CHM 103

ORGANIC CHEMSTRY I

Department of Chemical Sciences
Faculty of Science and Technology
Bingham University, Karu

Course Lecturer: Joseph C. Oguegbulu
Joseph.oguegbulu@binghamuni.edu.ng

COURSE CONTENT

• Introduction. History, classifications	0.5 week
• Carbon: Bonding in organic compounds, structure	0.5 week
• Functional groups	0.5 week
• IUPAC nomenclature	1 week
• Isomerism – Structural & Stereo-isomerism	2 weeks
• Hybridisation – Resonance effects & others	2 weeks
• Alkanes, Alkenes, Alkynes	1.5 weeks
• Alkyl halides, Alkanols	1 week
• Carbonyl compounds: Alkanals and Alkanones.	0.5 week

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LECTURE V

- ISOMERISM

- STRUCTURAL ISOMERISM
  - Chain
  - Position and
  - Functional Group Isomerism

OBJECTIVES: At the end, you should be able to…

- Apply IUPAC rules to naming simple and semi-complex compounds
- Show the structural formulars of cmpds based on their IUPAC names
- Explain isomerism and its types
- Differentiate between structural and stereo-isomerism
- Differentiate & show e.g. of various types of structural isomerism

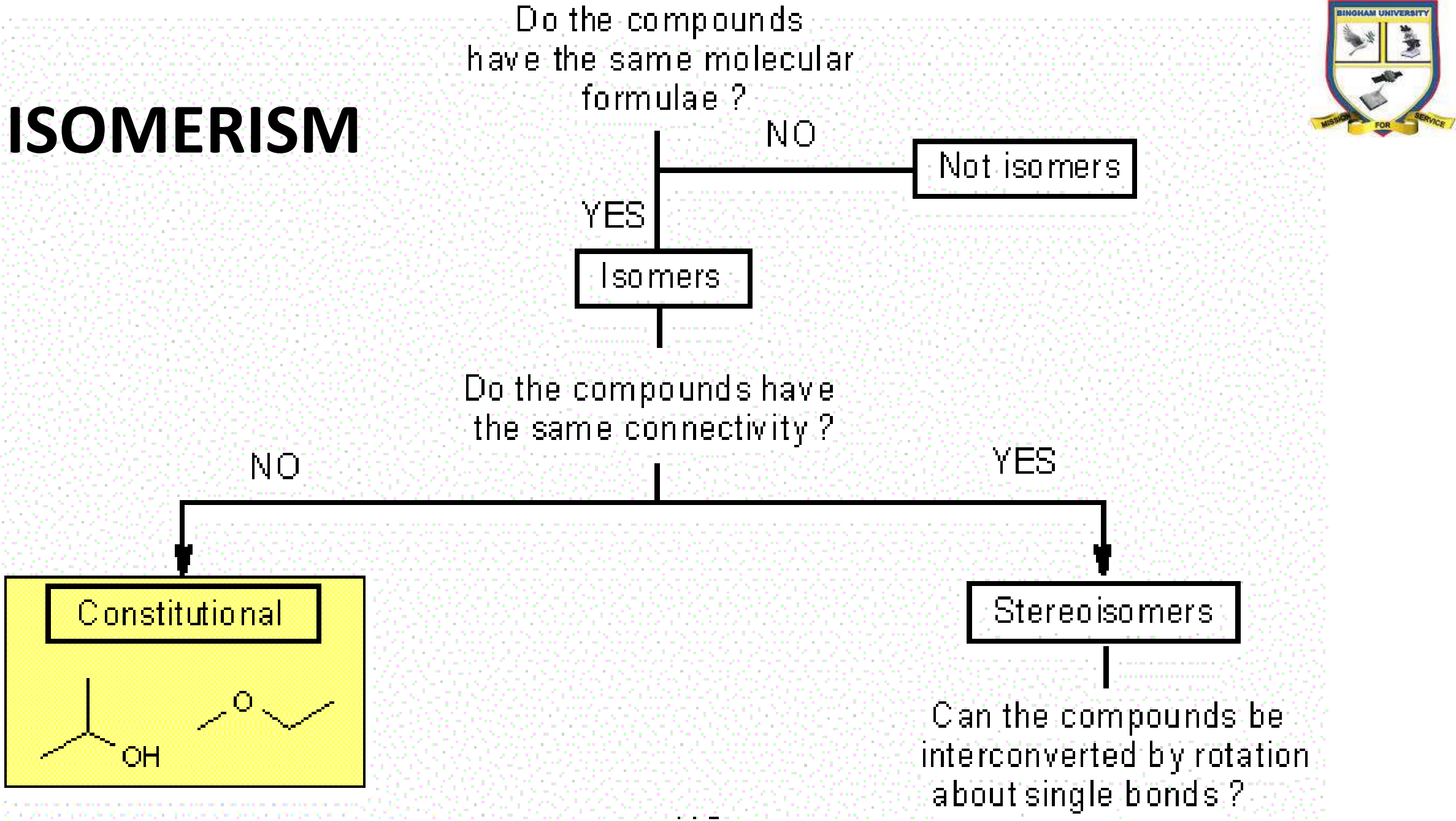
ISOMERISM

- The existence of compounds with **same molecular formula** but **different structural formulas**

- Types
  - **Structural/Constitutional Isomerism**: Same constitution, different connectivities

  - **Stereoisomerism:** Same constitution, same connectivities, different *spatial arrangements (spatial orientation)*

ISOMERISM

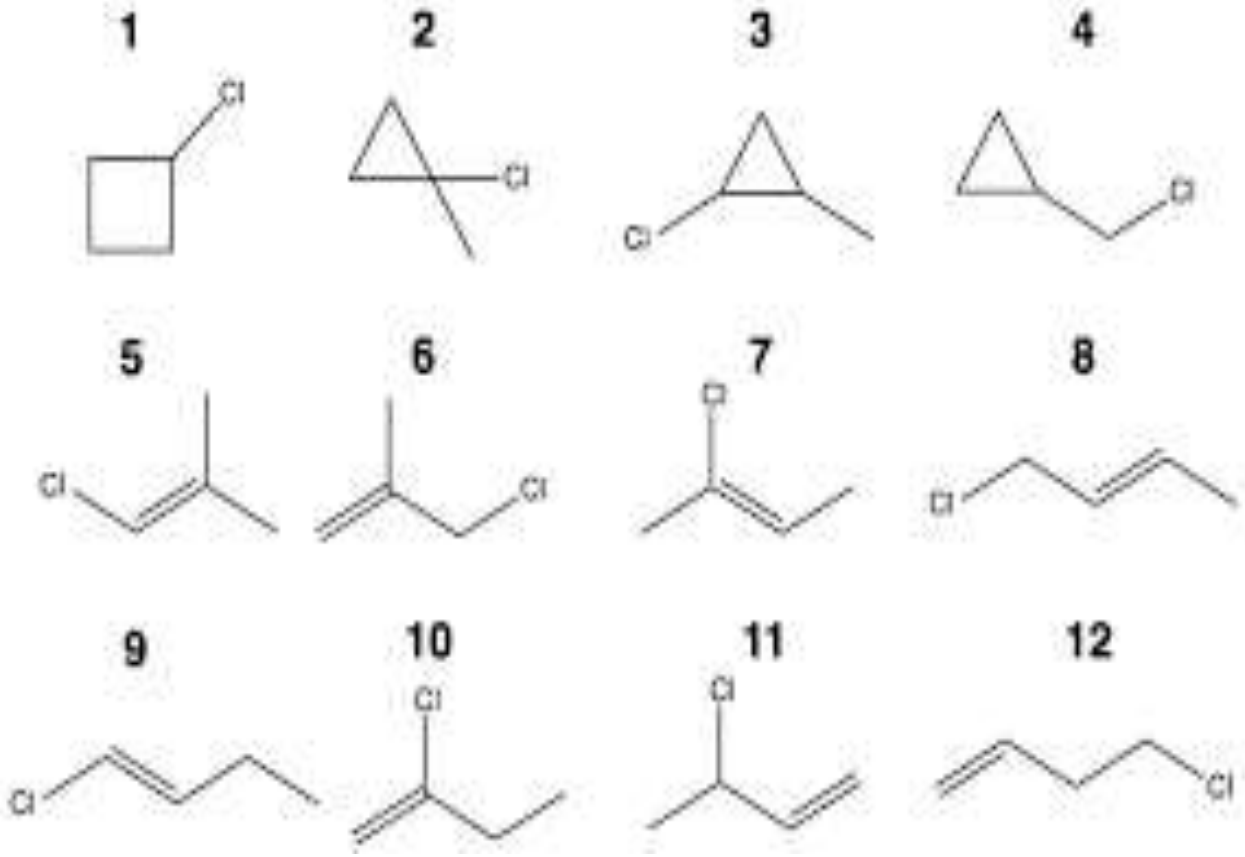

Do the compounds have the same molecular formulae ?
NO
Not isomers
YES
Isomers
Do the compounds have the same connectivity ?
NO
YES
Constitutional
OH
O
Stereoisomers
Can the compounds be interconverted by rotation about single bonds ?

STRUCTURAL ISOMERISM

- Also called *constitutional isomerism*
- All these cmpds have the same molecular formula:
  - What is it?

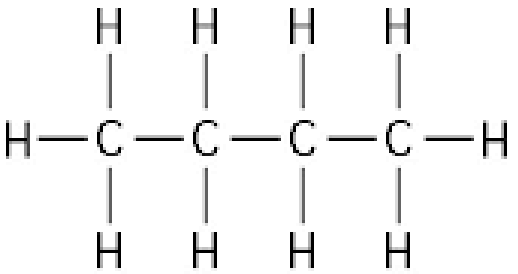
$$C_4H_7Cl$$

- Types:
  - **Chain Isomerism**
  - **Position Isomerism**
  - **Functional Group Isom.**

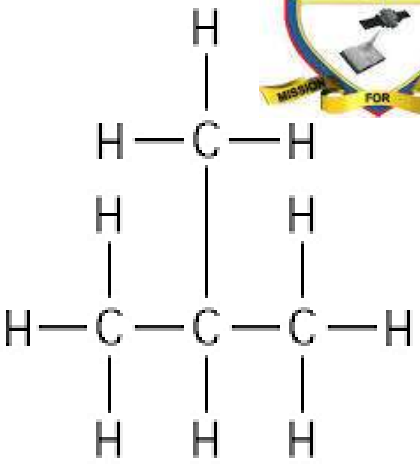


CHAIN ISOMERISM (Struct. Iso. Types)

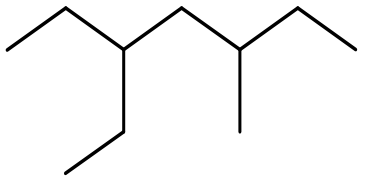
- Two compounds can have different chains or branching
  - Also called branching Isomerism
- Examples…
  - Butane **&** 2-Methylbutane
  - 3-ethyl,5-methylheptane **&** Decane
  - Cyclohexane **&** methylcyclopentane
- **Q5: Show all the chain isomers of hexane (C_6H_{14}) Name them???**

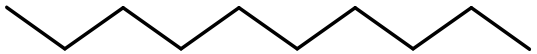


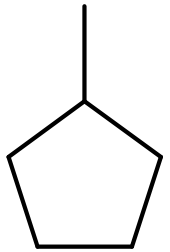
Butane
(n-Butane)

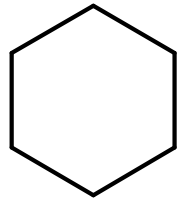


2-Methylpropane
(Isobutane)



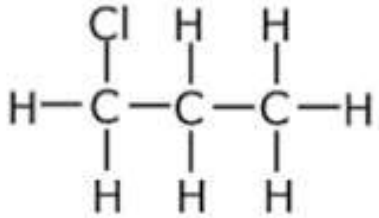




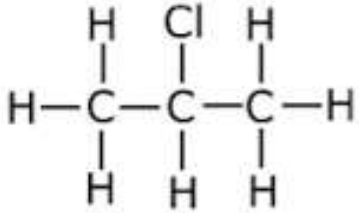


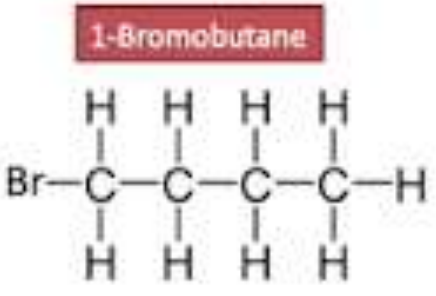
POSITION ISOMERISM (Struct. Iso. Types)

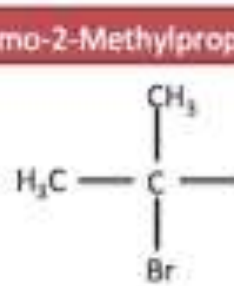
- Just like in chain isomerism but when other elements are present
- Examples…
  - C_4H_9Br
  - C_3H_7Cl
  - C_3H_7OH
  - $C_6H_4NH_2OH$
- **Q6**
  - **C_5H_9Br** ***(take home)***

