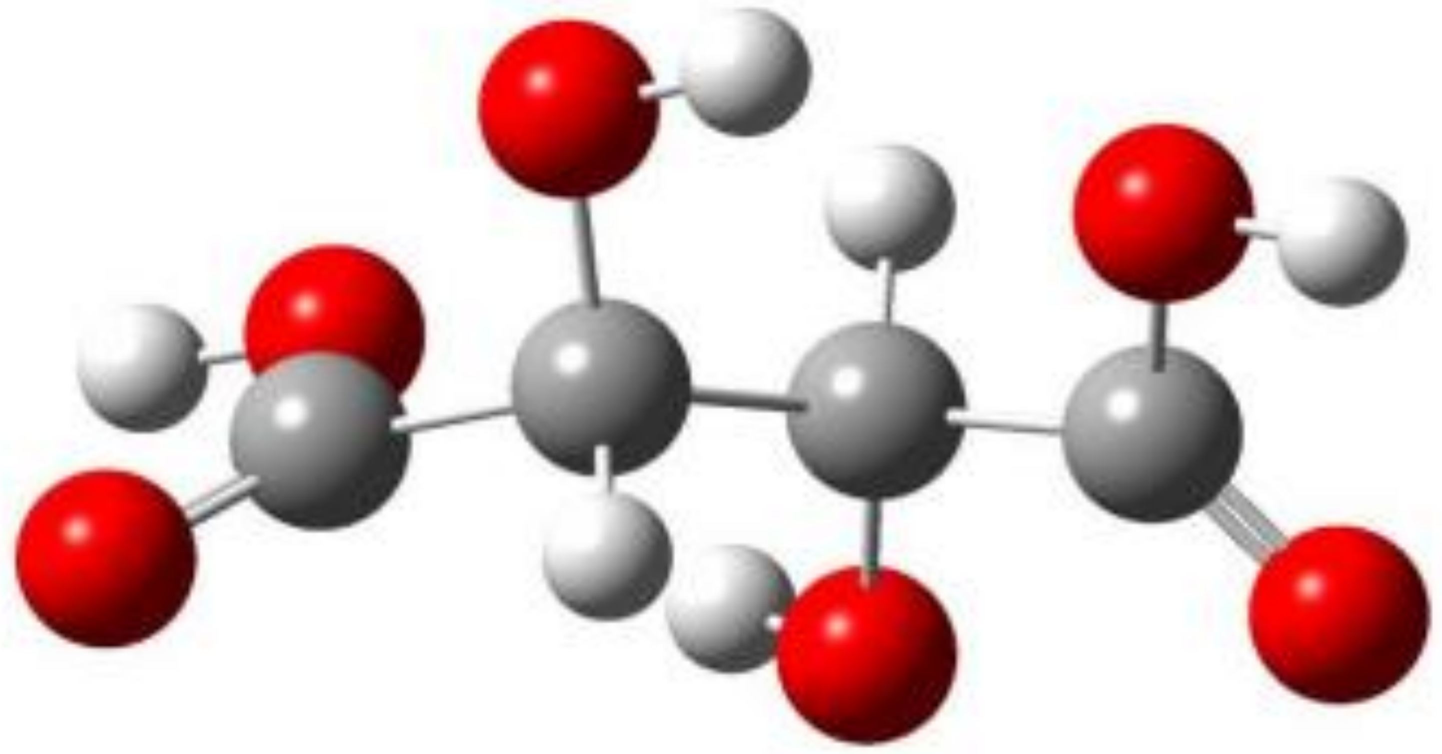
النادي الطبي

Organic chemistry

Chapter [redacted] : 5

Done by: Shahed Zaytoon



Chapter 5: Stereoisomerism

* صغرت الخط نوعًا ما وكتبت كلشي بمكانه
← حفاظًا على نفسيتكم الحلوة ت
← احذفوا هاي البيج كمان
عشان 45 احسن من 46 ت

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*Note:
اللي كانوا بيختلفوا بترتيب
ال Atoms هم ال
structural or constitutional isomers

Stereochemistry

نوع من ال isomers الهم نفس ترتيب
ال Atoms لكن الترتيب الفراغي (3D structure)
الهم بختلف

Chiral

Stereochemistry is the study of the 3D aspects of molecules. *Stereoisomers* are molecules that differ only in the 3D arrangement of their atoms. Stereoisomers posses one or more *chiral* centers. Chiral objects are ones where the mirror image has a different 3D structure, i.e. the mirror image is not *superimposable* on the original object.

The chiral or chirality

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

أي اشي بالدنيا حطيته قدام المرآة، وحاولت اطابق الاشي مع انعكاسه على المرآة وما زبط ← بطلق عليه chiral

← فبالتالي ال function تبع الاشي وانعكاسه رح يختلف

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Photo by Michael Watson for John Wiley & Sons, Inc.

← فالفكرة انه لو اجيت تطابق الايد اليمين مع انعكاسها على المرآة (as ايدك اليسار) ما رح يتطابقوا (can't superposed)

← وظيفة ايدك اليمين بتختلف عن اليسار

*Note: تختلف الوظيفة في ال chiral

hand هي كلمة تعني chiral

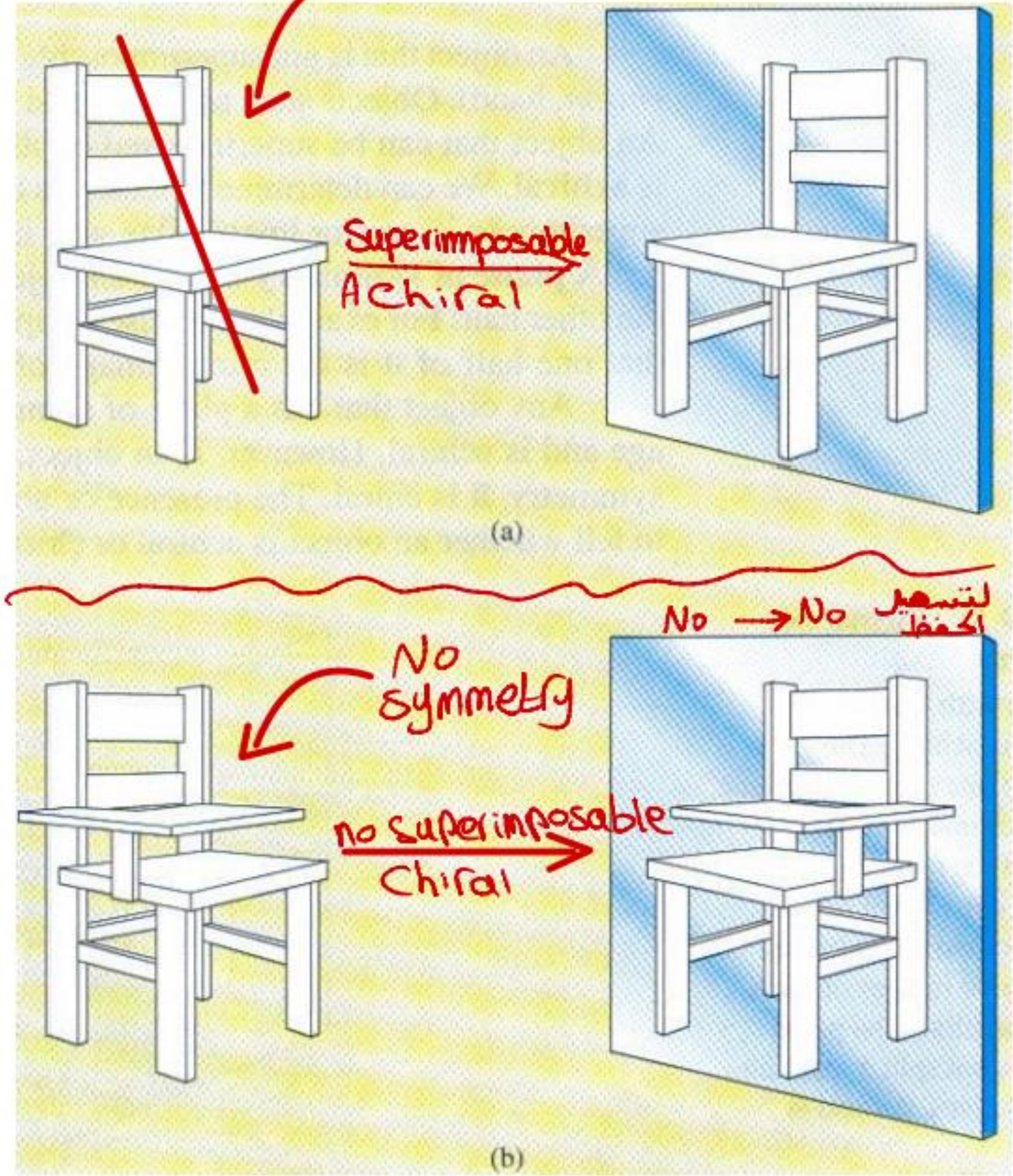
*If you put your right hand in front of mirror → you will see it as your left hand

Chirality

Objects can be chiral or achiral, i.e.

The top chair is achiral (mirror image is superimposable)

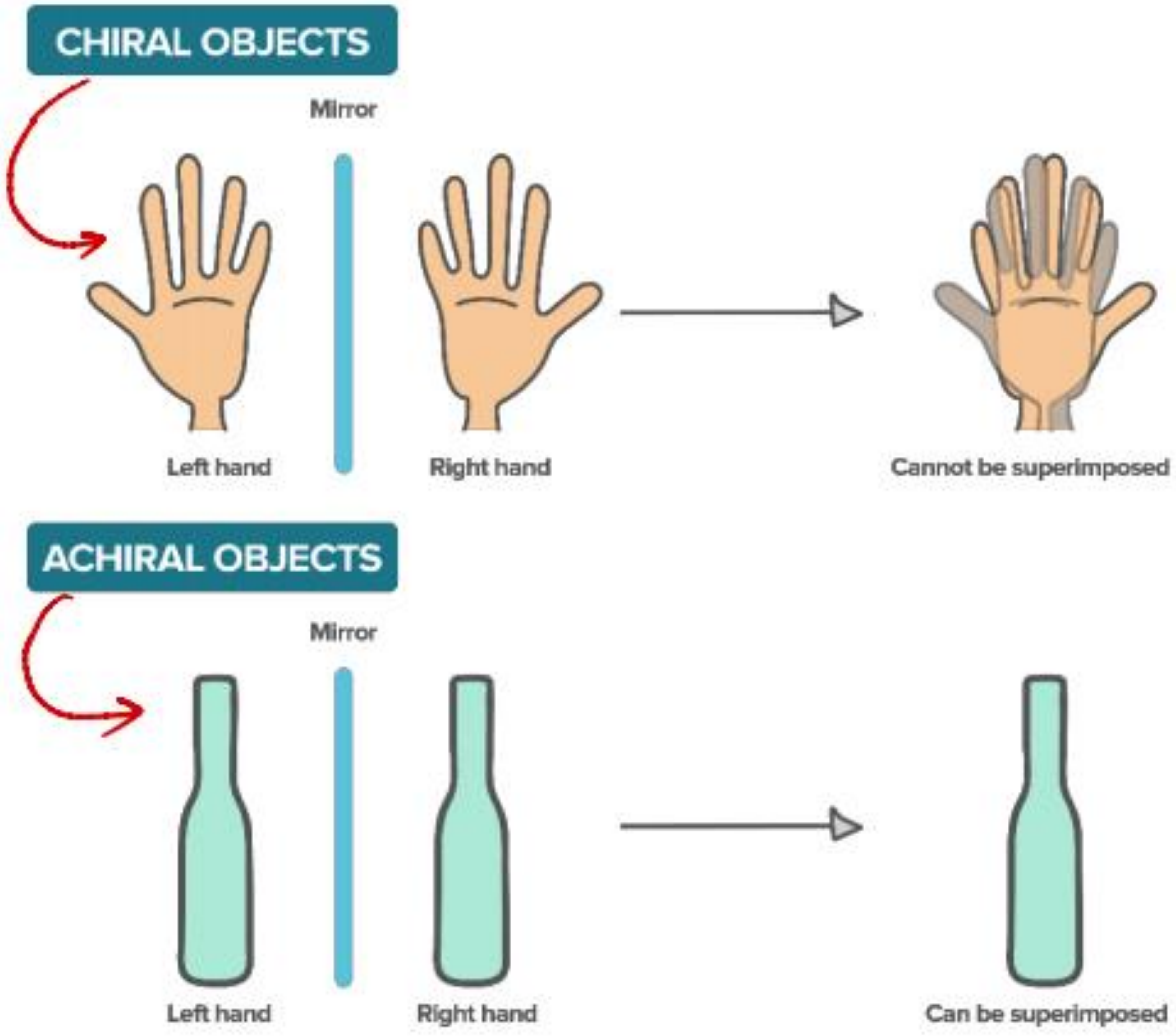
The bottom chair is chiral (mirror image is not superimposable)

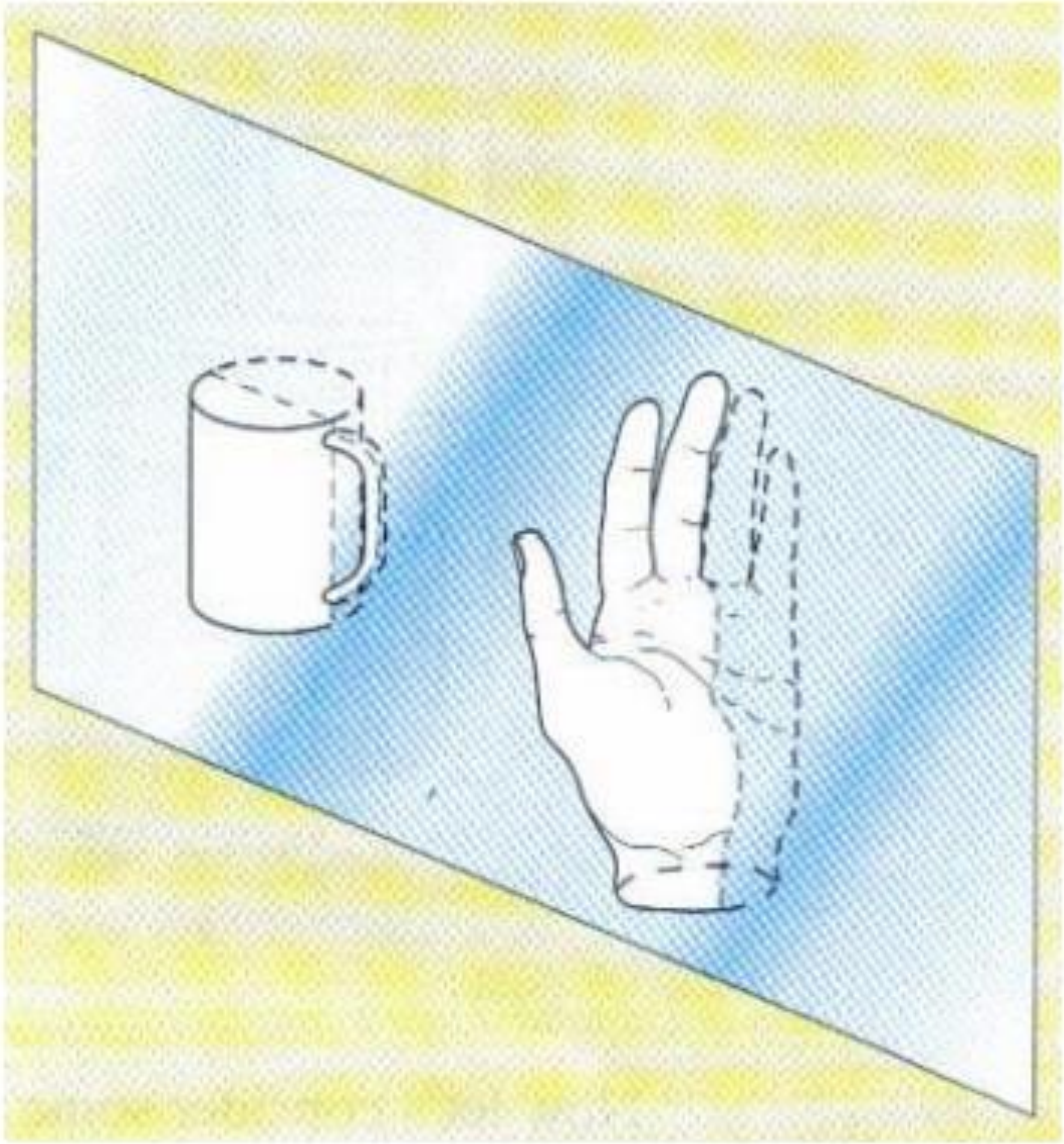


An achiral object will have a ***plane of symmetry*** in it, i.e. a mirror plane through the object so that one half is a mirror image of the other.

The coffee cup is achrial

While the hand is chiral

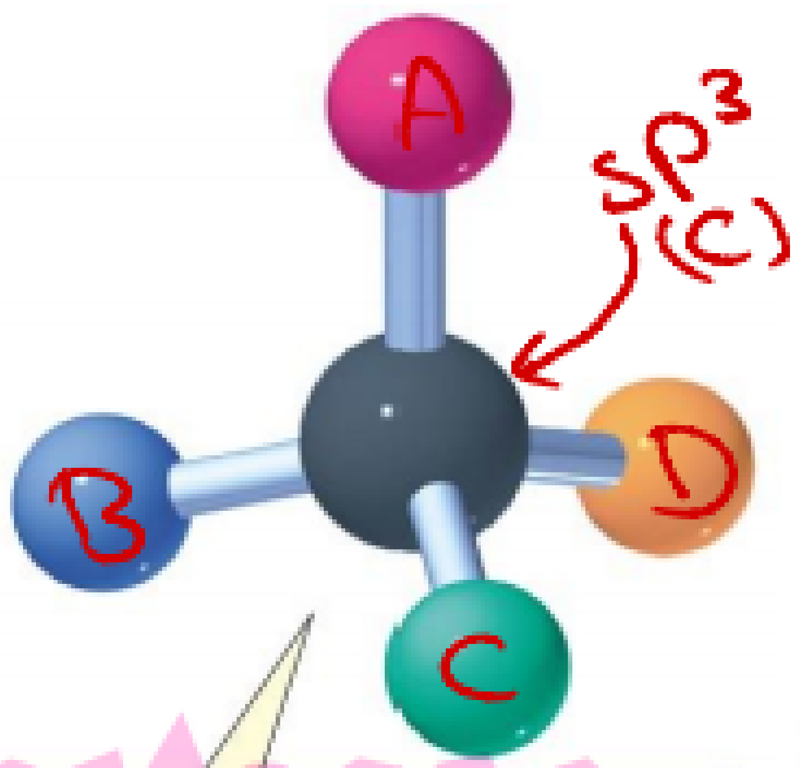




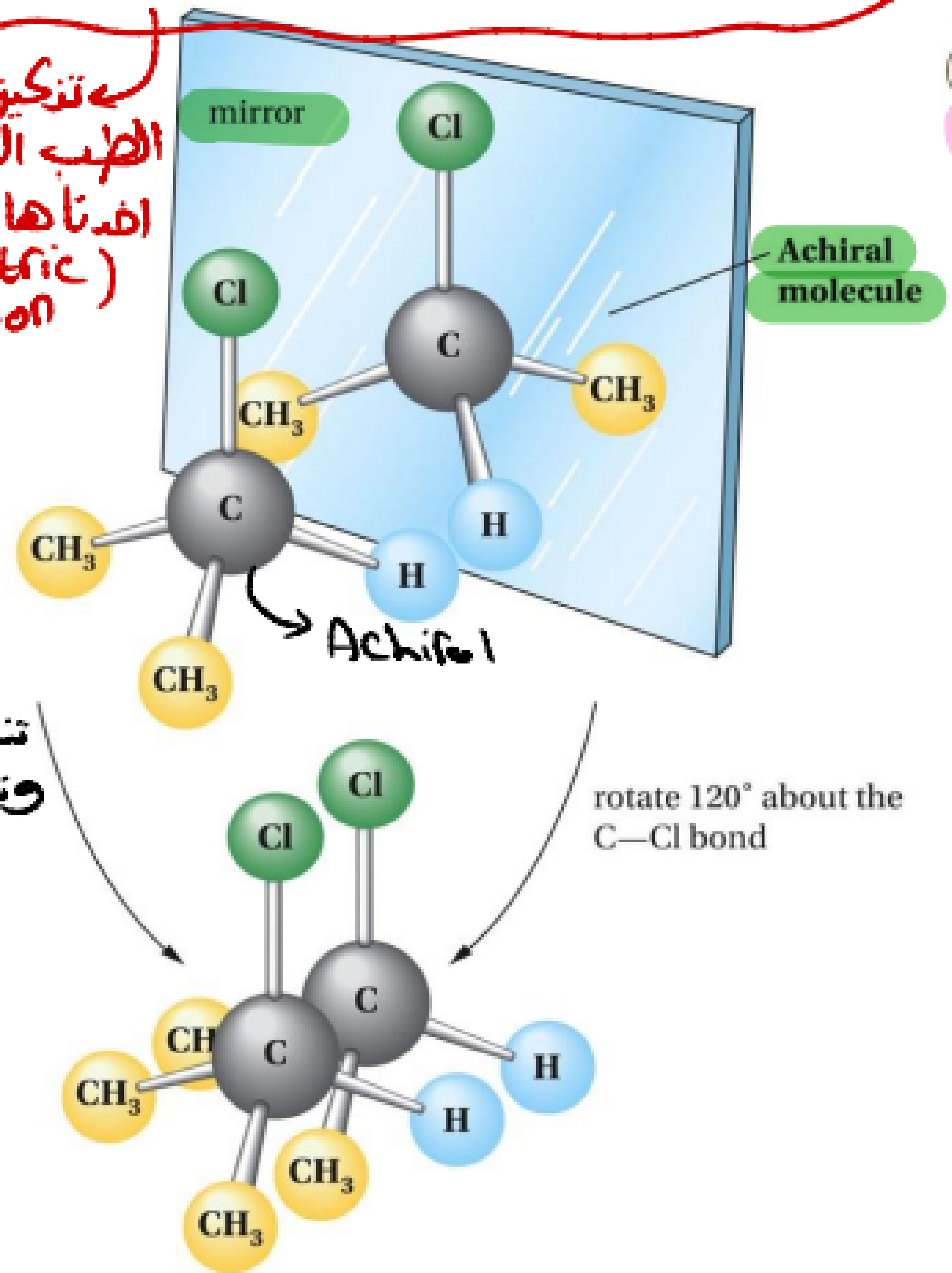
For molecules a chiral center is an sp^3 hybridized C atom with four different groups (atoms) attached. If two or more groups are identical then the molecule will posses a plane of symmetry.

