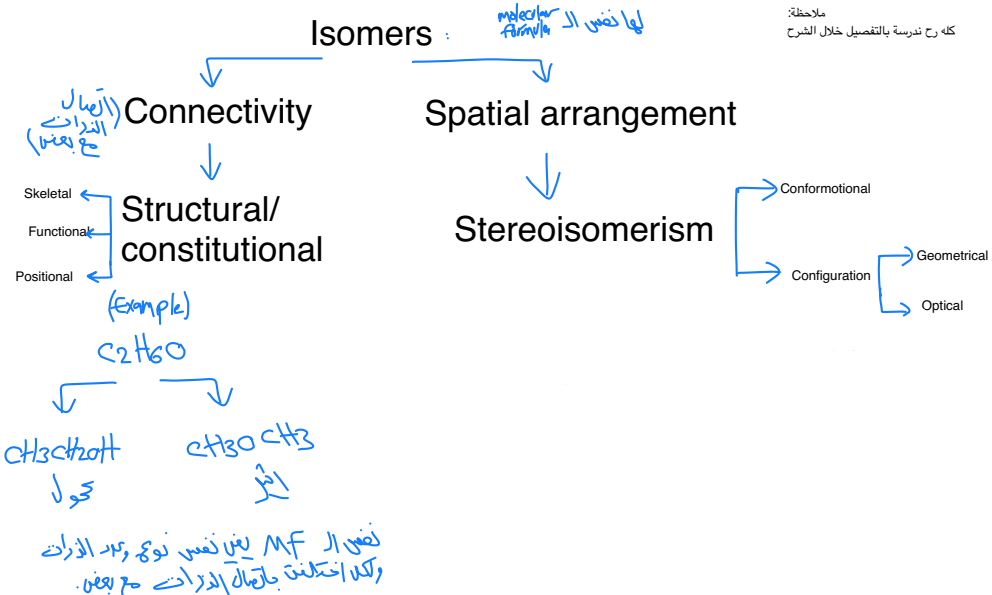
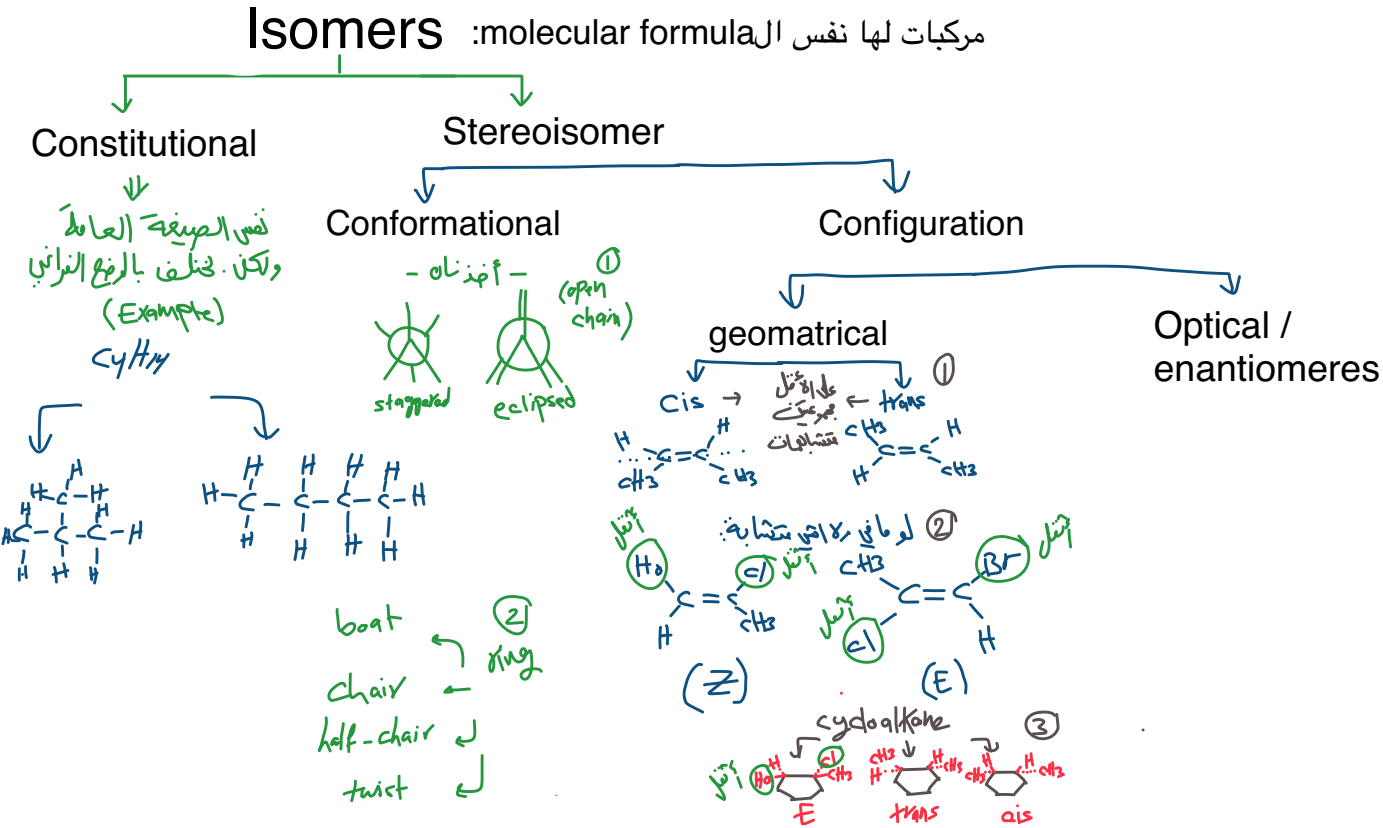
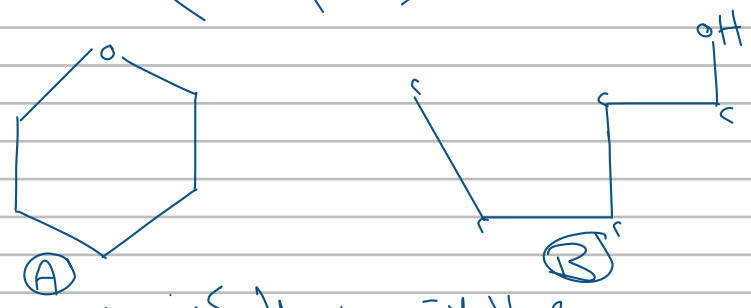


Chapter-5: Stereoisomerism



(Examples)

① 

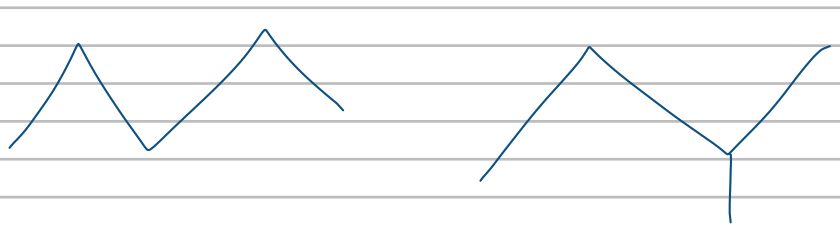
شو العلاقة بين المركبين؟

① نعد الذرات ونوعها

A → $C_5H_{10}O$

B → $C_5H_{12}O$

(Different compounds)

② 

A

B

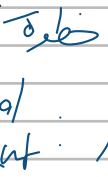
① نعد الذرات ونوعها

C_5H_{12} C_5H_{12}

② Connectivity : not the same connectivity

(constitutional / structural)

③ A 

B 

C

what is the relation?

① نعد الذرات ونوعها

A $C_4H_{10}O$

B $C_4H_{10}O$

C $C_4H_{10}O$

② Connectivity ⇒ B constitutional isomer for A and C.

Connectivity لأن الذرات مرتبطة بطريقة مختلفة

③ لأن الـ 2 عندهم Connectivity نفسها A, C

③ Spatial arrangement:

Same

A and C identical

السؤال بالامتحان:

What is the relation between the following compounds

Same compound ← isomers هاي من انواع ← different compounds

different compounds ← constitutional isomers ← stereoisomers

خطوات الحل:

① نعد الذرات ونوعهم

② Connectivity نحقق من الـ

Constitutional / structural ← not the same connectivity

نفس الخطوة ③ ← the same connectivity

③ نحقق من الـ spatial arrangement

stereoisomers ← different

identical ← same

Chirality & Stereochemistry

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

Achiral

example

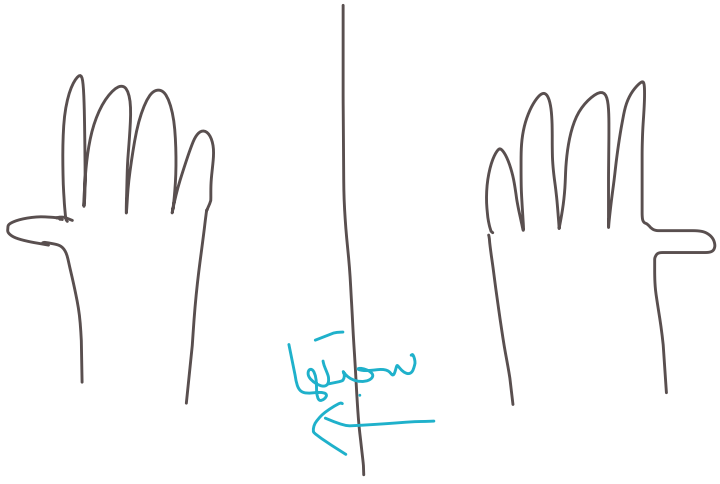
achiral

achiral

Chiral
Assymatric
Stereogenic
Stereocenter

(example)

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



chiral ⇐ الايد تعتبر
لأنه ما انطبقت مع صورتها بالمراي.

chiral / achiral

A) → achiral

B) → chiral

كيف اعرف بطريقة سهلة اذا الاشي وصورته بالمراي منطبقين:
ارسم خط بحيث يقسم الاشيً قسمين متماثلين اذا قدرت ترسم
معناته achiral ..... اذا ما قدرت معناته chiral.

1. Isomerism: Constitutional Isomers & Stereoisomers

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

❖ Examples

different in connectivity — same M.F

Molecular Formula

Constitutional Isomers

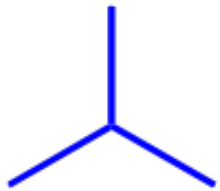
طريقة لتميزن أن تقوم بتسمية المركب اذا طلعوا مختلفين بيكونا constitutional

C_4H_{10}

same MF

Butane

and

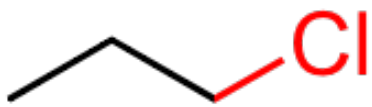


2-Methylpropane

connectivity يختلفوا بال

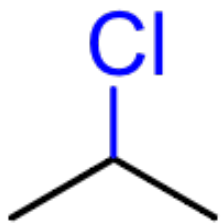
C_3H_7Cl

same MF



1-Chloropropane

and



2-Chloropropane

different connectivity

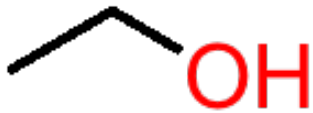
❖ Examples

Molecular Formula

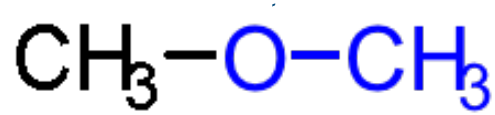
Constitutional Isomers

C_2H_6O

same M.F



Ethanol and

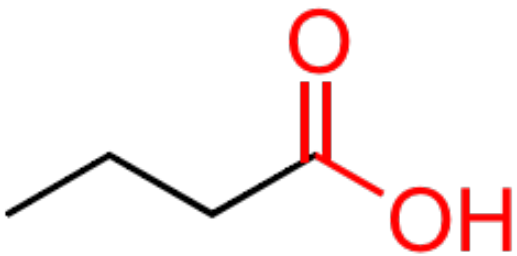


Methoxymethane

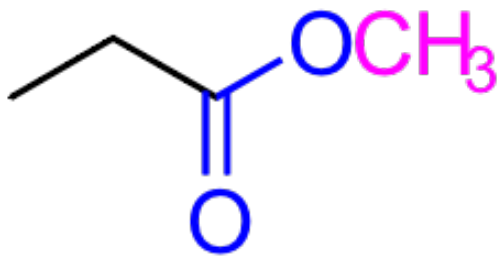
Functional

different connectivity

$C_4H_8O_2$



Butanoic acid and



Methyl propanoate

Functional

Isomers

Constitutional

Functional

في حال اختلاف الـ functional group

example

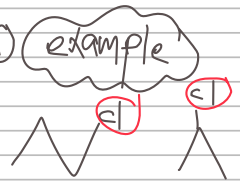
C_2H_6O → Same M.F ← C_2H_6O

different connectivity ⇒ Constitutional و كمان Functional

Positional

اختلاف مكان الـ Functional group

① example



C_3H_7Cl → Same MF ← C_3H_7Cl

different connectivity ⇒ Constitutional positional و كمان

② example

constitutional → positional

Skeletal

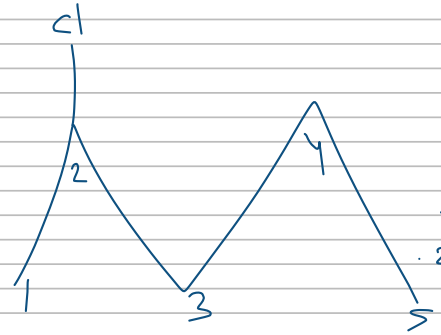
اختلاف مكان الكربونات

example

Constitutional → Skeletal

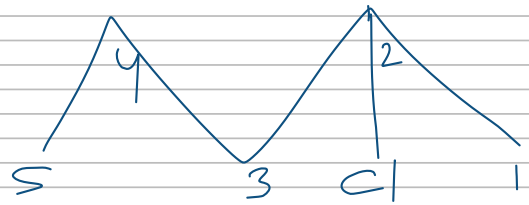
مثال

A



5 C
ال ا ك على
كربونة رقم 2

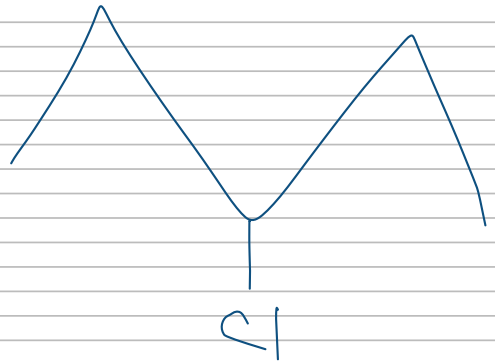
B



5 C
ا ك على كربونة
رقم 2

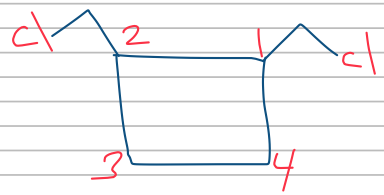
A and B not constitutional
والسبب لو سميتهم ا ك يكون الهم نفس الاسم

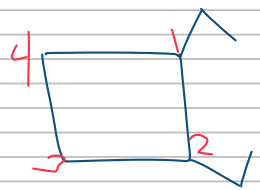
C



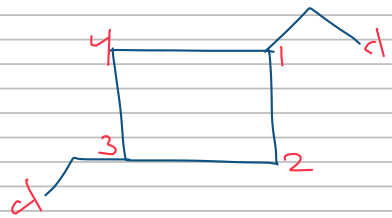
5 C
ا ك على كربونة
رقم 3

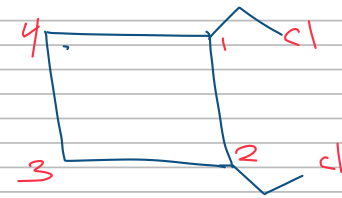
C is constitutional for A and B
وتوجه Positional.