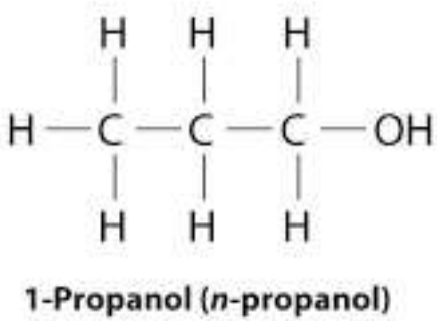

Chloropropane

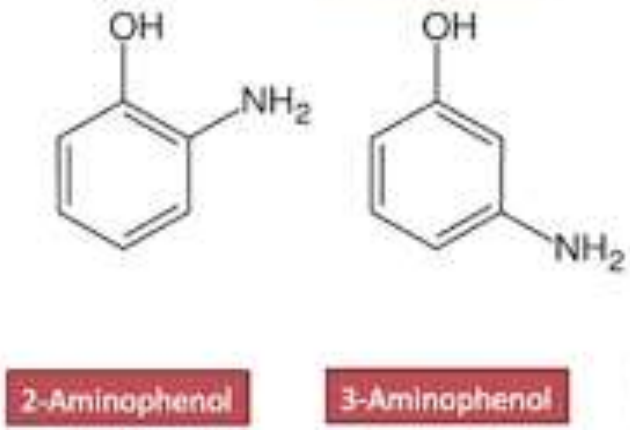
and

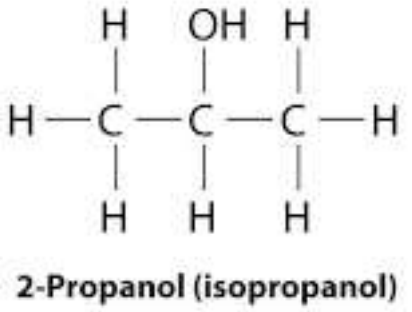

2-Chloropropane




2-Bromo-2-Methylprop


1-Propanol (*n*-propanol)

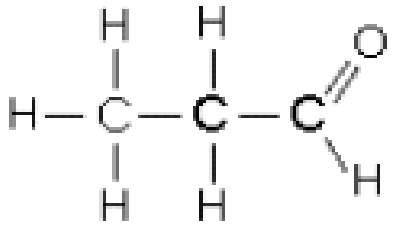



2-Propanol (isopropanol)

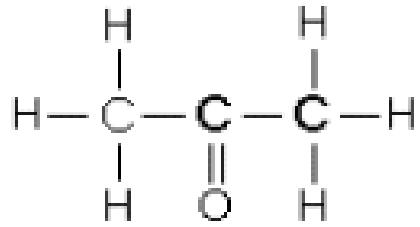
FUNCTIONAL GROUP ISO (Struct. Iso. Types)

- A new functional group may form bc of change in position of an atom

propanal

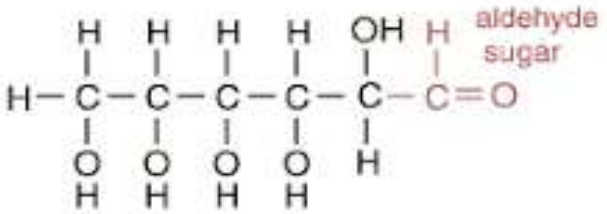


propanone (acetone)

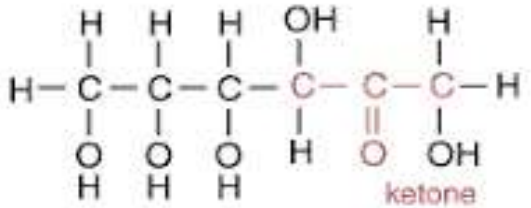


Examples…

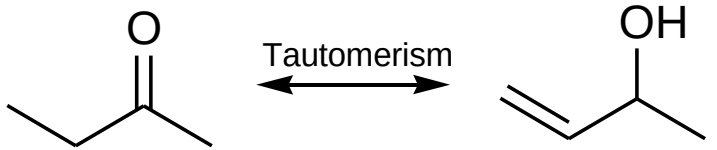
- Aldehydes and ketones
  - E.g. propanal and propanone
- Aldoses vs Ketoses
  - eg Glucose vs Fructose
- Keto/Enol Tautomerism
  - e.g. Butan-2-one and But-3-en-2-ol



Glucose



Fructose



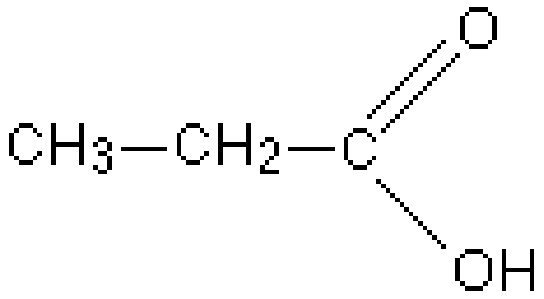
butan-2-one

but-3-en-2-ol
OR
3-Hydroxybutene

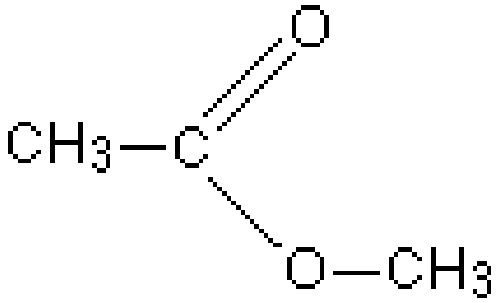
TUTORIAL 5: Structural Isomerism

Q7

- Show any functional group isomers of **propanoic acid ($C_3H_6O_2$)**



propanoic acid

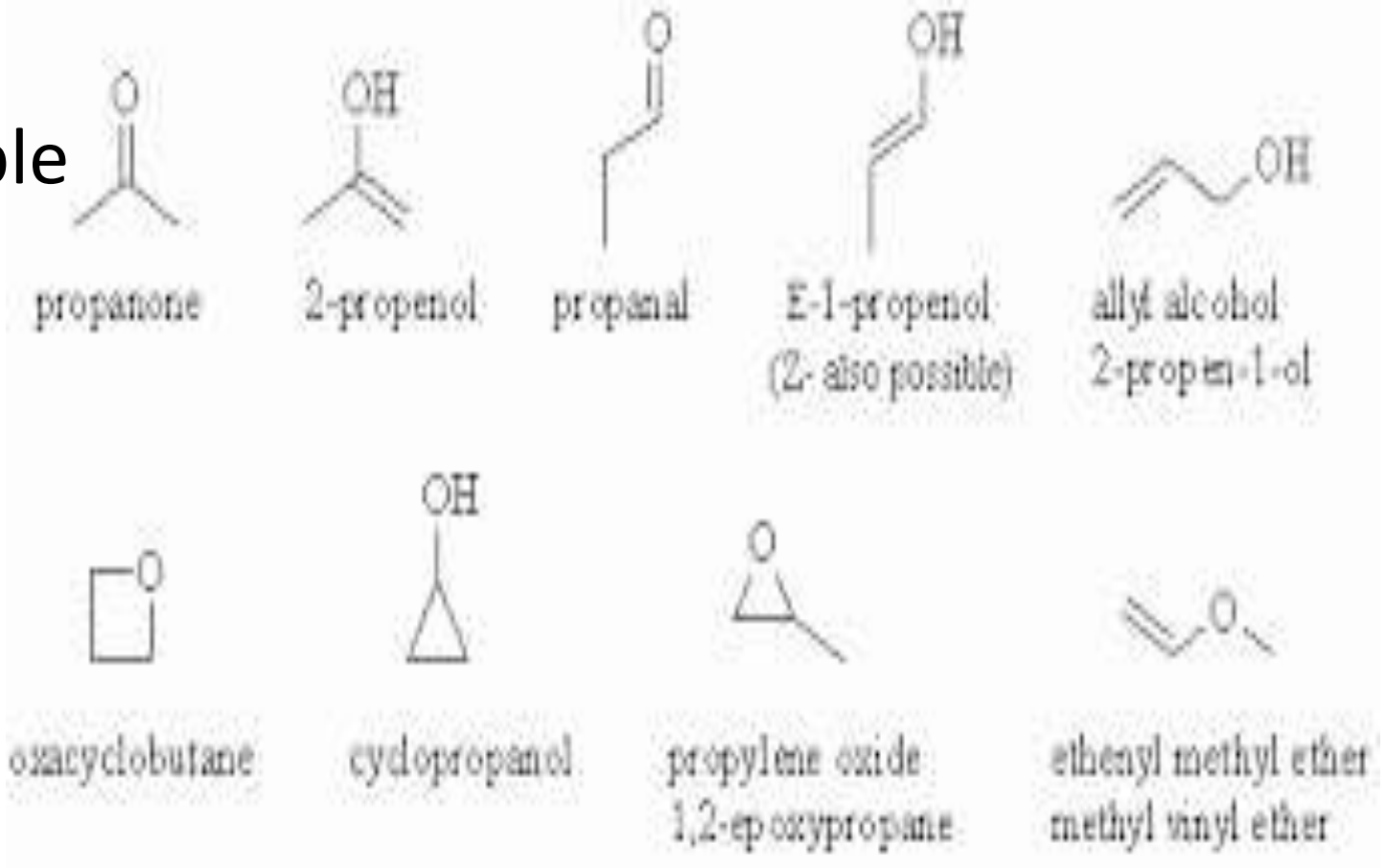


methyl ethanoate

TUTORIAL 5: Structural Isomerism

Q8

- Show **ALL** the possible isomers of **C_3H_6O**




Question

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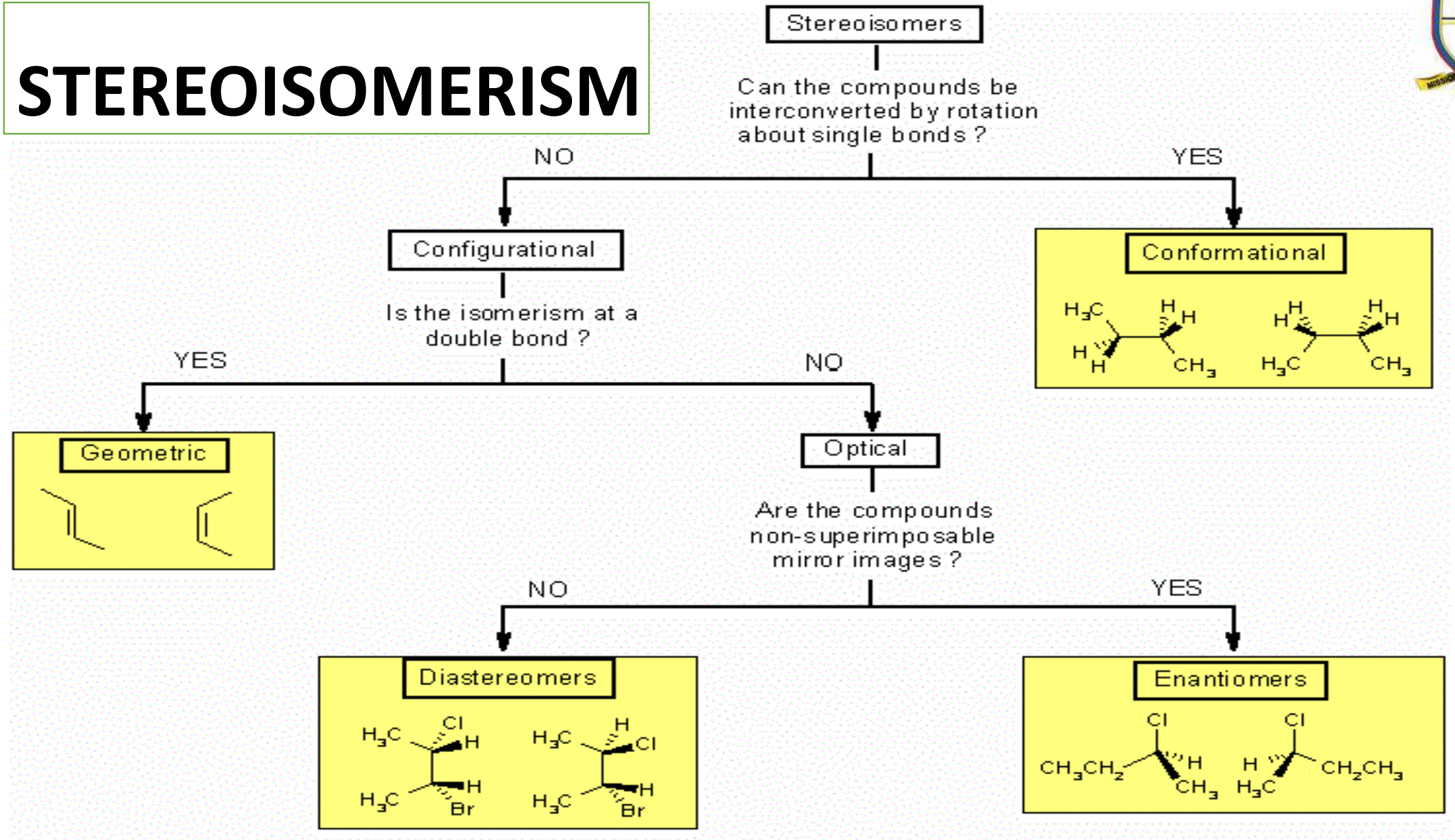
LECTURE VI