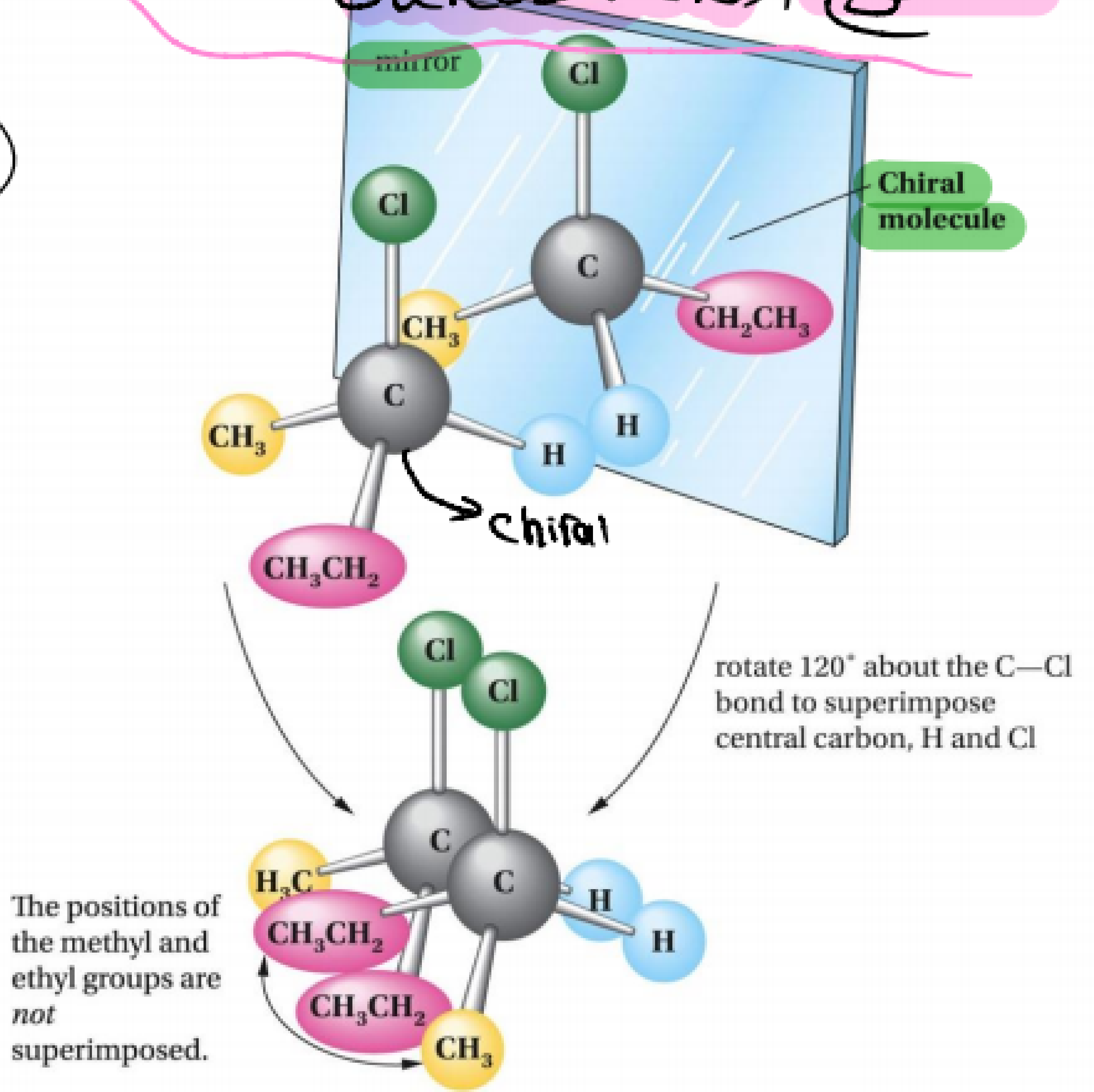
when is an organic molecule chiral?
لازم تحقق شرطين :-
1- sp^3 (C) has 4 يعني كربونة مع atoms or groups
2- 4 Different atoms or groups ← الاربع مجموعات حوليها يكونوا مختلفين

وهذا الكلام بنطبق على الـ molecules اي molecule ما عنده خاصية الـ symmetric إذاً هو وصورته على المرايا رح يختلفوا عن بعض إذاً وظيفتهم رح تختلف عن بعض إذاً هاد بيعتبر نوع من انواع الـ stereoisomers



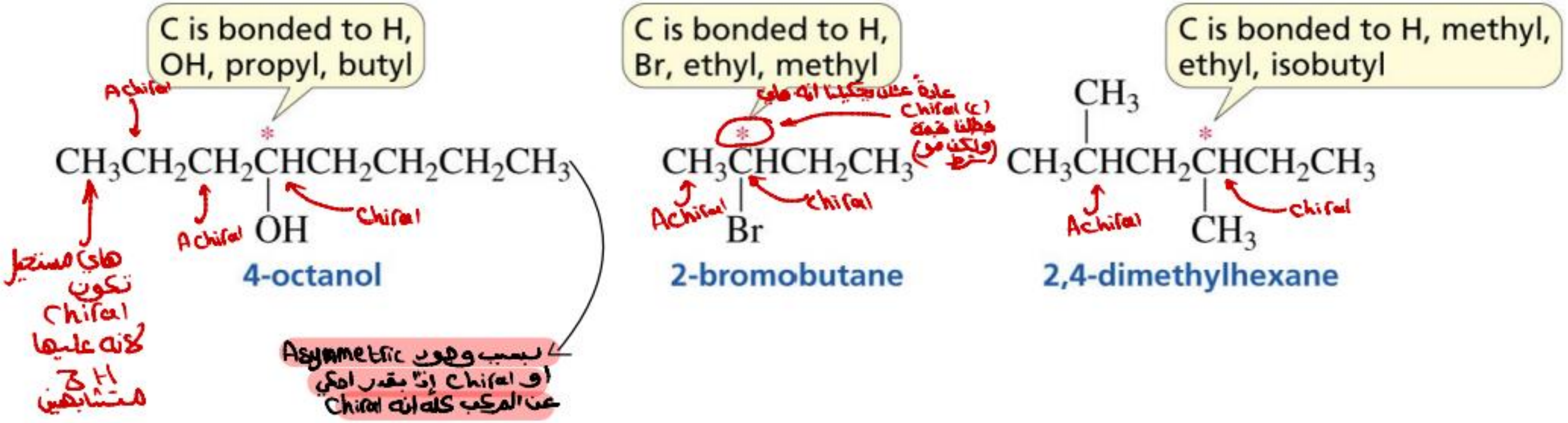
تركيز الطلاب ← الطب البشري: اخدنا هالحكي بالحرف (Asymmetric carbon)





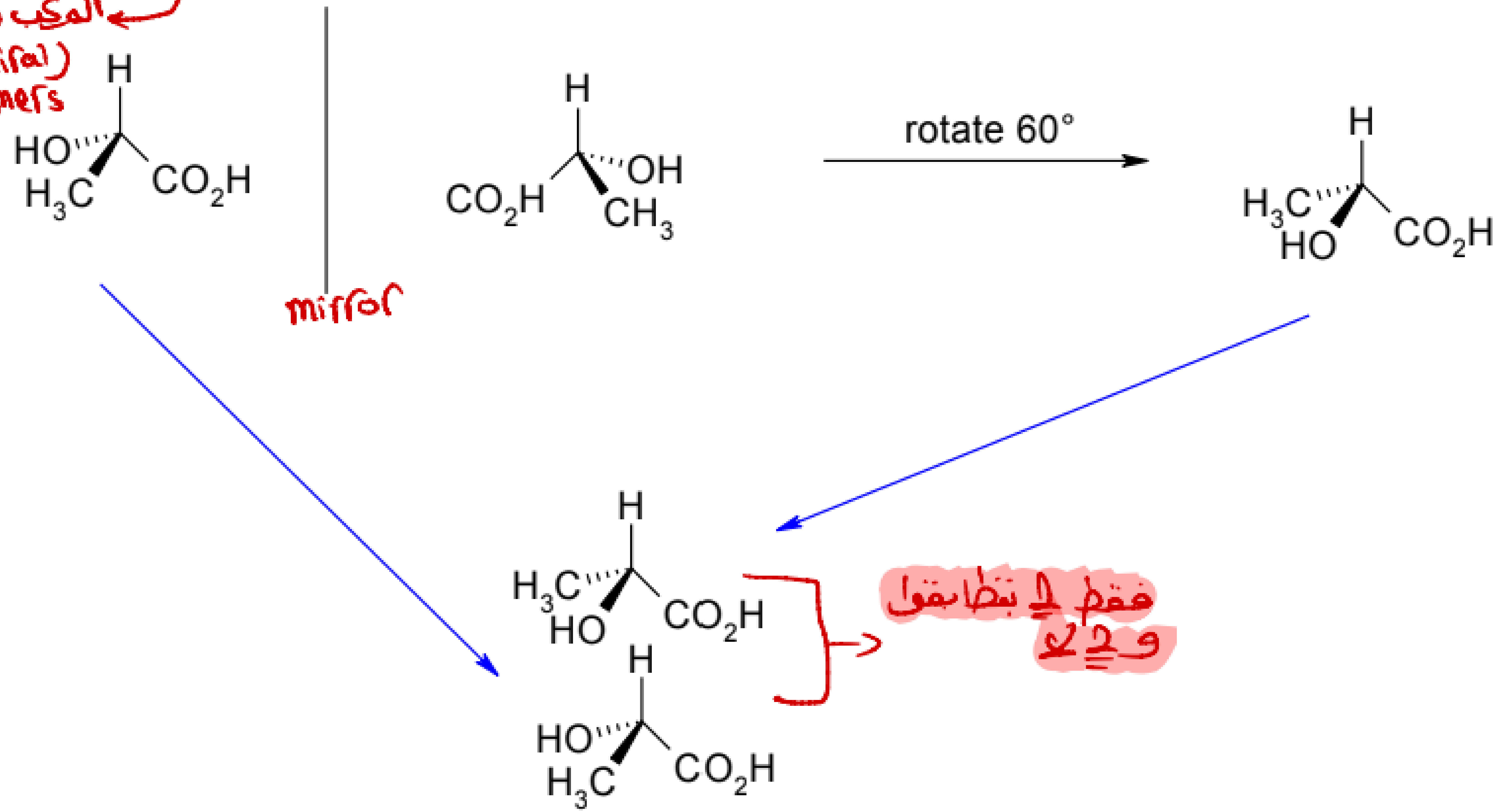
Compounds with an Asymmetric Center

So, they are chiral molecules



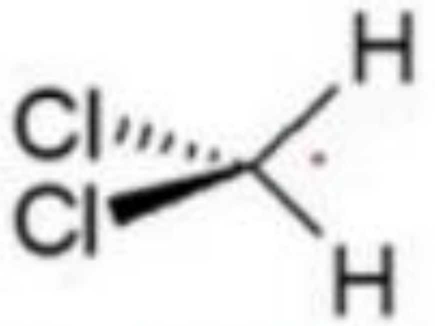
Chirality (cont'd)

Molecules which are non-superimposable mirror images (because they have a chiral or stereogenic center) are *enantiomers*, i.e.

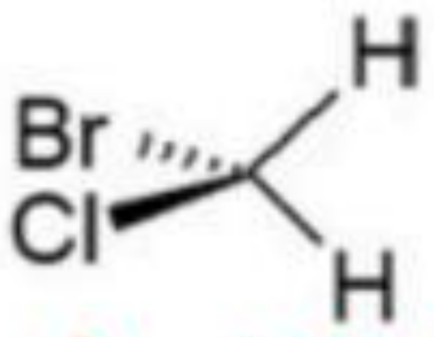


Enantiomers (cont'd)

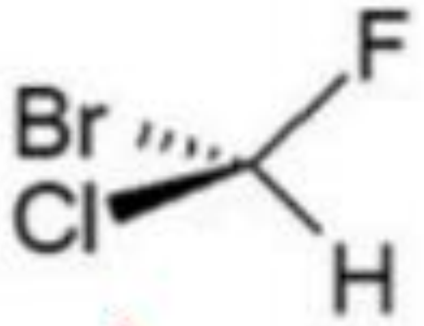
Chiral or not?



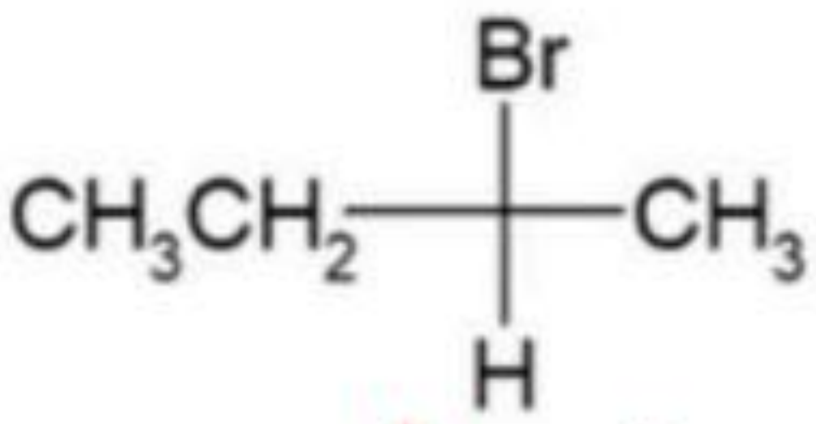
Achiral



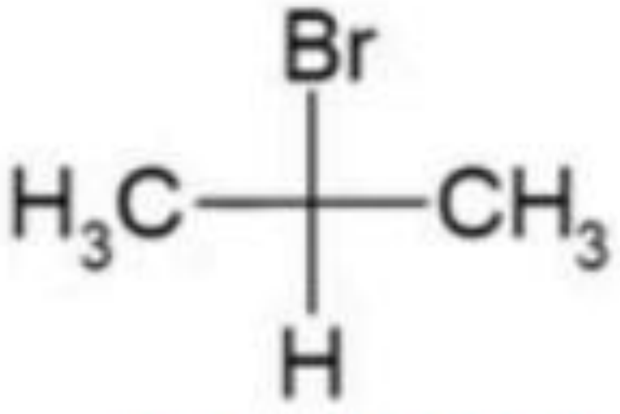
Achiral



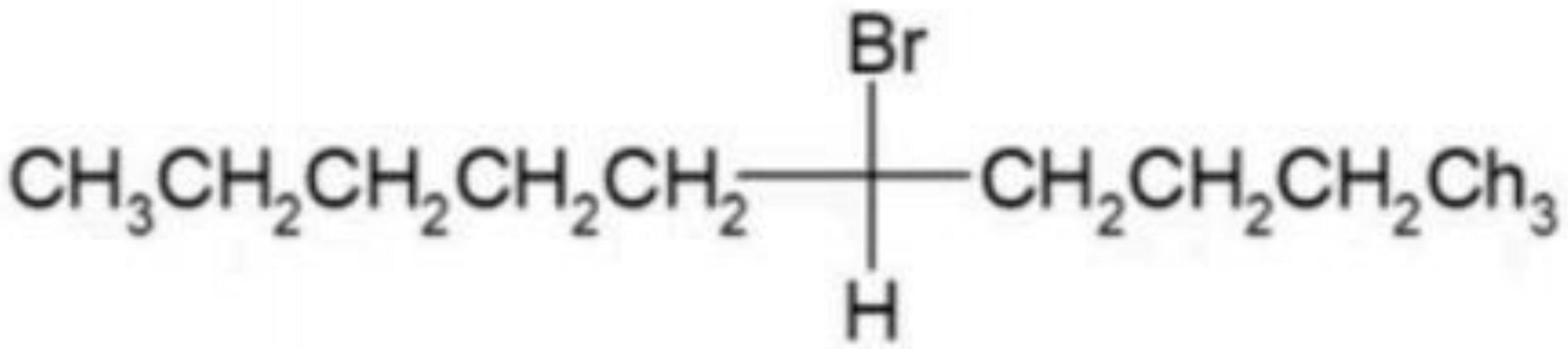
Chiral



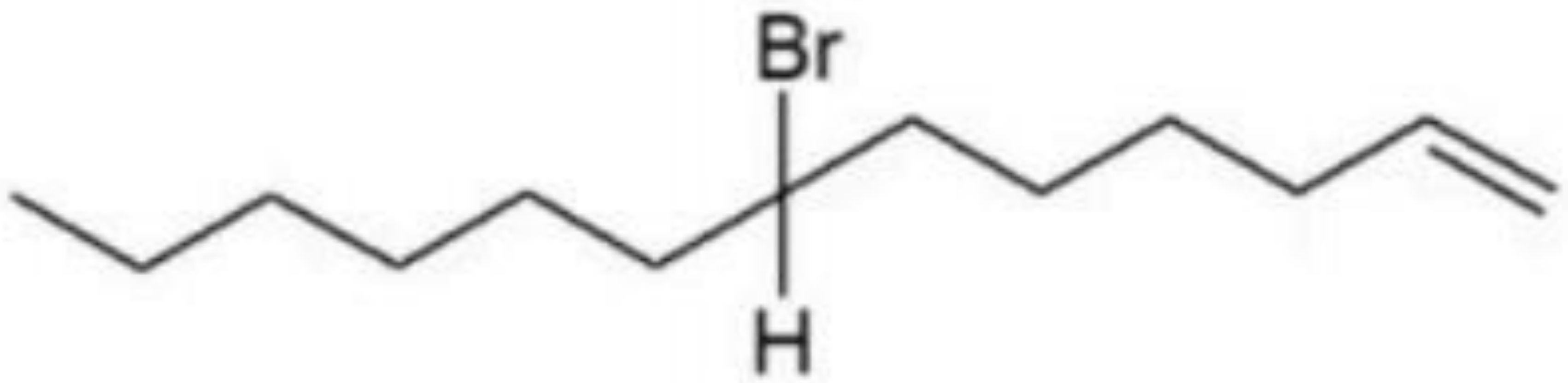
Chiral



Achiral



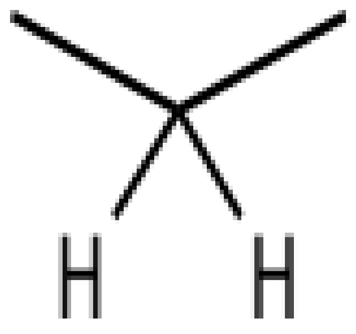
Chiral



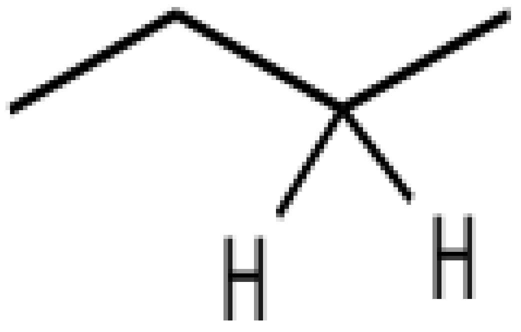
Chiral

Chemically Equivalent Atoms

Atoms that are related to one another by a mirror plane are chemically equivalent and have the same chemical properties, i.e. propane and butane