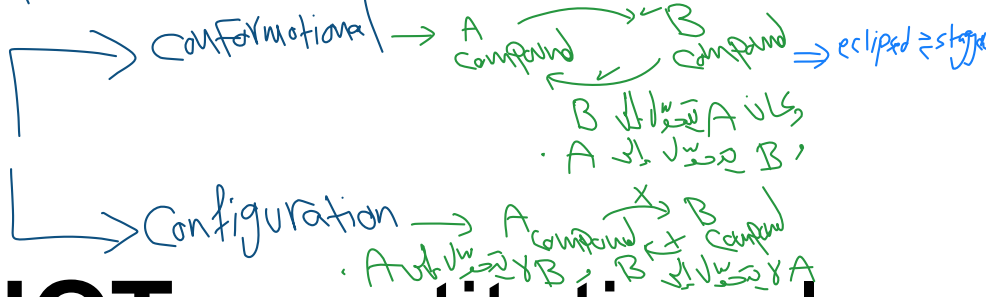
not constitutional





Constitutional → Positional

1B. Stereoisomers



- Stereoisomers are **NOT** constitutional isomers

- **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***

Stereoisomers

Conformational

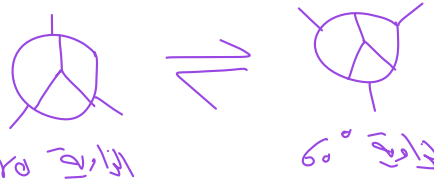
- newman
- Ring flip

A compound ⇌ B compound

B يتحول إلى A

A يتحول إلى B

① eclipsed ⇌ staggered



الزاوية zero — الزاوية 60°

stereoisomers → conformational → newman

② 

stereoisomers → conformational → ring flip

Configurational

- geomatrical /diastereomers
- optical /enantiomers

compound A ⇌ compound B

B سعولة يتحول إلى A

A سعولة يتحول إلى B

① geomatrical /diastereomers

cis / trans (على الأقل مجموعتين متشابهات)

- double bonds
- Rings

cis ⇌ trans

cis: مجموعات متشابهة على نفس الجهة

stereoisomers → configuration → geomatrical /diastereomers

(2) optical/enantiomers

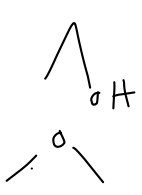
Isomers

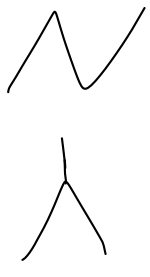
connectivity

Spatial arrangement

Constitutional / structural

- Functional
- Positional
- Skeletal



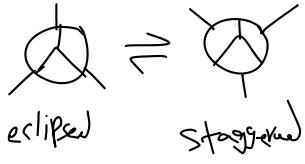


Stereoisomers

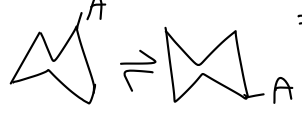
- Conformational
- Configurational

Conformational

Newman Projection



Ring flip



Configurational

- geometrical / diastereomers
  - cis/trans
  - ring
- optical / enantiomers
  - chiral

1C. Enantiomers & Diastereomers

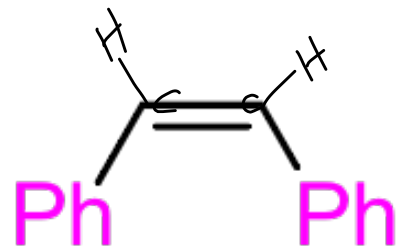
- Stereoisomers can be subdivided into two general categories: *enantiomers* & *diasteromers*
  - **Enantiomers** – stereoisomers whose molecules are nonsuperposable mirror images of each other
  - **Diastereomers** – stereoisomers whose molecules are not mirror images of each other

- Geometrical isomers (*cis* & *trans* isomers) are: (diastereomers) ⇒ cis/trans

  - *Diastereomers*

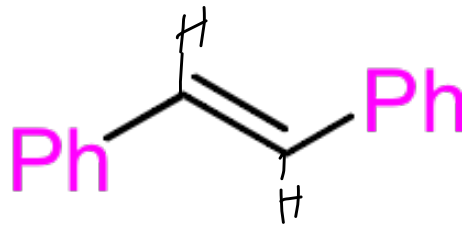
① يلزم الكربون تحمل تفرعين مختلفين.
② يلزم على الأقل تشابه تفرع ما الكربون الأول مع تفرع من الكربون الثانية.

e.g.

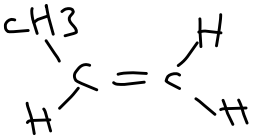


(*cis*)

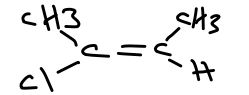
and



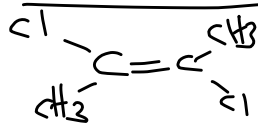
(*trans*)



no cis
no trans

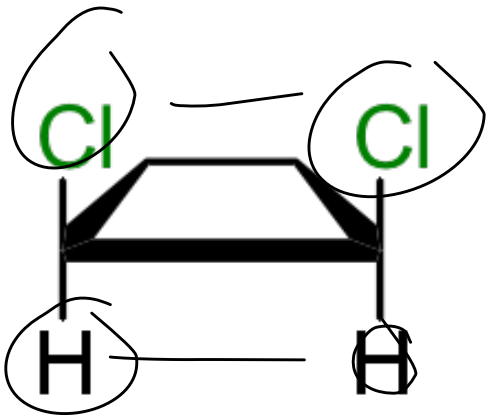


cis



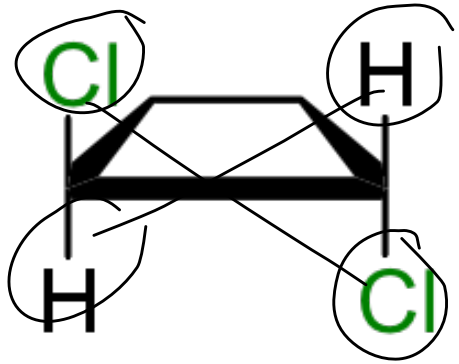
trans

Ring

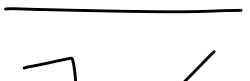


(*cis*)

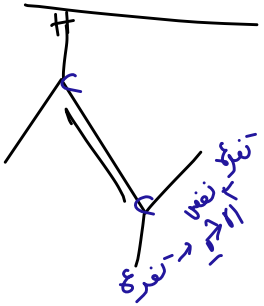
and



(*trans*)

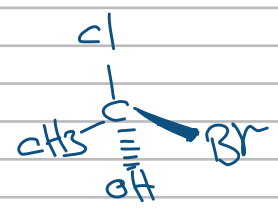


trans

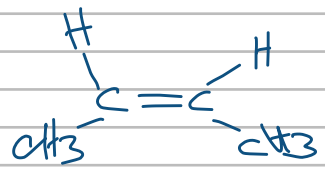


no cis
no trans

Examples

① 

- assymatric carbon

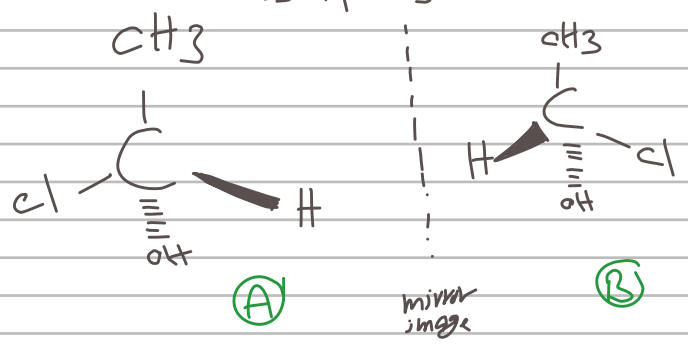
② 

- stereo center carbon
- geomatric (cis)

③ 

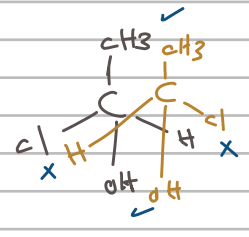
- stered center carbon
- geomatrical (cis)

Chiral compound حقيقة تمام المرآة



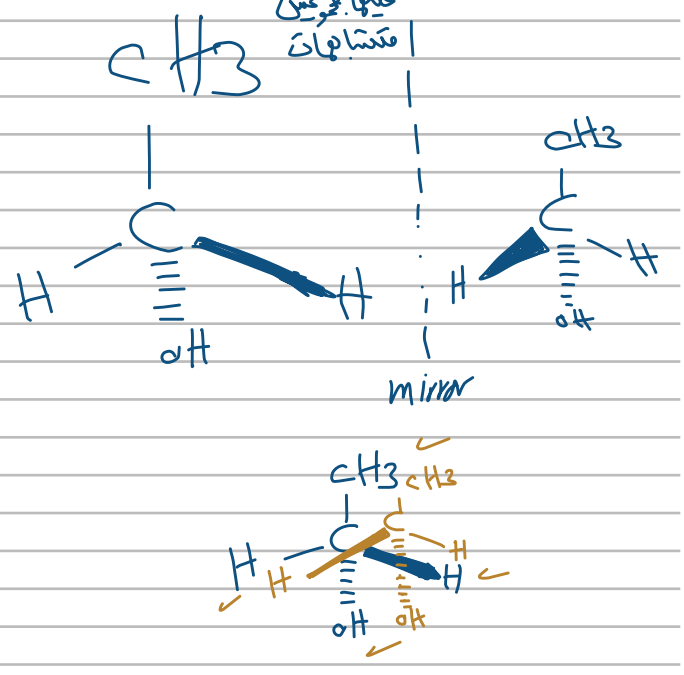
Chiral compound : كربون عليها أربع مجموعات مختلفة.

لو سكنت B تلاقيها هي وحقيقة A على ؛

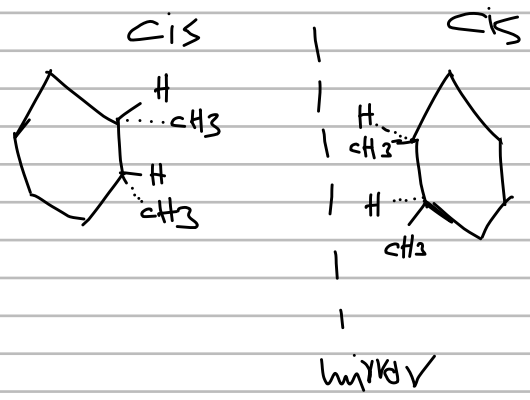


achiral compound : كربون عليها مجموعتين متشابهات

achiral compound

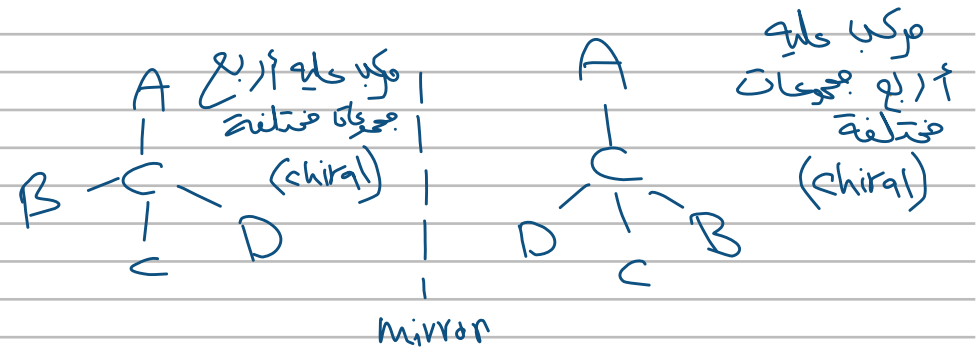


examples



6

Diastereomeres

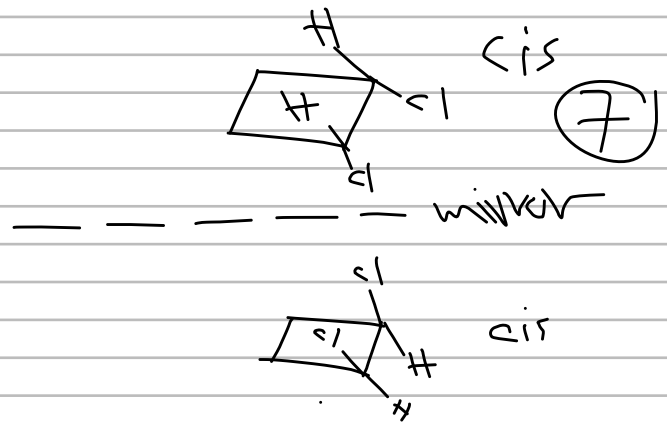


مركب حلي أربع مجموعات مختلفة (chiral)

مركب حلي أربع مجموعات مختلفة (chiral)