- STEREOISOMERISM
  - CONFORMATIONAL ISOMERISM
  - CIS/TRANS (or GEOMETRIC ISOMERISM)
  - OPTICAL ISOMERISM
    - ENANTIOMERISM
    - DIASTEREOMERISM
    - MESOMERS
    - RACEMIC MIXTURES
- SOME IMPORTANT CHIRAL COMPOUNDS IN NATURE

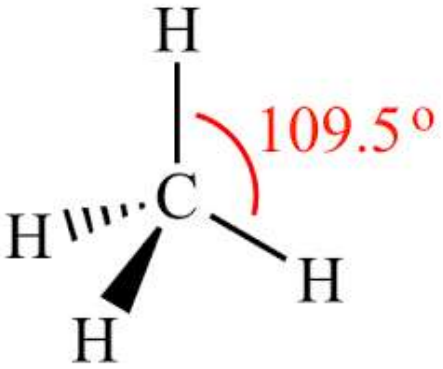
OBJECTIVES: At the end, you should be able to…

- Appreciate the three dimensional orientation of atoms in a stereoisomer
- Explain conformations
- Differentiate b/w conformational and configurational isomerism
- Explain cis/trans ism with examples
- Explain chirality and optical iso with e.g.
- Differentiate between enantiomers and diastereomers
- Explain Mesomers, recemisation, etc

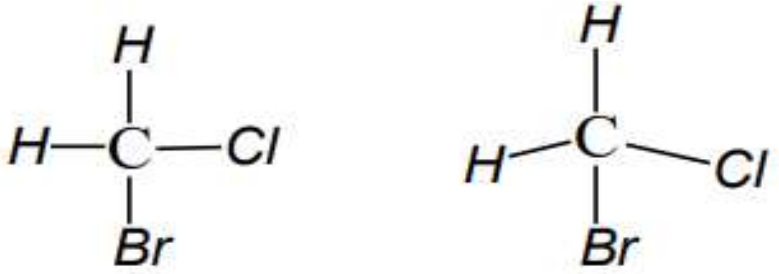
STEREOISOMERISM



STEREOCHEMISTRY



- The study of the arrangement of atoms of a mol. in space
- And effects of these arrangements on their phys&chem props
- You could also think of it as **the *study of Stereoisomerism***



2D drawing

Not appropriate for Stereochem

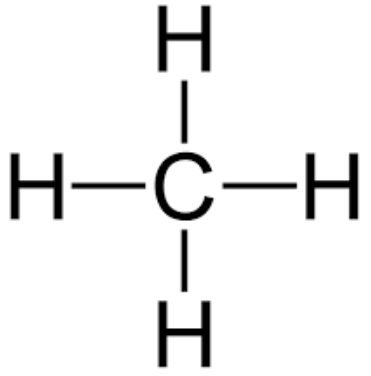
≡

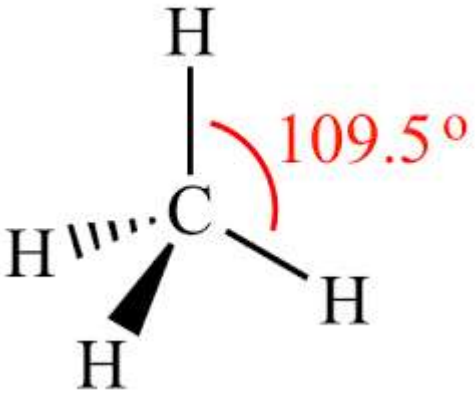
3D drawing

Appropriate for Stereochem

STEREOCHEMISTRY: Notation

- Dash = Pointing away from you
- Wedge = Pointing towards you
- Line = On the same plane of the paper/screen





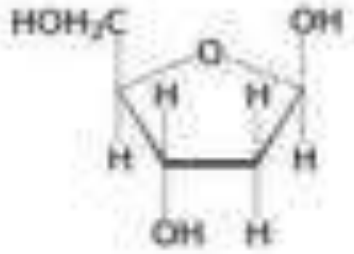
in the plane of the page

comes *forwards* out of the plane of the page ∴ **infront**

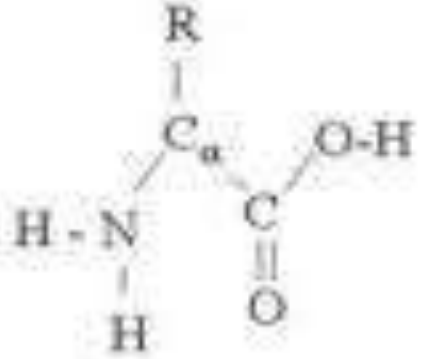
goes *backwards* out of the plane of the page ∴ **behind**

STEREOISOMERISM: Terms

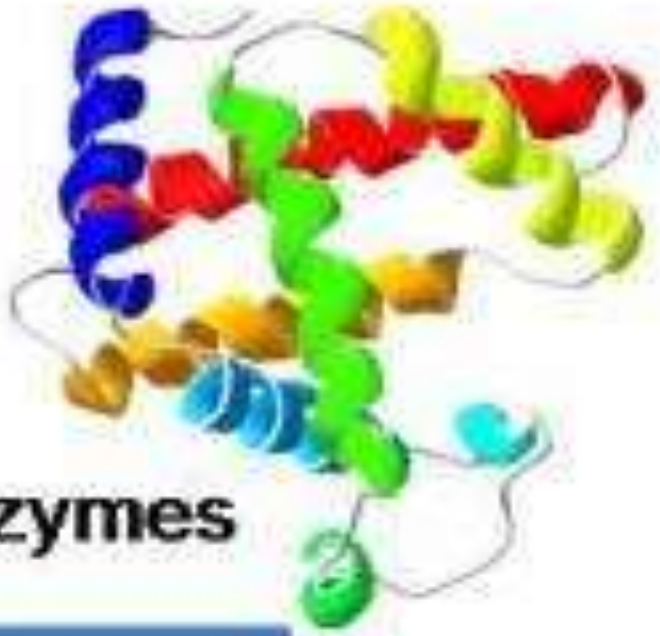
- **Chirality** is the property of an object (e.g. a molecule) of being non-superimposable on another object that is its mirror image
- It is characterized by an atom e.g. Carbon which has four **different groups bound** to it so that its mirror image is **nonsuperimposable**
- Hence, any mirror images of a chiral compound will be nonsuperimposable on each other
- **A stereogenic center** is another name for a chiral centre



sugars

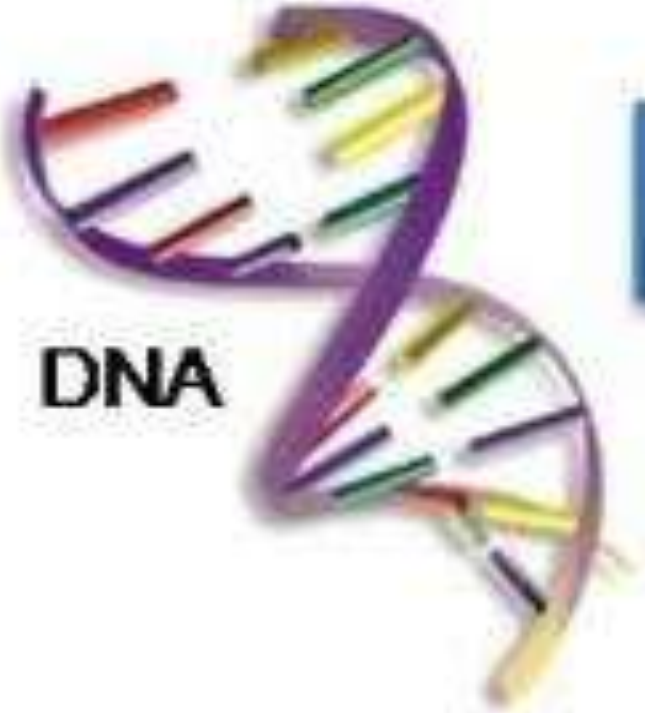


amino-acids

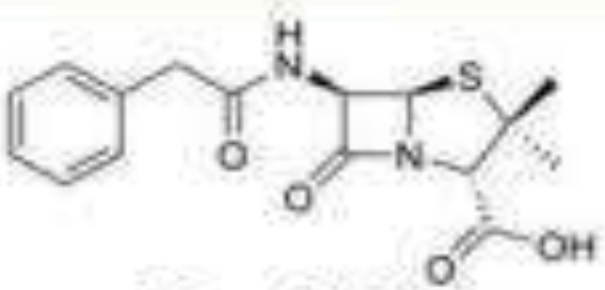


enzymes

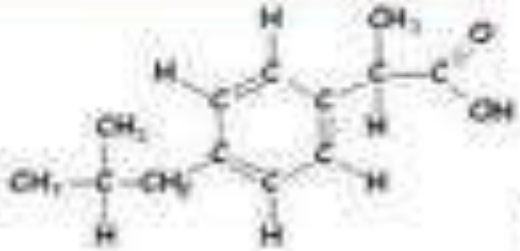
CHIRAL MOLECULES



DNA



Penicillin

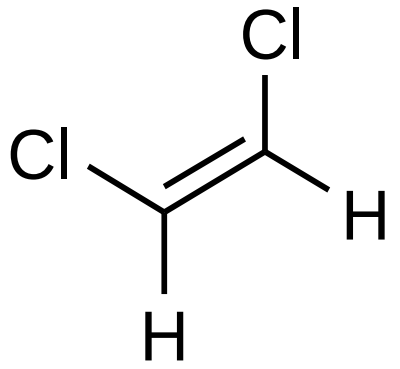


Ibuprofen

carbon nanotubes

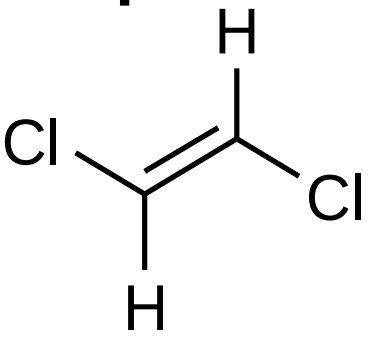
STEREOCHEMISTRY: Importance

- The study of stereochemistry is important because…
- The stereochemistry of two different isomers of the same compound can affect their
  - Physical properties
  - Chemistry properties
- Hence, their **chemical reactivities** & **biological functions** can be very different!



