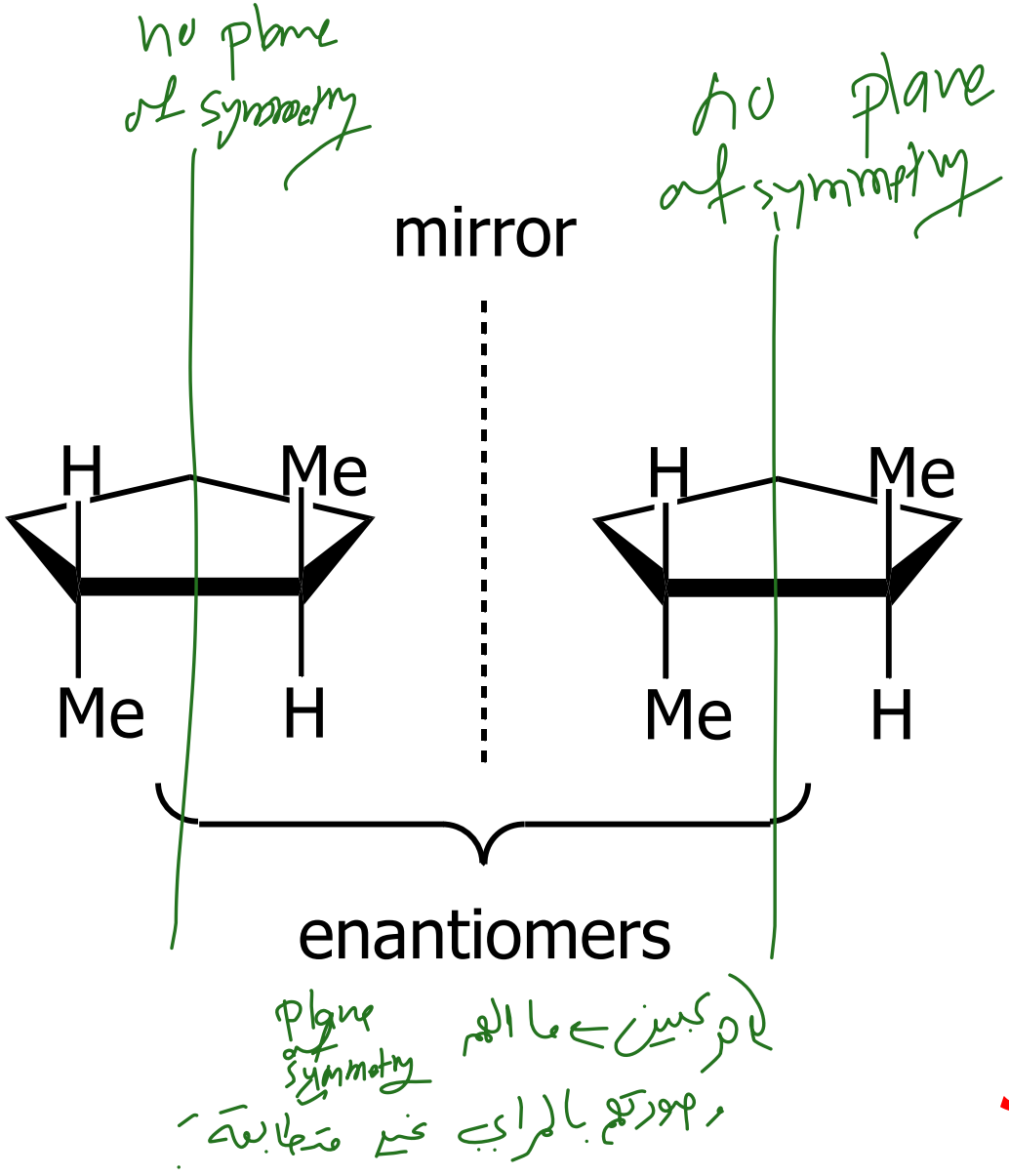
③ Stereoisomers ←
- cis / trans , =
- cis / trans , حلقة
- Geometrical