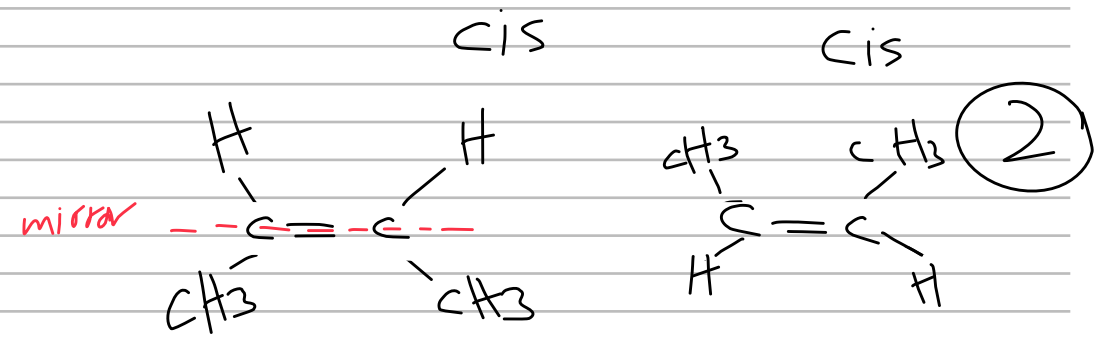
1

Enantiomers = chiral + mirror chiral



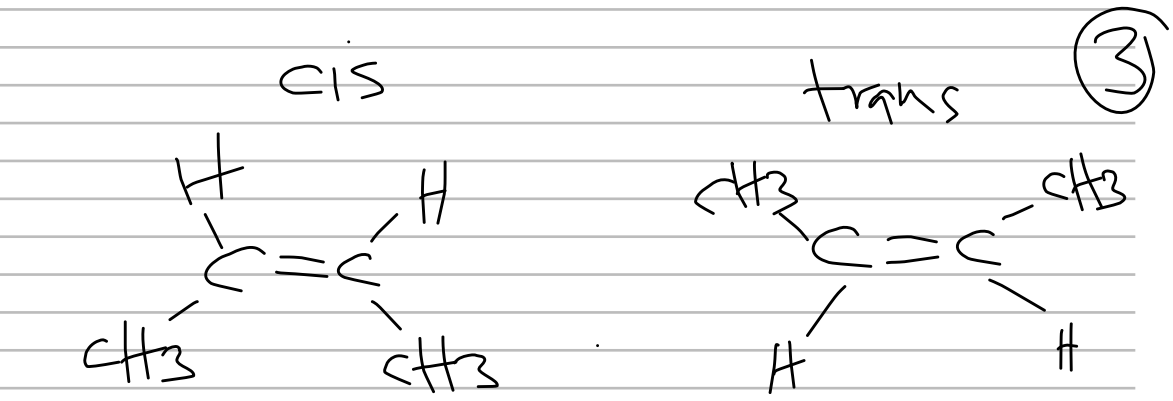
7

Diastereomeres



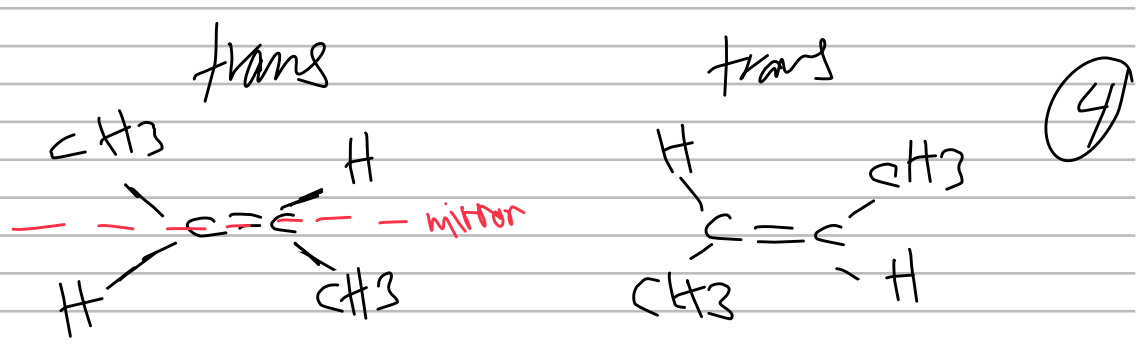
2

Diastereomeres



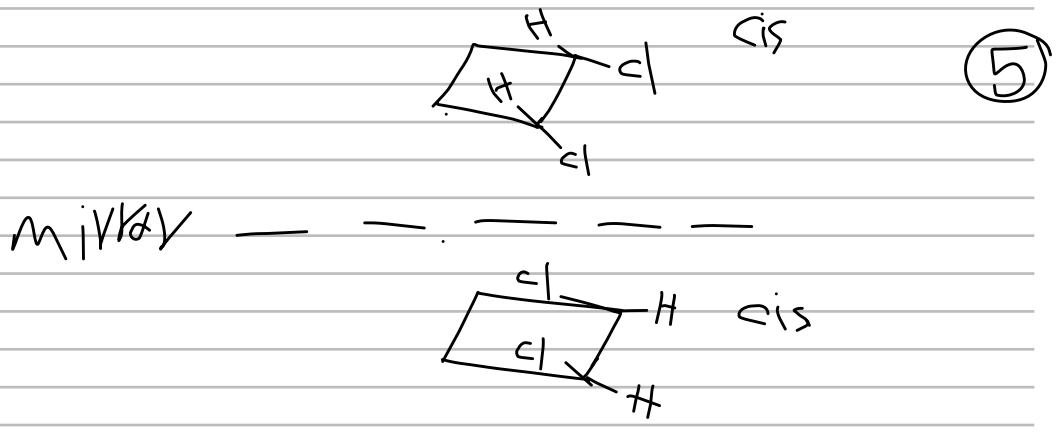
3

Diastereomeres



4

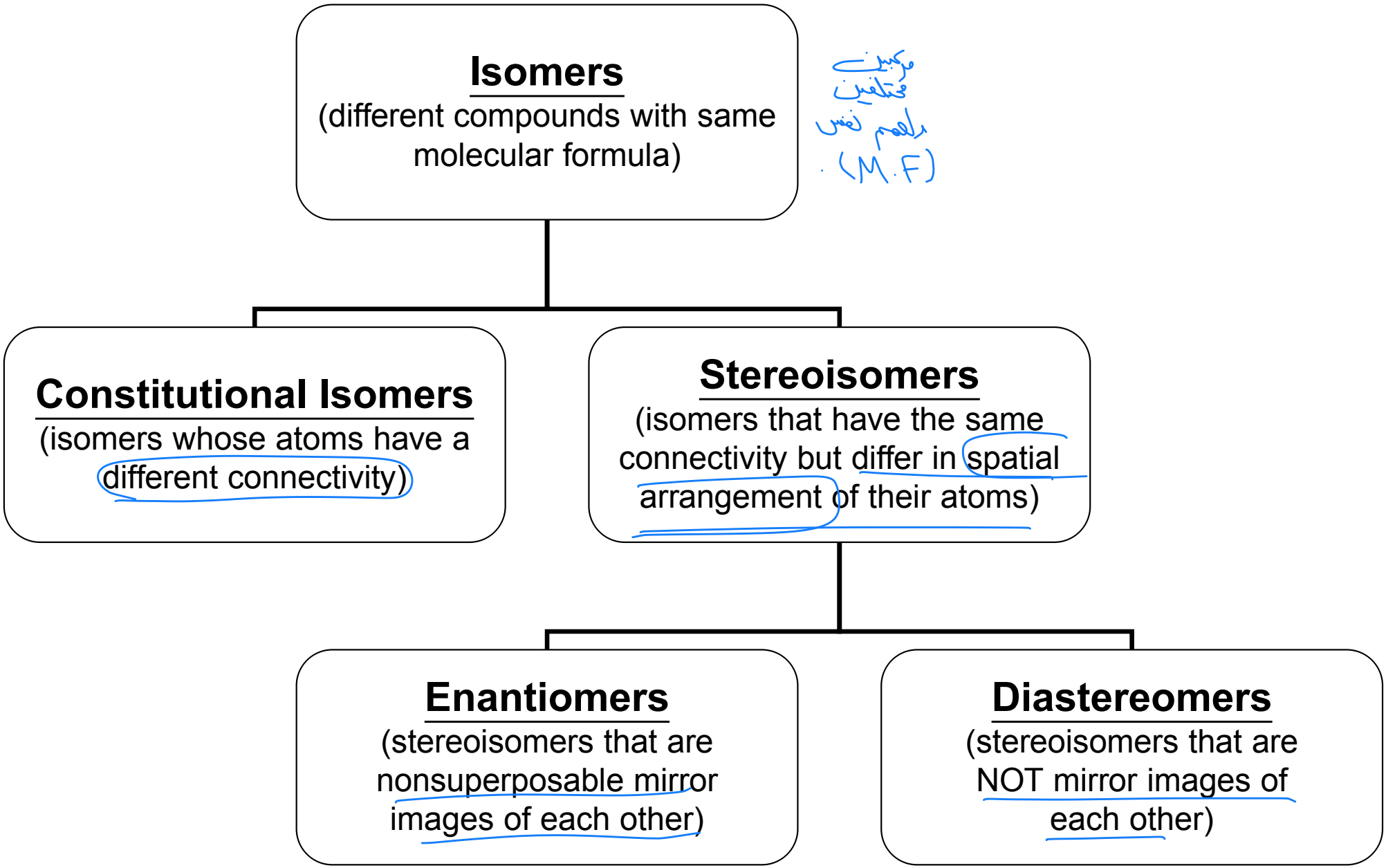
Diastereomeres



5

Diastereomeres

Subdivision of Isomers



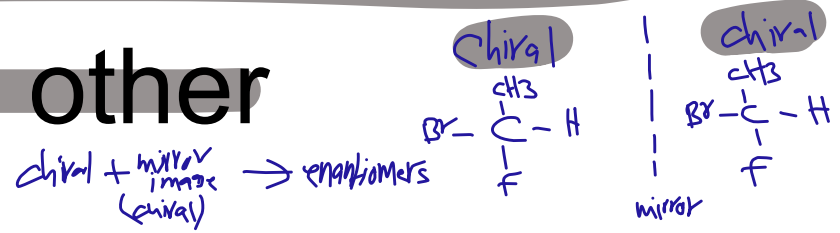
2. Enantiomers and Chiral Molecules

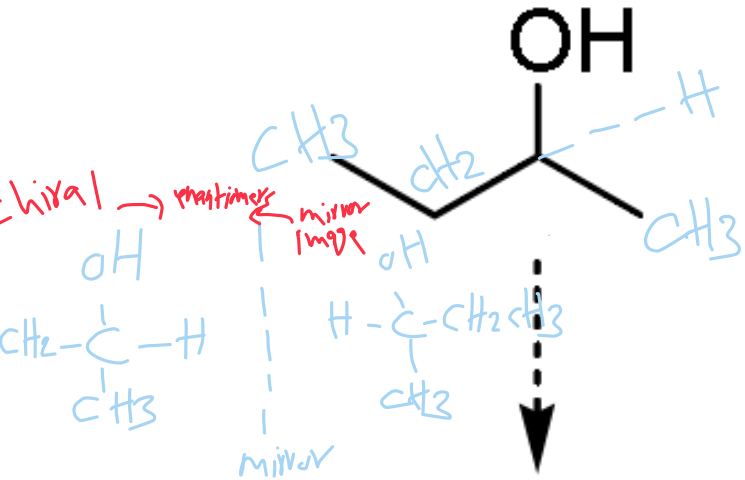
chiral + mirror image of chiral → Enantiomers

- Enantiomers occur only with compounds whose molecules are **chiral**
- A chiral molecule is one that is **NOT** superposable on its mirror image

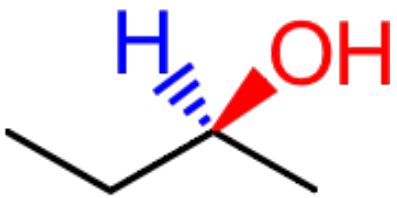
Chiral ⇓ كربون حراميا أربع مجموعات مختلفة وصورتها بالمرايا لا تنطبق عليها.

- 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

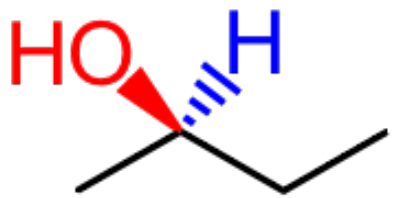




(2-Butanol)



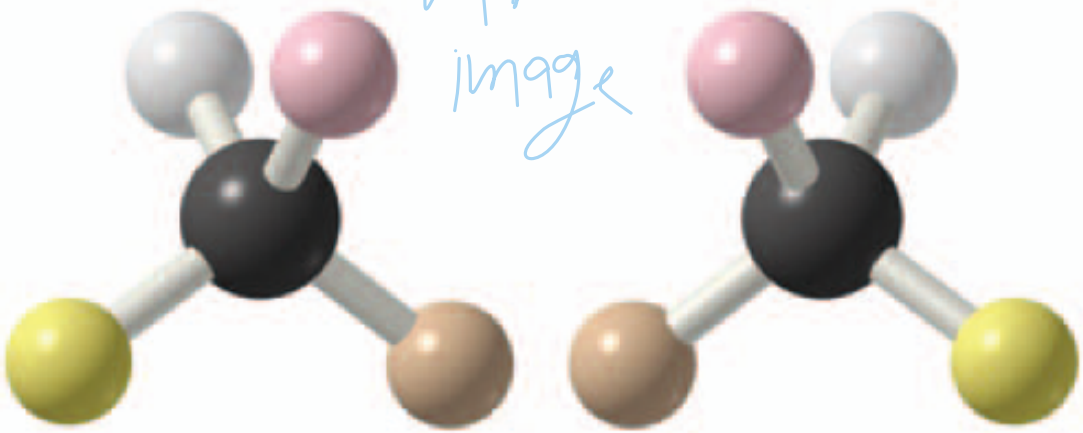
(I)

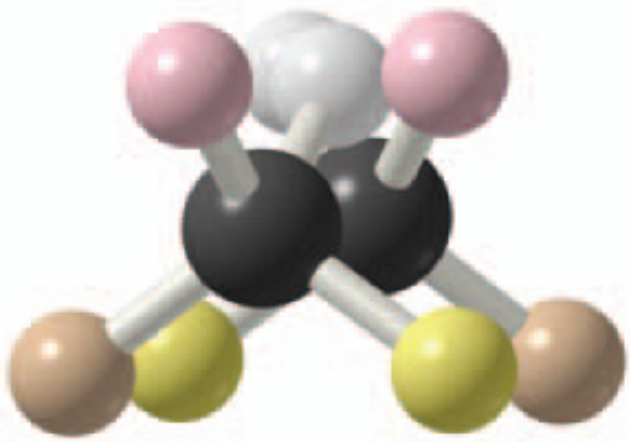


(II)