cis-1,2-Dichloroethane

bp = 60^{o} C

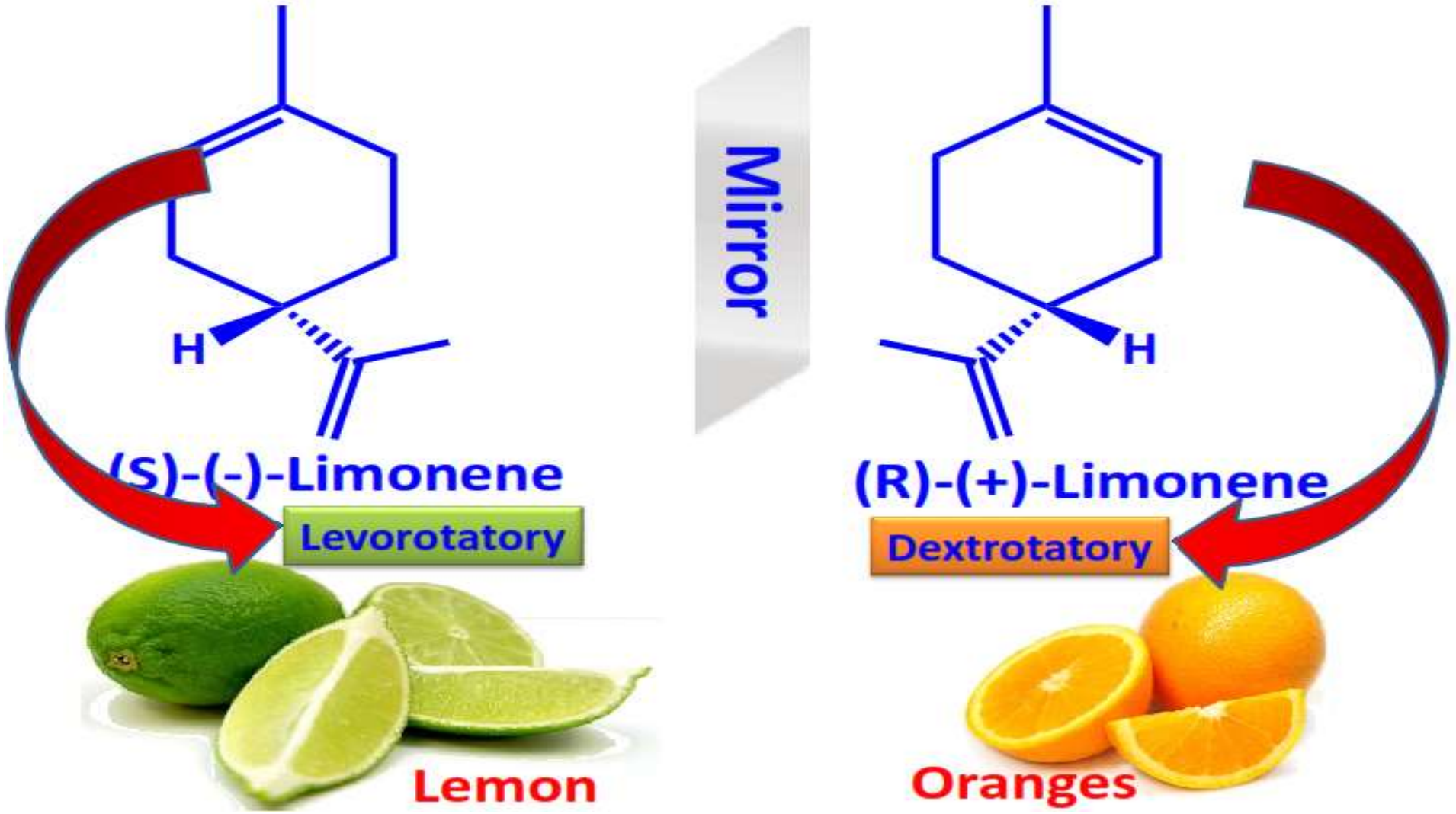


trans-1,2-Dichloroethane

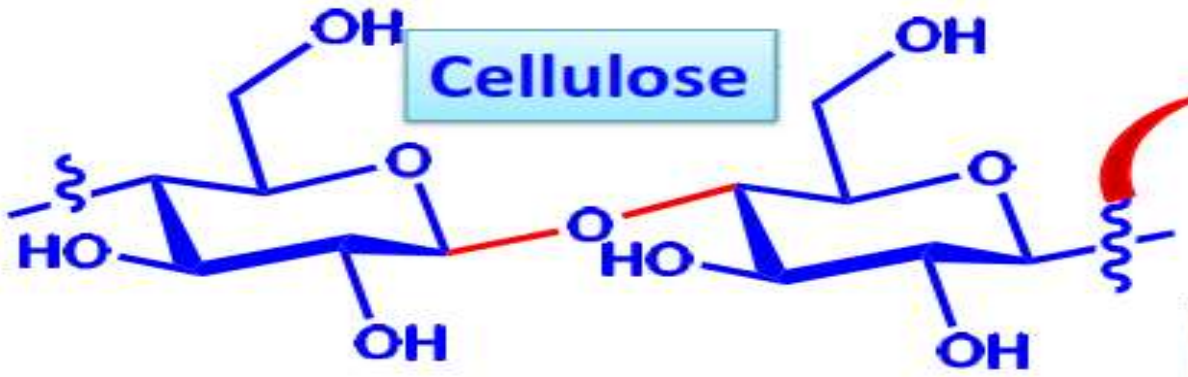
bp = 48^{o} C

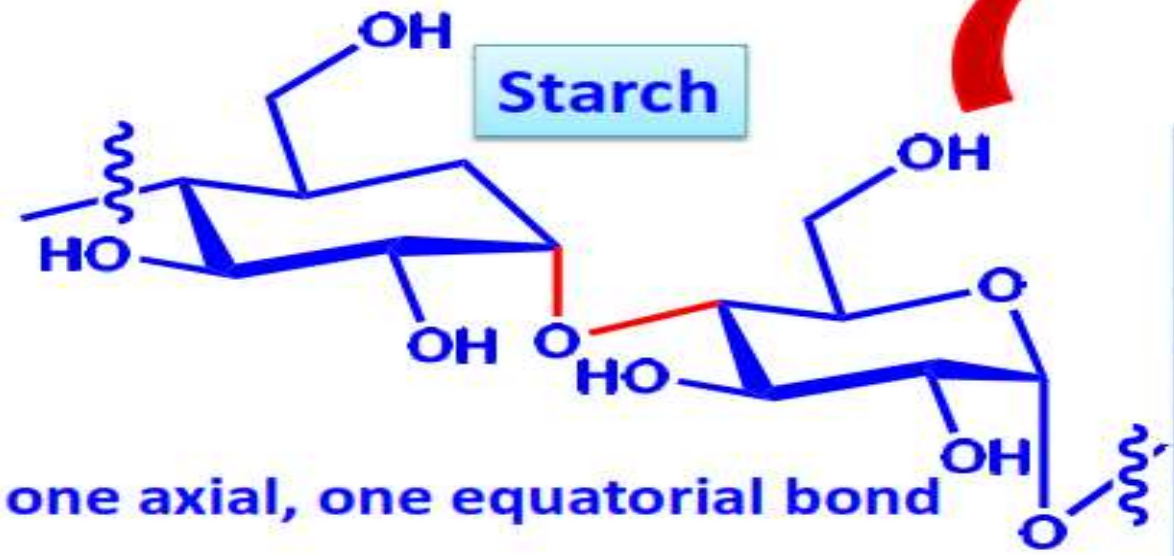
STEREOCHEMISTRY: Importance

- A



STEREOCHEMISTRY: Importance





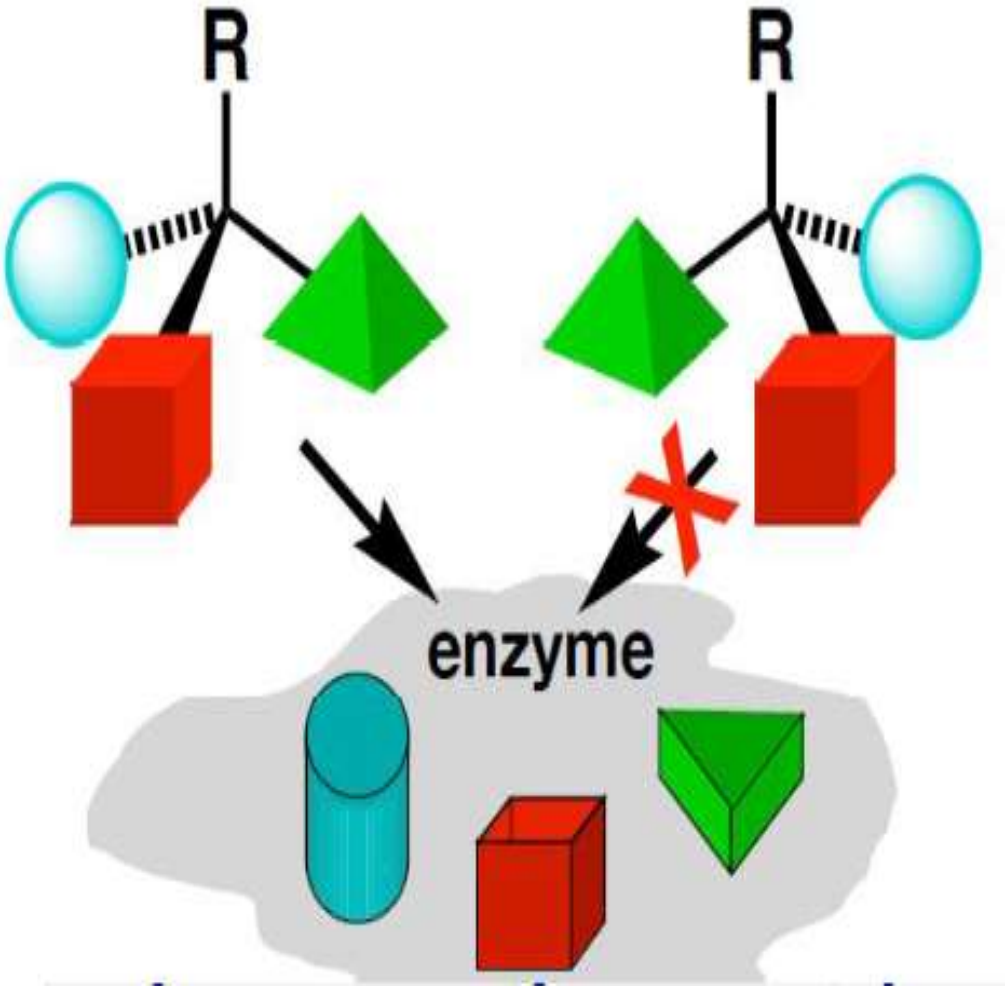
Thus, an apparently minor difference in the three-dimensional arrangement of atoms confers very different properties on starch and cellulose.

STEREOCHEMISTRY: Importance

- Many biological processes such as
  - Drug action
  - Enxyme catalysis
  - Metabolism and catabolism, etc

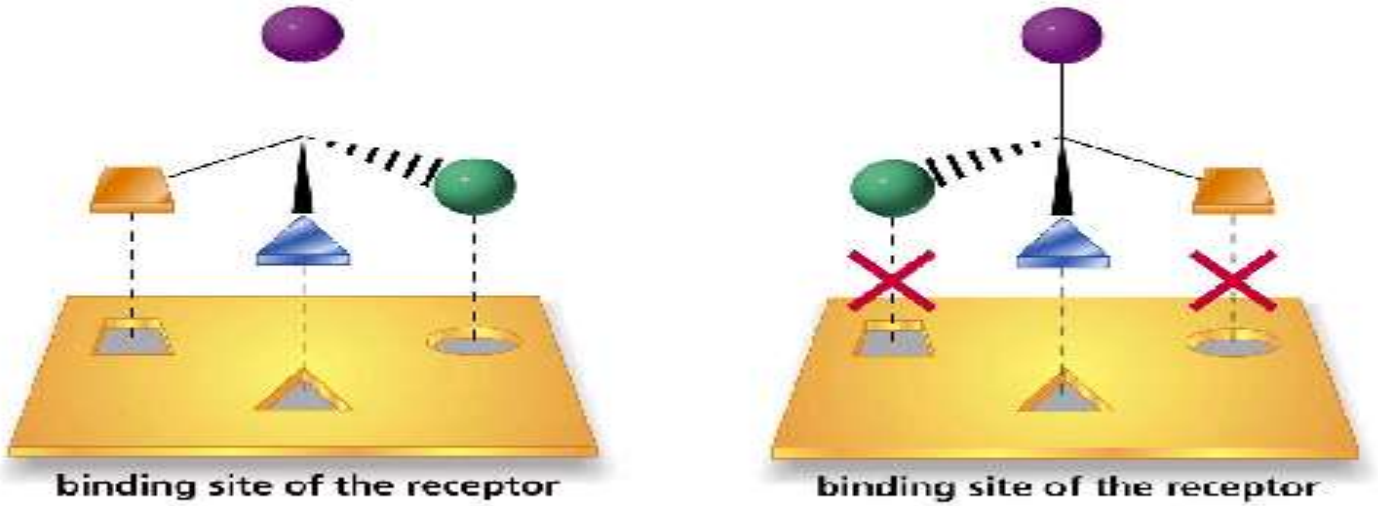
Depend on the

  - **Structure Activity Relationships (SAR)** of molecules to receptors
- i.e. They fuction via a ***Lock and Key*** mechanism