homotopic H

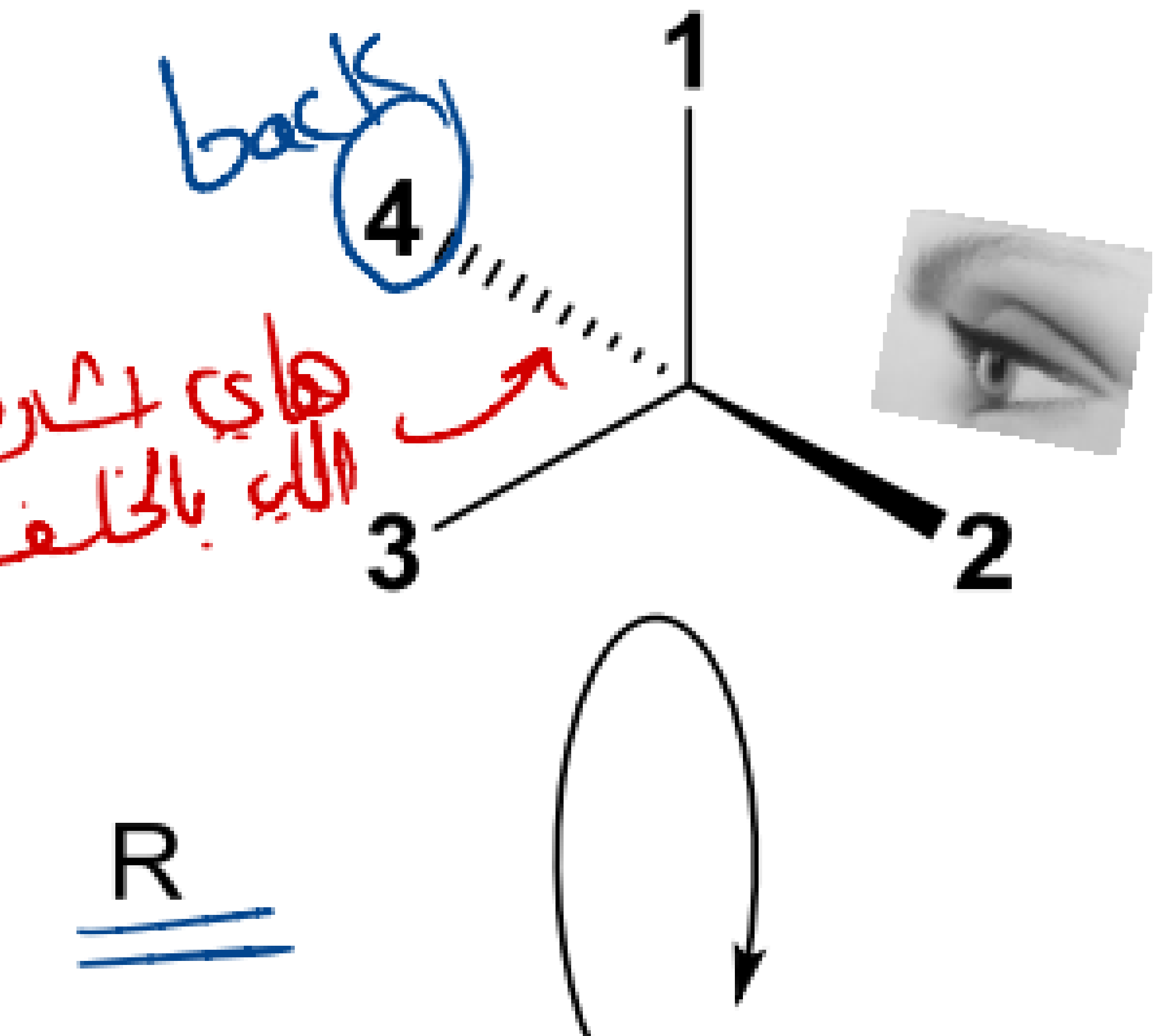


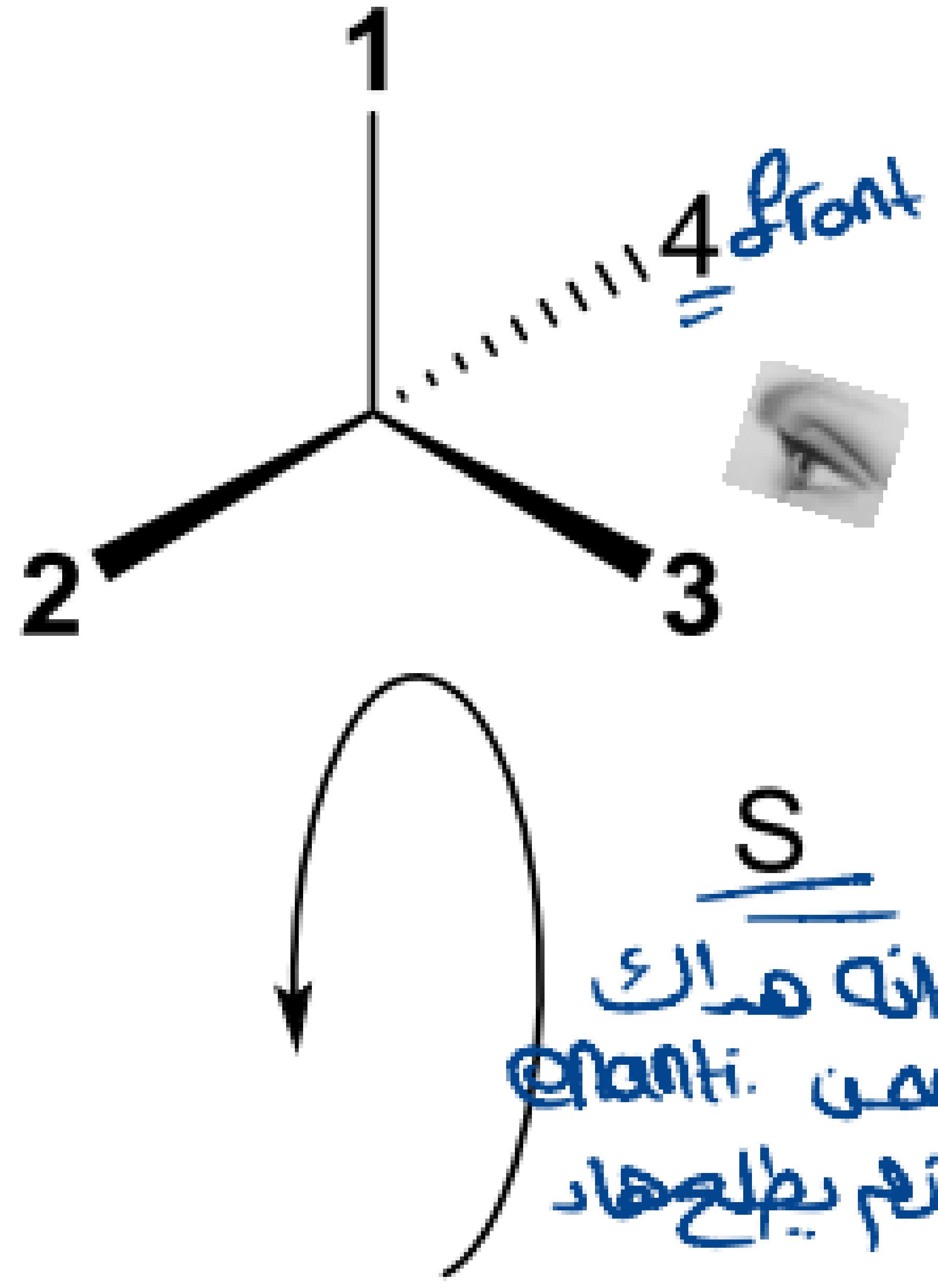
enantiotopic H

Configuration: R/S Nomenclature

The R/S nomenclature system is used to distinguish between two enantiomers. The methods relies on three simple rules for assigning priority to the four groups attached to assign a configuration of R (clockwise) or S (counterclockwise).

The lowest (#4) priority group Pointing away from us (.....)





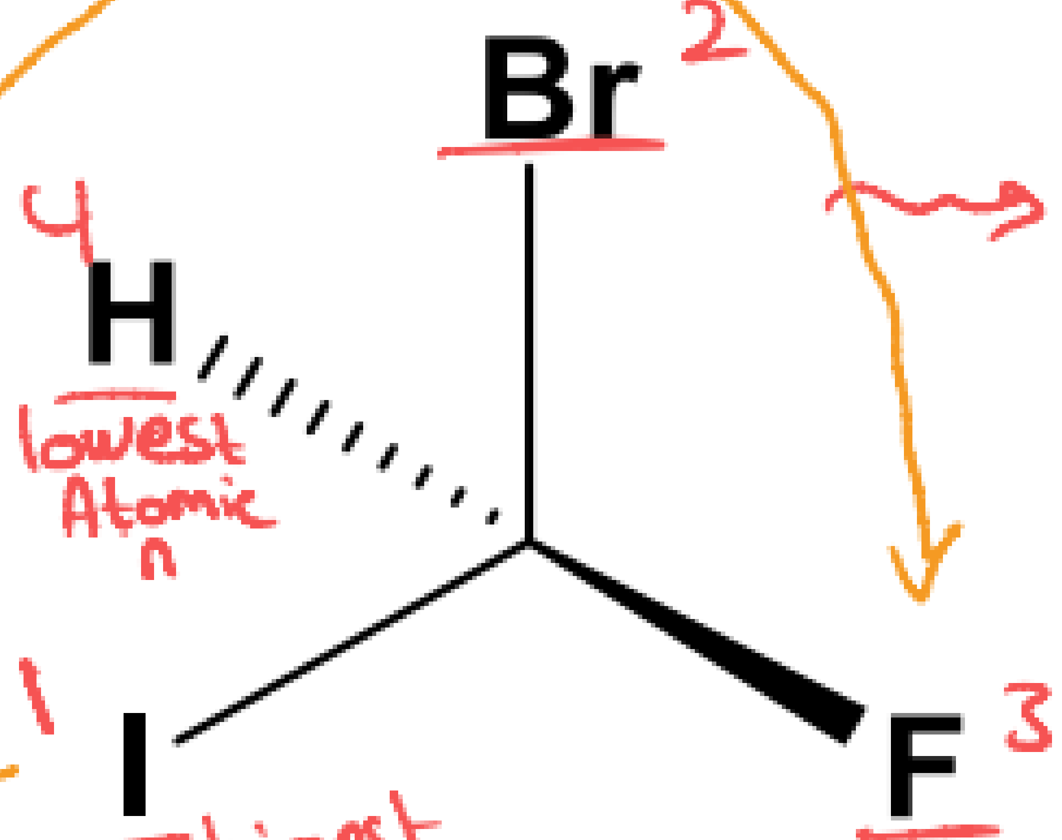
كيف بدي استقبل هاي R وهاي S ؟
عنا مجموعة قواعد

The rules are:

1) Atoms attached to the stereogenic center are ranked to atomic numbers (the higher the atomic number the higher the priority

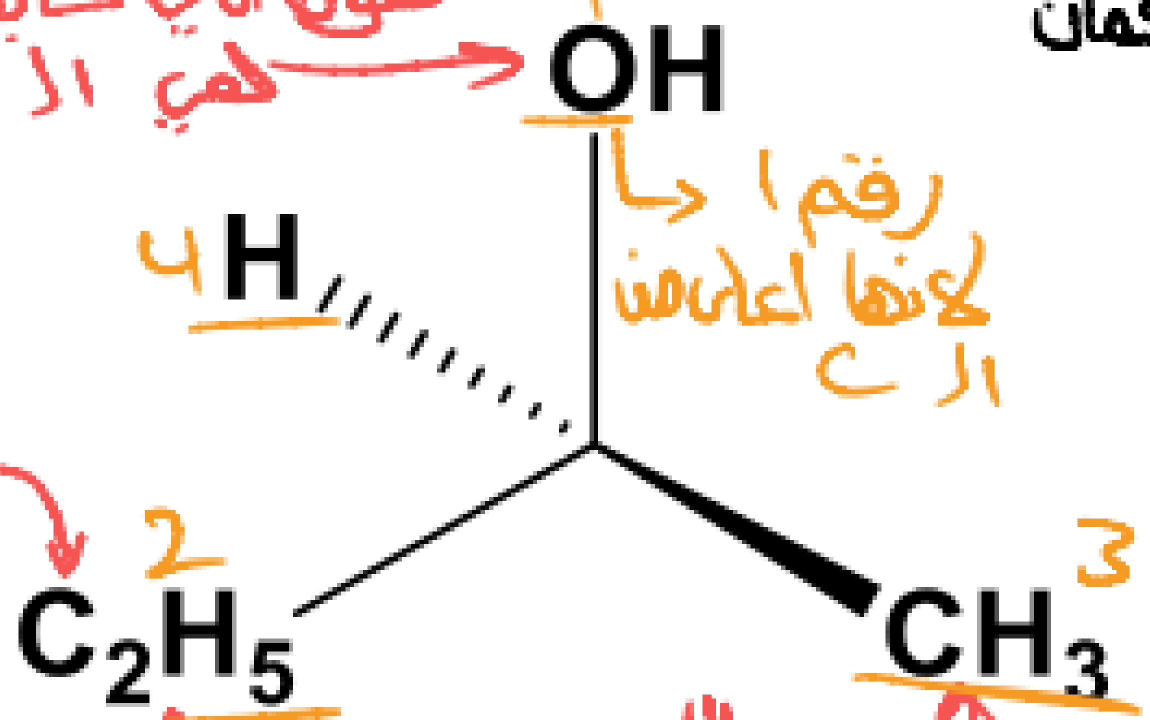
حسب الجدول الدوري

اول شغلة برقم من 1-4
1 → highest priority
4 → lowest priority



I, Br, F, then H

2) Compare the next atom out in the chain



Counter clockwise (S)

$-CH_3$ vs. $-CH_2CH_3$

H,H,H

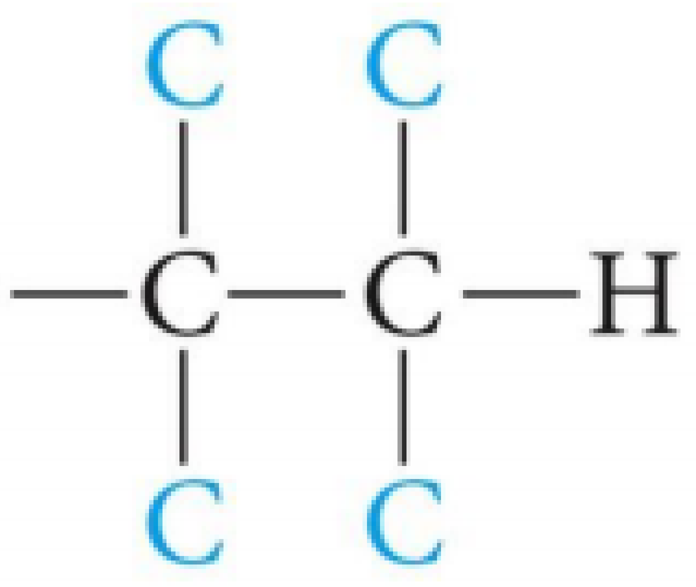
H,H,C

Higher priority

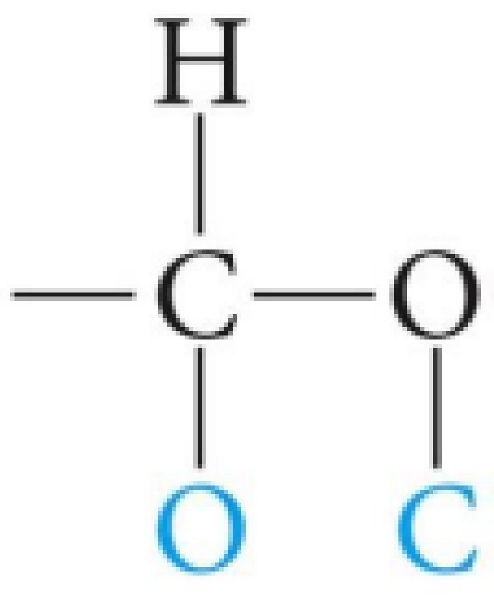
3) Multiple bonds: open the bond as equivalent atom types, i.e.

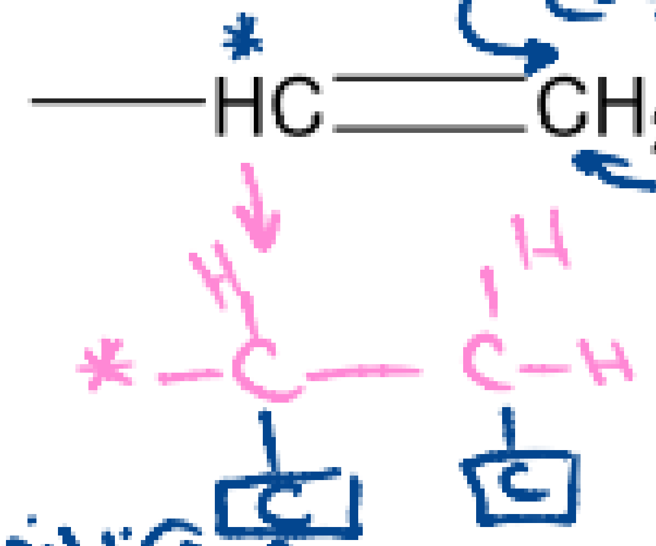
هون لوقارنا بينها وبين الـ كتنها الـ double منلاقي انه الـ triple هي اعلى priority

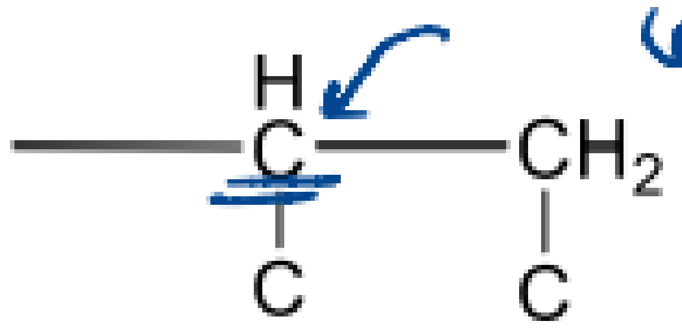
$-C\equiv CH$ is treated as



$-CH=O$ is treated as



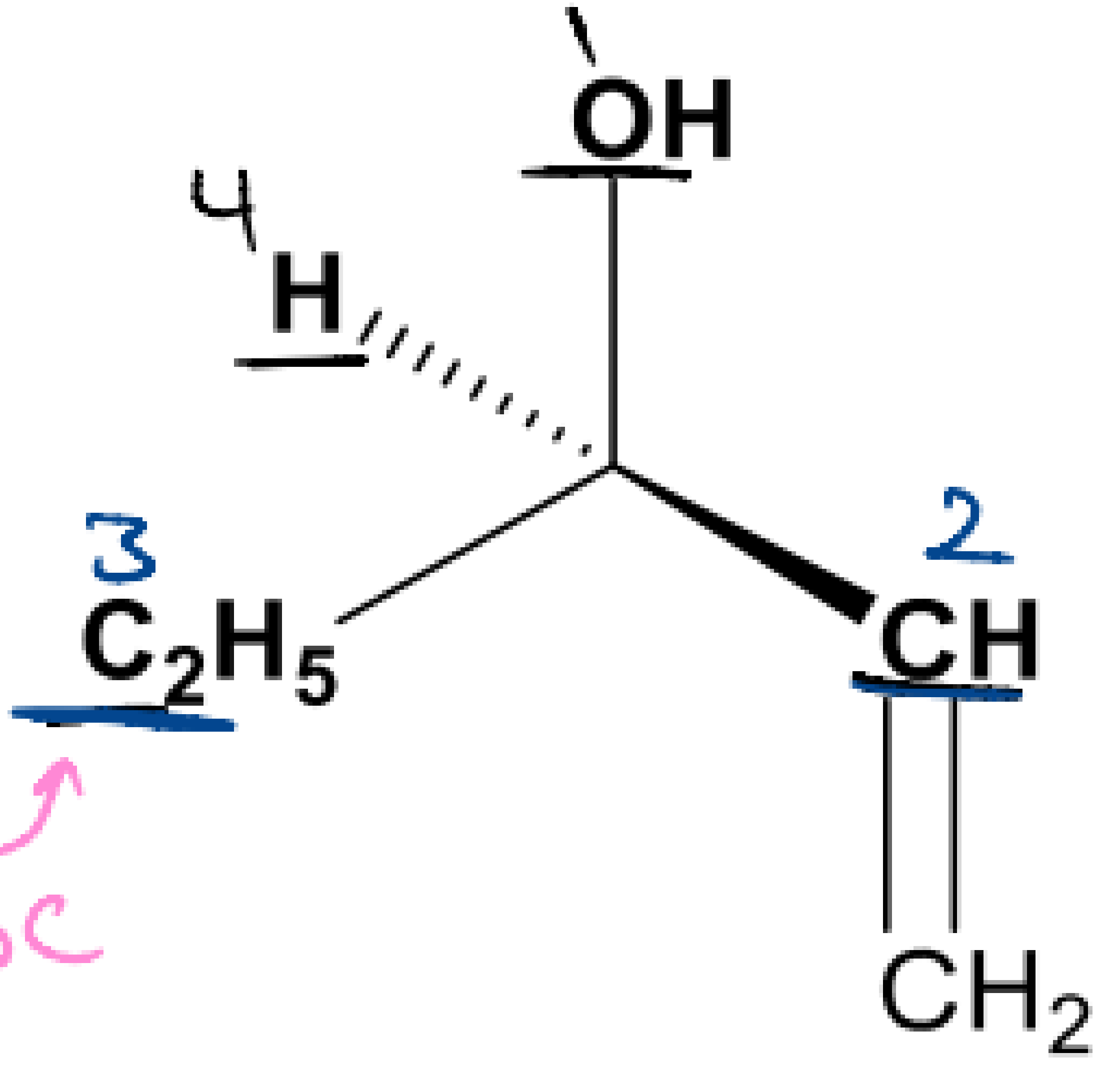




Note:

eg R Or S

Clock wise



(هنا حكينا لما يكونوا متشابهات (C)
كانحل مباشرة حكينا اول خطوة
لقدام وقارن بعيدًا عن الـ C
ولكن نلاحظ هون انه المقارنة
عبر عائلة واحد عليه single
والثاني double bonds

هون بدنا نفكك الـ double
شوف فوق يسار عشان تفهم

Naming Enantiomers

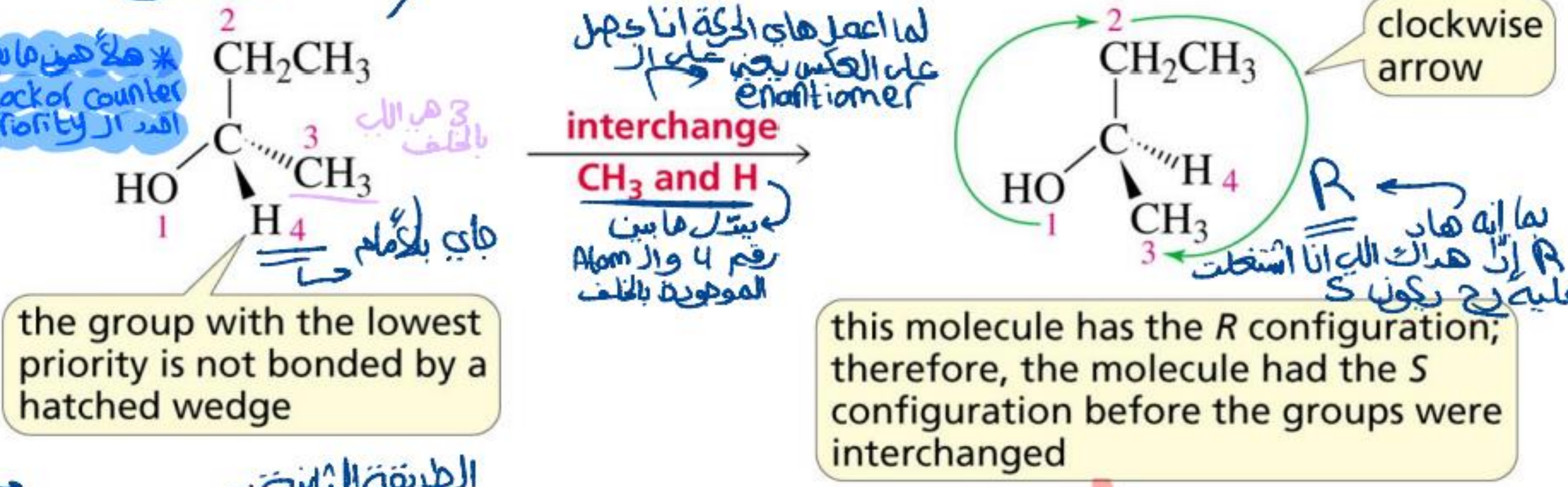
هل دائمًا المركب بكون كيف انه دائمًا الرقم 4 بكون بالخلف؟ الجواب لا

<u>If the lowest priority group is</u> <u>not</u> on a hatched wedge (#4), switch a pair so it is on a hatched wedge.