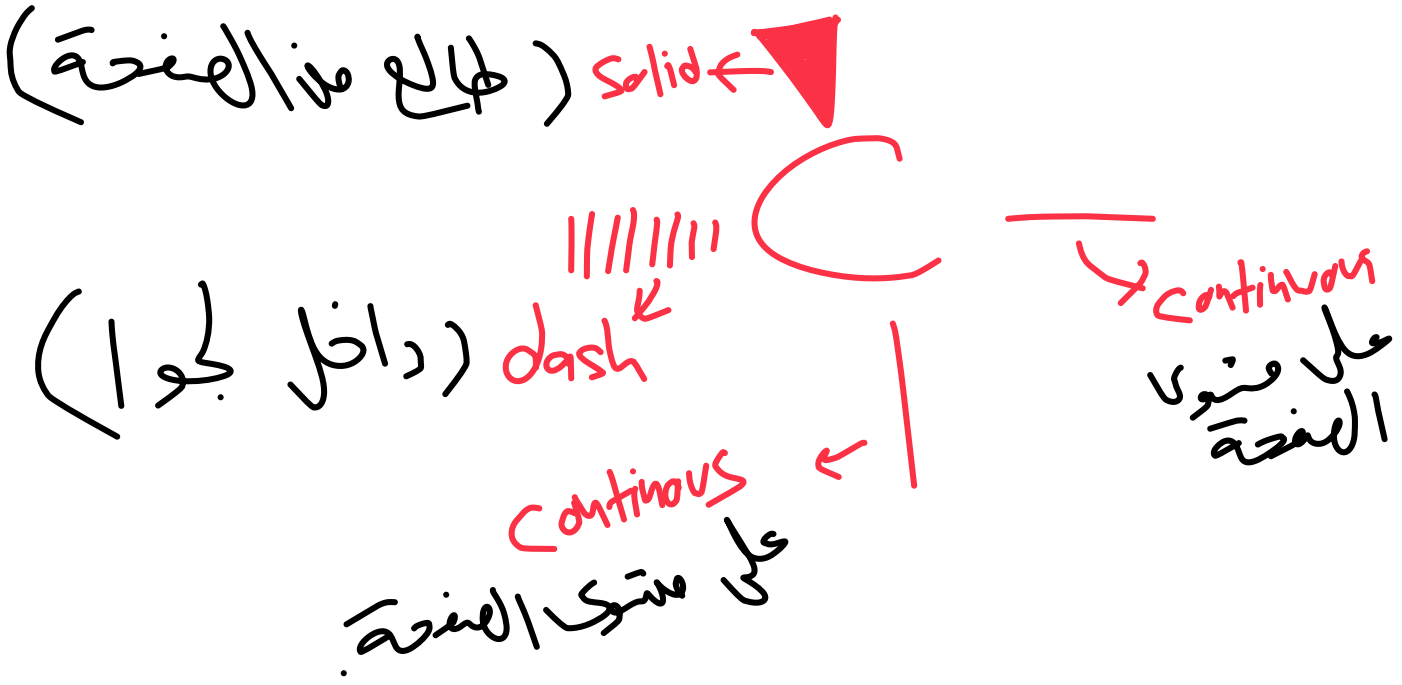
(I) and (II) are غير متطابقتين
nonsuperposable
mirror images of
each other

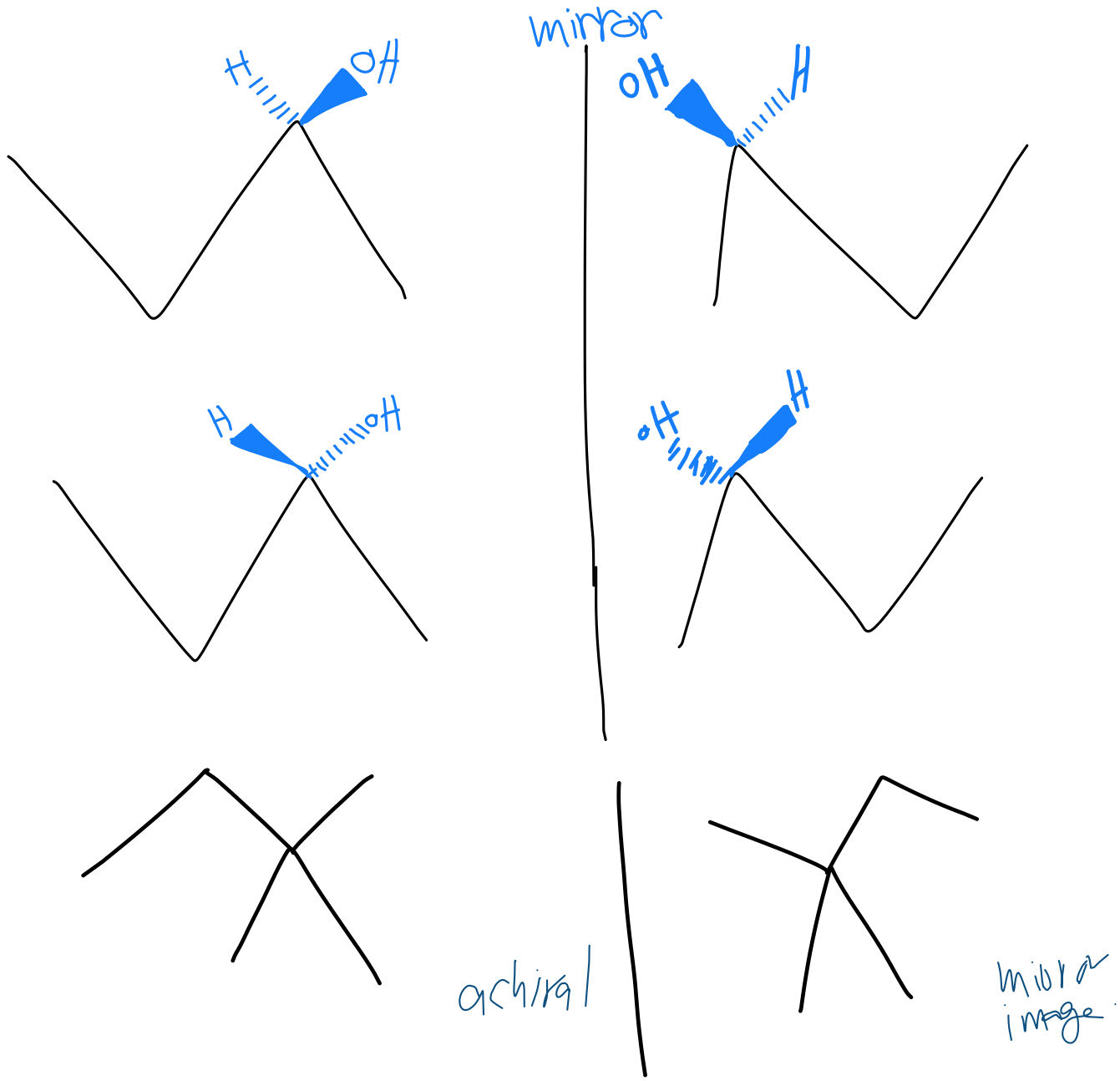
mirror image





Solid – dash


(طالع من الصفحة)
solid
dash (داخل لجوا)
continuous
على مستوى الصفحة
continuous
على مستوى الصفحة


mirror
achiral
mirror image

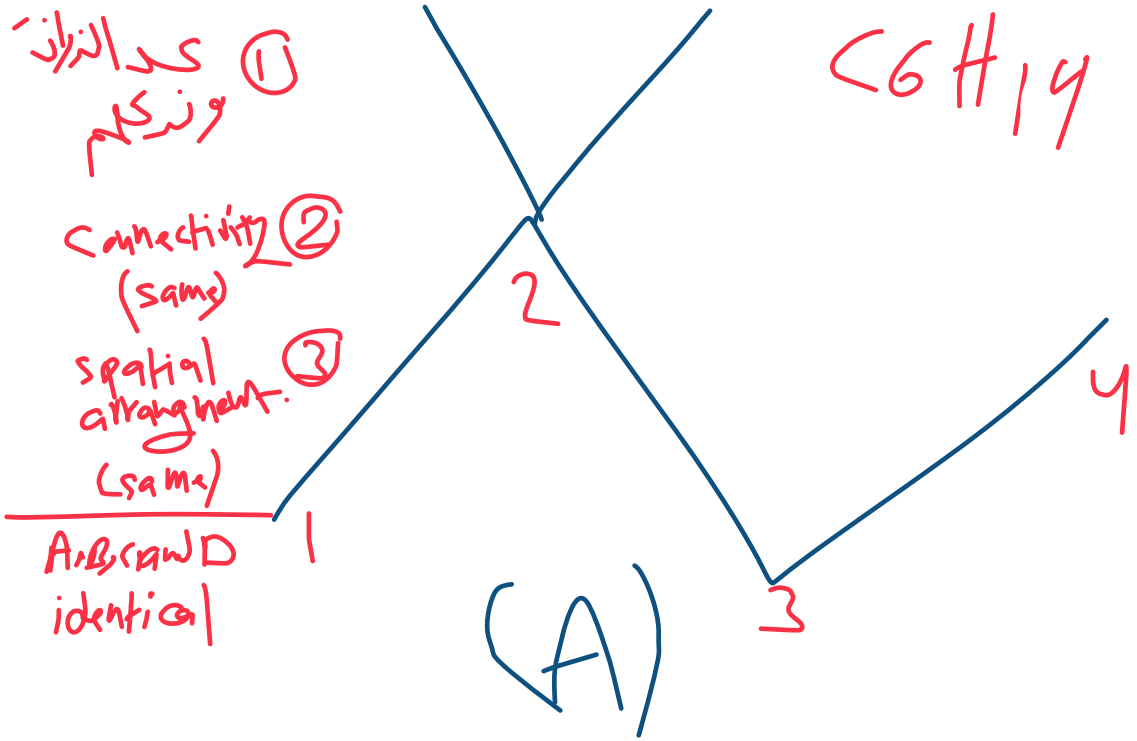
كد الزاك ①
وتركيم

Connectivity ②
(same)

spatial arrangement ③
(same)

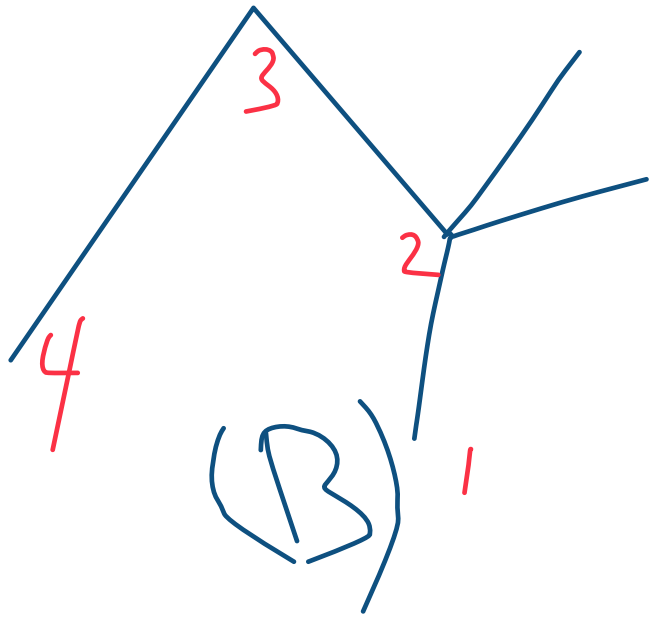
A, B, C and D identical

C_6H_{14}

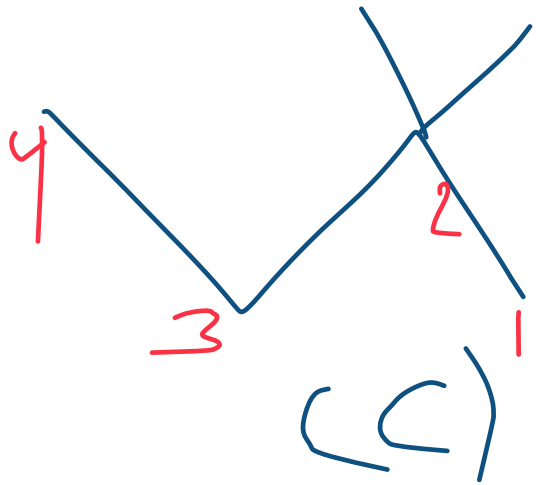


(A)

C_6H_{14}



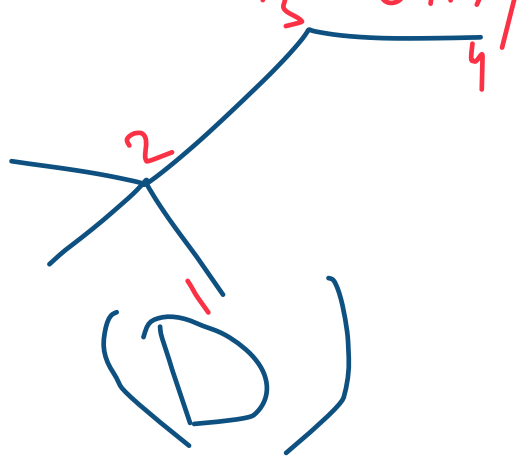
(B)



C_6H_{14}

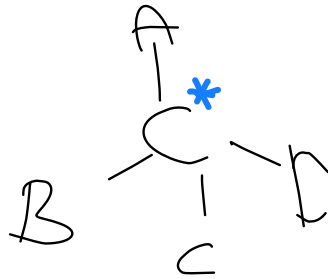
(C)

C_6H_{14}



(D)

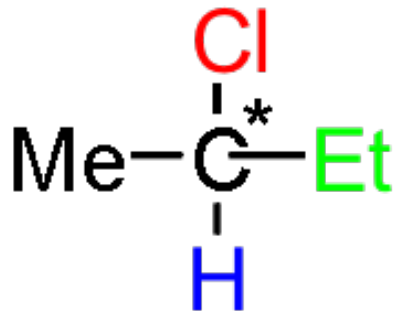
3. A Single Chirality Center Causes a Molecule to Be Chiral



- 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 (*)

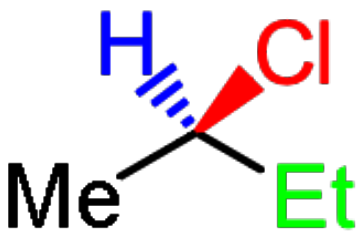
(chiral/asymmetric/stereogenic/stereocenter) + star

example (1)



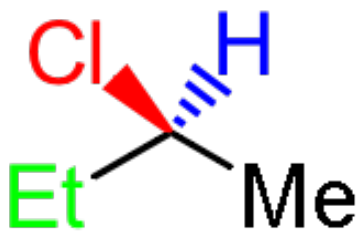
الكربون chiral يعني مرتبط بأربع مجموعات مختلفة.

chiral



(III)

mirror image



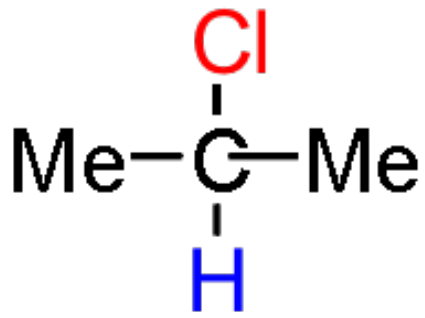
(IV)

mirror

chiral + mirror image → enantiomers

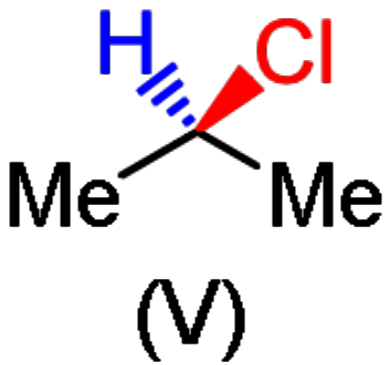
(III) and (IV) are nonsuperposable mirror images of each other

example 2

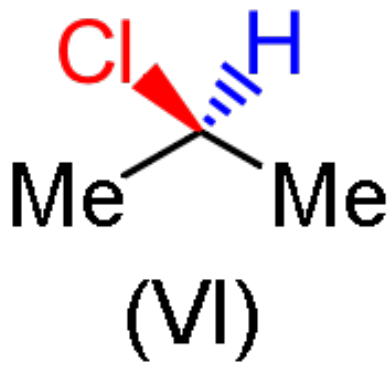


(achiral)

ذرة كربون غير متصلة بأربع مجموعات مختلفة.