STEREOCHEMISTRY: Importance

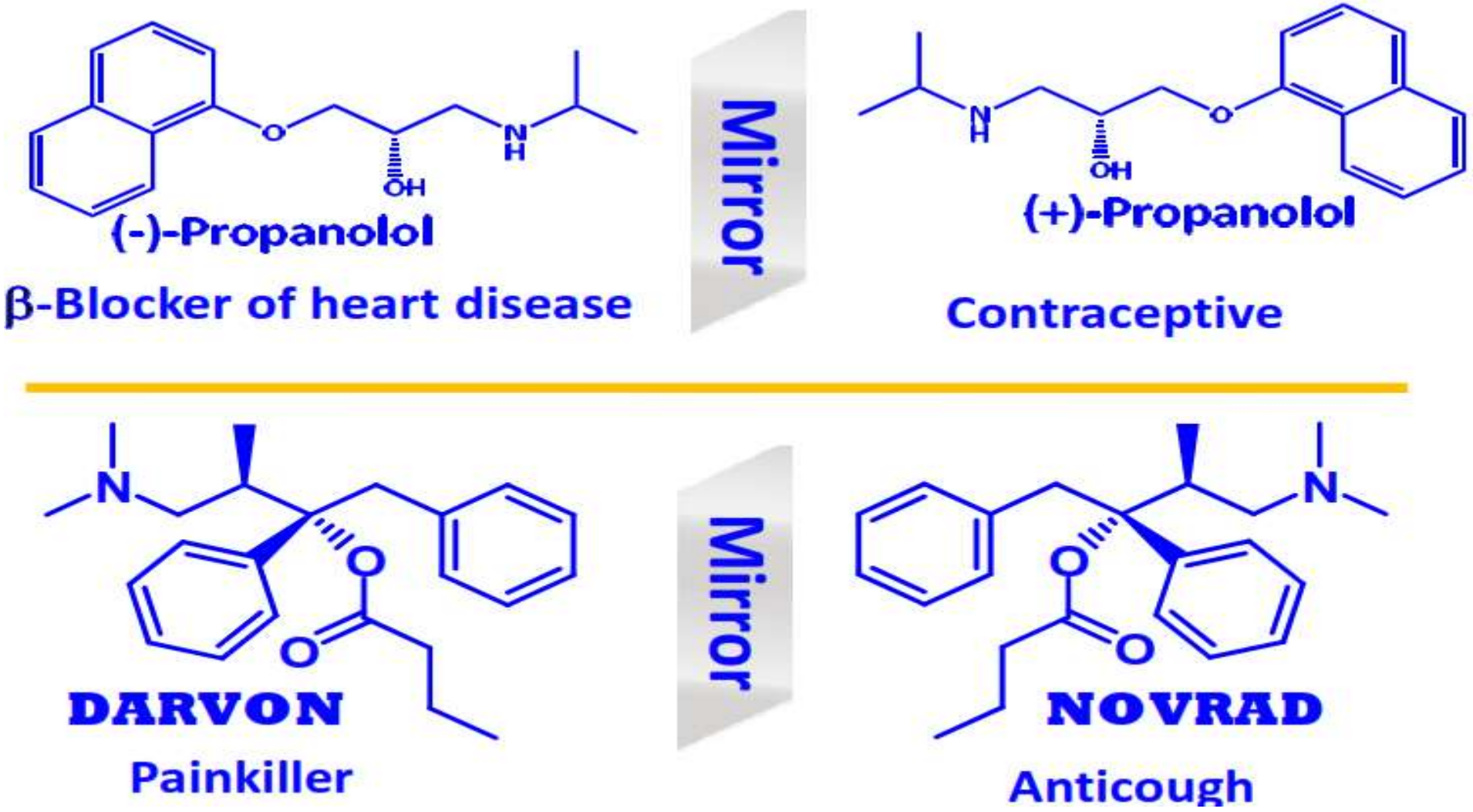
Many drugs are chiral and often must react with a chiral receptor or chiral enzyme to be effective. One enantiomer of a drug may effectively treat a disease whereas its mirror image may be ineffective or toxic.



That is why it is absolutely necessary you determine the absolute configuration of your compounds !!!

STEREOCHEMISTRY: Importance

- A



STEREOCHEMISTRY: Importance

The thalidomide tragedy

Thalidomide

Thalidomide was hailed as a "wonder drug" that provided a "safe, sound sleep". It was a sedative that was found to be effective when given to pregnant women to combat many of the symptoms associated with morning sickness.

(S)-Thalidomide

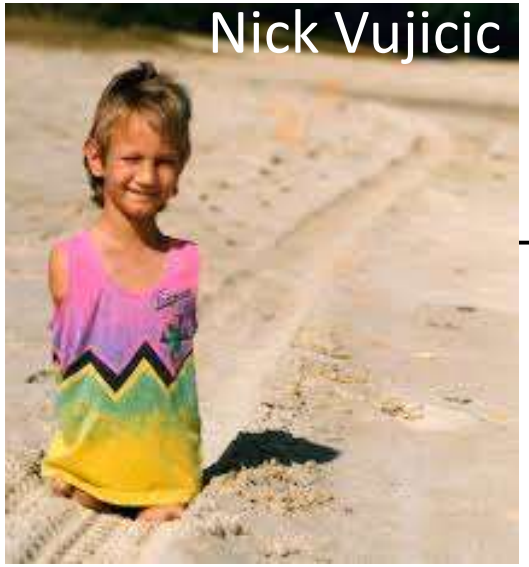
(R)-Thalidomide

Sedative

Teratogen

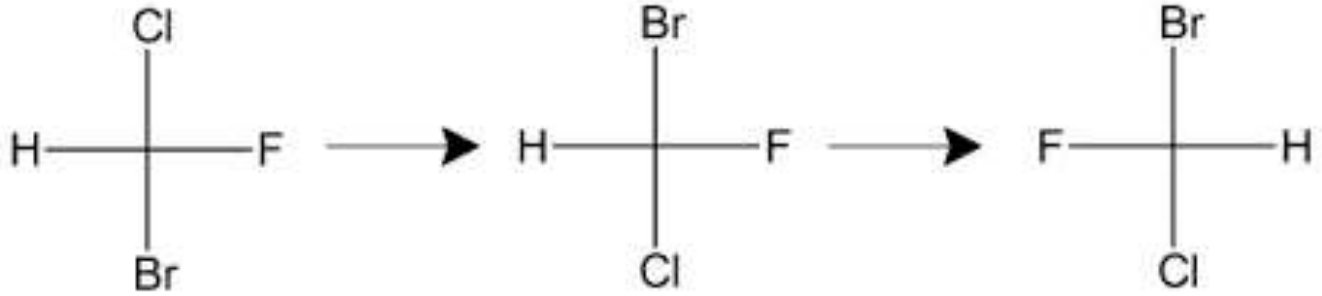
Agents that cause malformations in a developing embryo

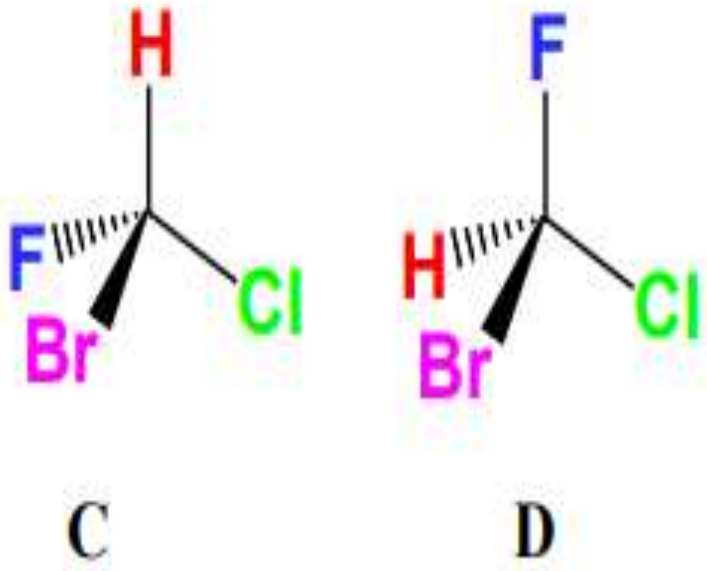
THALIDOMIDE EFFECT



STEREOISOMERISM

- Consider CHFBrCl



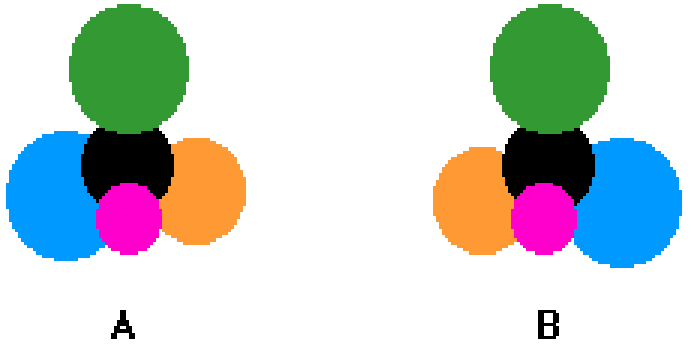


- same molecular formula (CHFBrCl)
- same atom connectivity
- nonsuperposable

stereoisomers
(two different compounds)

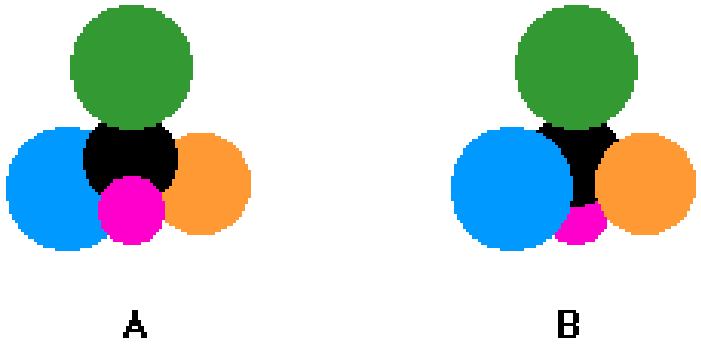
STEREOISOMERISM

- Stereoisomerism is the existence of compounds which have…
  - Same formula (e.g. CHFBrCl)
  - Same linkage (H, F, Br and Cl all linked to C)
  - Different spatial arrangements/orientations (clockwise, anticlockwise, etc.)



Two types:

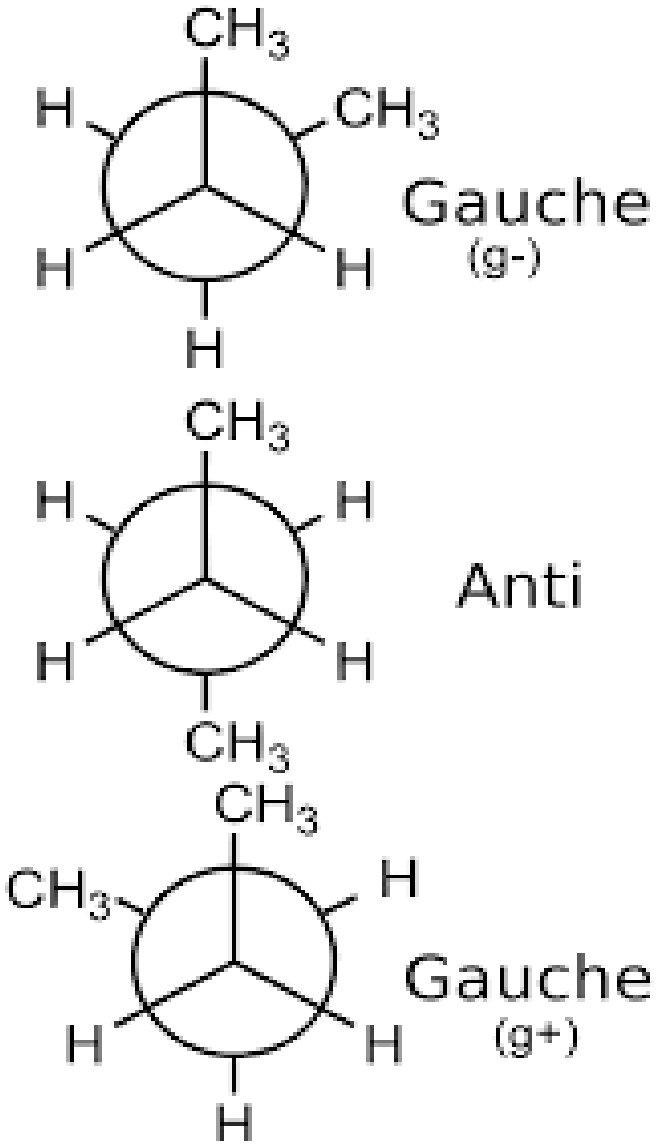
- ***Configurational and***
- ***Conformational***



STEREOISOMERISM: Types

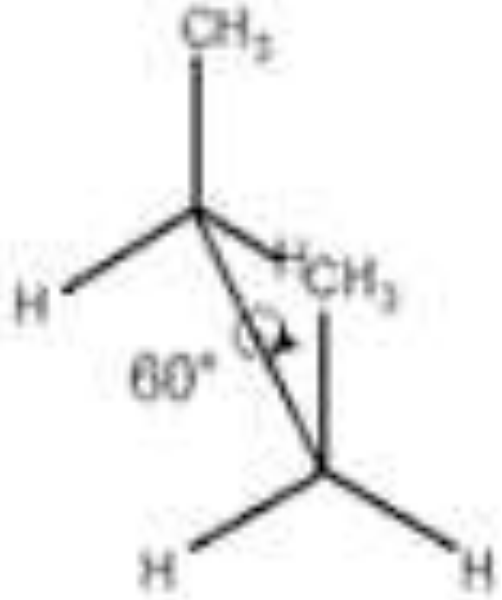
CONFORMATINAL ISOMERISM

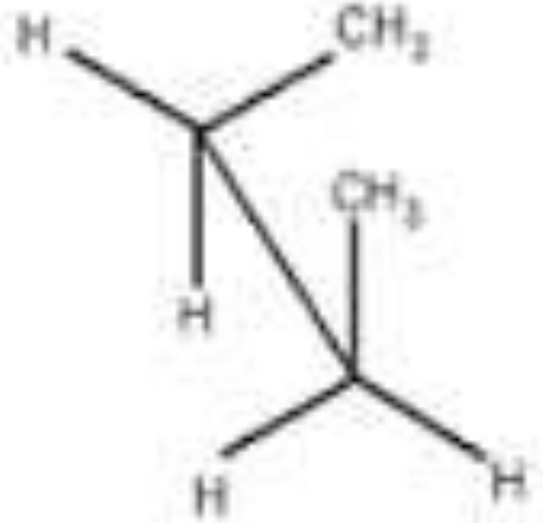
- The **conformation** of a molecule is the precise spatial arrangement of the groups of atoms in it **as a result of rotation about single bonds**
- Infinite number of possible conformations
- However, only those conformational isomers possessing energy minima (e.g. anti (180^0), syn (0^0), gauche (60^0) etc) are denoted **conformers**