عندي طريقتين للتعامل لما تكون 4 مو بالخلف:-
1- هو اني اعمل دوران للمركب واتخيل انه 4 صارت بالخلف ← وهاي الطريقة مو كثير مضمونة

Then, name the new compound.

*Note: لما ابدّل ما بغير الروابط (شكلهم) + كل ذرة بتاخذ معها رقمها



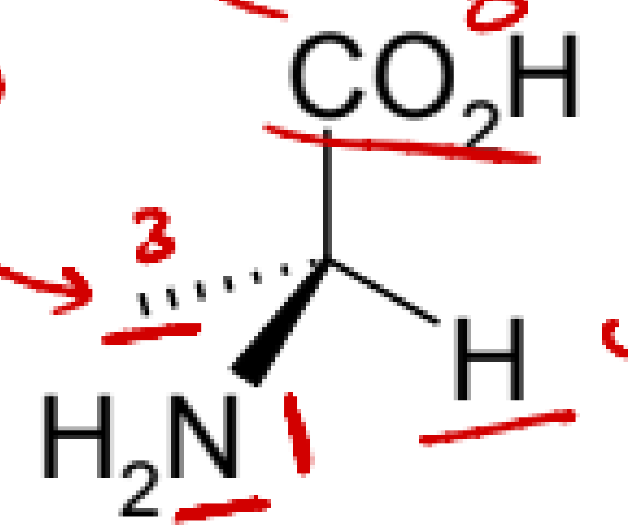
الطريقة الثانية:-
*اذا انت بدّلت اي مجموعتين ببعض بتحصل على الـ opposite configuration
← هذا الكلام بفيد بشغلة انه 4 مو بالخلف
هون بهاد المثال اللي بالخلف هي CH_3 رقم 3
← لكن لو بدلت بين H و CH_3 ← H لانها هي اللي رقمها 4 و CH_3 لانها هي اللي بالخلف

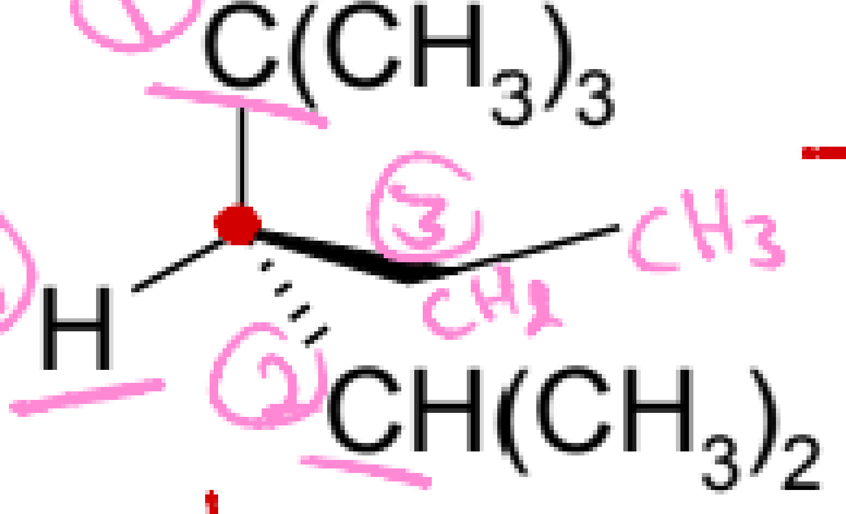
*لما نعمل interchange الـ S متحوله لـ R والـ R متحوله لـ S

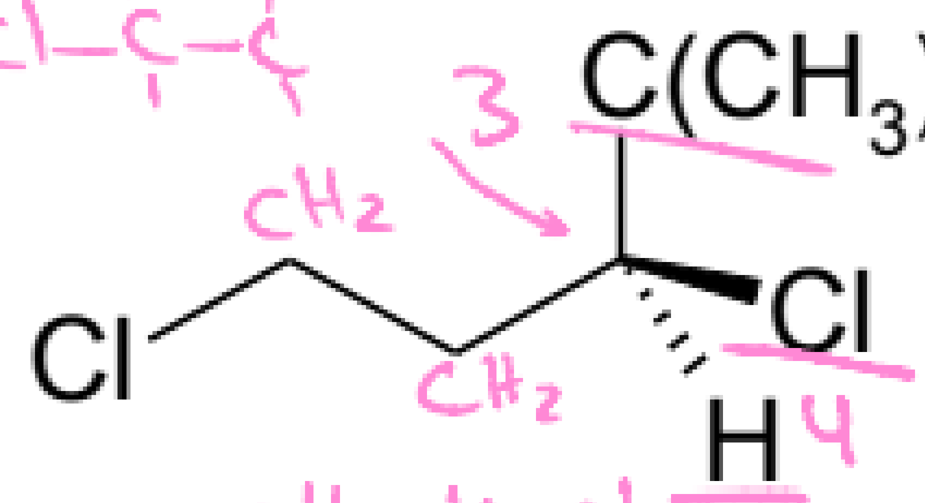
*Note:- مو دائمًا اللي بالخلف لح تاخذ رقم 4

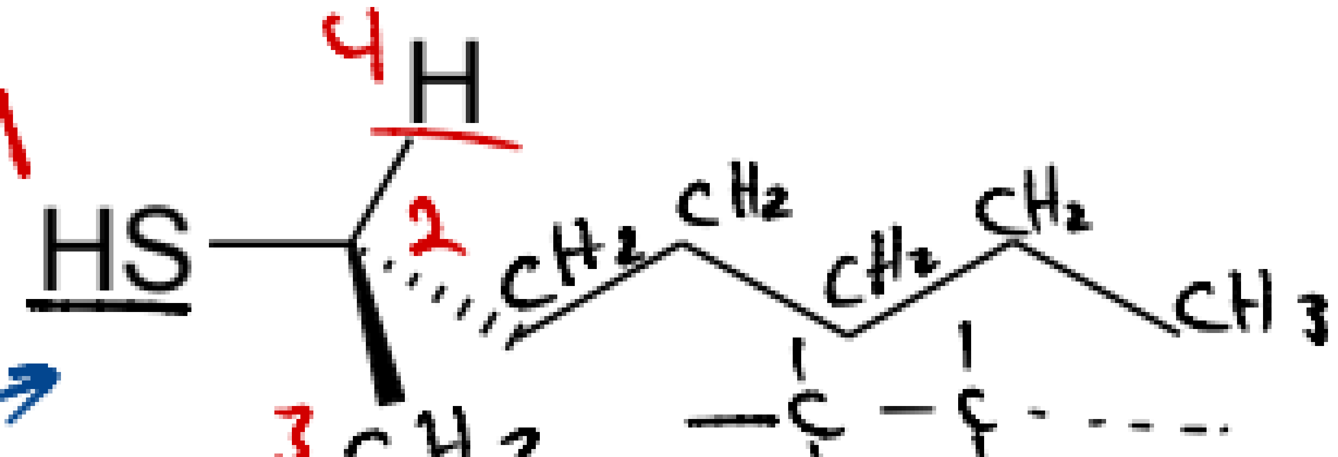
Configuration: R/S Nomenclature

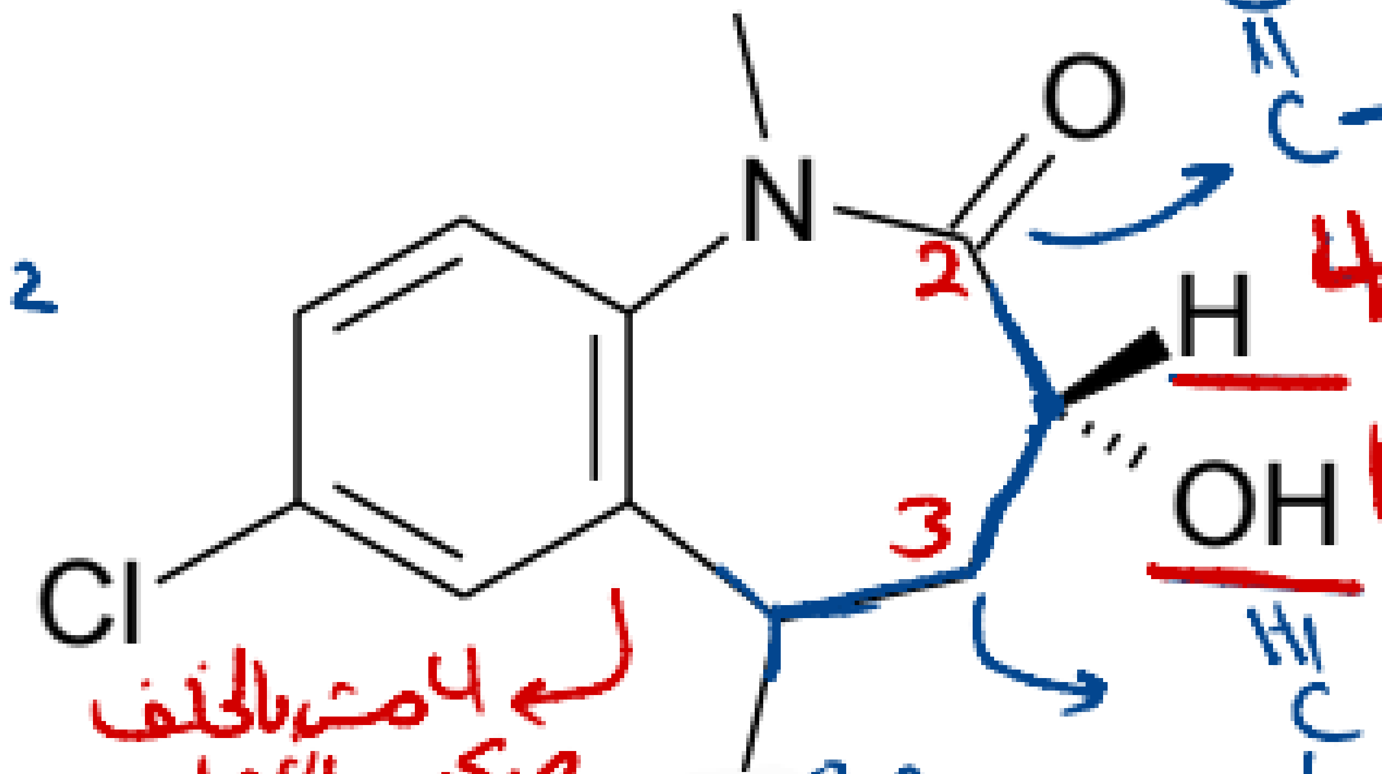
Examples:











عبّر عن ال chiral molecule في 2D structure

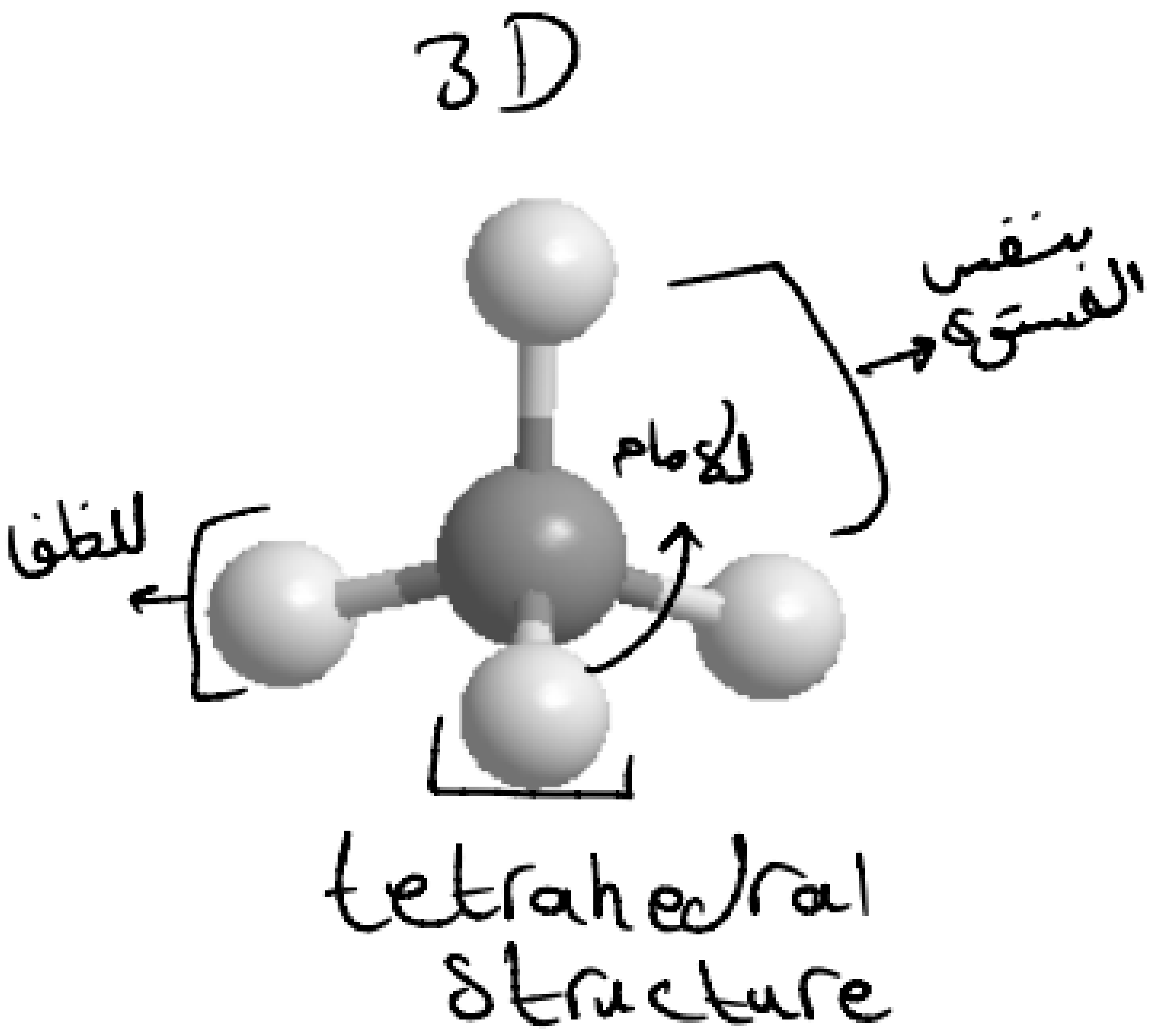
Fisher Projections

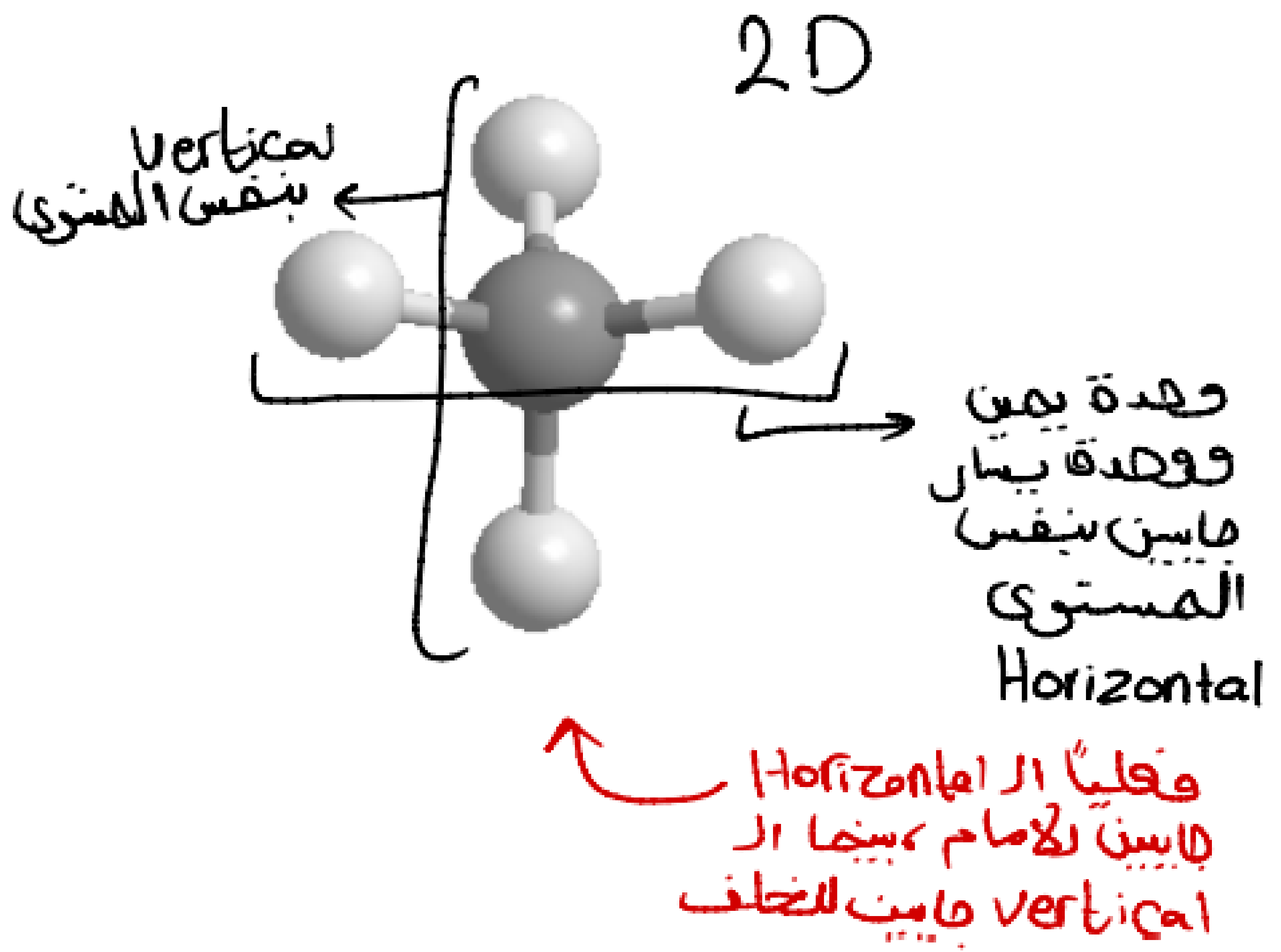
Fisher projections are a stylized way of conveying 3D info in a 2D drawing. They are very common in biochemistry. The convention is a cross where the horizontal arms are coming out of the page towards you and the vertical arms are going back into the page. For 2 adjacent chiral centers the middle vertical bond is in the plane of the page, i.e.