(V)



(VI)

mirror

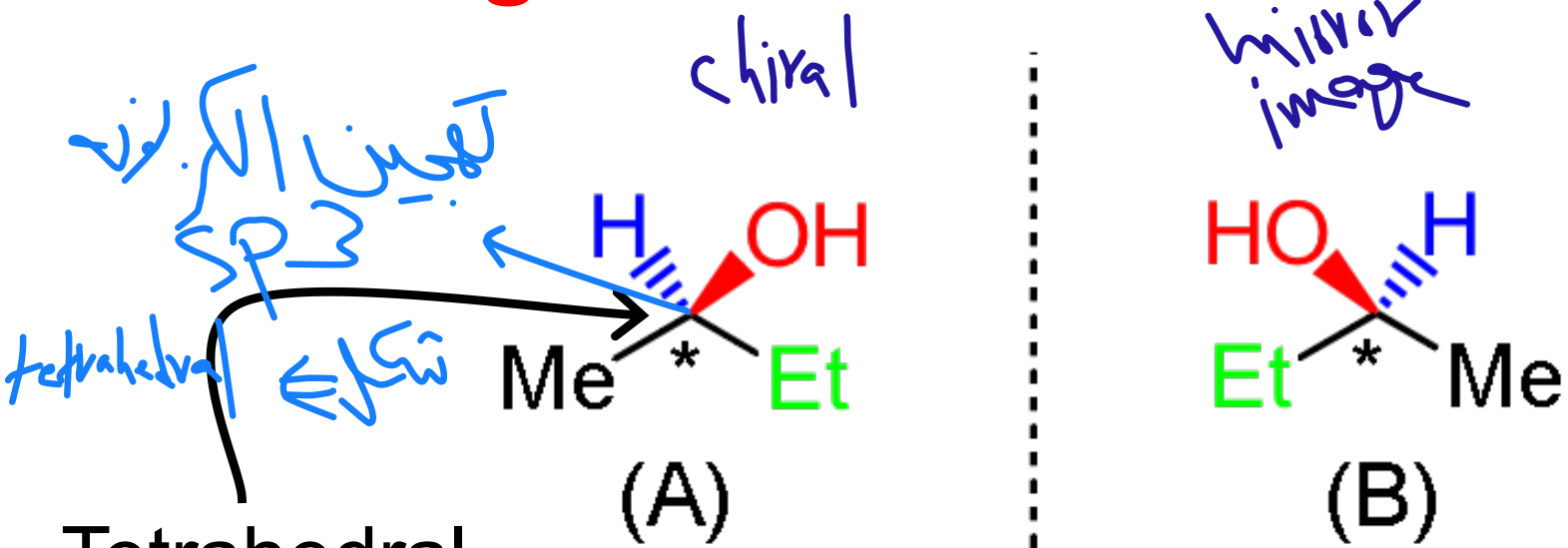
متطابقتين

(V) and (VI) are superposable

⇒ not enantiomers ⇒ **achiral**

3A. Tetrahedral vs. Trigonal Stereogenic Centers

- Chirality centers are ***tetrahedral stereogenic*** centers

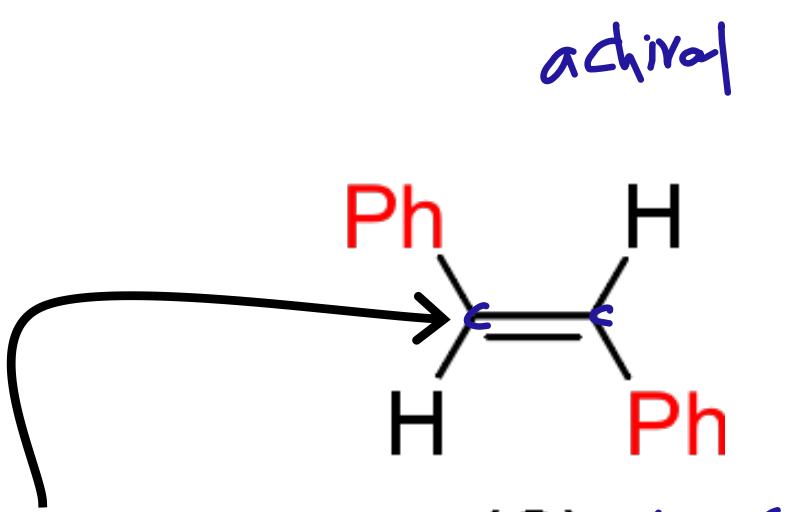


Tetrahedral stereogenic center ⇒ chiral

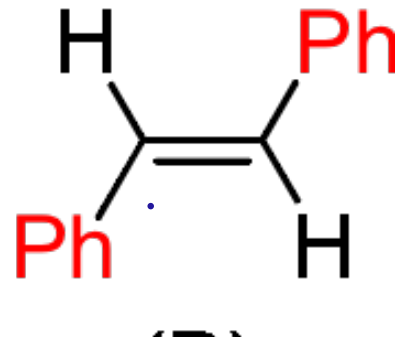
mirror

(A) & (B) are enantiomers

- *Cis* and *trans* alkene isomers contain trigonal stereogenic centers



(C)



(D)

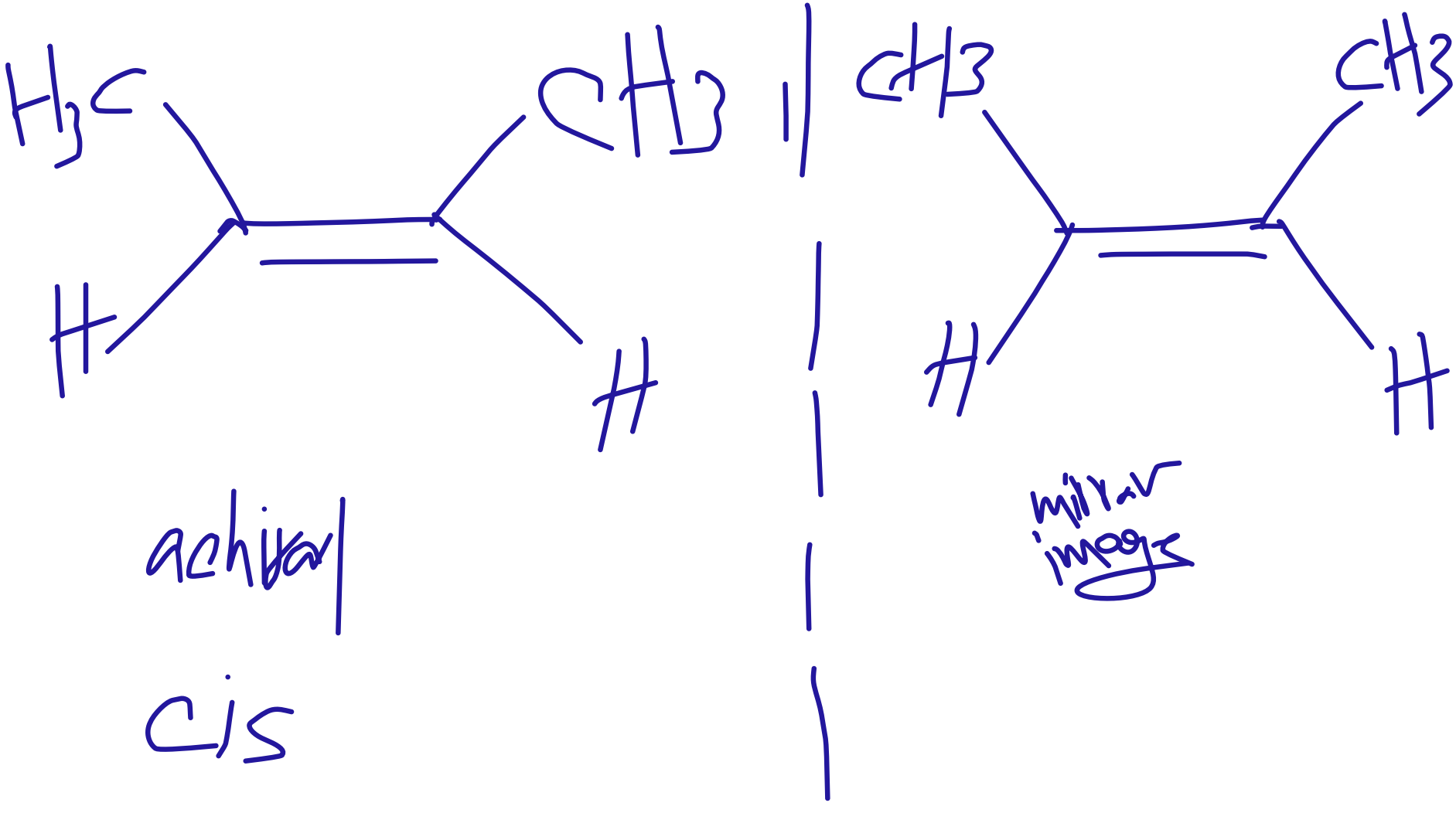
mirror

Trigonal stereogenic center

⇒ achiral

(C) & (D) are identical

17



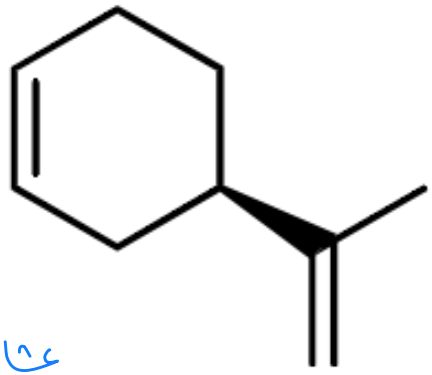
achiral

cis

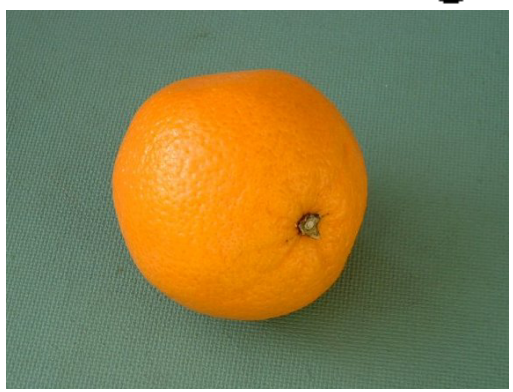
mirror image

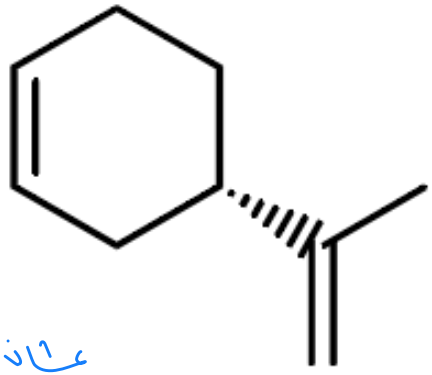
not enantiomers

4. More about the Biological Importance of Chirality

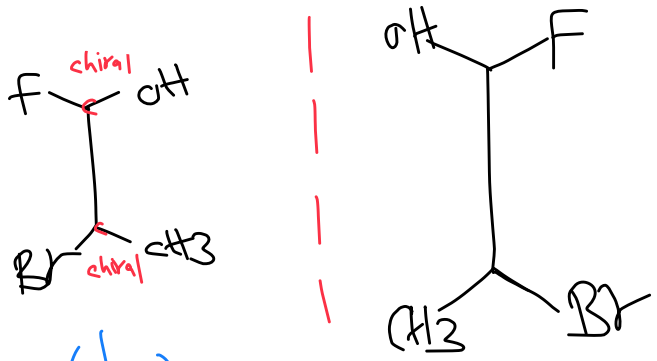


(+)-Limonene
(limonene enantiomer found in oranges)





(-)-Limonene
(limonene enantiomer found in lemons)



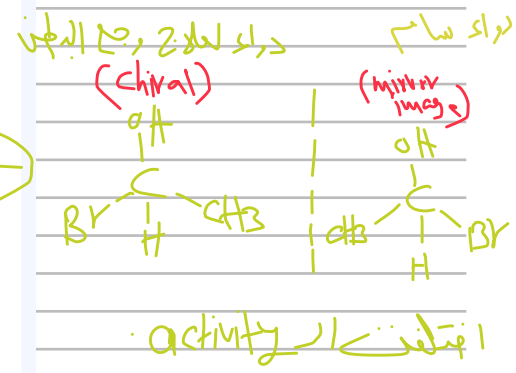
دواء

صورة الدواء

ممكن يكون واحد دواء ممتاز وبعالج ومرتاح
دواء سام أو العكس

Thalidomide

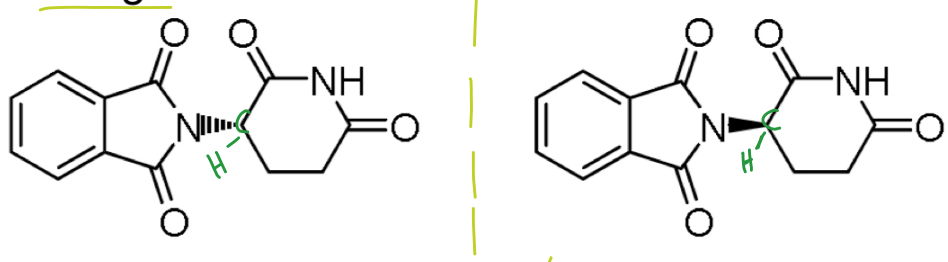
- The activity of drugs containing chirality centers can vary between enantiomers, sometimes with serious or even tragic consequences



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

مركب اقترحوه للحوامل لحتى ينمو الجنين بشكل أفضل
وخصوصا النخاع الشوكي، اسمه الthalidomide,عملوا
تجارب بالمختبر وكانت النتائج ممتازة،نزلوه ع الاسواق وبعد
فترة بلشت تزيد حالات ولادة اطفال مشوهين، رجعوا
للامهات ووجدوا انهم كانوا يوخذوا thalidomide,
مع انه بالمختبر كان وضعه تمام,
السبب انه لما كان هذا المركب بالوضع المخبري كان بوضع
فراغي مختلف عن يلي نزل ع الاسواق....
بالوضع المخبري كان R
وبالوضع الصناعي كان
R 40%
S 60%
وتم سحب الدواء من الاسواق
وحالياً اله بديل بتوخذه الحوامل
folic acid

- 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)

mirror

enantiomer of Thalidomide
(causes birth defects)