↳ Newman / ring flip → conformational

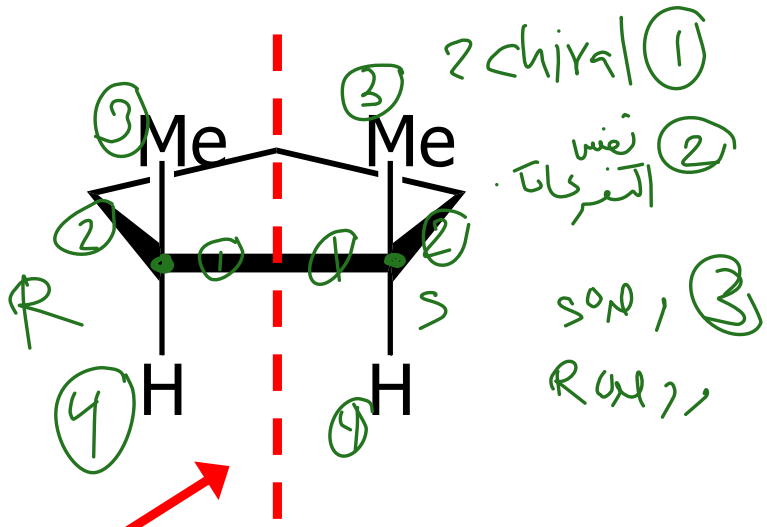
↳ chiral ← R واحد و S الثاني ← enantiomers, لكن اذا كانوا R , R أو S , S ← same compound

↳ no chiral ← same compound

12. Stereoisomerism of Cyclic Compounds



a meso compound
achiral



Plane of symmetry

1. chiral carbon → cis → meso → Plane of symmetry → achiral compound

(نفس التفرع) up اذين

(نفس التفرع) down أو اذين

---

2. chiral carbon → trans → enantiomers → no plane of symmetry.

down على، up على

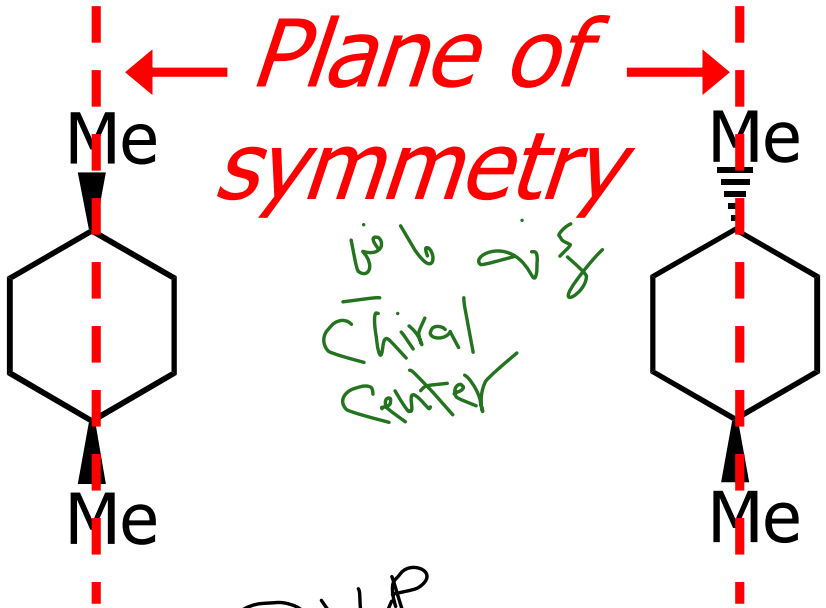
(نفس التفرع)