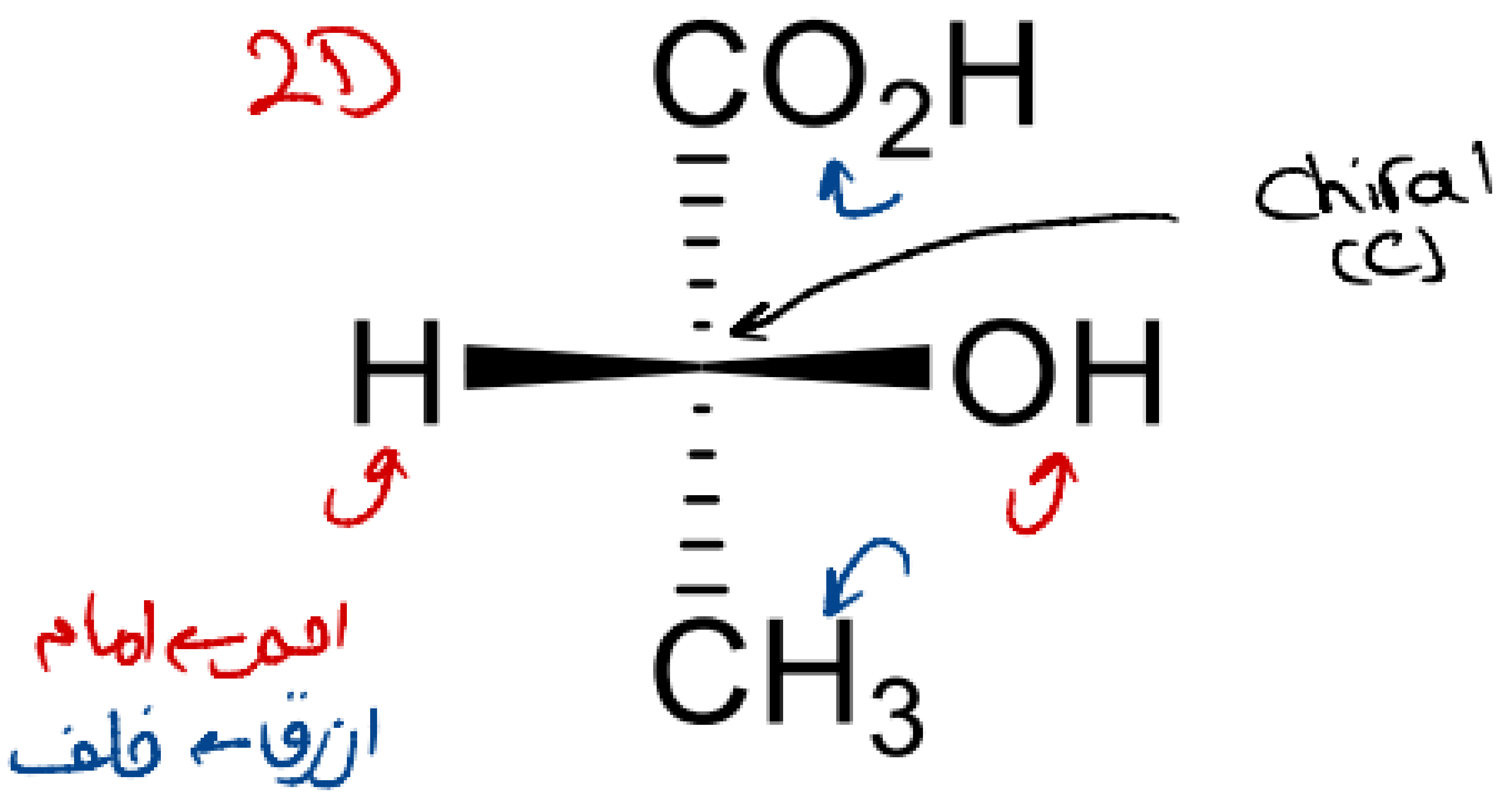
* لما اعبّر بطريقة Fisher او في ال 2D :

ال Horizontal جايين للأمام

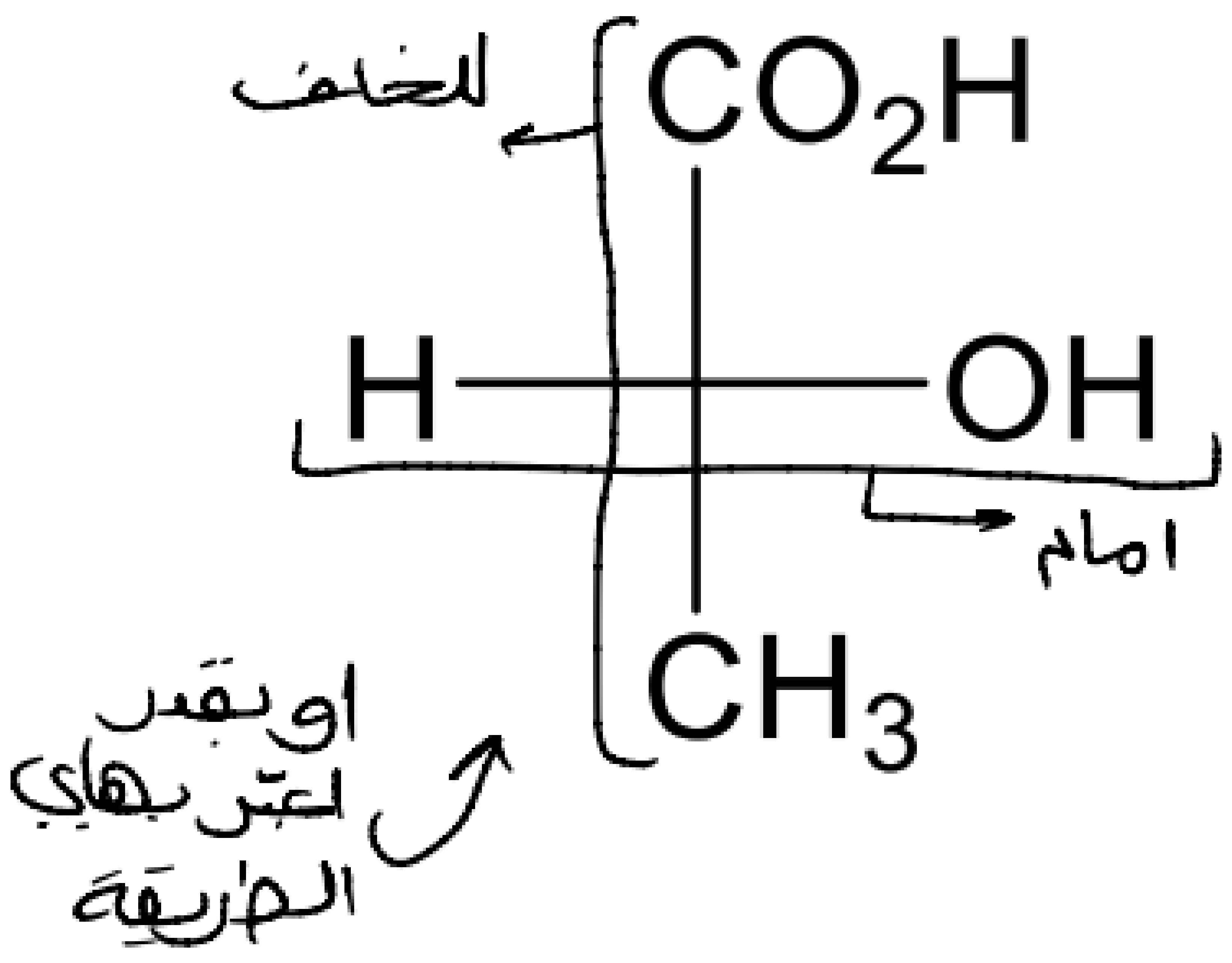
ال Vertical جايين للخلف


3D
بنفس المستوى
للامام
للخلف
tetrahedral structure


2D
Vertical
بنفس المستوى
وحدة يمين ووحدة يسار جايين بنفس المستوى
Horizontal
فعلياً ال Horizontal جايين للامام، بينما ال vertical جايين للخلف

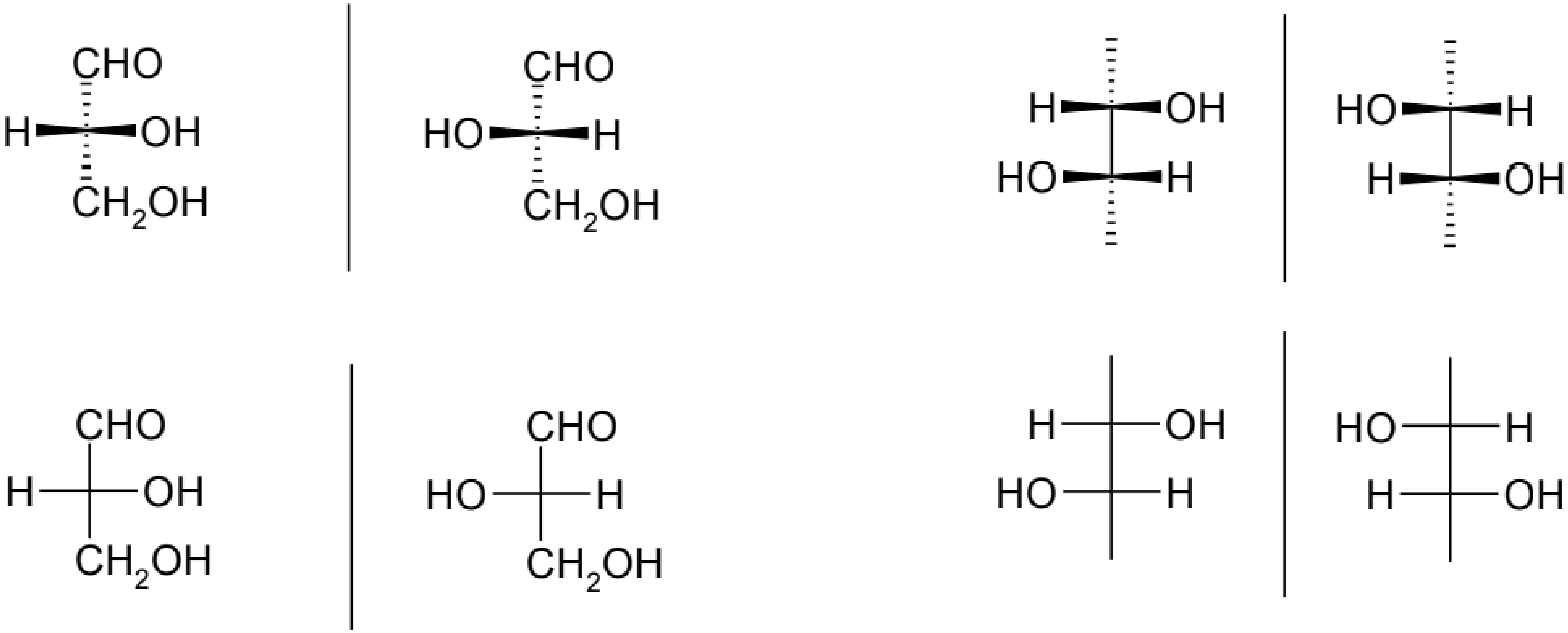

2D
CO_2H
H
OH
CH_3
chiral (C)
احمر ← امام
ازرق ← خلف

=


للخلف
CO_2H
H
OH
CH_3
امام
او بقدر اعتبر بهاي الطريقة

Fisher Projections

Examples:



بحالة ال Fisher انا ما بقدر اعمل rotation (90°)

Fisher Projections

بقدر اعمل Rotation (180°) بحيث انه بلف المركب كامل
بس ما رح يتغير ال Configuration

Manipulating Fisher diagrams:

– Entire diagram: Rotation by 180° but not 90° (90° inverts the configuration)

– Three groups: can be rotated by any amount

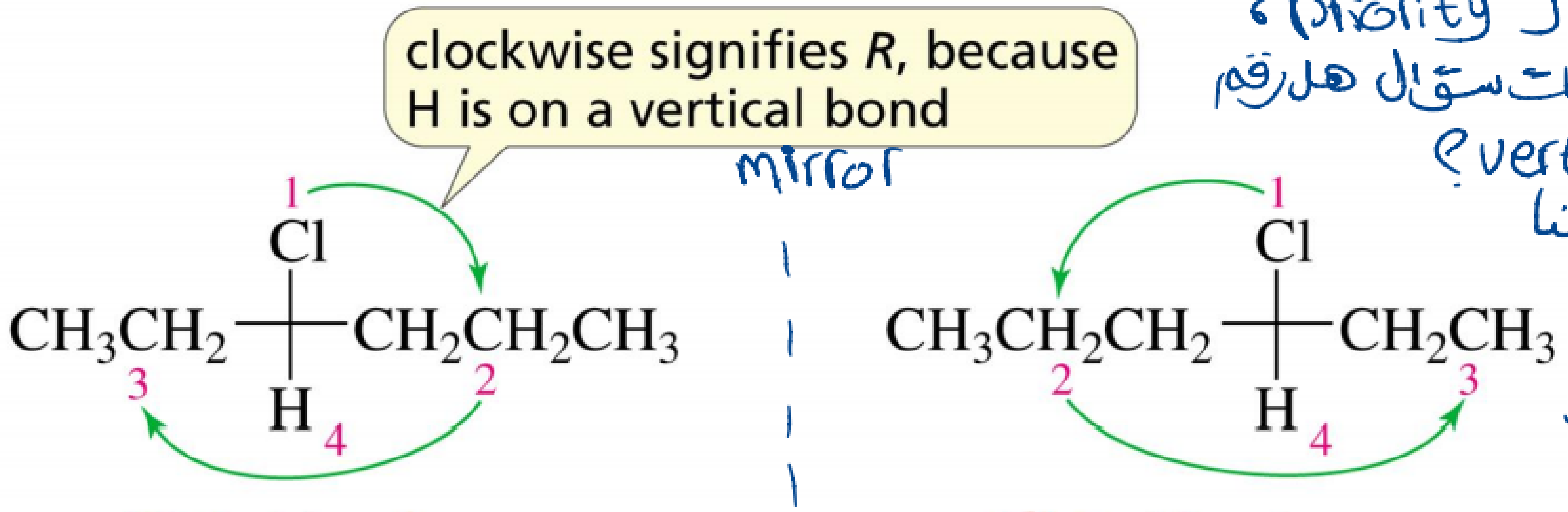
– Two groups: exchange of any two groups inverts the configuration

* إذا بدلت اي two groups رح تنعكس ال Configuration
* اذا بدلت 3 رح ترجع إلى ما كنت عليه

← نفس الأفكار السابقة

Naming Enantiomers

هلأ كيف بدي احدد ال R/S :-



(*R*)-3-chlorohexane

(*S*)-3-chlorohexane

بعد ما أخذ ال priority ،
الآن اسأل نفسك سؤال هل رقم
4 على ال vertical ؟
لأنه إذا اتفقنا
ال vertical
يكون بالكلف
سواء فوق أو
تحت

If yes:
clock → R
Counter → S

If the lowest priority group is on a vertical bond, then

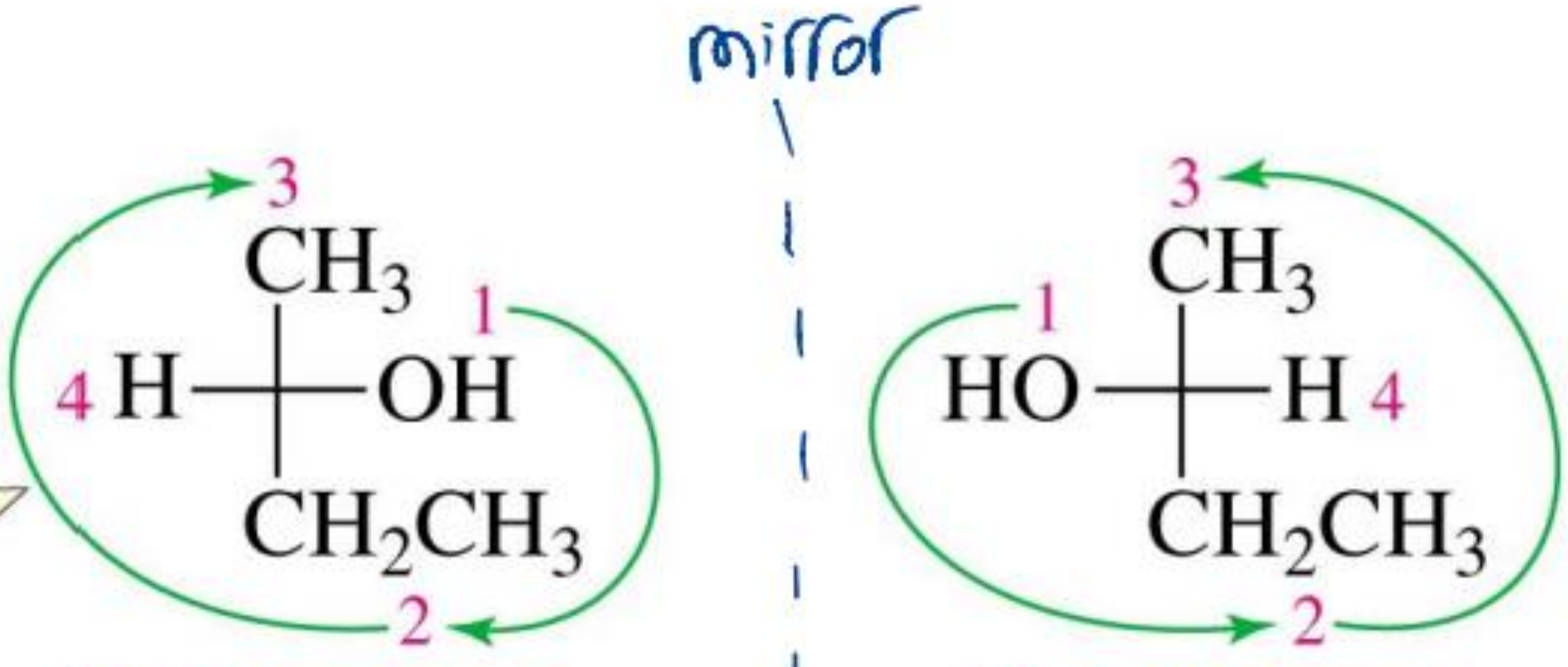
clockwise = *R*

and

counterclockwise = *S*

Naming Enantiomers

clockwise signifies *S*,
because H is on a horizontal bond



(*S*)-2-butanol (*R*)-2-butanol

Clockwise معناته
المفروض تطلع R
ولكن عكسناها

front

If the lowest priority group is on a horizontal bond, then

يعني ما رح نعكس ال groups

بهاي الحالة رح نخذ ال priority ونمشي عادي ونجيب منعكس الناتج مباشرة

counterclockwise = *R*

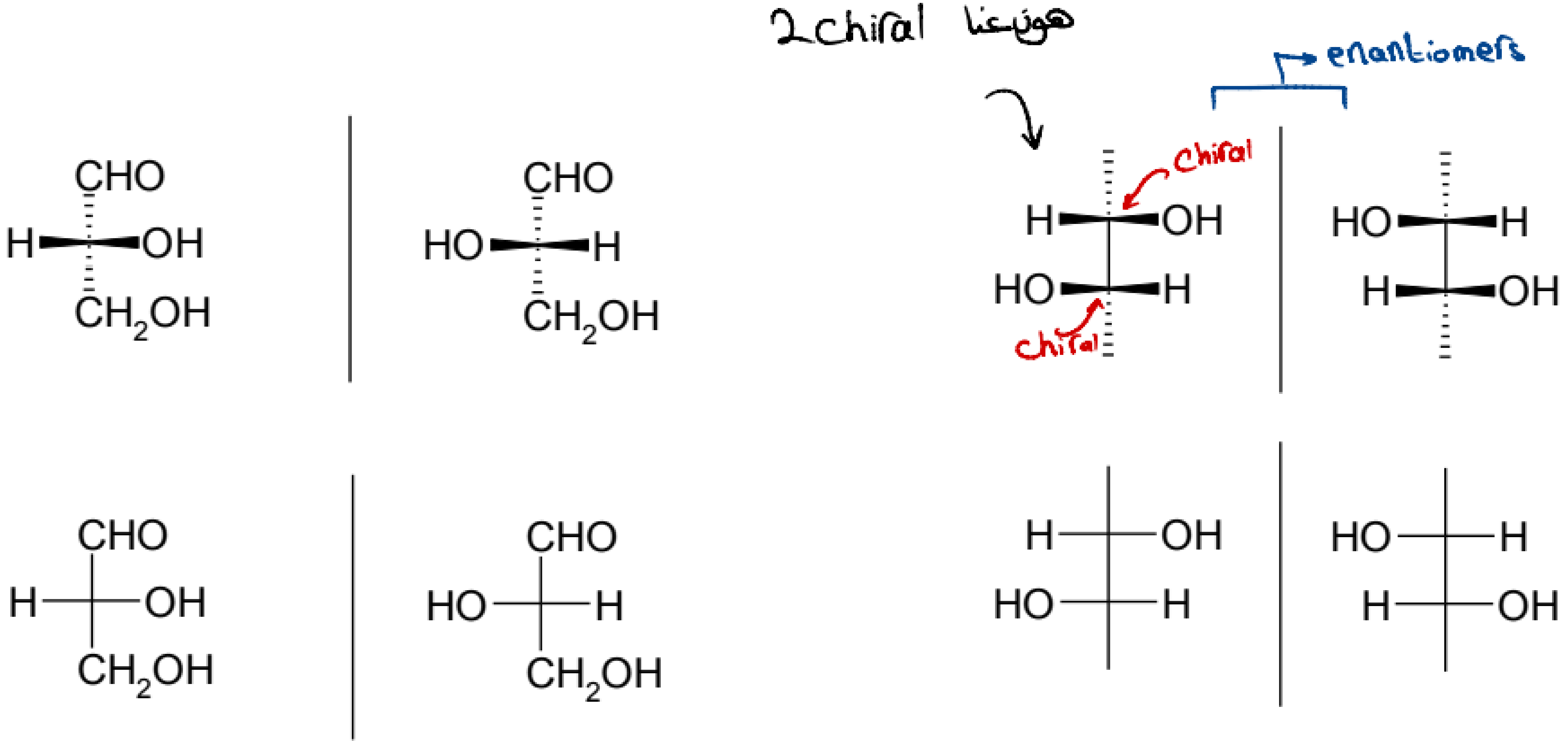
and

clockwise = *S*

هاد الحكي فقط لل (fisher) 2D

Fisher Projections

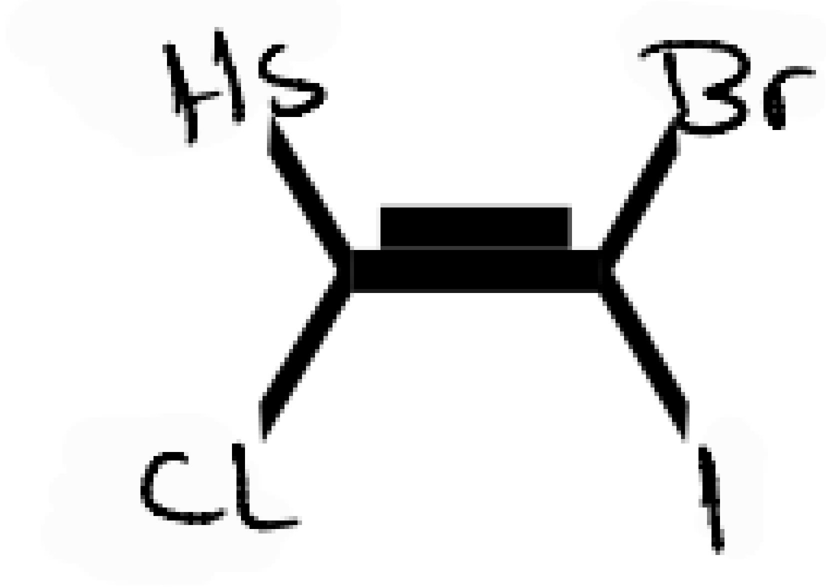
Assign the following stereochemistry

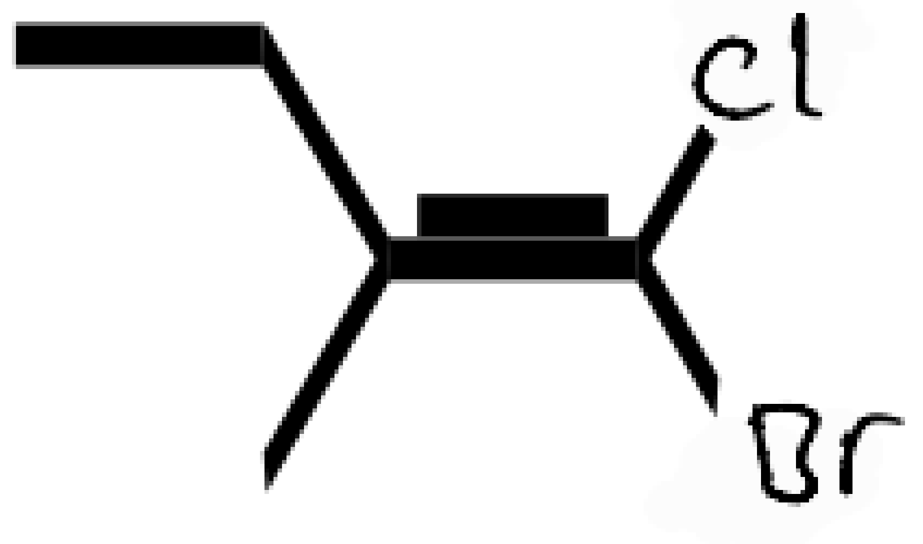


D-glyceraldehyde | L-glyceraldehyde | S,S-butane-2,3-diol | R,R-butane-2,3-diol

5.4: Configuration: E/Z Nomenclature

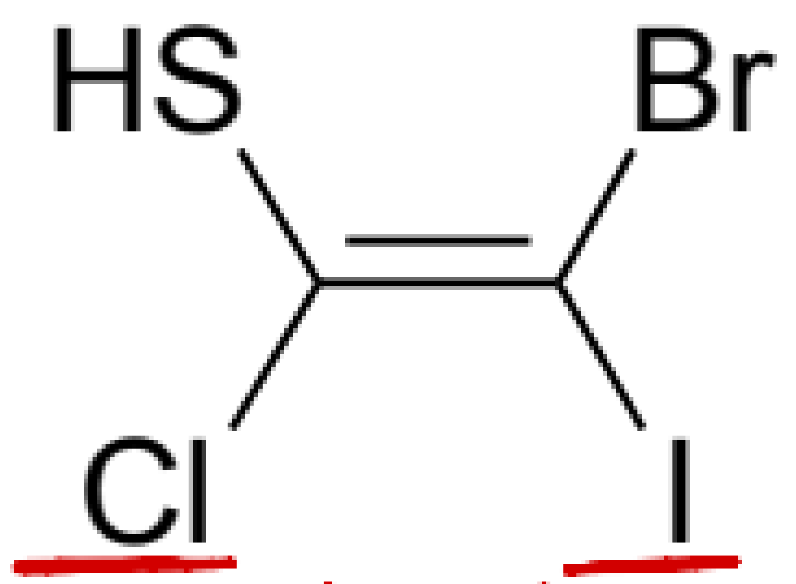
We have already seen geometric isomers when we discussed cyclic alkanes, the cis-/trans-isomers. Generally cis & trans only refer to hydrocarbons, what happens for other non C & H systems?