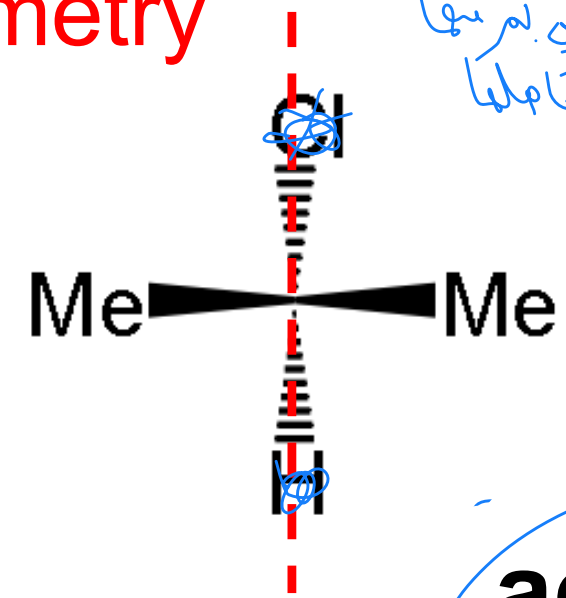
أطفال مشوهين
وبنتهم مثل في نمو الأطراف

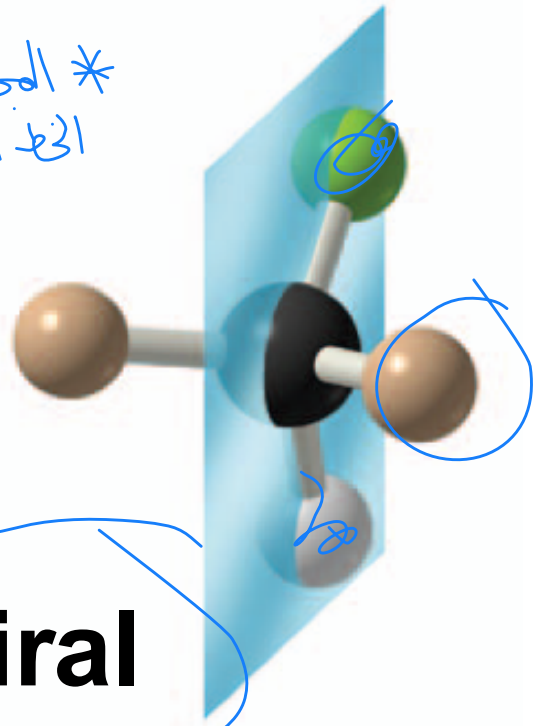
5. How to Test for Chirality: Planes of Symmetry

- 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***

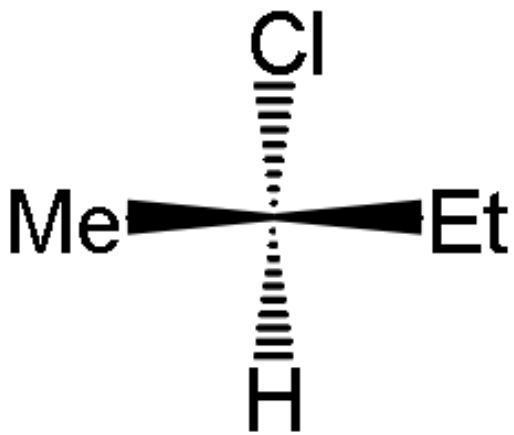
Plane of symmetry

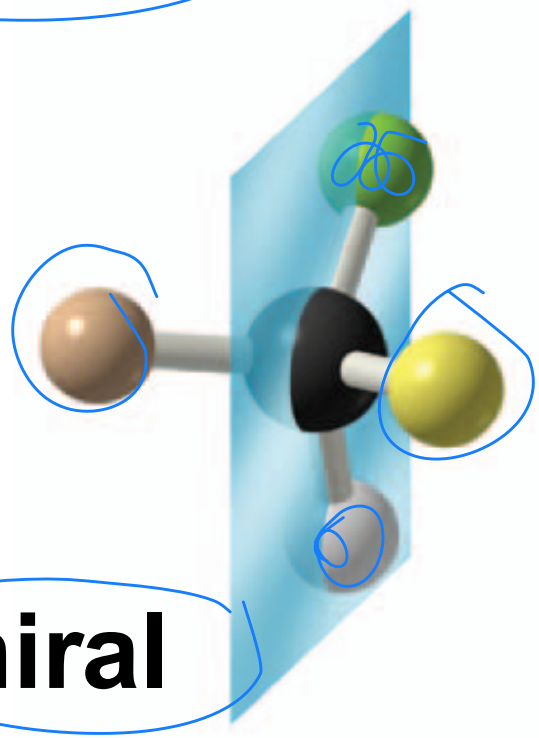
* المجموعة اللي بمر بنها الخط الرهمي بتماثلها





achiral

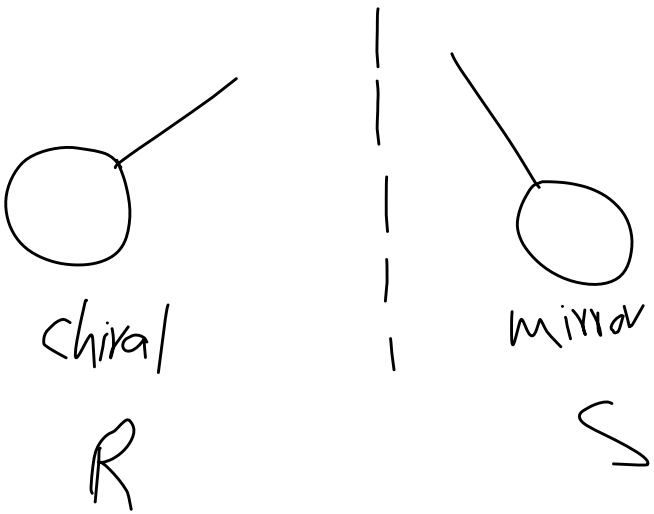


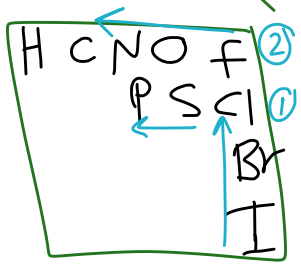


chiral

No plane of symmetry

(خاصية التماثل لا chiral)



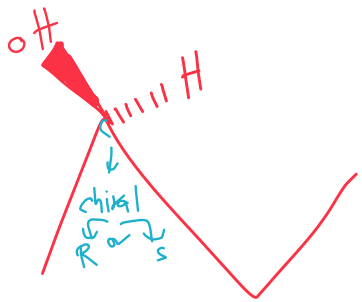


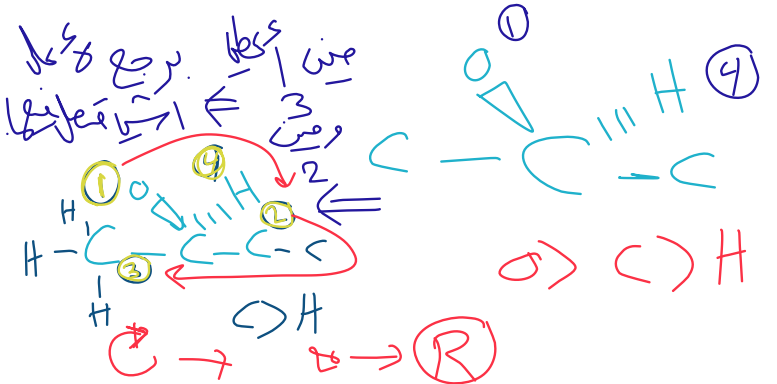
① ترقم 1,2,3,4

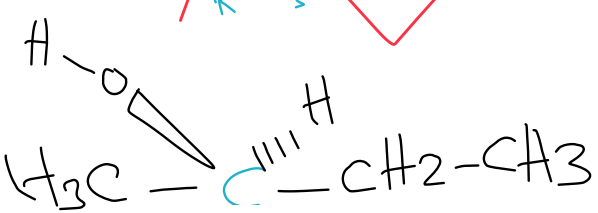
② نعتبر أربعة شي موجودة

③ بتمشي مع واحد إلى ثلاث
- إذا كان عكس عقارب الساعة ↺ ⇓ S
- إذا كان مع عقارب الساعة ↻ ⇓ R

Example

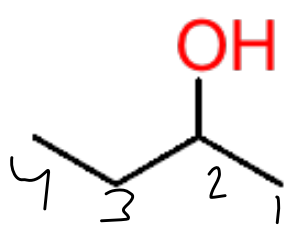




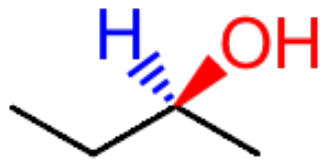


6. Naming Enantiomers: *R*,*S*-System

Recall:

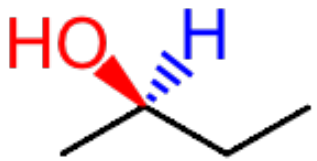


2-butanol



(I)

(R) 2-butanol



(II)

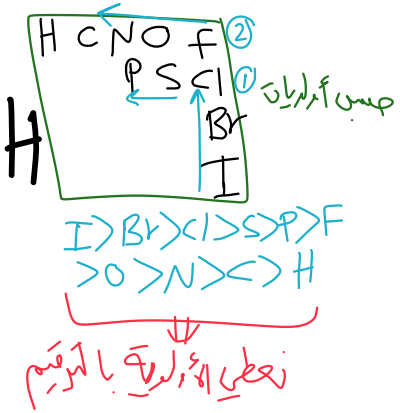
(S) 2-butanol

- 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)

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



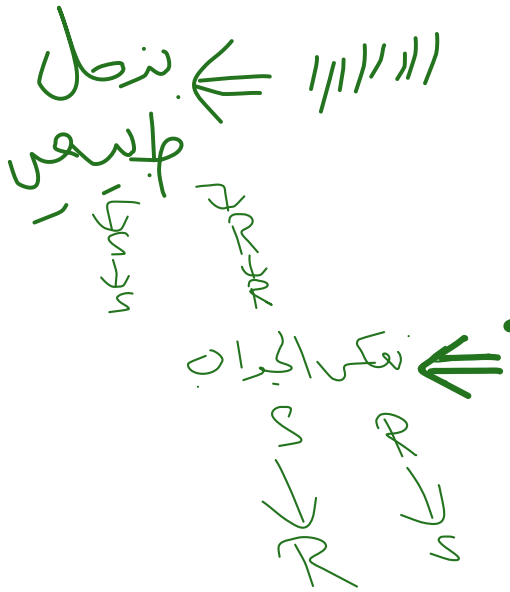
- في حال الذرات المتصلة بشكل مباشر مع الـ chiral carbon

لهم نفس الأولوية، نعود إلى كل ذرة ونشوف أعلى ذرة متصلة في كل وحدة ومن ثم تقارن بينهم الأعلى نعطي المتصل بها الأولوية بالترقيم.

- 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.

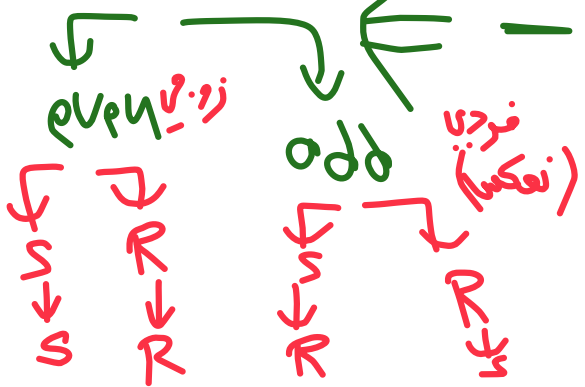
3 حالات

① - يكون رقمها أربعة على الأقل dash



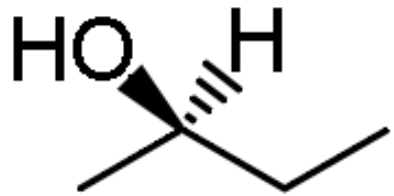
② - يكون رقمها أربعة على الأقل solid

③ - يكون رقمها أربعة على الأقل continuous

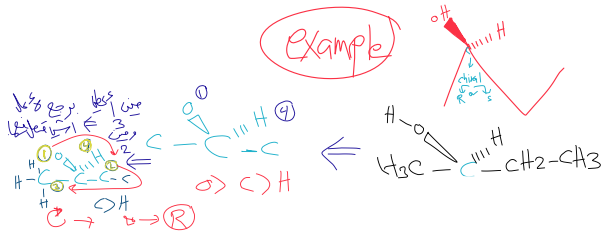


- Rule 3
  - Visualize the molecule so that the lowest priority group is directed away from you, then trace a path from highest to lowest priority. If the path is a clockwise motion, then the configuration at the asymmetric carbon is (*R*). If the path is a counter-clockwise motion, then the configuration is (*S*)

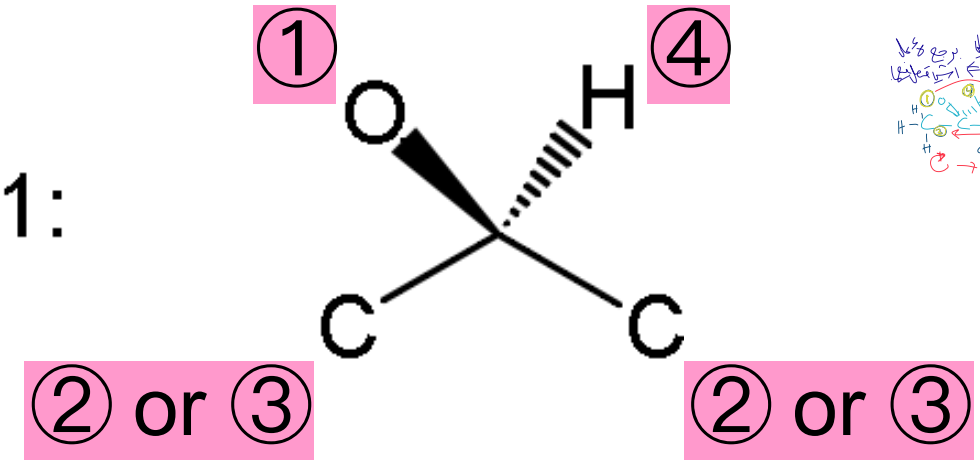
❖ Example



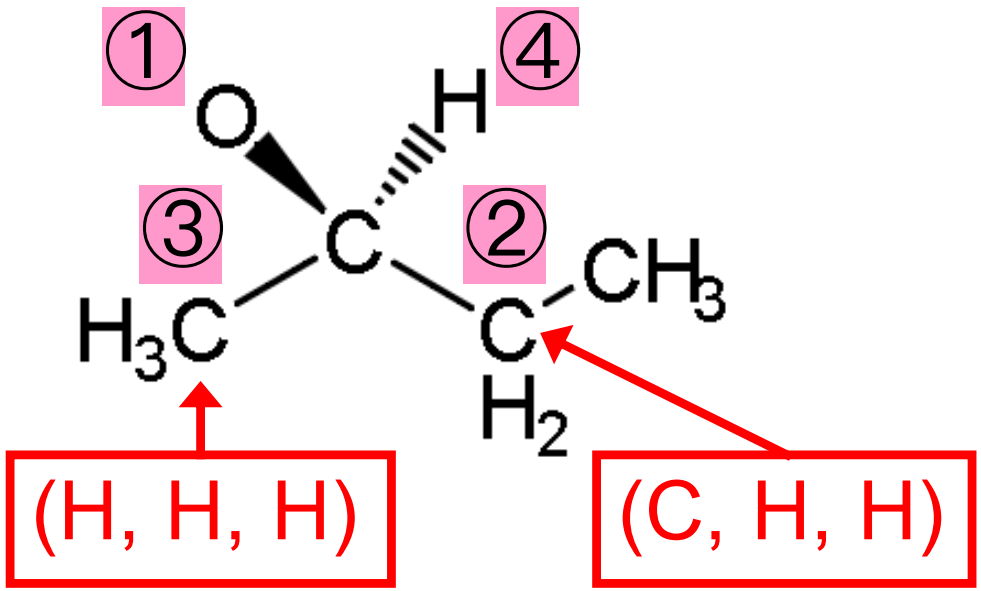
(2-Butanol)