---

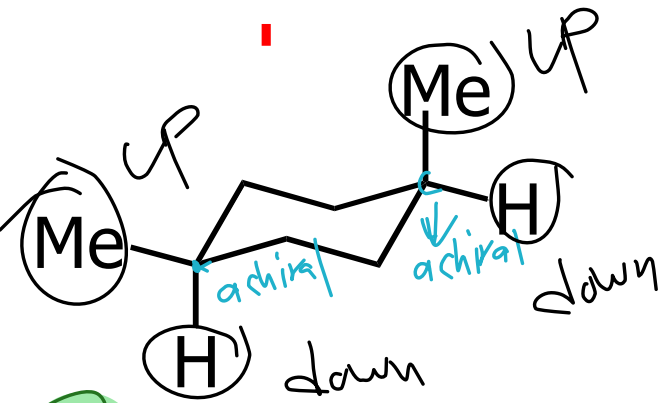
3. no chiral carbon → plane of symmetry

12A. Cyclohexane Derivatives

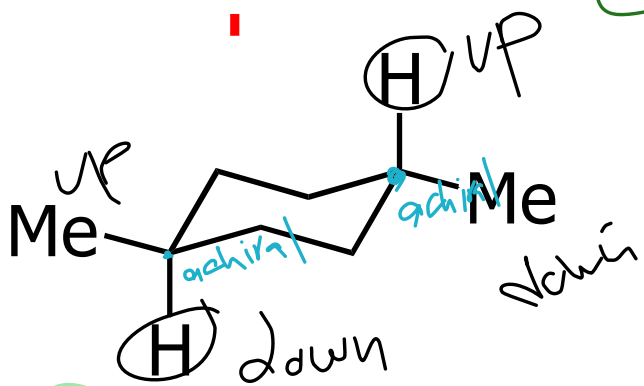
- 1,4-Dimethylcyclohexane



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