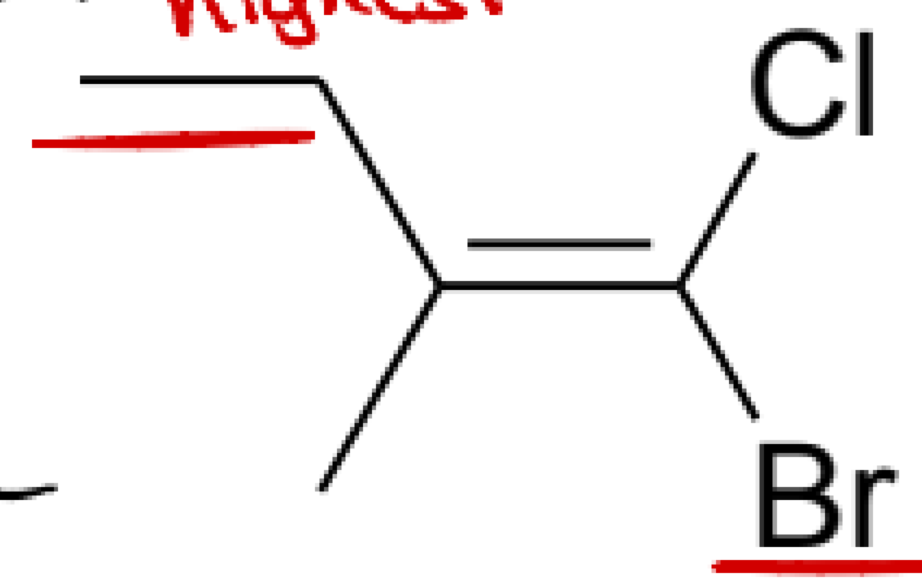




Configuration: E/Z Nomenclature

In this case we can use the same rules for chiral centers to assign a priority to each group on the double bond. When the two high priority groups are on the same side of the double bond: Z (zusammen (together)), on opposite sides: E (entgegen (opposite)).





(*E*)-1-bromo-1-chloro-2-methylbut-1-ene

ممكن يخطر ببالنا سؤال، انه لما احكي عن pair of enantiomer بكون ترتيب الذرات وحدة
فقط في عندي اختلاف في الترتيب الفراغي ← وهاد اللي احنا حكينا عنه Stereoisomers وتحديداً همن enantiomers

Enantiomers

فالسؤال هون... هل في بينهم اختلاف؟
اكيد في
لما انا احكي عن R/S enantiomers ← بلاقيهم تتشابهوا بأشياء

Definition: non-superimposable mirror images.

– Identical non-chiral properties, i.e. MP or BP, interaction with other non-chiral objects/molecules

physical properties — Melting p. — Boiling p.

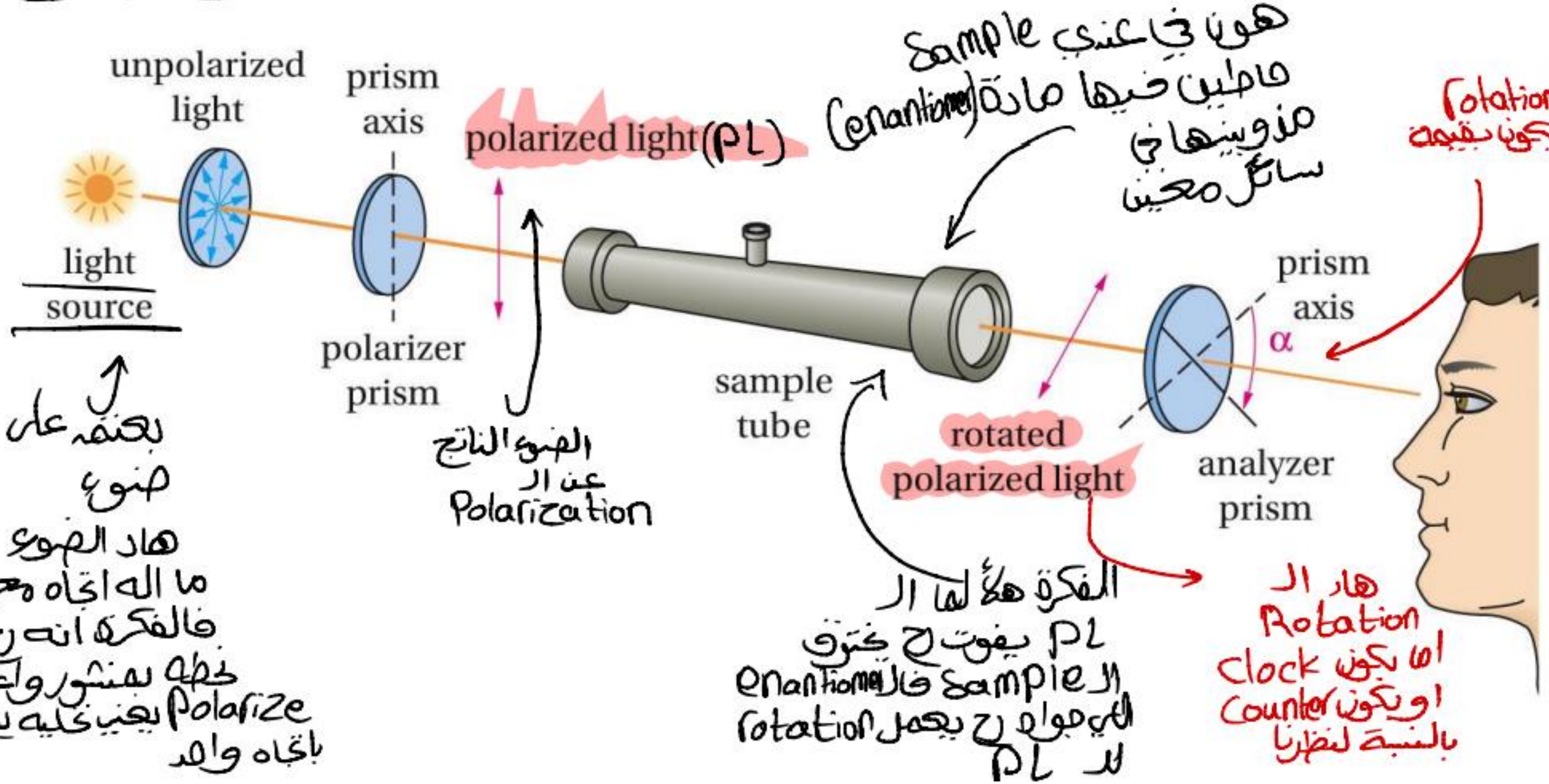
يختلفوا عن بعض

– Different chiral properties, i.e. optical activity, interactions with other chiral objects/molecules

Optical Activity

The experiment is performed using a polarimeter.

الجهاز اللي منستخدمه



إذا ال rotation ال بكون اما مع او عكس عقارب الساعة

Optical Activity

Optical activity refers to a molecule's ability to interact with plane polarized light (PPL). Optically active compounds will rotate PPL due to the electron distribution in the molecule either clockwise (dextrorotatory (+)) or counterclockwise (levorotatory (-)).

Optical Activity

The polarimeter measures the observed rotation (α, degrees), but since the rotation is dependent on the concentration, temperature, wavelength of light and device it is more common to report the *specific rotation*, where *l* is the pathlength through the polarimeter and *c* is the concentration.

*ما تهتموا كثير بالتطبيق على المعادلة

المشكلة انه قيمة α بتعتمد على عدة عوامل مثل" التركيز للـ sample او على الطول مثلا" لذلك هم حطوا قانون كلها وسموه specific rotation

$$[\alpha]_\lambda^T = \frac{\alpha}{lc}$$

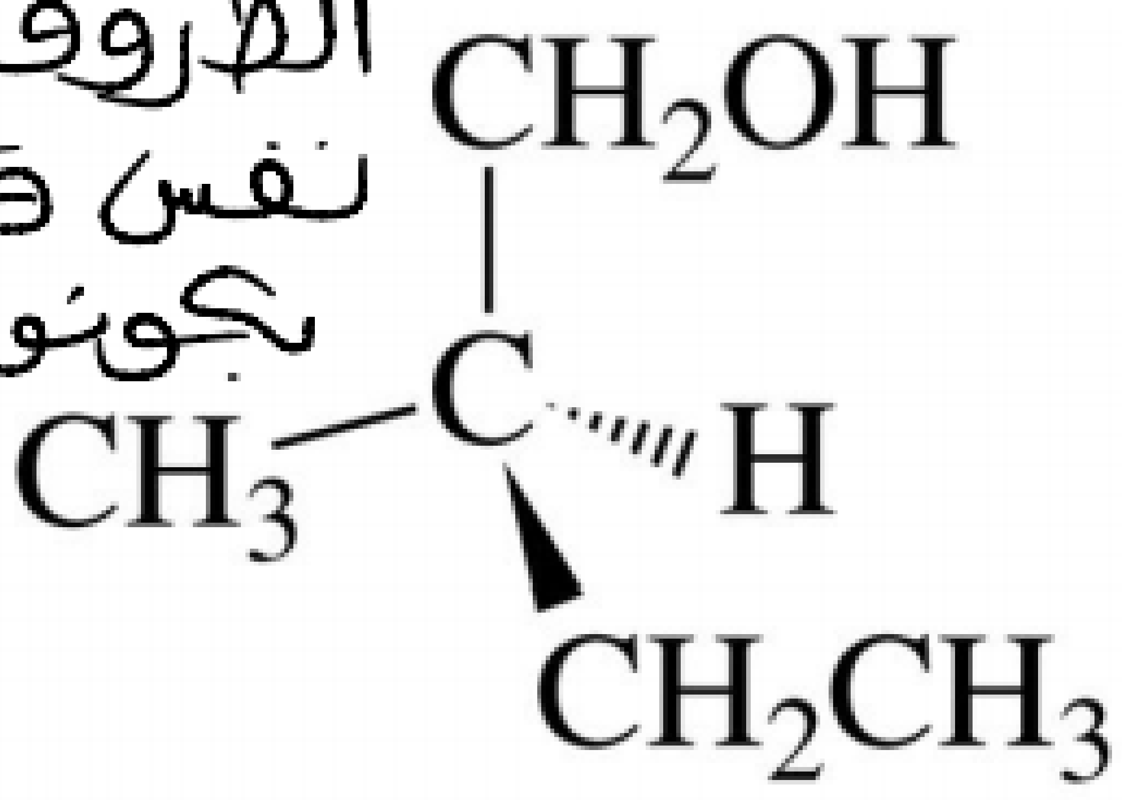
بال length (dcm)

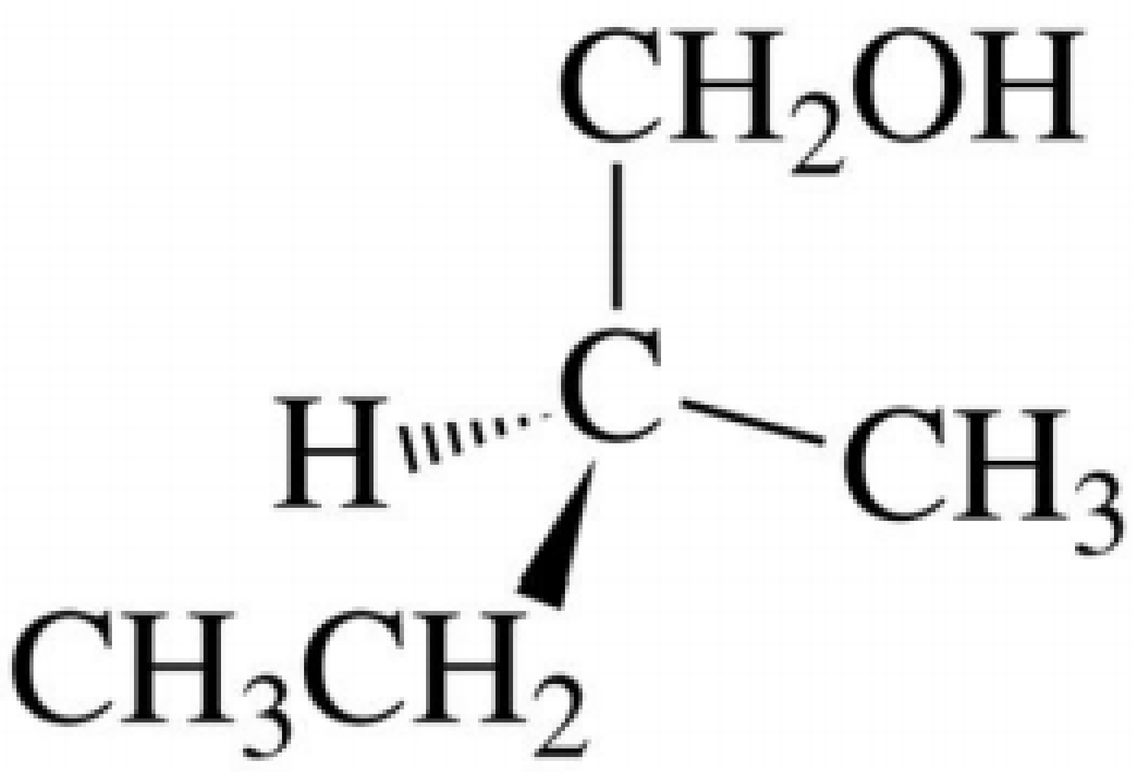
ضرب ال concentration

If One Enantiomer is (+), the Other is (–)

هاي قيمة اسمها observe rotation
وهاي قيمة بتكونا نفسها للenantiomers عند نفس الظروف بحصل على نفس قيمة d لكن بكونوا opposite direction

هدول enantiomers





*الإشارة فقط للتعبير عن ال direction of P.L. هل clockwise or counter

(*R*)-2-methyl-1-butanol

$$[\alpha]_{D}^{20\,°C} = +5.75$$

مع العقارب (clock)

(*S*)-2-methyl-1-butanol

$$[\alpha]_{D}^{20\,°C} = -5.75$$

عكس counter

إذا واحد منهم عمل rotation (clockwise) الثاني رح يعمل عكسه (counterclockwise) rotation

هاي القيمة بدون الإشارة هي قيمة (d)

الهم نفس قيمة d فقط بختلفوا عن بعض بال rotation

تخيلوا اني اخدت المركبين (اخدت من كل واحد نسبة 50%)
اللي فوق ← الهم نفس قيمة
α ولكن يختلفوا بال direction
of rotation
↲ وحطيتهم بال tube وعرضت
عليهم P.L
هل رح يصير في rotation ؟
لا • وقيمة α رح تكون Zero
فهاد بيسمى optical inactive
↲ هلأ انه يكون عندي 50% من
هدول اسمهم Pair of enantiomer
Racemic mixture
↲ يعني نسبة متساوية من ال
enantiomer
فبكونوا optical inactive

R and *S* *versus* (+) and (–)

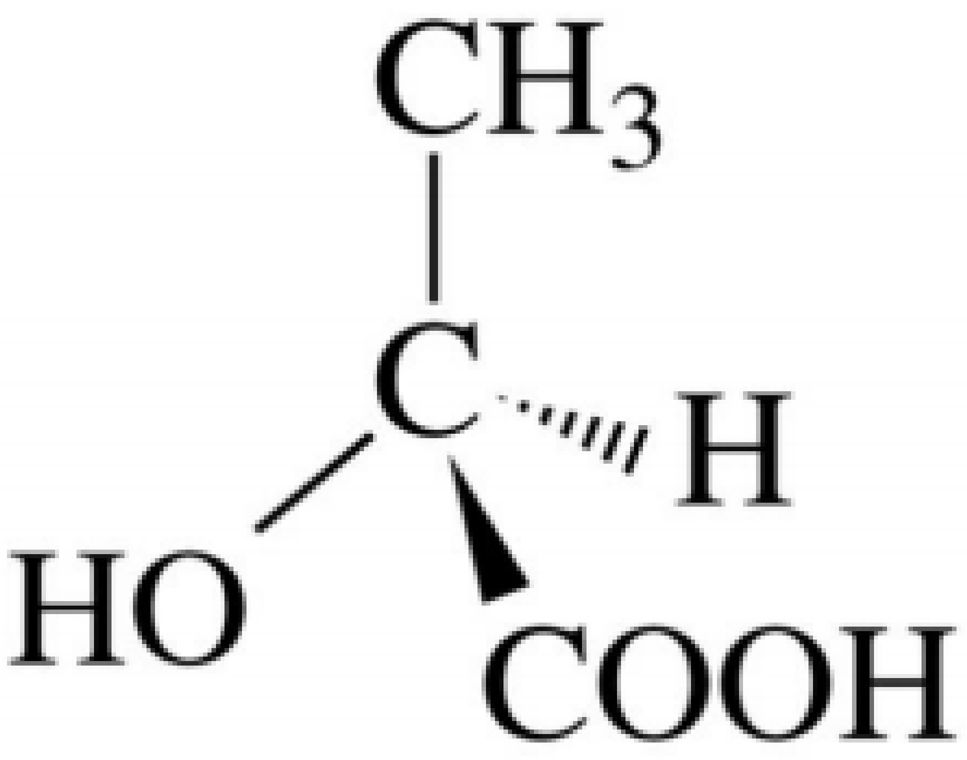
ما في علاقة بين R/S وال(+,-)

There is no relationship between (R/S) and (+/ -)

حسب القوانين اللي حكيناهم — experimental results

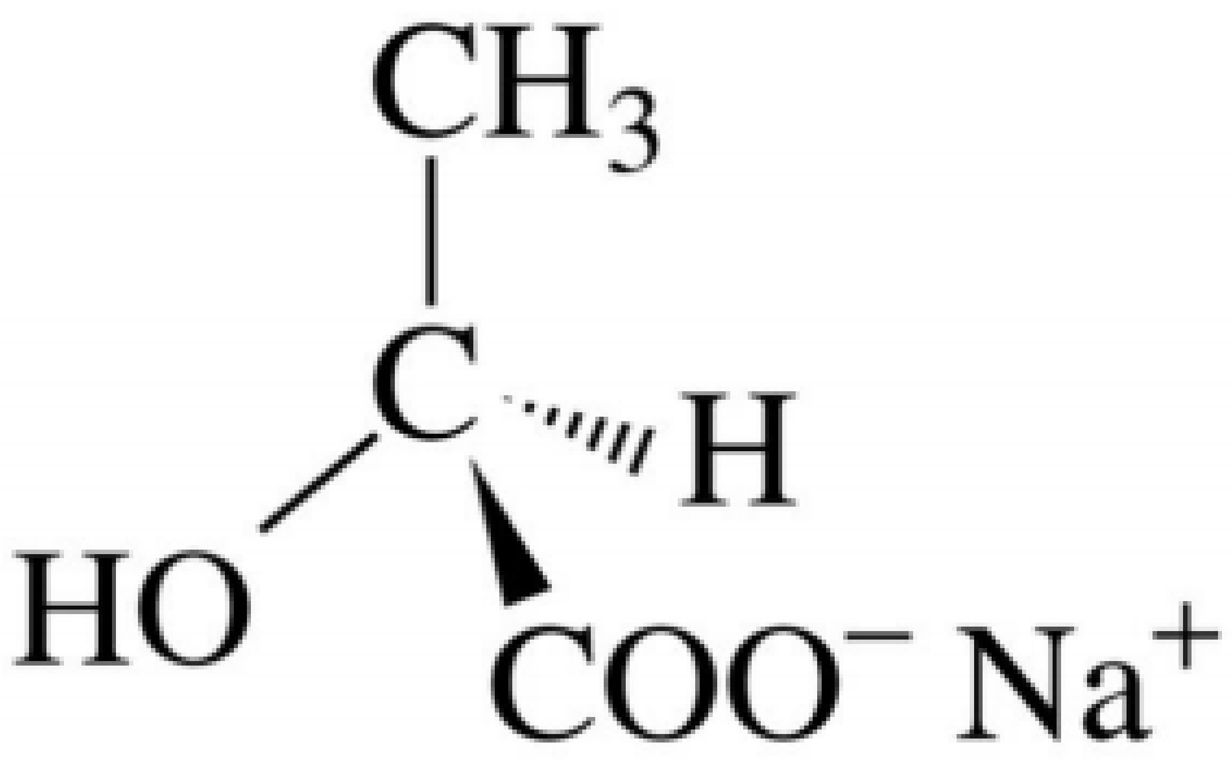
Some *R* enantiomers are (+) and some are (–).