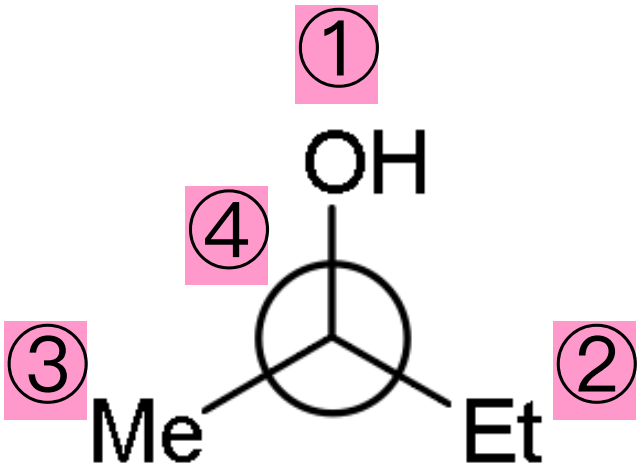


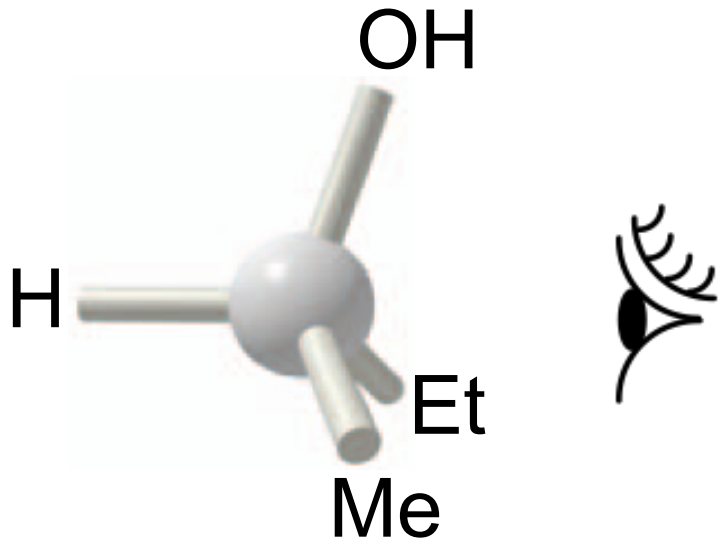
Step 1:

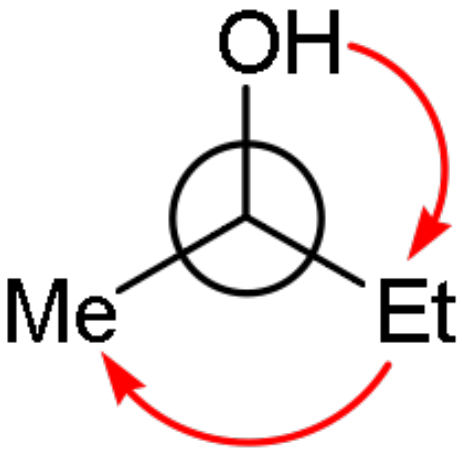


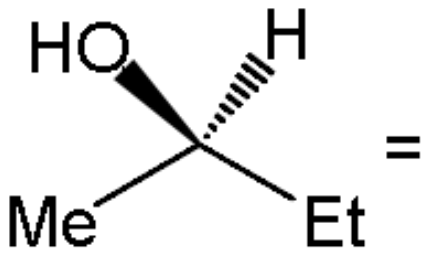
Step 2:











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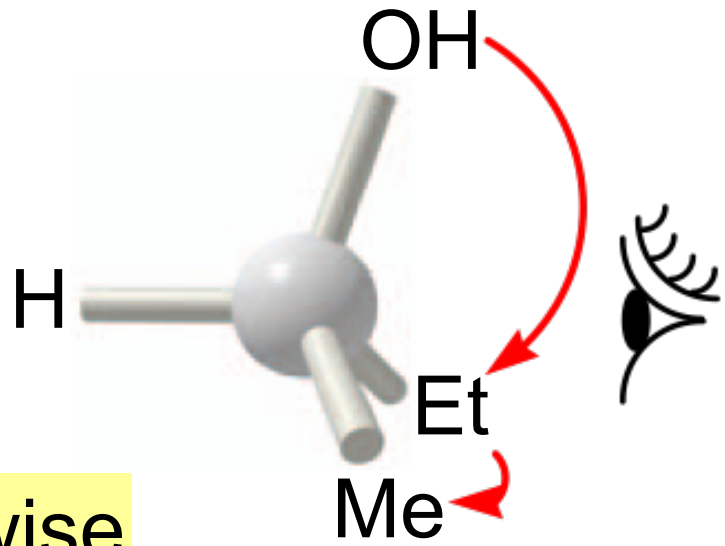
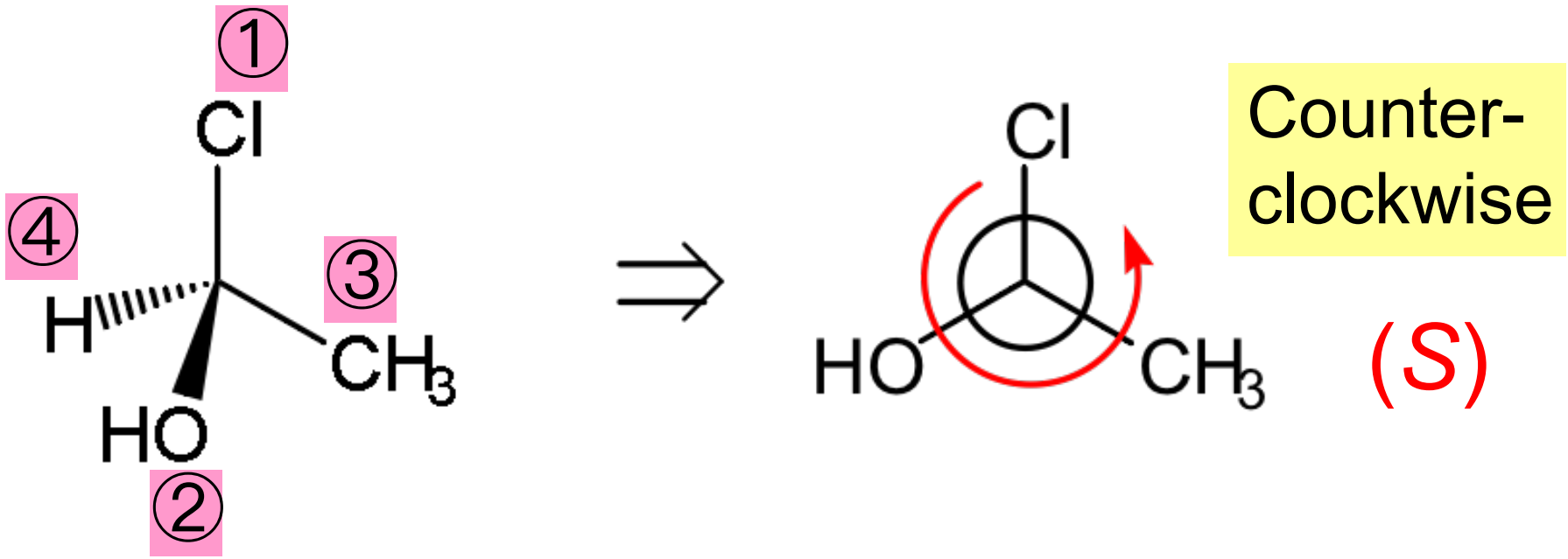
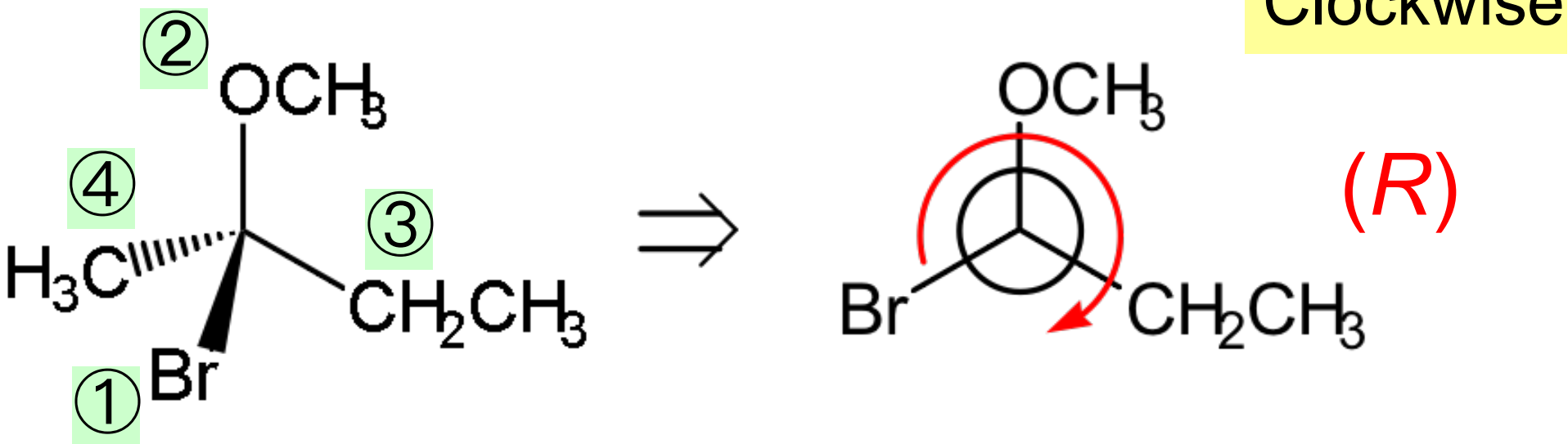