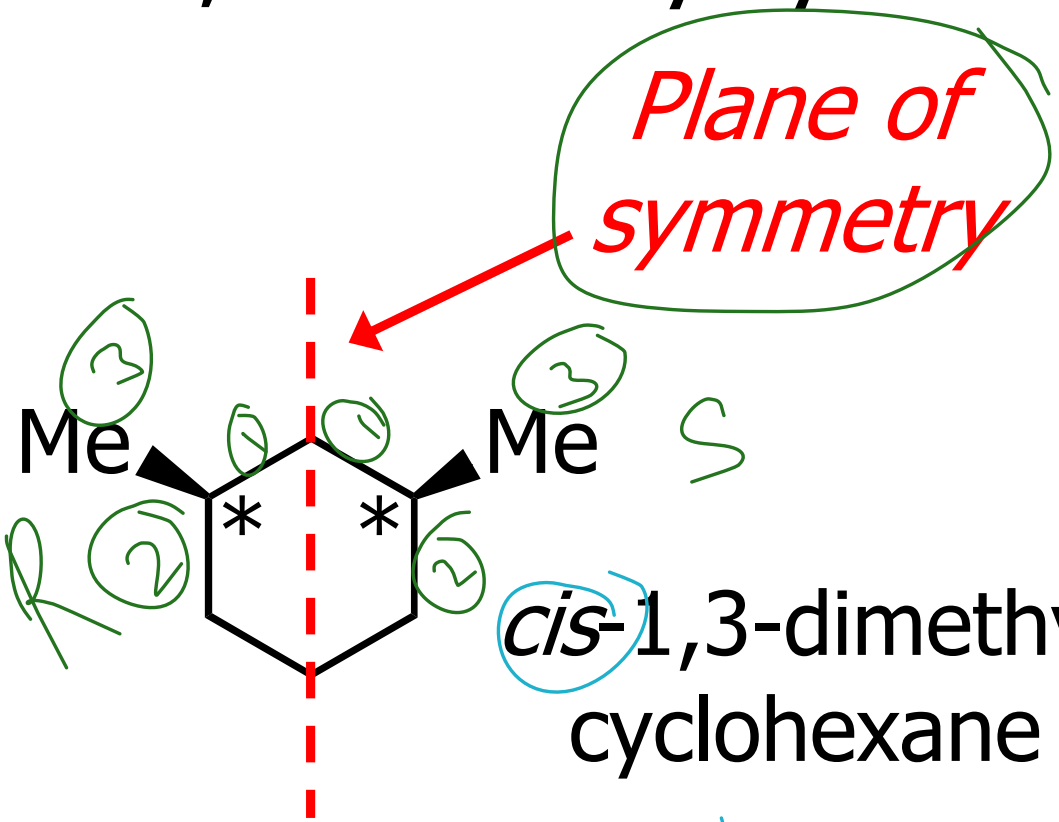


cis-1,4-dimethyl cyclohexane

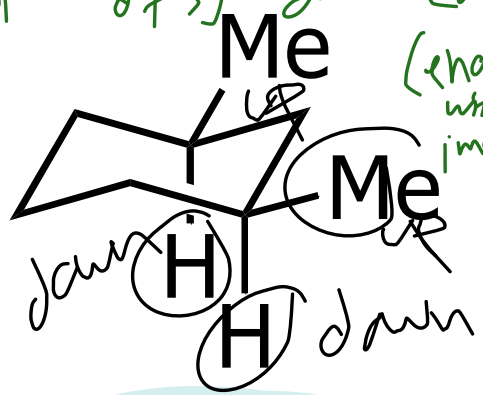


trans-1,4-dimethyl cyclohexane

❖ 1,3-Dimethylcyclohexane



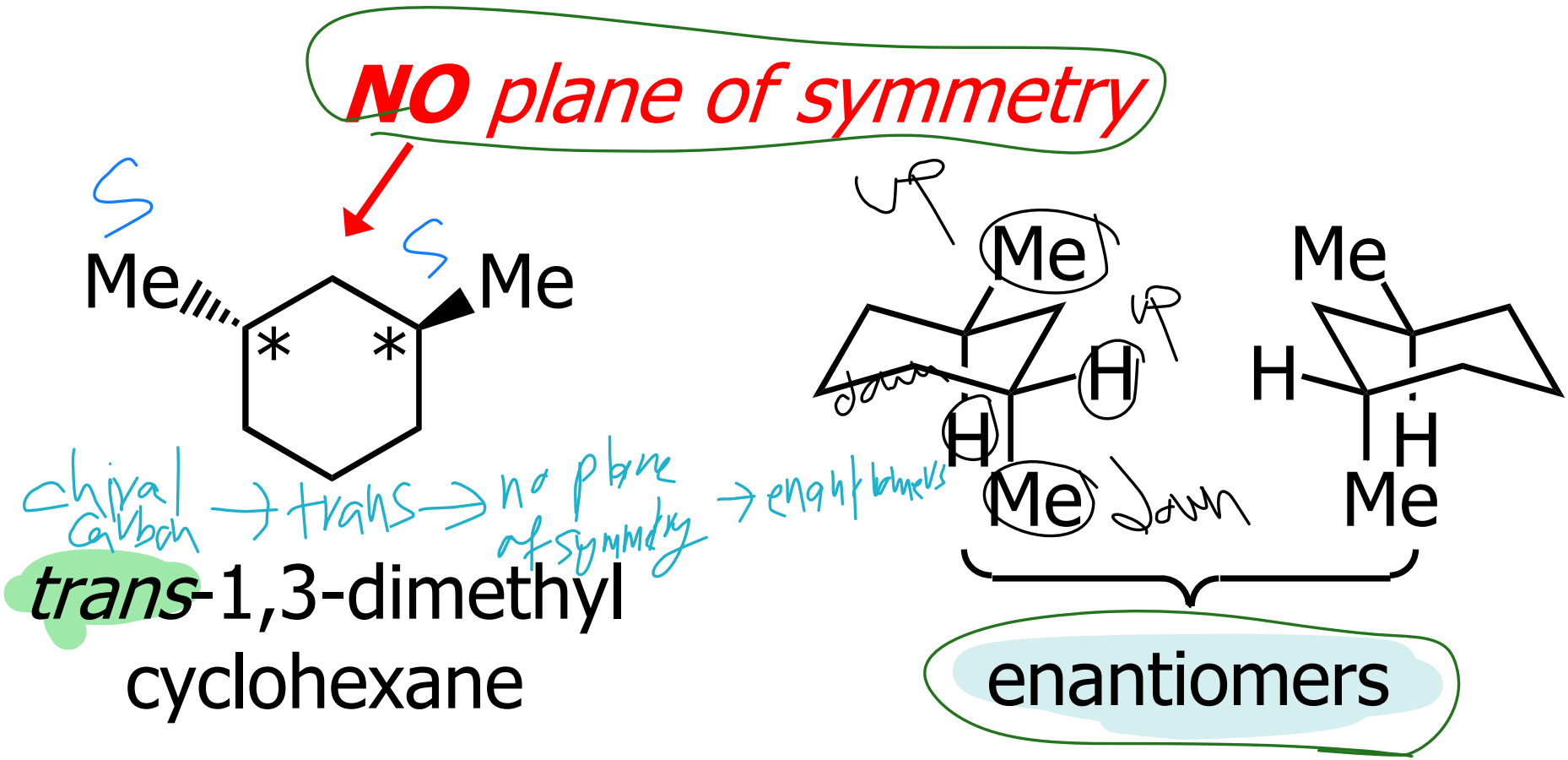
cis-1,3-dimethyl cyclohexane



(meso)