Some *S* enantiomers are (+) and some are (–).



(*S*)-(+)-lactic acid

observed



(*S*)-(–)-sodium lactate

Biological properties of enantiomers

interaction with other Chiral molecule ← هون بدنا نفهم الاختلاف الثاني

A Receptor is a Protein
Proteins are Chiral Molecules

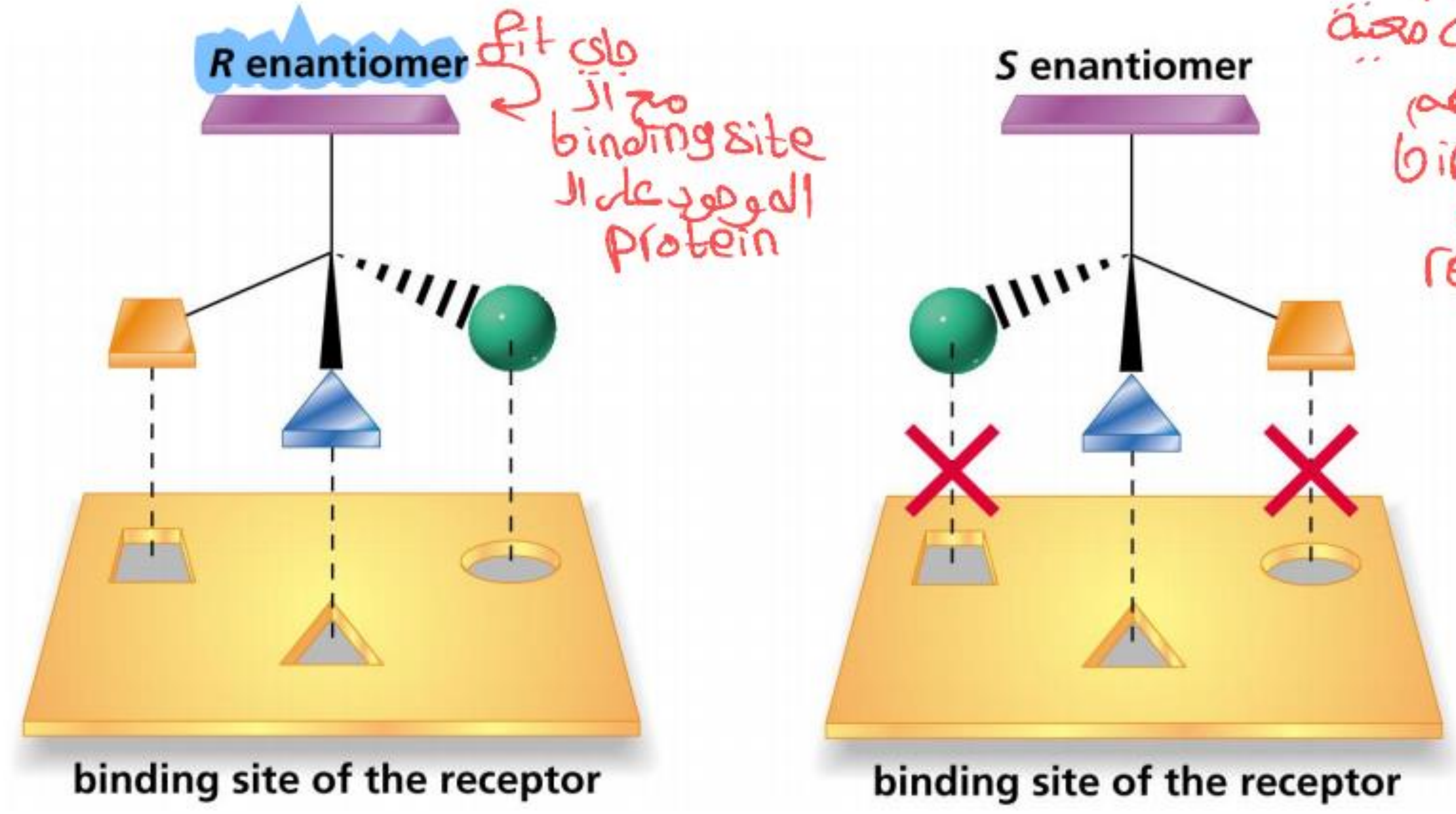
* هاي ال binding sites بكونوا ماشيين على نظام ال Key and lock

الفكرة انه مركبات ال Chiral اللي احنا ممكن نستخدمهم as drugs او proteins الهم مهمة معينة هون في الهم binding site موجود as receptor

Because a receptor is chiral, it binds one enantiomer.

لـ اذا ماكانوا مثل بعض مارح يشتغلوا

A right-handed glove fits only a right hand.



fit جاي مع ال binding site الموجود على ال protein

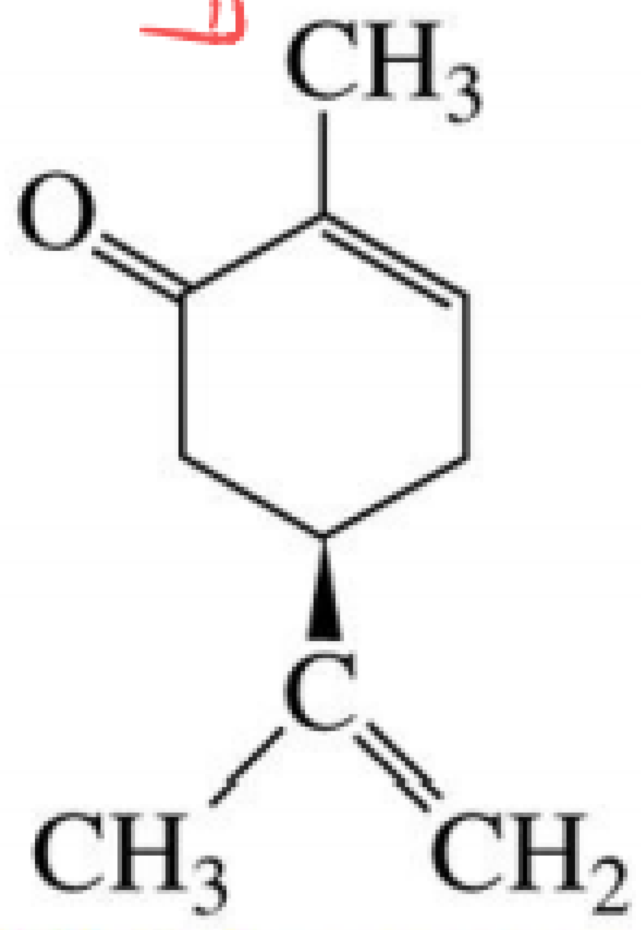
A Receptor Binds One Enantiomer

كل enantiomer الهم smell مختلفة عن الآخر بعود هذا الكلام إلى ال different receptors in our nose

pair of enantiomer

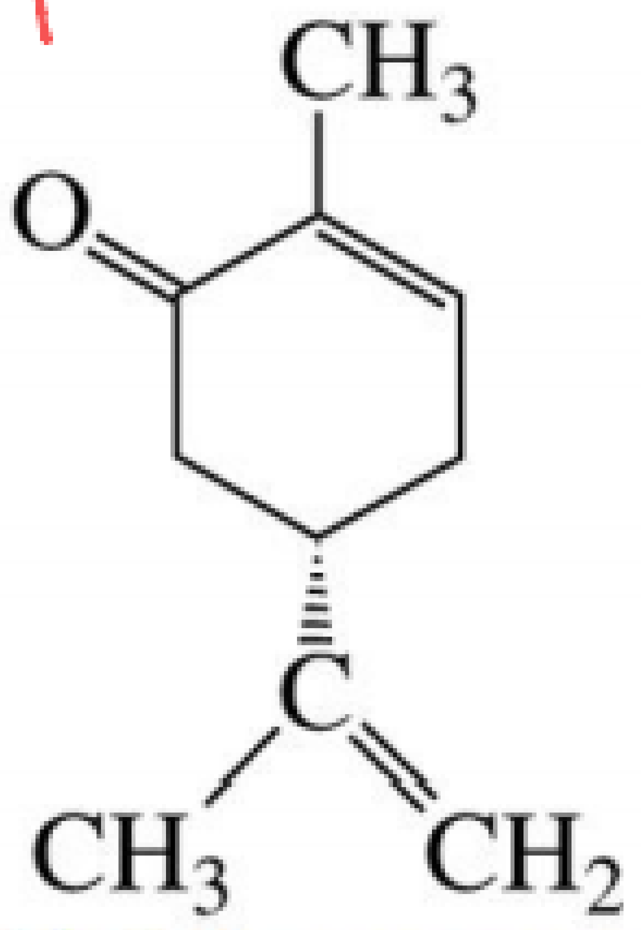
* هدول الأشكال مش للحفظ

(*R*)-(−)-carvone smells like spearmint



(*R*)-(−)-carvone

$[\alpha]_D^{20\,°C} = -62.5$



(*S*)-(+)-carvone

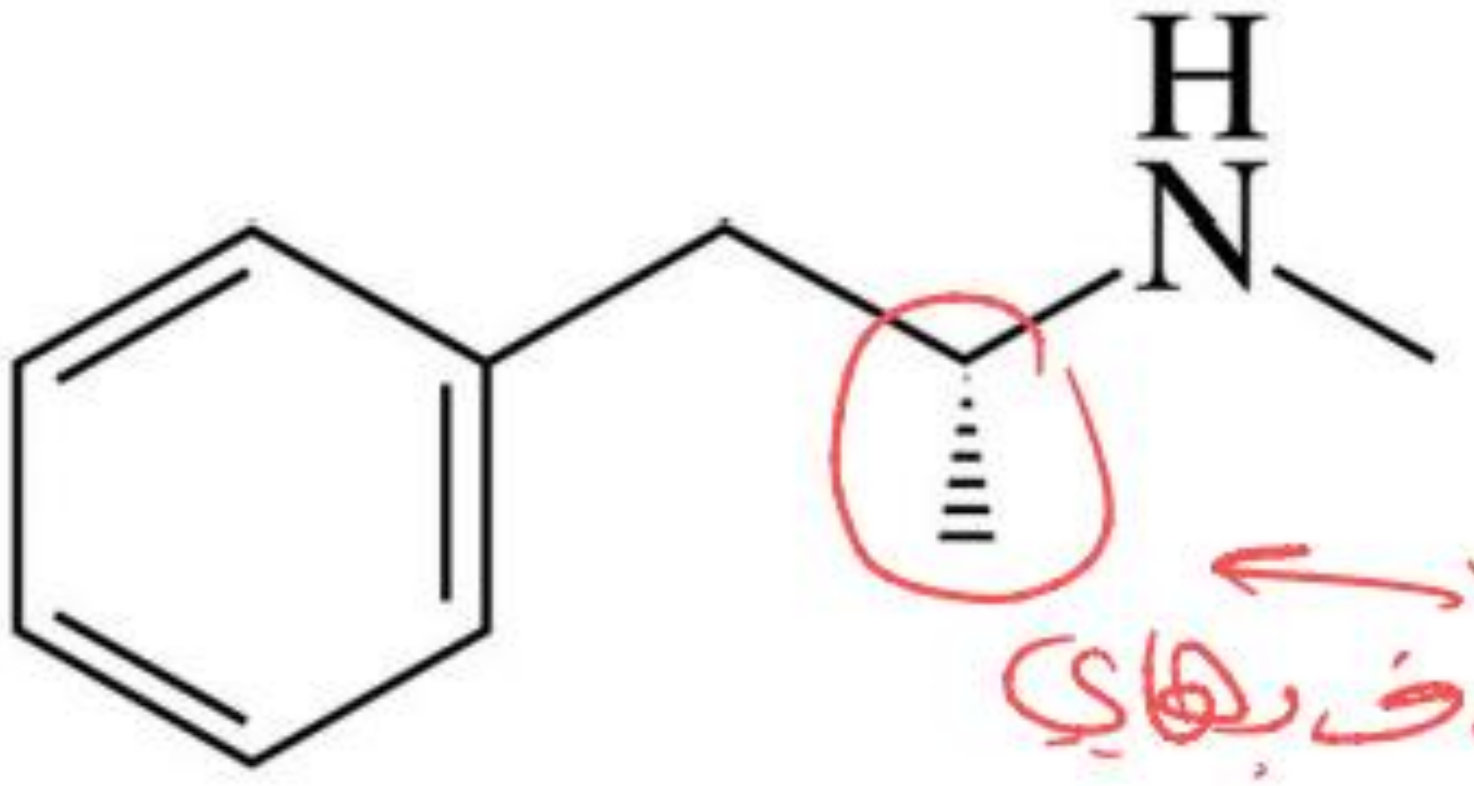
$[\alpha]_D^{20\,°C} = +62.5$

(*S*)-(+)-carvone smells like caraway seeds

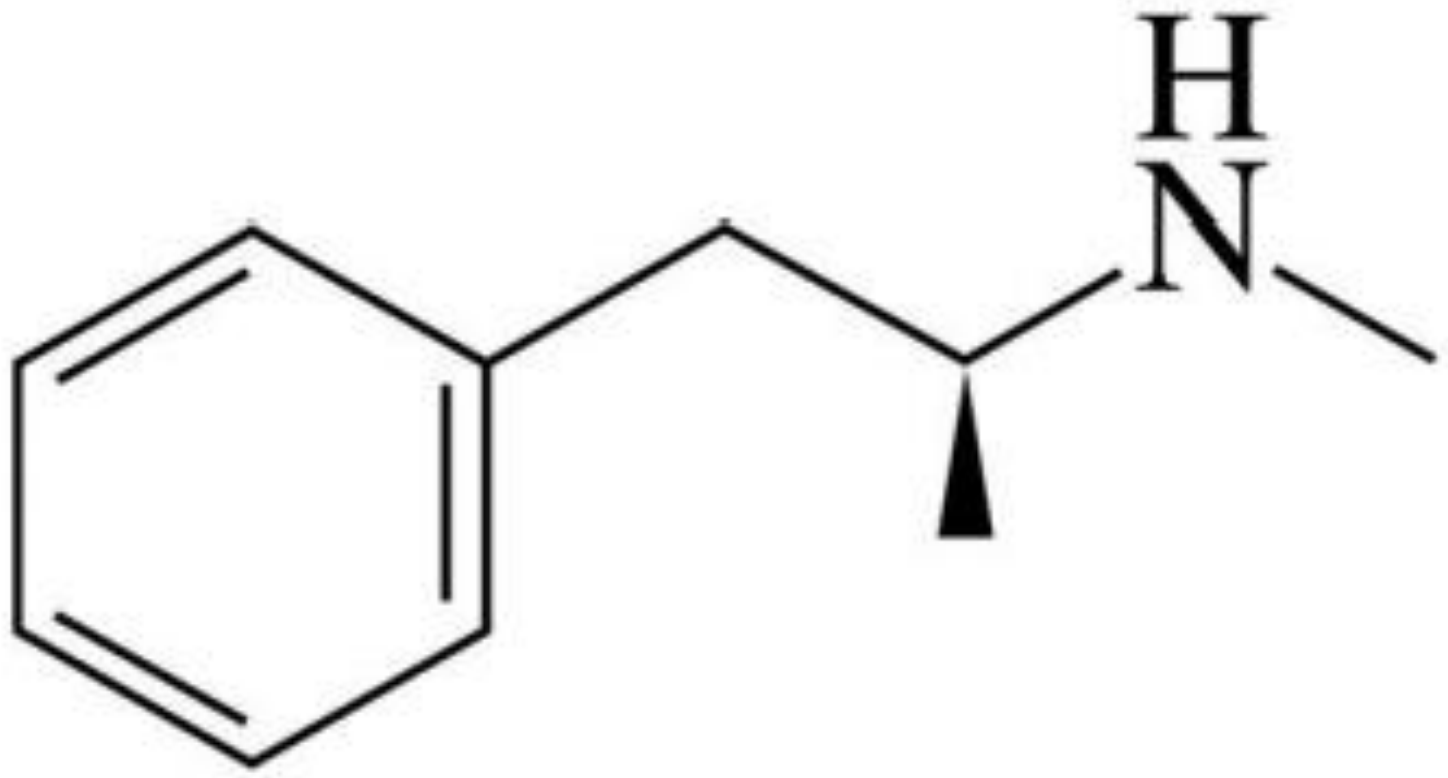
Each enantiomer binds to a different receptor in the nose.

Physiological Properties of Enantiomers

Enantiomers can have very different physiological properties.



فقط الاختلاف بهاي



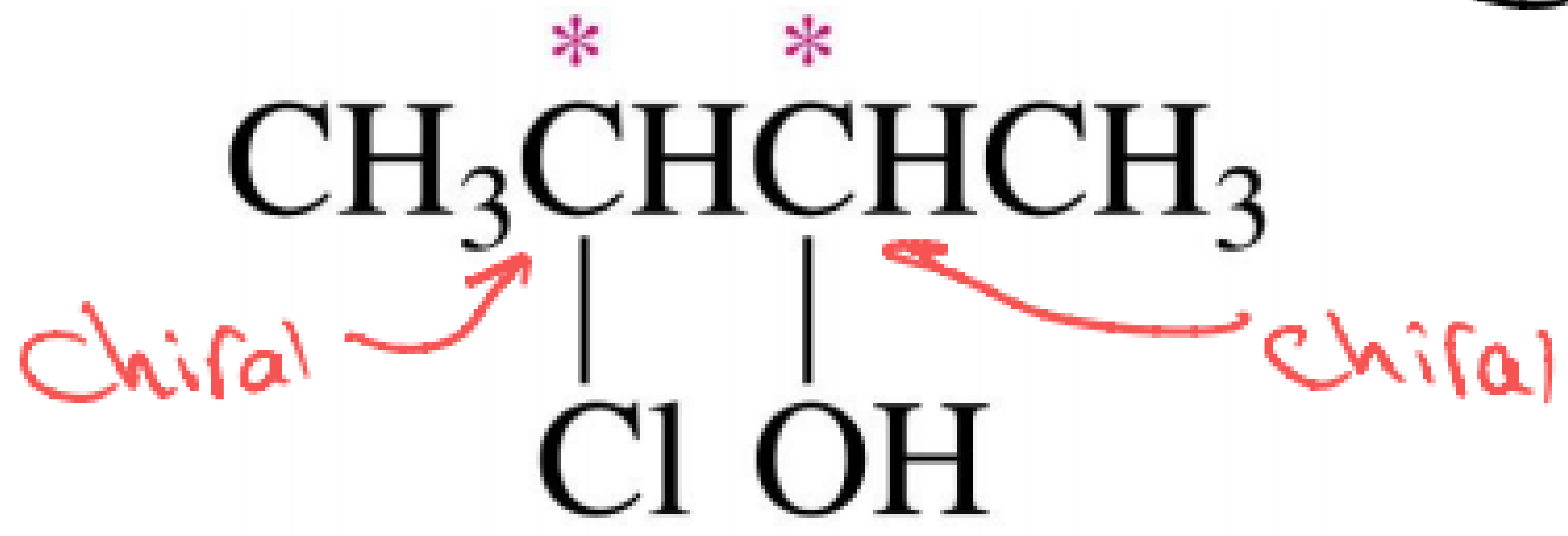
the active ingredient in Vicks Vapor Inhaler® → **methamphetamine "meth"**

موسّع قصبات

ال enantiomer تبعه لهناك ما بشتغل وكمان اله side effects

Compounds with Two Asymmetric Centers

يعني كلامنا سابقاً كان انه يكون عندي 1 Chiral (C) ← الآن عندي
اكثر من Chiral (C) سطيب اديه stereoisomers رح يكون عندي بهاي الحالة؟



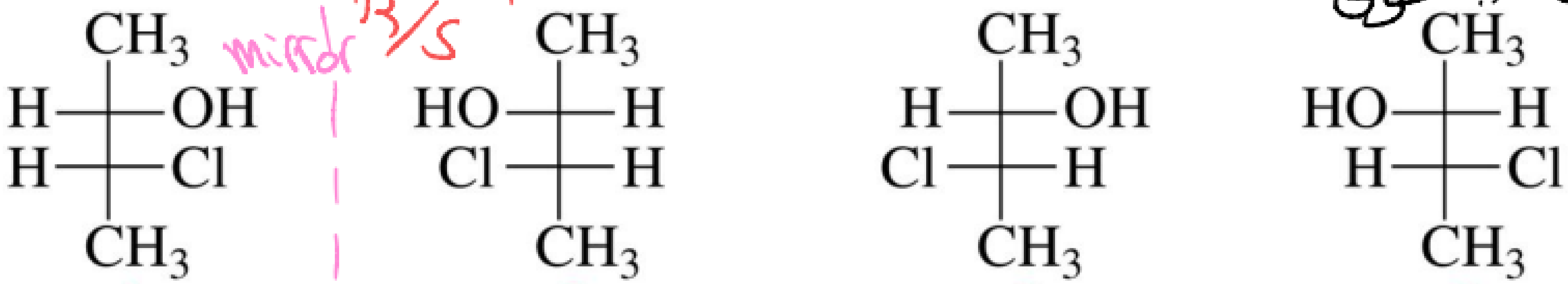
3-chloro-2-butanol

$2^n = 2^2 = 4$ (R/R, S/S, S/R, R/S)

maximum # (number) of stereoisomers = 2^n

(n = # (عدد) of asymmetric centers (chiral carbons))

هون جربنا نرسم ال 4 enantiomers المحتملين للمركب اللي فوق



1 2 3 4

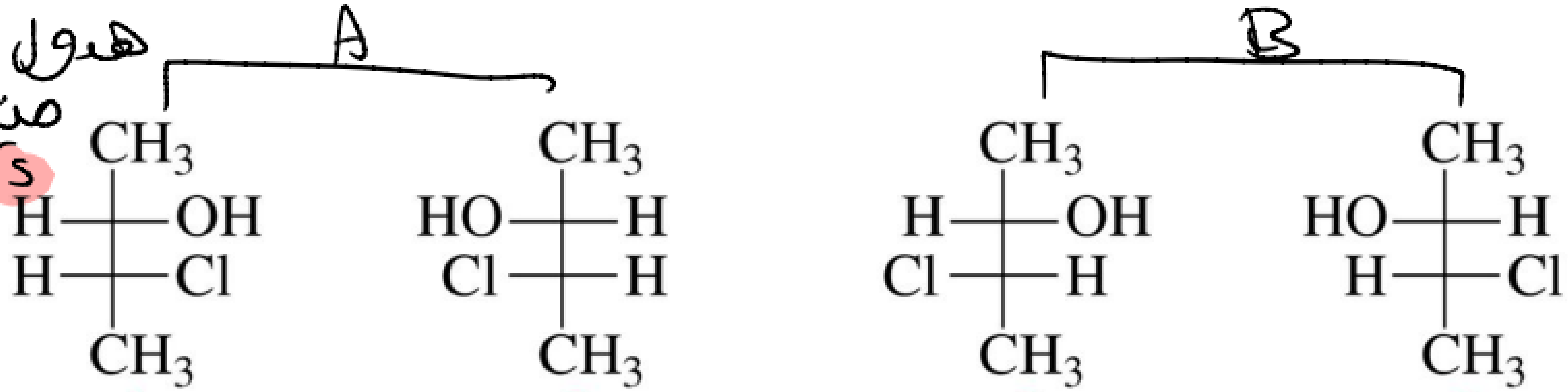
erythro enantiomers — threo enantiomers

Fischer projections of the stereoisomers of 3-chloro-2-butanol (eclipsed)

1 and 2 are enantiomers. 3 and 4 are enantiomers.