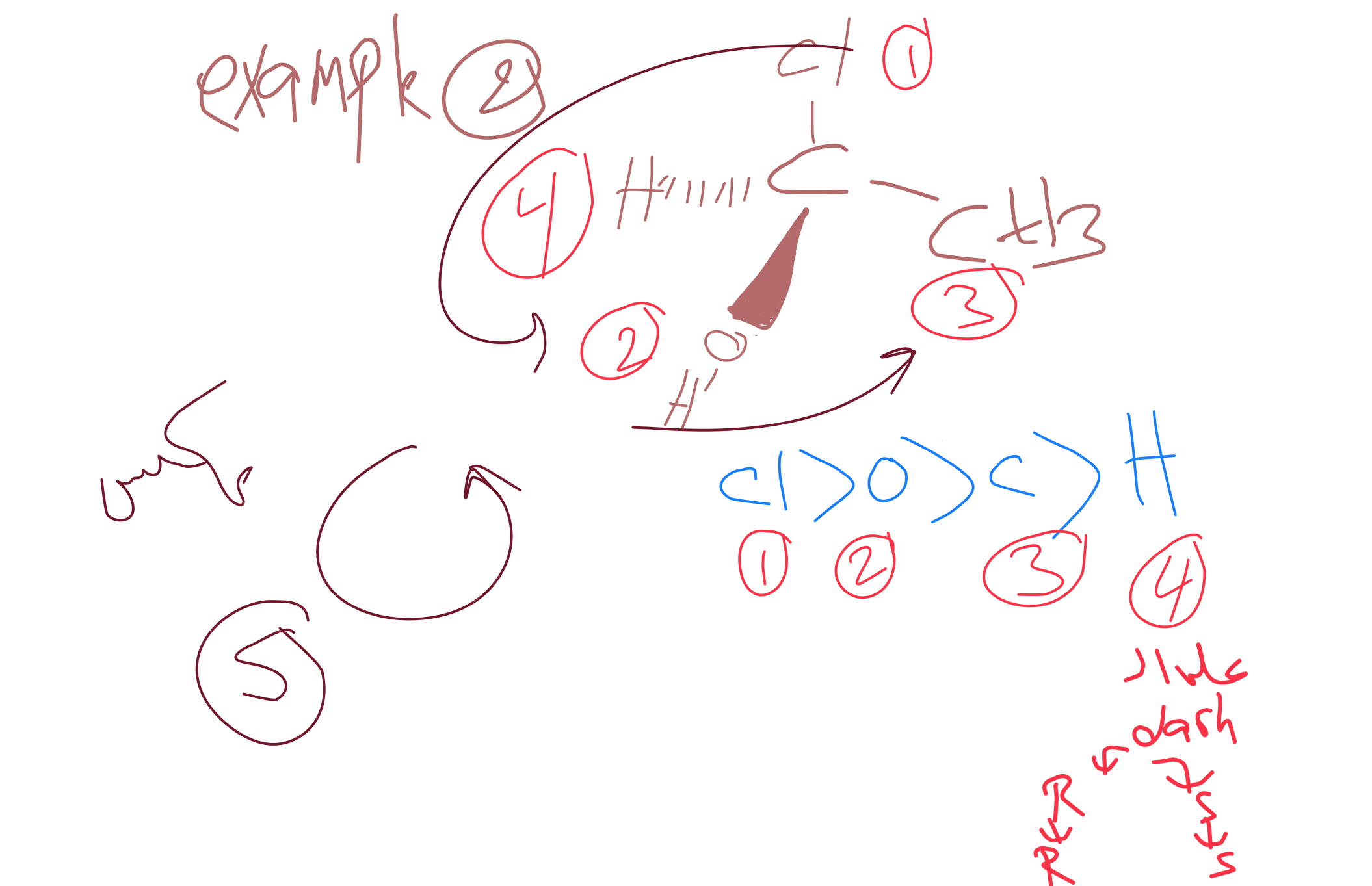
Arrows are clockwise

(*R*)-2-Butanol

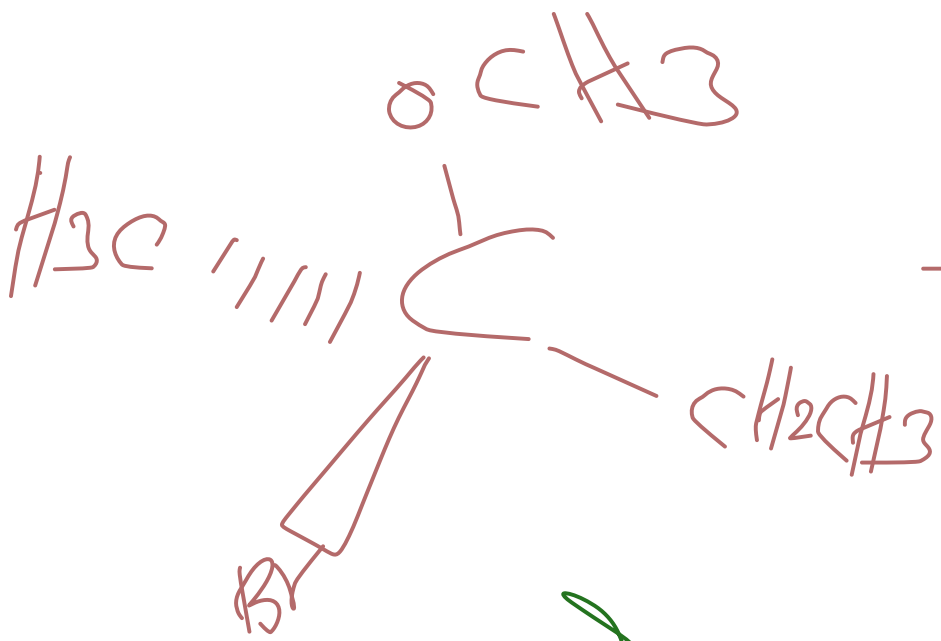
❖ Other examples

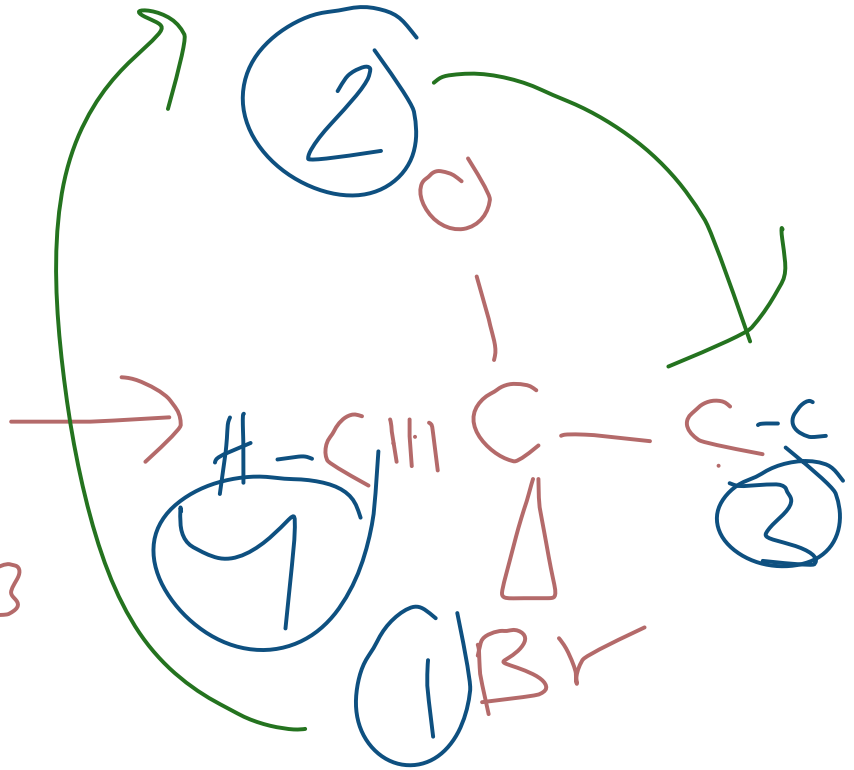





example 2
Cl
1
4
H
C
CH3
3
2
O
H
C
O
C
H
1
2
3
4
5
dash
R
S

example ③





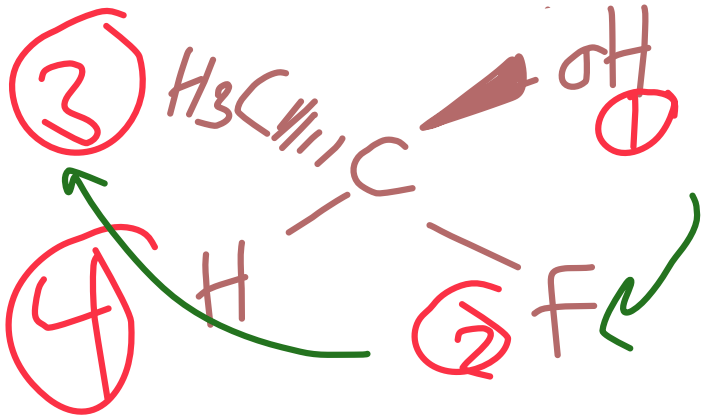
Br > O > C

① ② 3

dash wedge

R S

Example (4)



O > F > C > H

1 2 3 4

على continuous

ثم تغيير كما 2 لتصبح Dash على

نبدأ من 1 إلى 3

نعكس الجواب

الجواب قبل التبديل ← R

الجواب بعد التبديل ← S

الجواب النهائي S

example (5)

<1>F>O>H

على continuous → كم تغيير كل أصبع على dash → 1

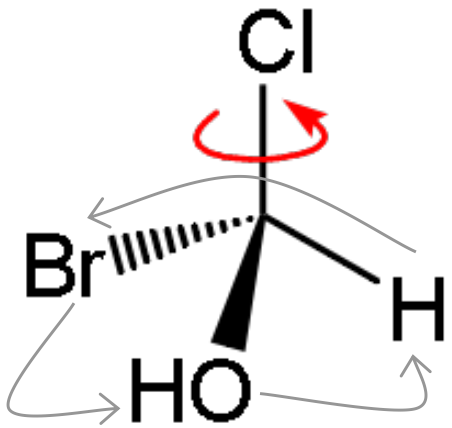
فردي ← نعكس الجواب

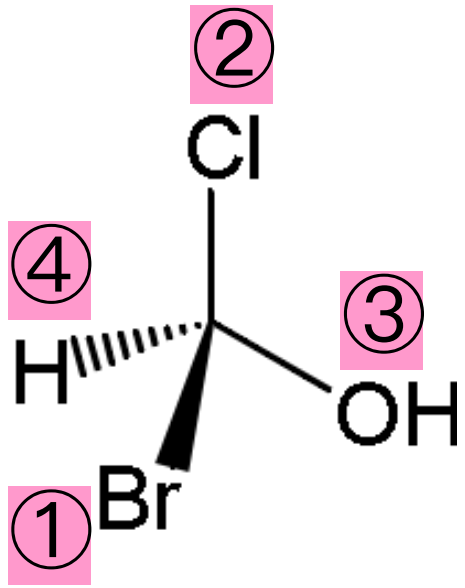
R الجواب النهائي ← نعكسه R

عكس S

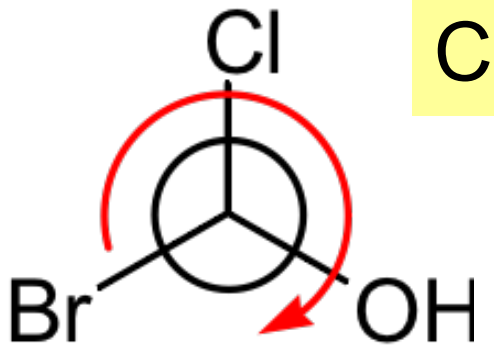
Other examples

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



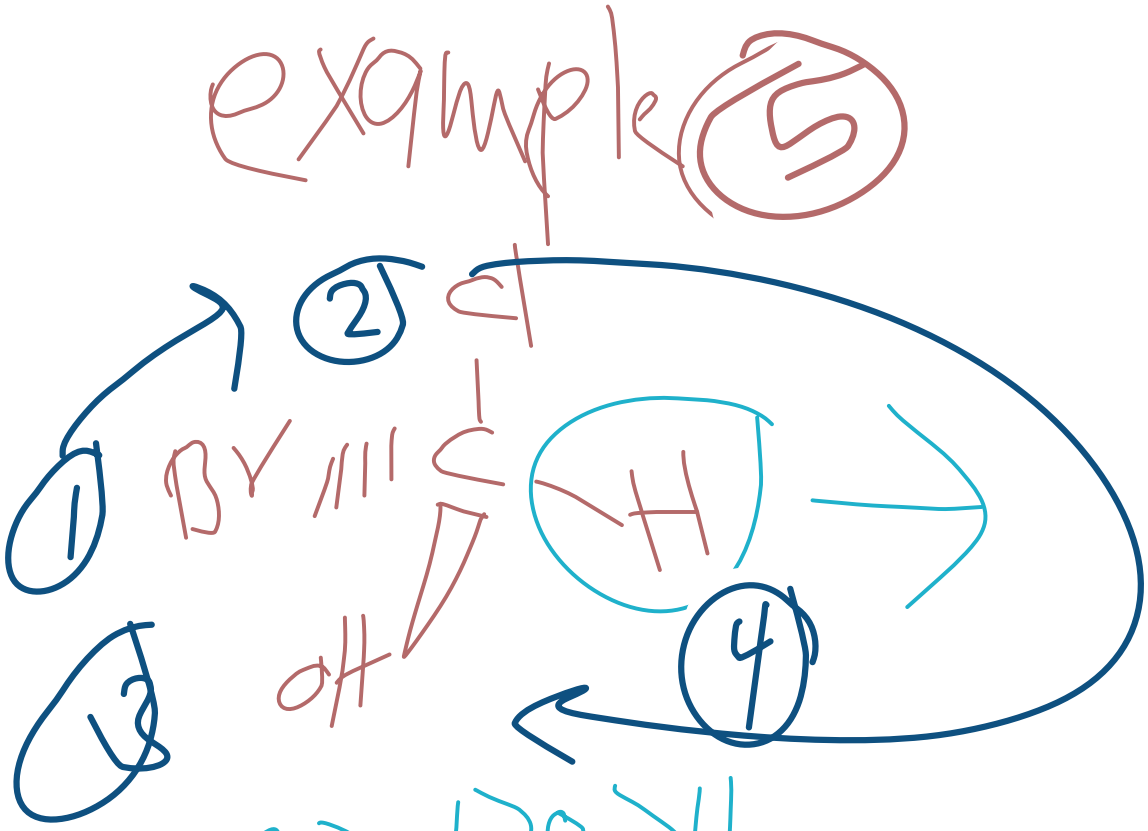


ملاحظه
دايما لازم
ترقيم أربعة
يكون على ال
dash
(/////)

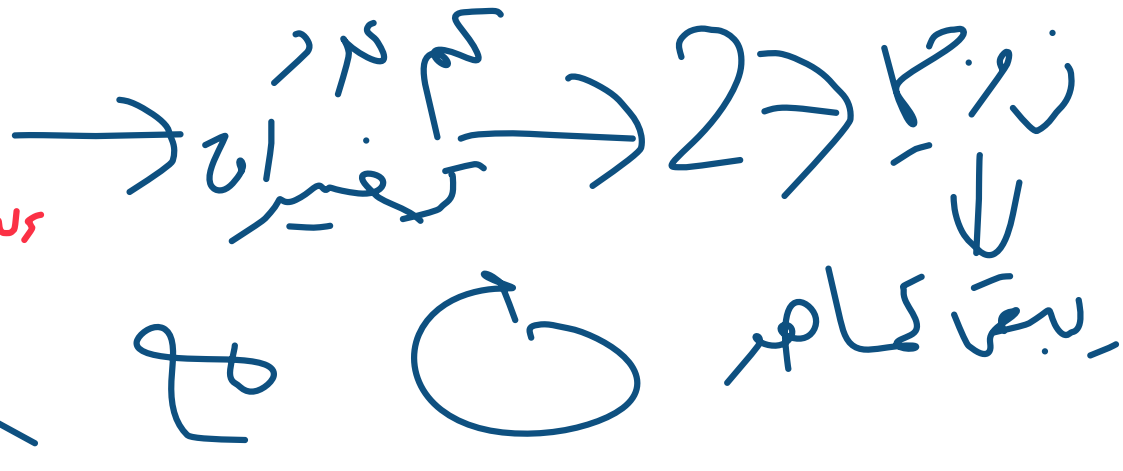


Clockwise

(*R*)

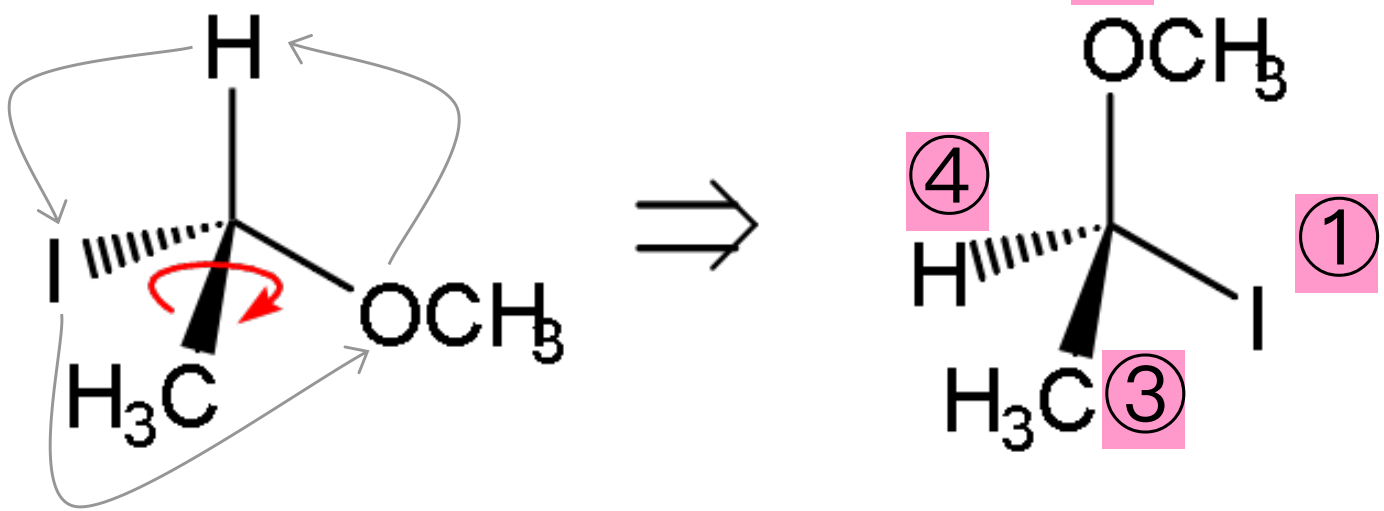


على continuous

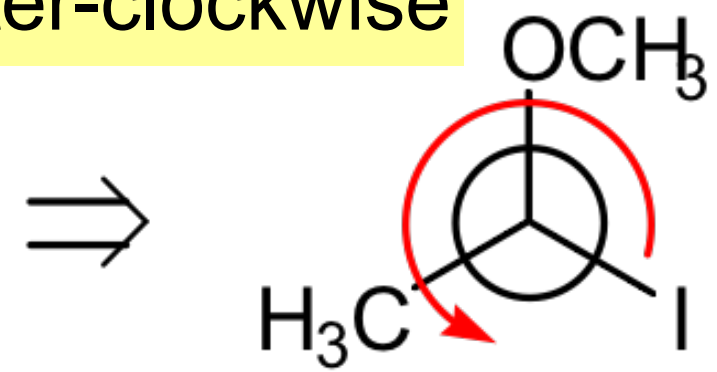


Other examples

- Rotate C–CH_3 bond such that H is pointed to the back



Counter-clockwise



(*S*)