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

❖ 1,3-Dimethylcyclohexane

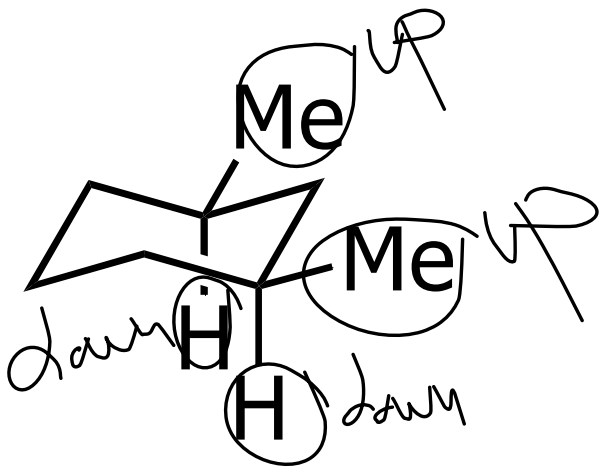


trans-1,3-dimethyl cyclohexane

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

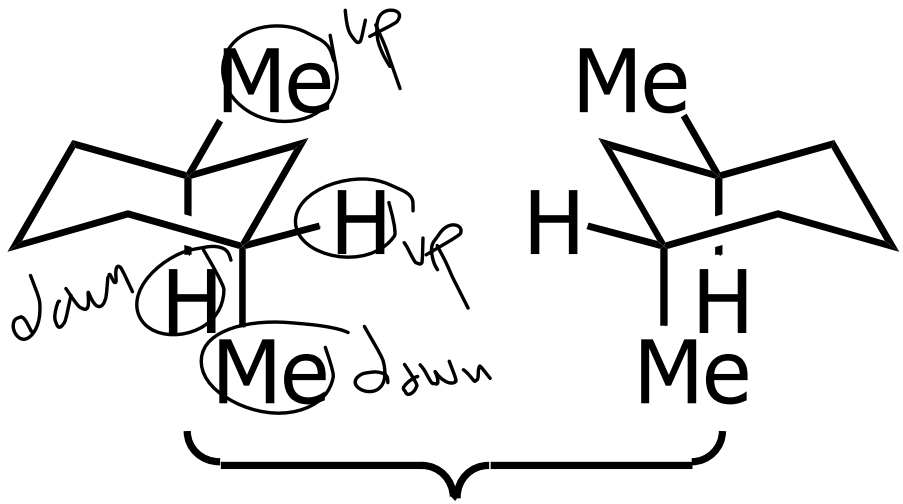
- 1,3-Dimethylcyclohexane
  - Has two chirality centers but only ***three*** stereoisomers