Diastereomers

ايش بيجري A علاقته مع جروب B enantiomers هدول stereoisomers من نوع diastereomers



1 2 3 4

erythro enantiomers — threo enantiomers

Fischer projections of the stereoisomers of 3-chloro-2-butanol (eclipsed)

1 and 2 are enantiomers. 3 and 4 are enantiomers.

Diastereomers are stereoisomers that are not enantiomers.

1 and 3 are diastereomers.

1 and 4 are diastereomers.

2 and 3 are diastereomers.

2 and 4 are diastereomers.

Diastereomers have different physical and chemical properties.

اما انفقنا الـ physical proprieties للـ enantiomers متساوية

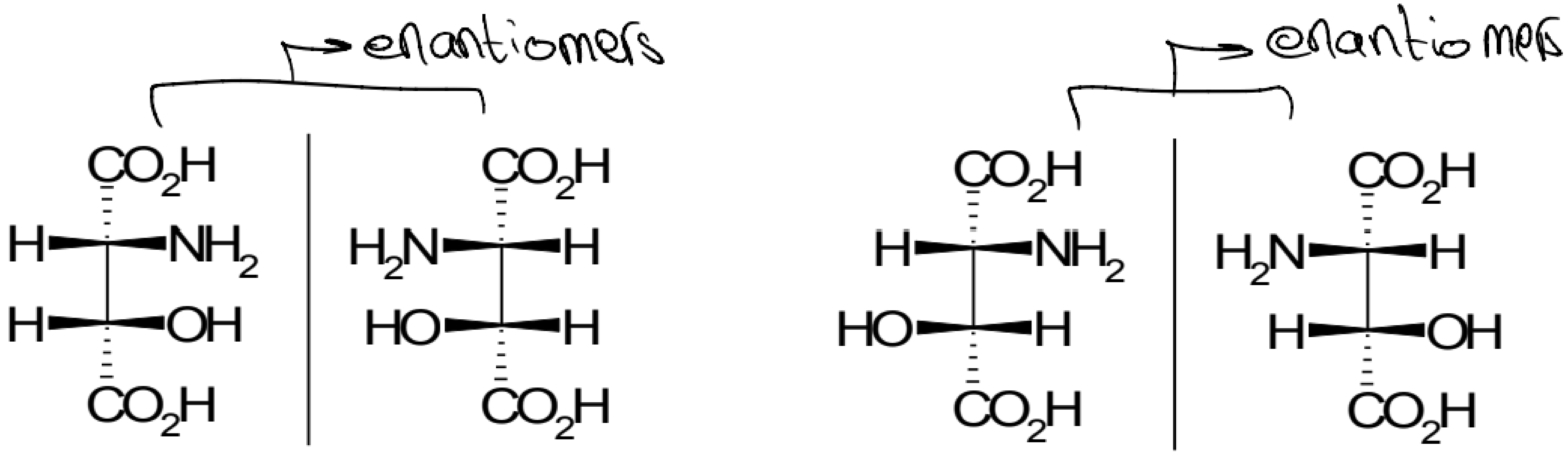
Diastereomers

Diastereomers are an additional class of stereoisomers. In contrast to enantiomers (non-superimposable mirror images) diastereomers are non-superimposable non-mirror images. This means they need to have two or more chiral centers (and/or geometric (E/Z) isomeric centers).

مثال على ال diastereomers
هو cis and trans
فعلاقة ال cis و trans
ببعض عبارة عن diastereomers

Diastereomers

Nonequivalent stereogenic centers:



2R,3R   2S,3S   2R,3S   2S,3R

optical inactive وهو بكون

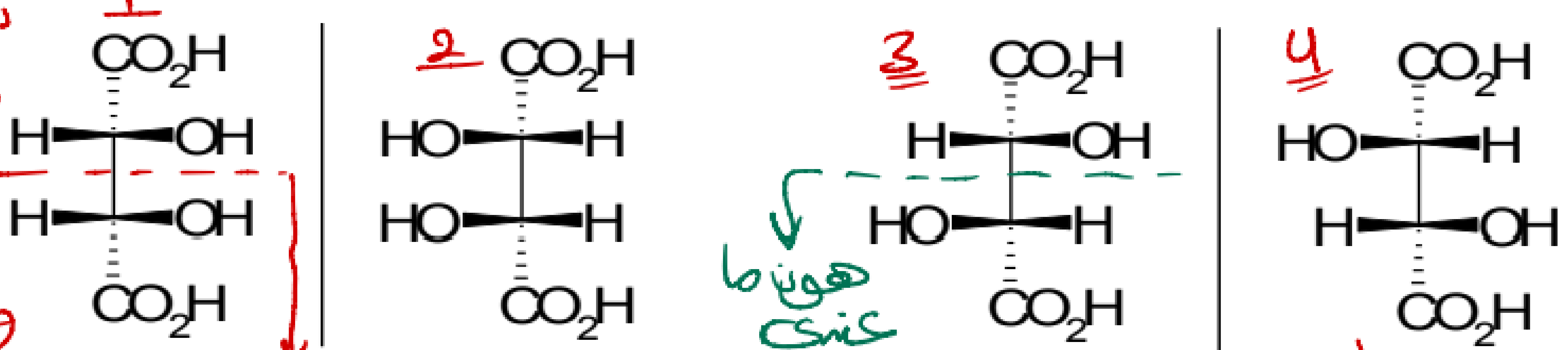
Diastereomers: Meso compounds

همن عبارة عن مركبين فيهم Chirality لكن بسبب ال symmetry رح يتطابق ال mirror image مع الأصل تبعه.

Equivalent stereogenic centers:

لو اتطلعنا هون على 1 منلاقي 2 هو ال mirror لـ 1

بس في خاصية بتخص Fisher انه انا بقدر اعمل rotation (180) ولو عملت هالحكي لواحد رح ينتج عني 2 فهموا انه نفس المركب ولكن بنفس الوقت انا عندي Chirality يعني هدول عبارة عن stereoisomers ولكن همن مش enantiomers همن Meso compounds

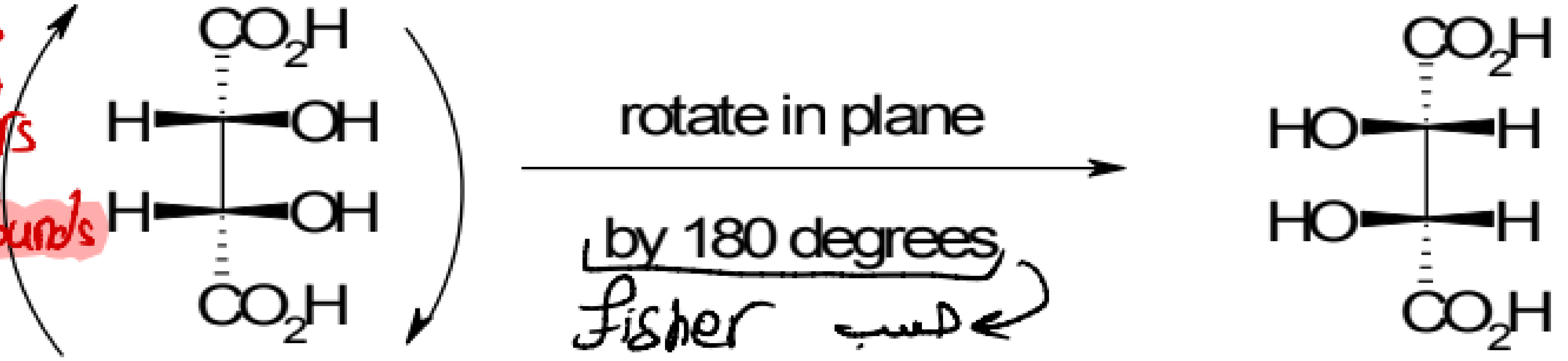


2R,3S 2R,3S 2R,3R 2S,3S

السبب للحكي هو وجود symmetry ولكن ما ننسى انه عندنا Chirality

هون ما عنا symmetry

3, 4: enantiomers → لانه ما في symmetry فهو وصورته بالمراي ما رح يتطابقوا



Fisher السبب

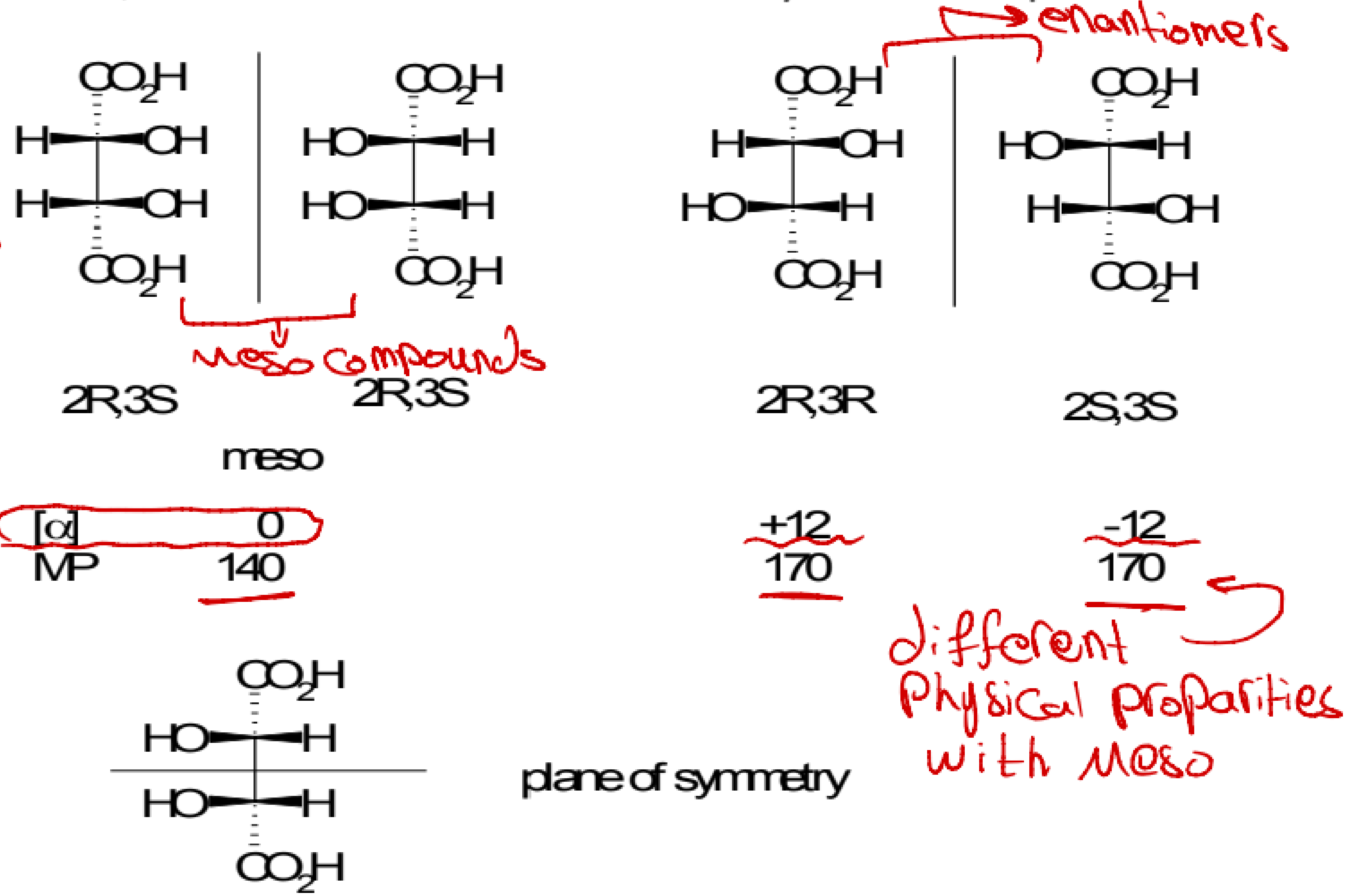
فوق مكاللا مملة maximum n. of stereoi. ليه هون maximum؟ لانه فعليا اكبر عدد ممكن يطلع هو 4 فهون لو امشينا عينيا رح يطلع معنا 3 ليه؟ لانه 1 و 2 the same ← 1 Meso 2 enantiomers

2 meso لأنها أصلاً 3 stereois. بطلعلي *

Diastereomers: Meso compounds

Equivalent stereogenic centers: meso compounds, although they contain multiple chiral centers, there are two configurations that are mirror images and superimposable, This results from the fact they contain a plane of symmetry

*الفرقة ال
Meso compounds
enantiomers ال مع
diastereomers هو



Diastereomers

The physical and chemical properties of diastereomers are different.

For meso compounds two isomers are actually enantiomeric so they will have the same non-chiral properties but different chiral properties. The meso isomers will have different physical and chemical properties to the other isomers.

Stereochemistry in Chemical Reactions

Stereochemistry is very important in chemistry as you are normally only interested in one of the stereoisomers.

There are two possibilities:

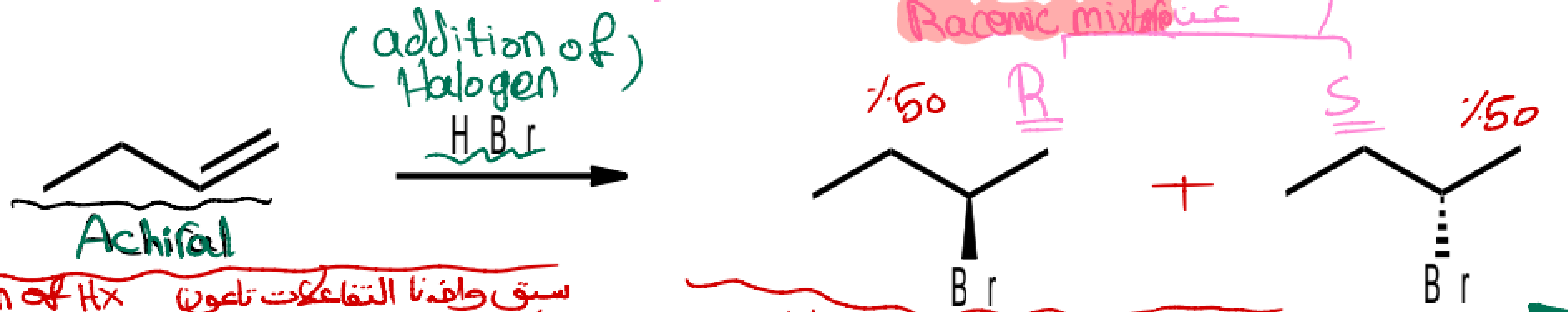
1. Chiral products from achiral reagents
2. Chiral products from chiral reagents

Stereochemistry in Chemical Reactions

Chiral products from achiral reagents:

This commonly results from addition type reactions that go through a carbocation intermediate, equal chance of reacting with either side of the carbocation. Usually results in a racemic mixture (50:50) of both enantiomers, i.e.

على افتراض انه وحدة R و وحدة S ونسبتهم 50% كل واحد ← (1:1) هدول عبارة عن Racemic mixture



addition of HX سبق وأخذنا التفاعلات تاعون على ال Alken بحيث انه ح تنضاف ال H ويطلع عنا carbocation وأخذنا كمان انه ال carbocation بكون Planer

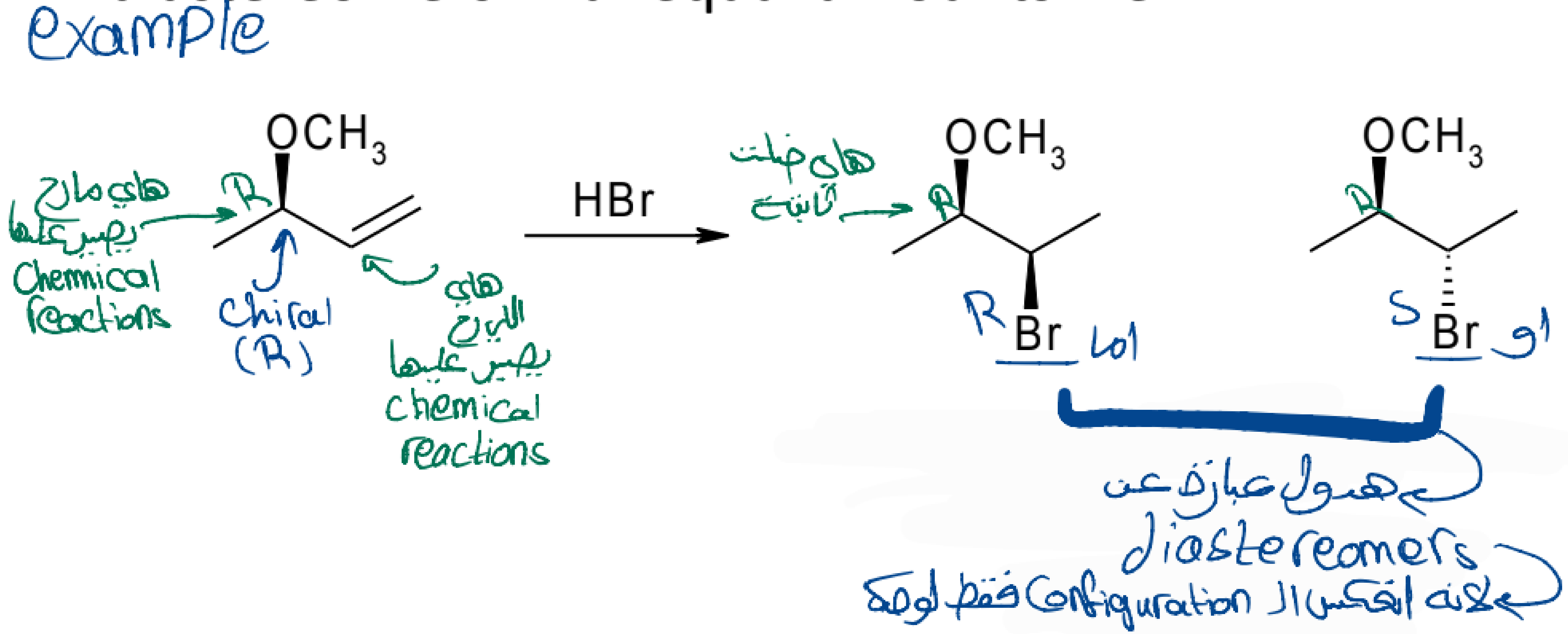
هلا لما نيجي نضيف ال Br عنا خيارين اما الاتجاه لفوق او للتحت والخيارين نسبتهم 1:1

نثبت انه النواتج chiral بالفعل

Stereochemistry in Chemical Reactions

Chiral products from chiral reagents:

Since the chiral reagents react with each other at different rates this results in the production of diastereomers in unequal amounts. i.e.



Chiral Resolution

A common problem is how to separate enantiomeric products from a reaction. This can be difficult as many of the common techniques to separate compounds rely of physical properties that are the same for enantiomers.

The solution? Change them into diastereomers using a chiral resolving agent. These can be easily separated as their physical properties are now different.

Chiral Resolution

i.e.

R + S → R-S

S + S → S-S

The two new products are easily separated.

This technique work best when the chiral resolving agent is easy to add and then remove, i.e.

Alcohol + acid → ester + water