CONFORMATIONAL ISOMERISM

- Consider the example of
- **$CH_3CH_2CH_2CH_3$ (Butane)**
- Viewing the molecule through Carbon2-Carbon3
- Imagine C_2-C_3 bond rotating
- There are a couple of possible conformers

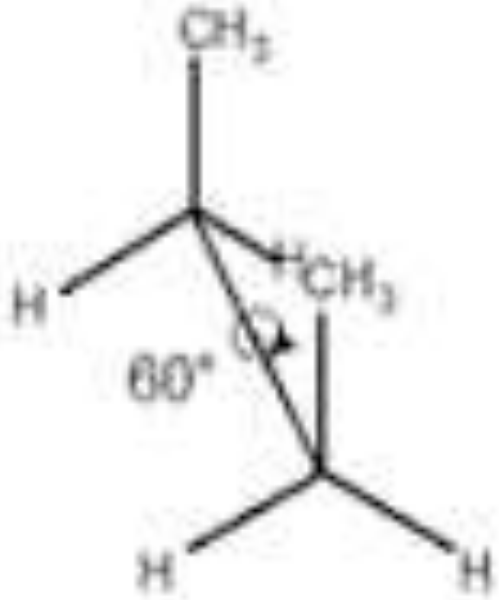


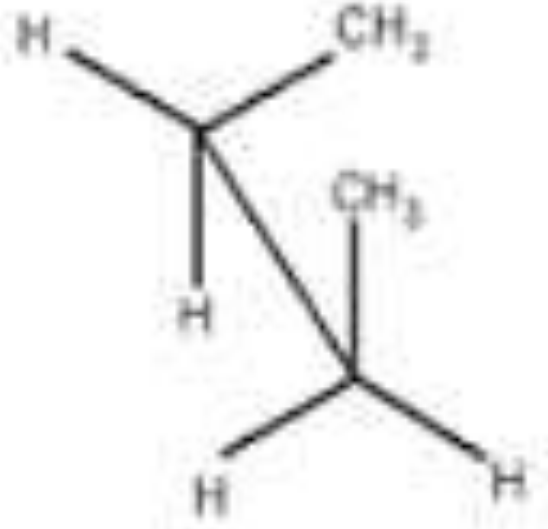


CONFORMATIONAL ISOMERISM

Q

- **Now try 2-Bromobutane viewing through C_2-C_3**





QUESTIONS???

STEREOISOMERISM: Types

CONFIGURATIONAL ISOMERISM

- The **configuration** of a molecule is the spatial arrangement of atoms or groups of atoms in the molecule that **DOES NOT DEPEND on rotation about any single bond**

- Two types of configurational isomerism
  - **Cis-Trans (or Geometric) isomerism &**
  - **Optical isomerism**

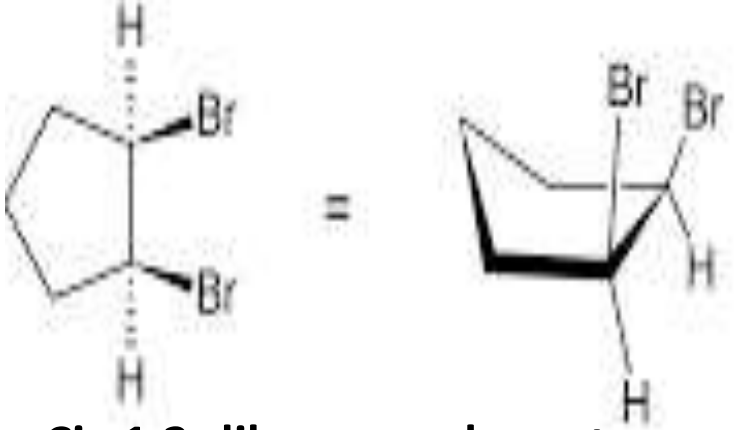
CIS-TRANS (GEOMETRIC) ISOMERISM

- A type of Configurational **Isomerism** where…
- **Restriction to rotation is because of A DOUBLE BOND or RING SYSTEM**

- Hence, a double bond or ring must be present in a molecule before it can exhibit *cis-trans* isomerism
- Isomers are denoted by the relative stereochemistry **(cis or trans)** of their chiral centres

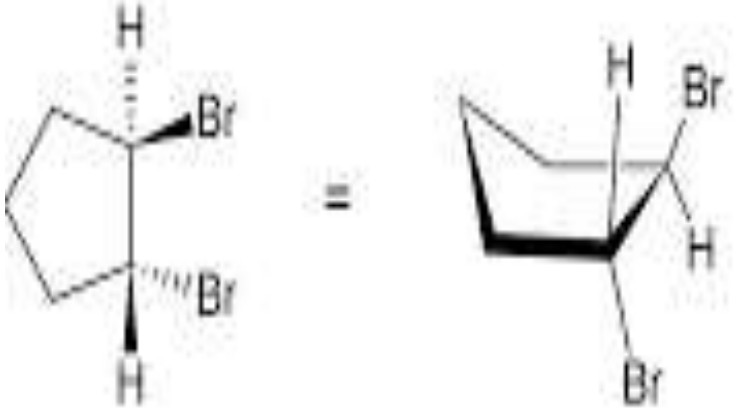
CIS-TRANS (GEOMETRIC) ISOMERISM

- **Relative Stereochemistry:** Refers to the stereochemistry of a chiral centre w.r.t another chiral centre on same molecule



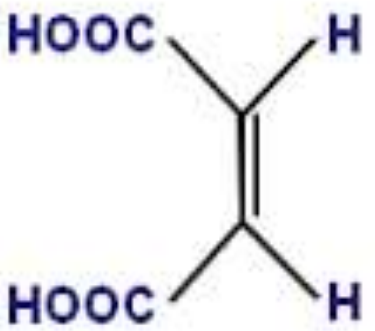
Cis-1,2-dibromocyclopentane

- E.g. **Cis and Trans** configurations
  - Two substituents are called **Cis** to one other if they're pointing in the **same direction**
  - Two substituents are **trans** to one another if they're pointing in **opposite directions**
- This is the basis of **CIS-TRANS ISOMERISM**

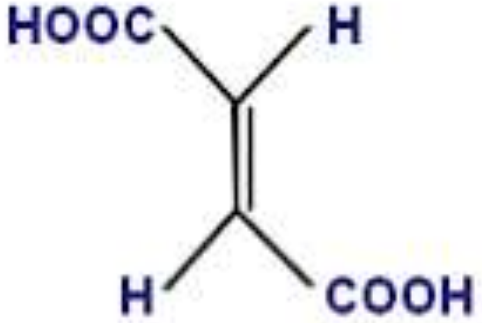


Trans-1,2-dibromocyclopentane

GEOMETRIC (CIS-TRANS) ISOMERISM

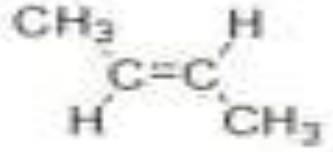


cis-butenedioic
(maleic acid)

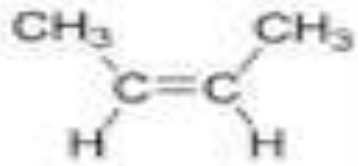


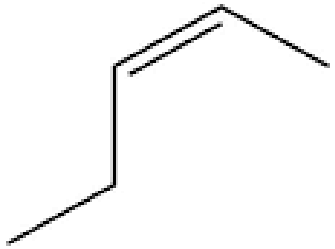
trans-butenedioic acid
(fumaric acid)

trans-but-2-ene



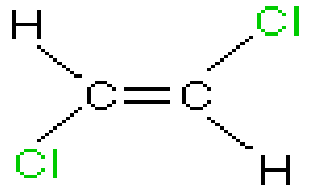
cis-but-2-ene



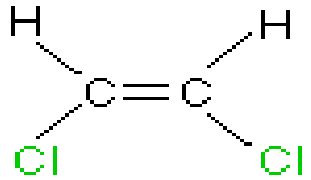


cis

trans

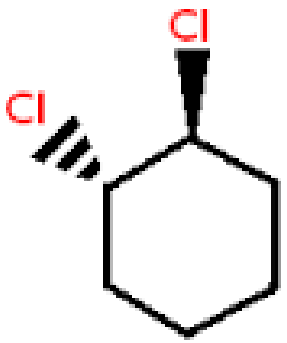


trans-1,2-dichloroethene

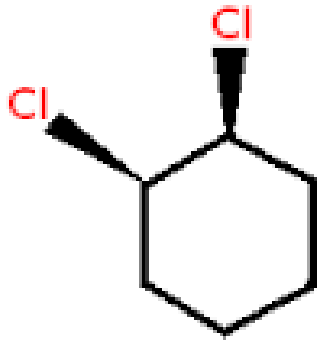


cis-1,2-dichloroethene

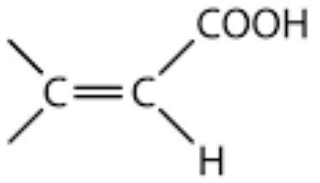
GEOMETRIC (CIS-TRANS) ISOMERISM

- 

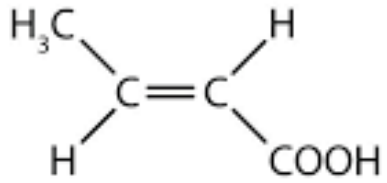
trans-1, 2-Dichlorocyclohexane



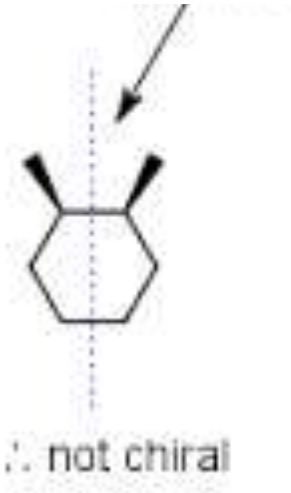
cis-1,2-Dichlorocyclohexane



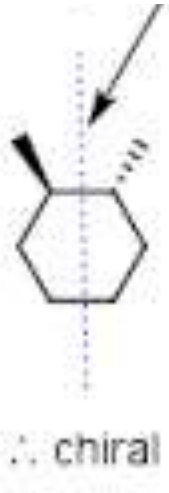
cis



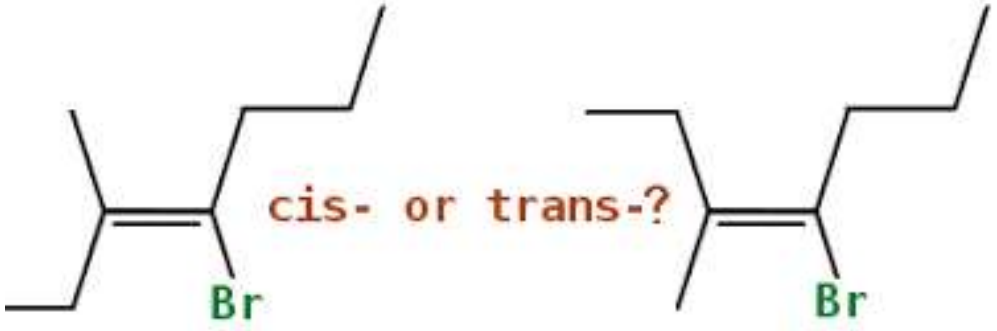
trans



∴ not chiral



∴ chiral



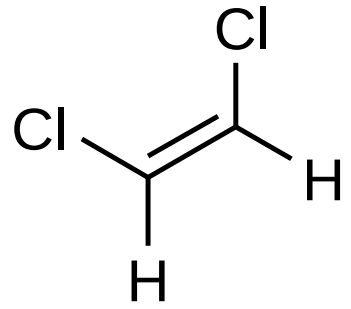
E/Z NUMENCLATURE IN CIS/TRANS ISO

- **E/Z notation** is used to denote **relative stereochemistry**

Where

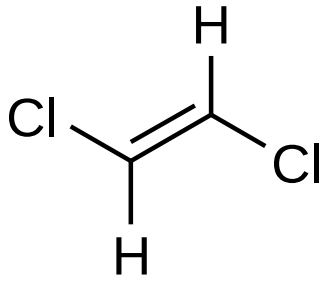
- E === Trans
- Z === Cis

- The determination of E or Z follows the Cahn-Ingold-Prelog (CIP) rules



cis-1,2-Dichloroethane

bp = 60^{o} C

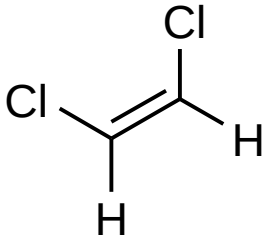


trans-1,2-Dichloroethane

bp = 48^{o} C

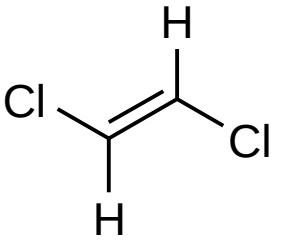
CIS/TRANS ISOMERISM: Conclusion

- Cis/trans Isomers vary one from another in their physical and chemical properties and hence must be treated carefully