cis-1,3-dimethyl cyclohexane



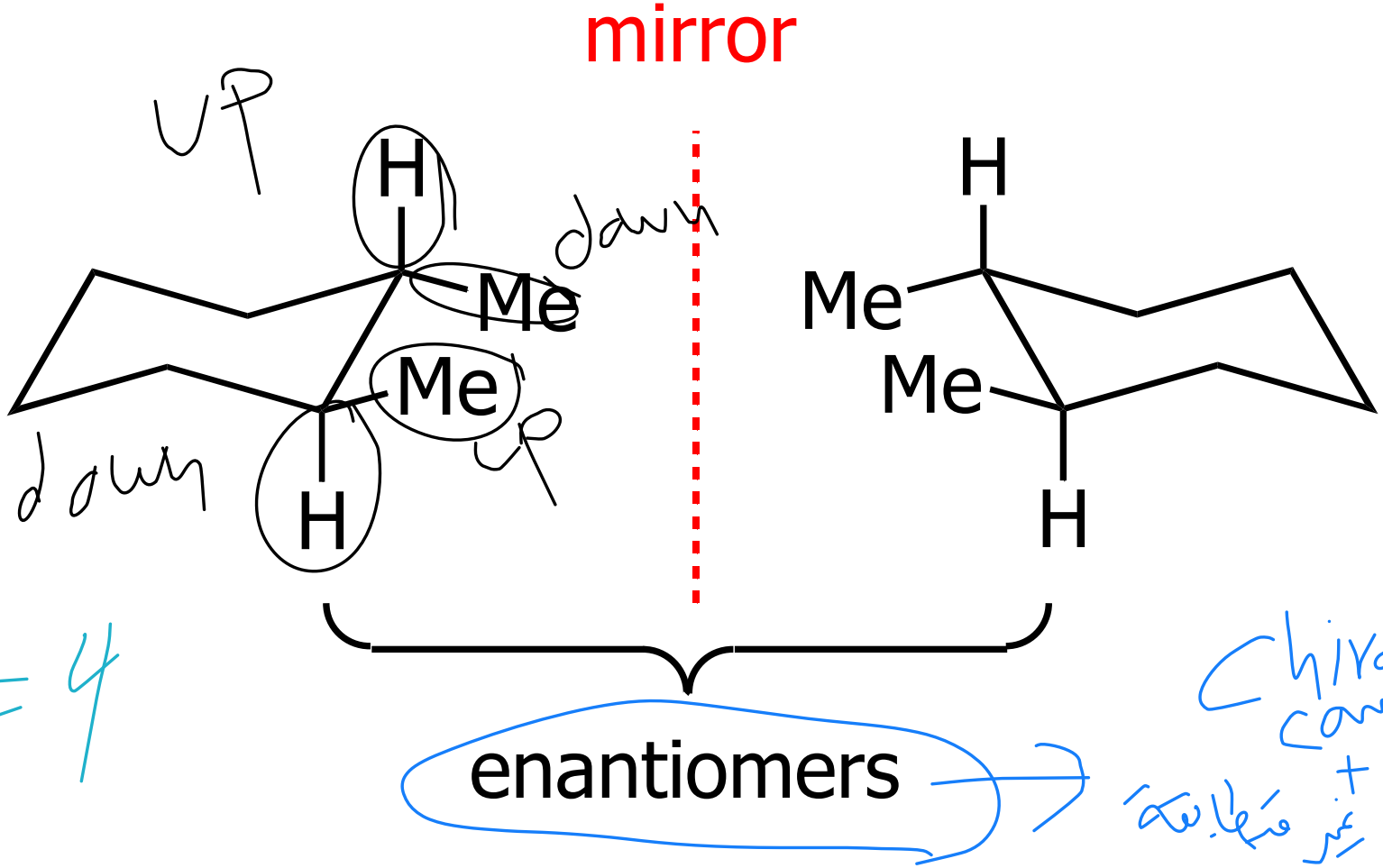
(meso)

trans-1,3-dimethyl cyclohexane



enantiomers

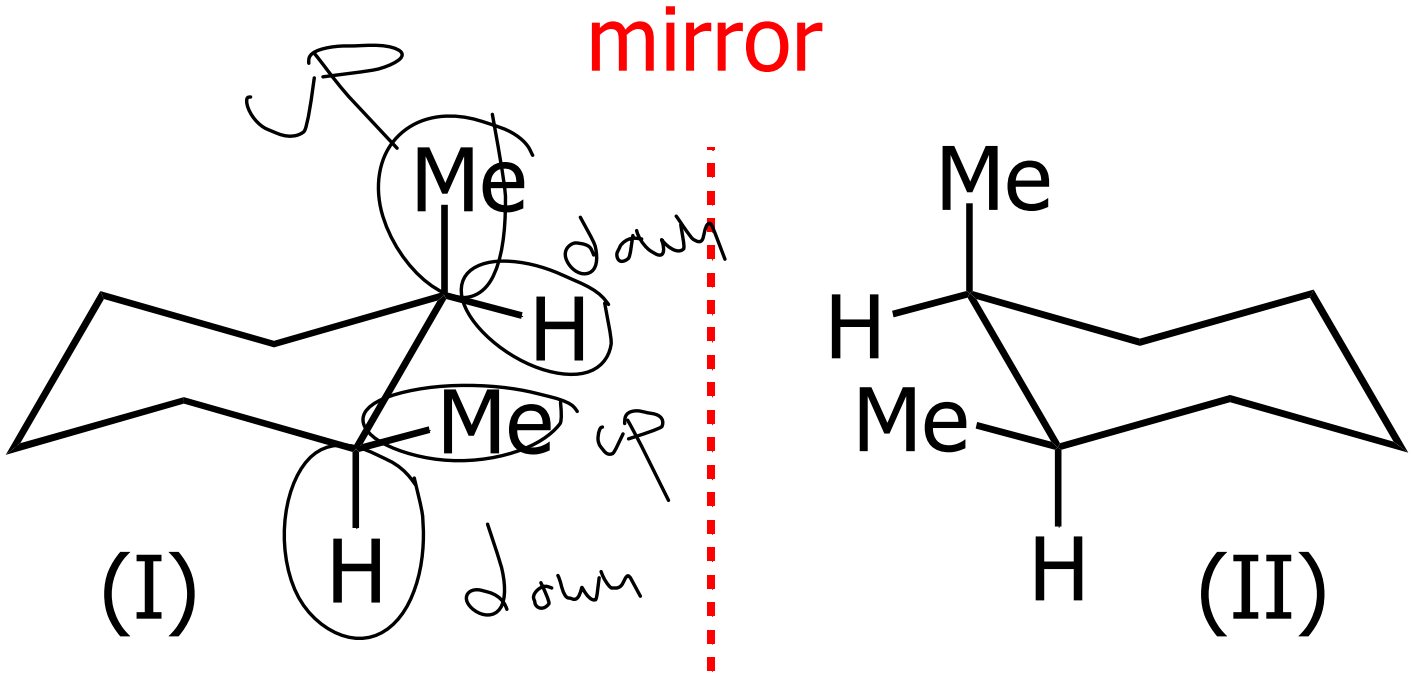
❖ 1,2-Dimethylcyclohexane



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

chiral carbon → trans → no plane of symmetry → enantiomers → 2^n

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



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

cis 1,4 } → no chirality
trans 1,4 }