cis-1,2-Dichloroethane

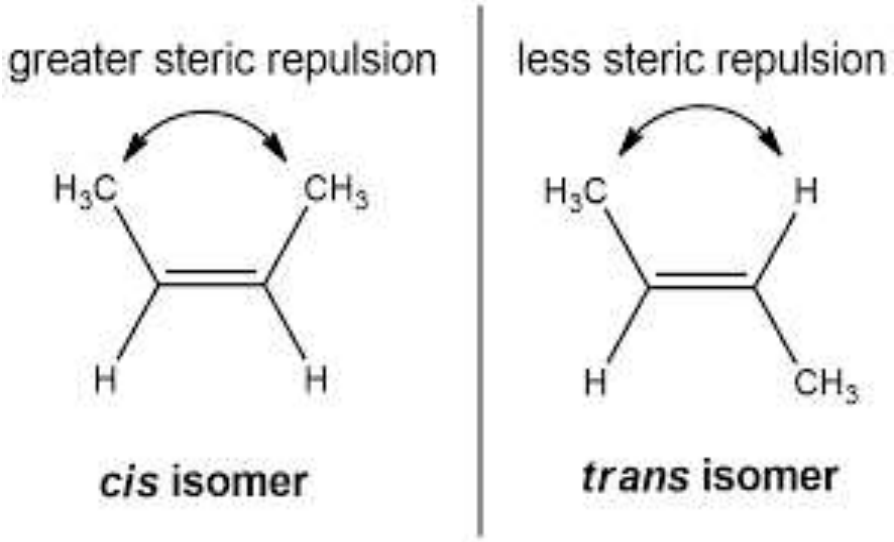
bp = 60^{o} C



trans-1,2-Dichloroethane

bp = 48^{o} C

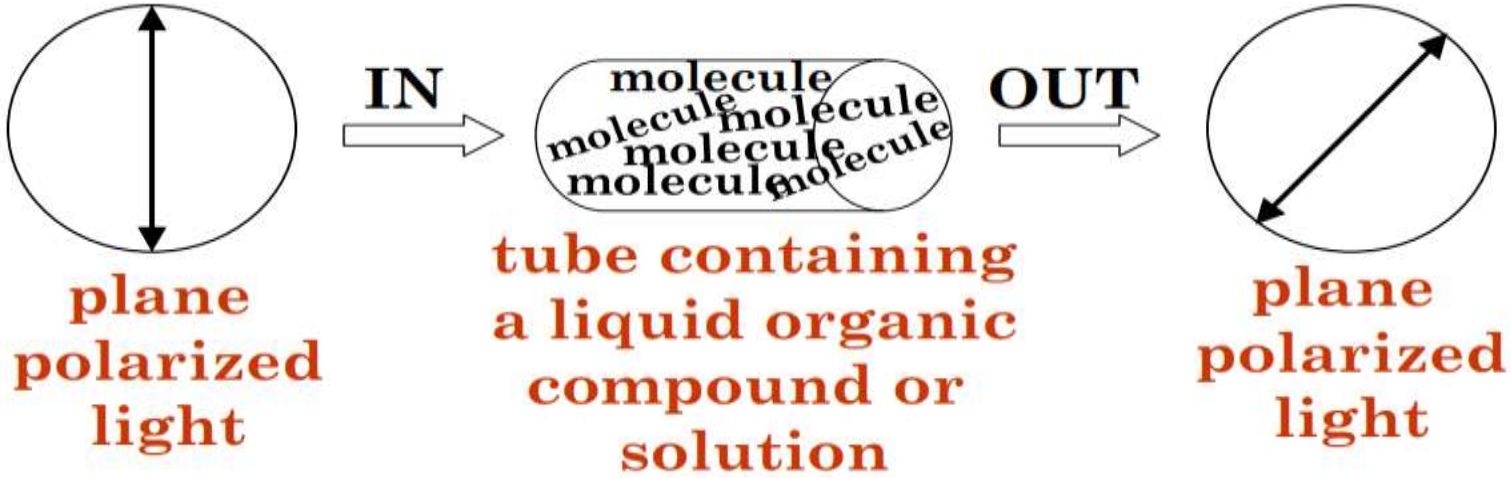
- These differences are mostly due to the differences in steric interaction between the substituents



- The greater the steric repulsion, the higher the energy of the molecule (lesser stability)

QUESTIONS???

STEREOISOMERISM: Terms



- **Optical activity:** The ability of chiral substances to rotate the plane of polarized light by a specific angle
- **Dextrorotatory:** Ability of chiral substances to rotate the plane of polarized light to the **RIGHT direction.** Denoted **(+)**
- **Levorotatory:** Ability of chiral substances to rotate the plane of polarized light to the **LEFT direction.** Denoted **(-)**

CHM 103

ORGANIC CHEMSTRY I

Department of Chemical Sciences

Faculty of Science and Technology

Bingham University, Karu

Course Lecturer: Joseph C. Oguegbulu

Joseph.oguegbulu@binghamuni.edu.ng

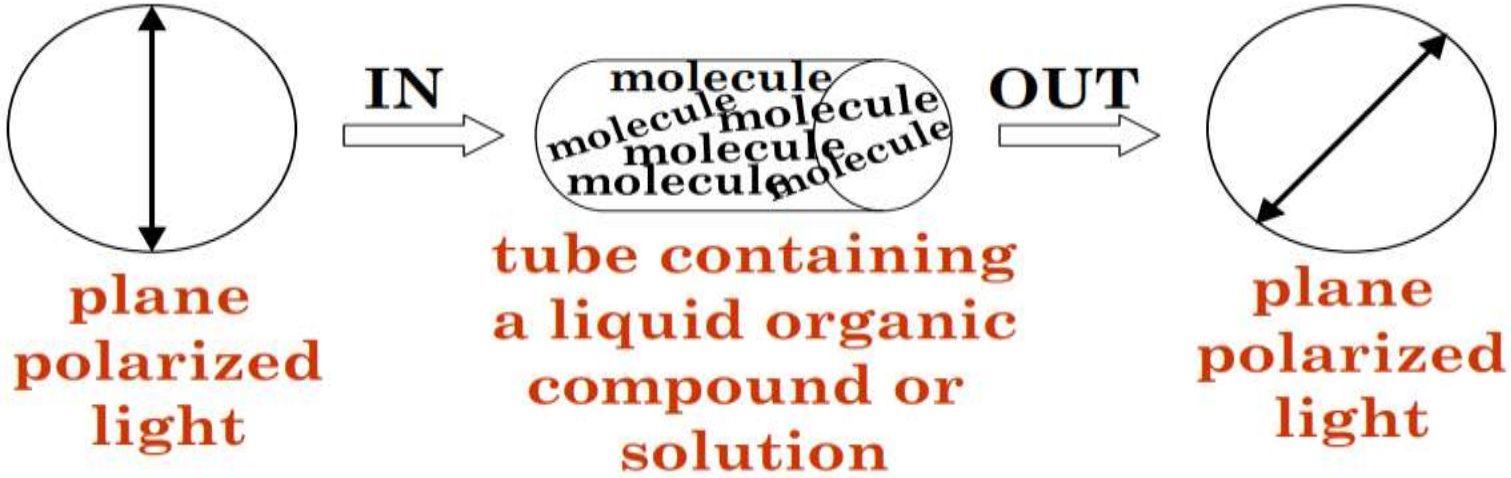
LECTURE VII

- OPTICAL ISOMERISM
  - ENANTIOMERISM
  - DIASTEREOMERISM
  - MESOMERS
  - RACEMIC MIXTURES

OBJECTIVES: At the end, you should be able to…

- Appreciate the 3-D orientation of atoms in a stereoisomer
- Explain chirality and optical isomerism with e.g.
- Differentiate between enantiomers and diastereomers
- Explain Mesomers, recemisation, etc

OPTICAL ISOMERISM



- **Optical activity:** The ability of chiral substances to rotate the plane of polarized light by a specific angle
- Hence **Optical Isomers** are stereoisomers that have **opposite optical activities.** i.e. one is dextrorotatory; the other, levorotatory
- Types of Optical Isomerisms; **Enantiomerism & Diastereomerism**

STEREOISOMERISM: Terms

- **Chirality** is the property of an object (e.g. a molecule) of being non-superimposable on another object that is its mirror image
- It is characterized by an atom e.g. Carbon which has four **different groups bound** to it so that its mirror image is **nonsuperimposable**
- Hence, any mirror images of a chiral compound will be nonsuperimposable on each other
- **A stereogenic center** is another name for a chiral centre

OPTICAL ISOMERISM: Types

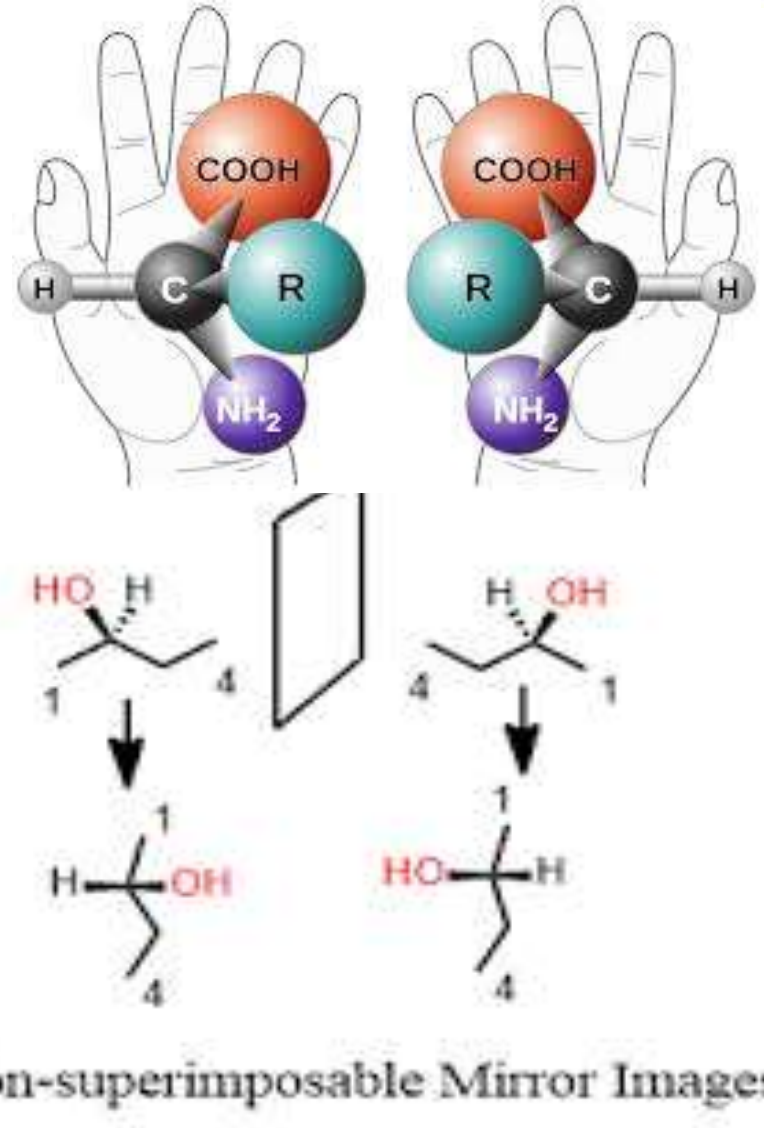
- **Enantiomerism**: Existence of stereoisomers that are nonsuperimposable mirror images
- **Diastereomers**: Simply put; stereoisomers that are ***not enantiomers***
- *Compounds with* ***multiple chiral centres*** *can exhibit both* ***enantiomerism and diastereomerism***
- *But compounds with a* ***single chiral centre can only exhibit Enantiomers***