chiral vs
center

---

cis 1,3 } → meso

---

trans 1,3 } → enantiomers

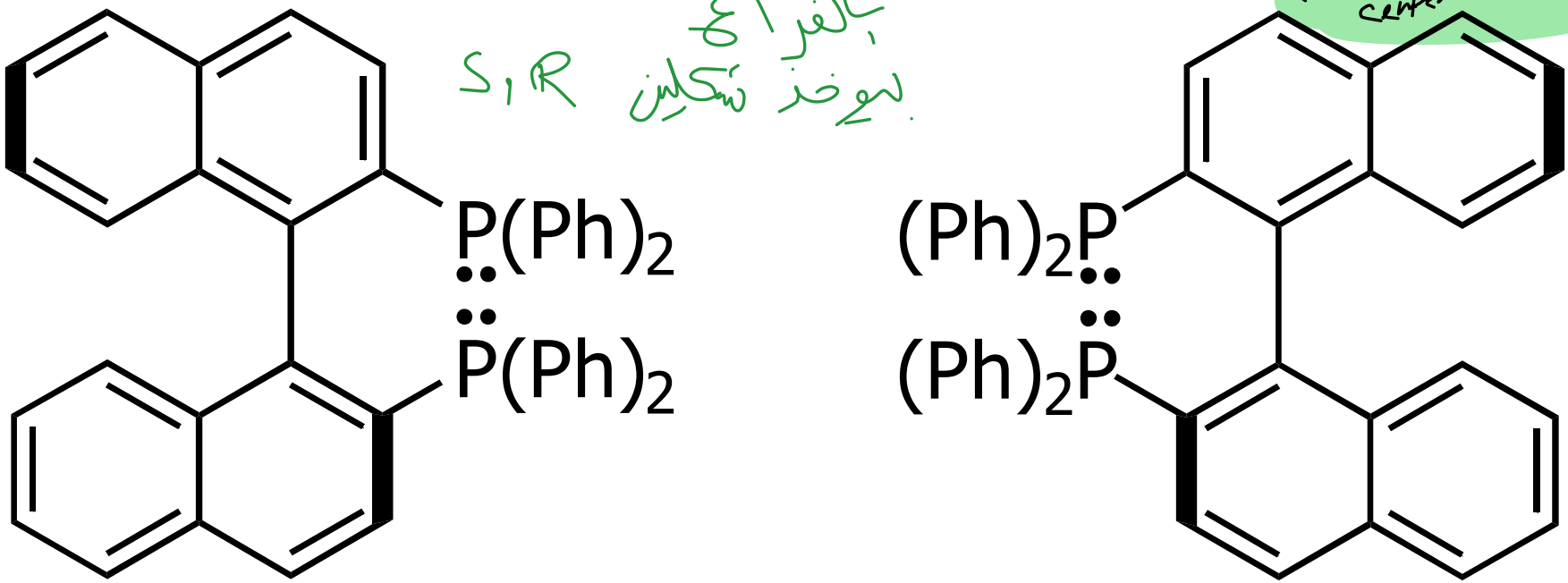
---

trans 1,2 → enantiomers

---

cis 1,2 → enantiomers

13. Chiral Molecules That Do Not Possess a Chirality Center

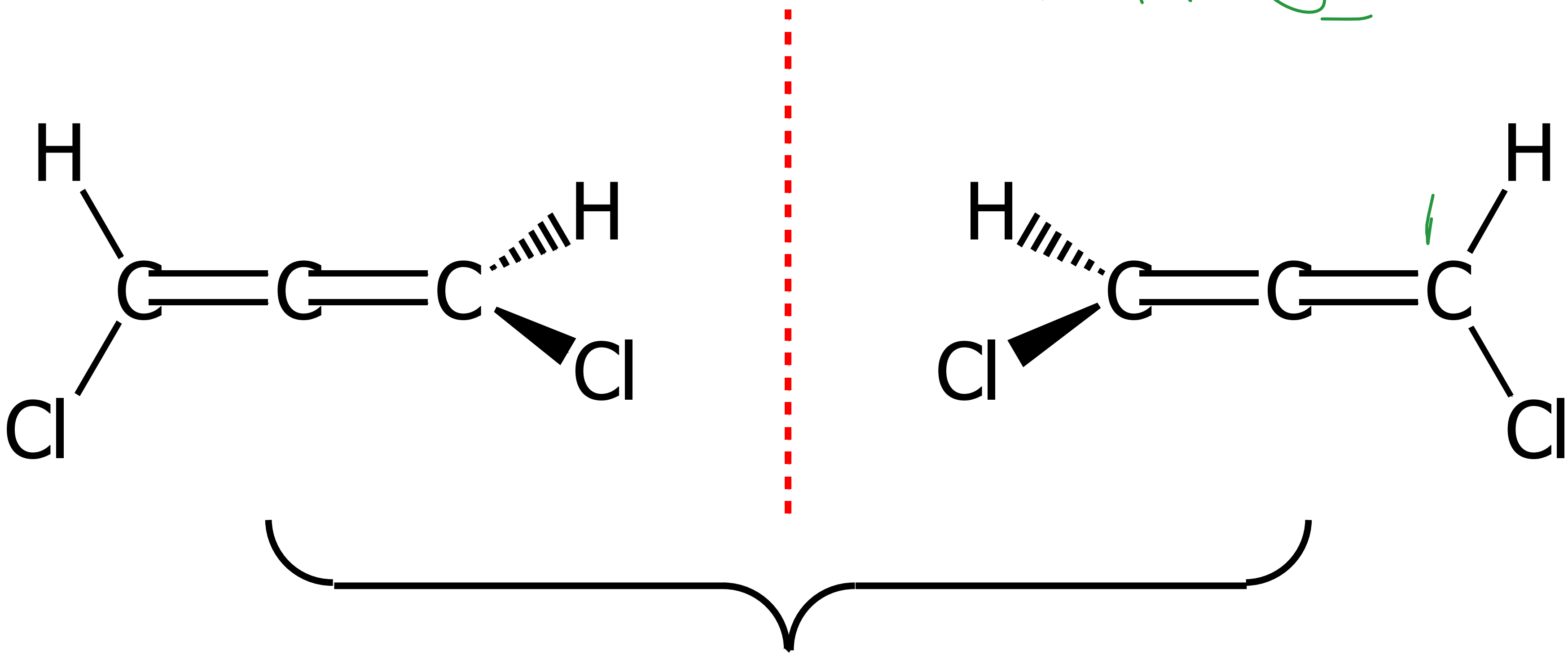


(*S*)-BINAP (*R*)-BINAP

enantiomers

no chiral center → ولكن المركب بالنزاع أخذ S و R شكلين

mirror



enantiomers