ENANTIOMERISM

- Stereoisomers that are **non-superimposable mirror images of each other**

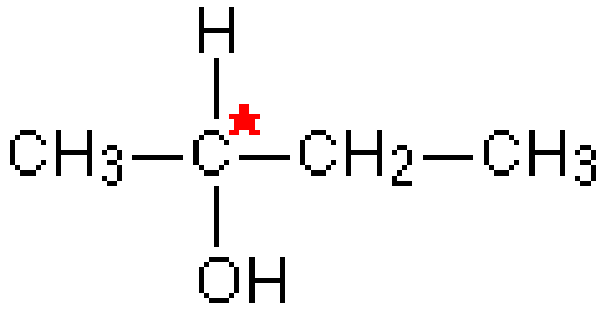
- Think of your **Left** & **Right** hands
  - They are non-superimposable
  - They are mirror images

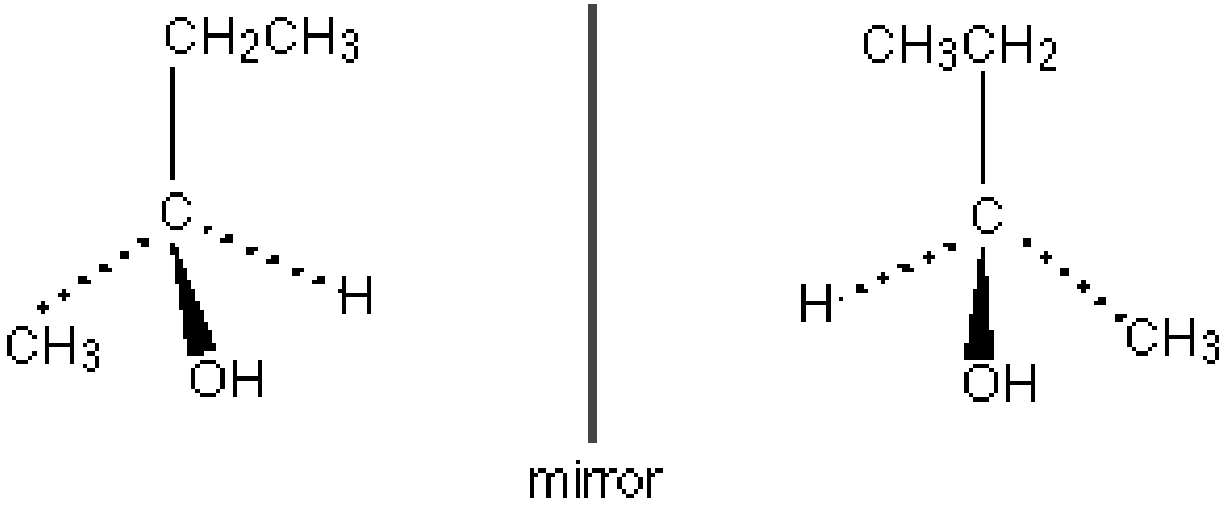
- Every pair of enantiomer have the same physical props but different optical rotations



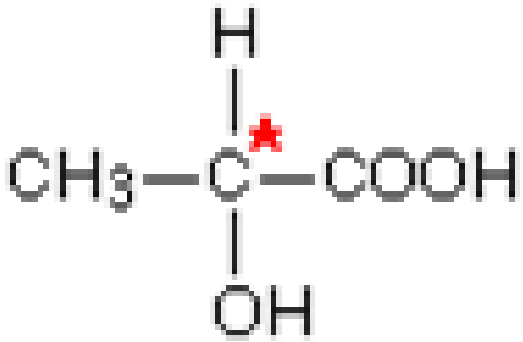
ENANTIOMERS: Examples

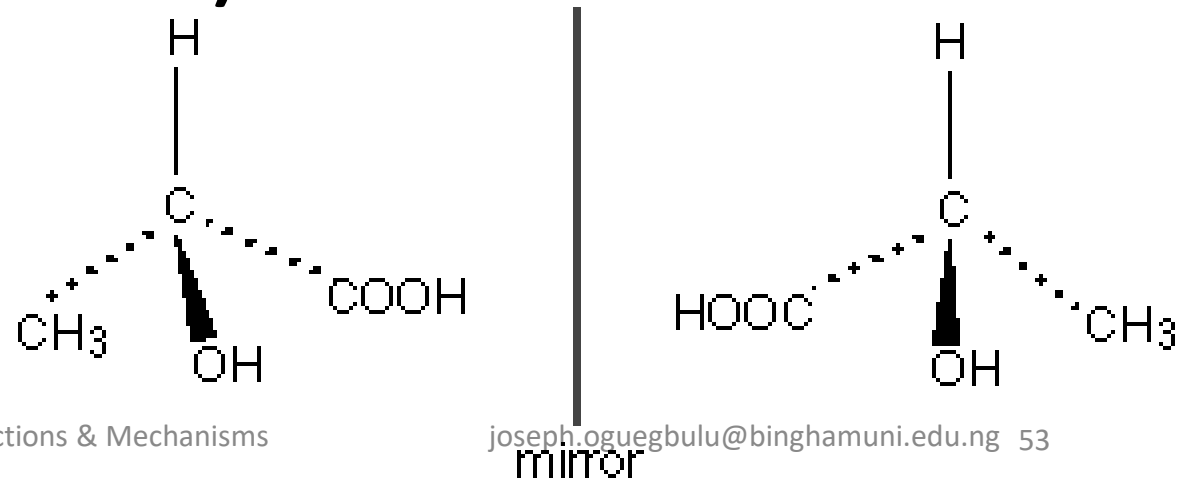
- **Butanol**





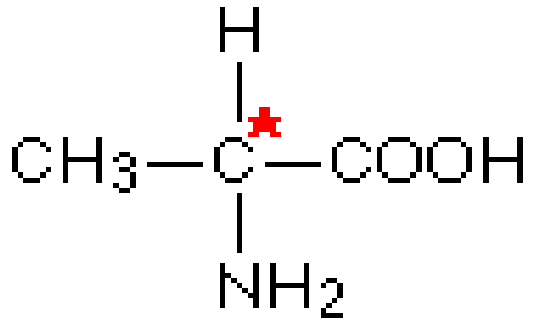
- **Lactic acid (2-hydroxypropanoic acid)**

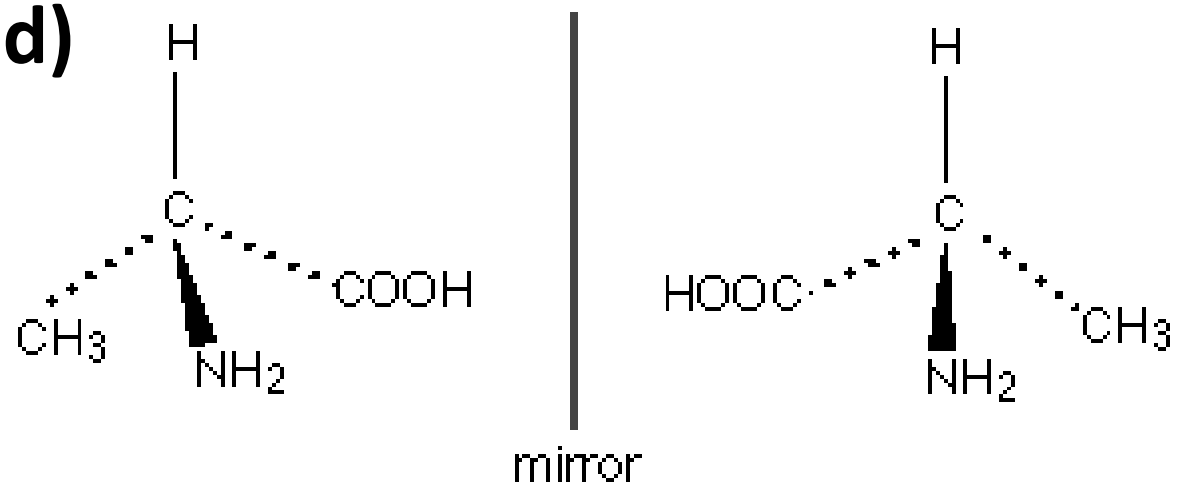




ENANTIOMERS: Examples

- **Alanine (2-Aminopropanoic acid)**

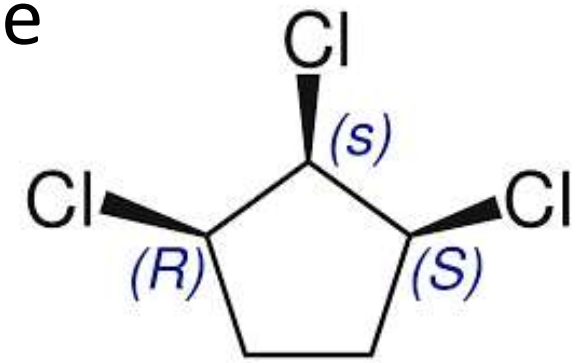




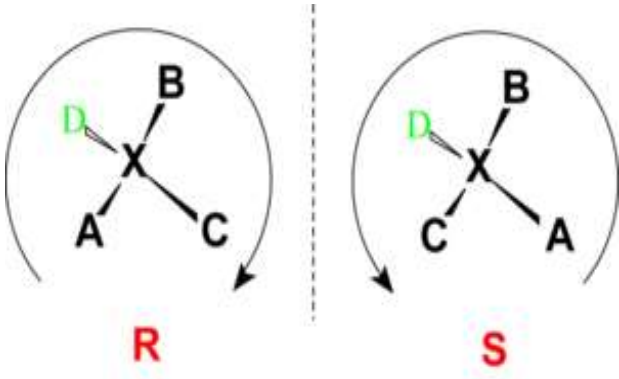
- **In protein/carbohydrate chemistry, R corresponds to D, while S corresponds to L**

R/S NOTATION (ABSOLUTE STEREOCHEM.)

- **Absolute stereochemistry:** Refers to the precise arrangement of substituents at a chrial centre
- **E/Z notation** denotes relative stereochemistry
- **R/S notation** denotes **absolute stereochemistry**
- **R** (Rectus) OR **S** (Sinister)

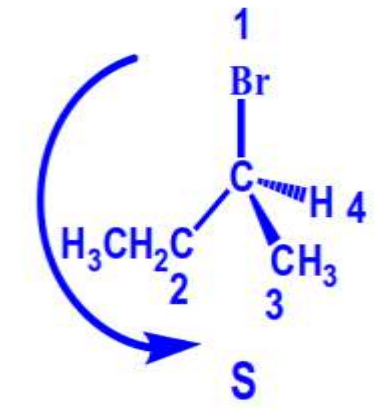


- It is determined by the **Cahn-Ingold-Prelog rules**
- Can also be determined by X-ray Crystallography

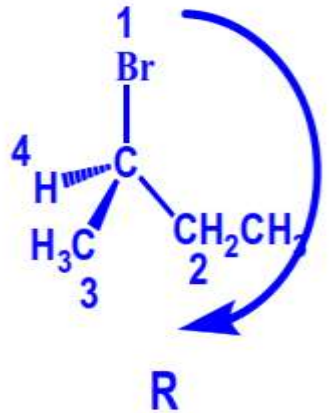


ABSOLUTE CONFIG vs OPTICAL ROTATION

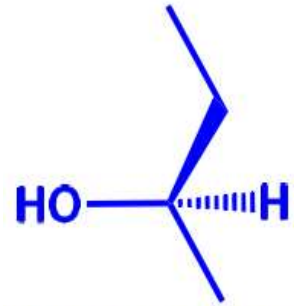
- **Optical Rotation** $[\alpha]^t_D$ is the angle through which the plane of polarized light that passes through an optically active substance is rotated
- It can only be determined experimentally
- **Note:** The absolute stereochemistry (R/S) of a chiral centre is **NOT** in any way related to its optical activity (-) or (+)



(S)-2-Bromobutane

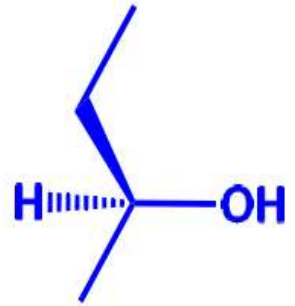


(R)-2-Bromobutane



(R)-Butan-2-ol

$[\alpha]^t_D = +13.5$

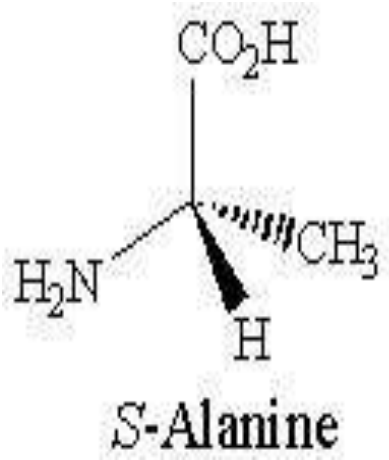


(S)-Butan-2-ol

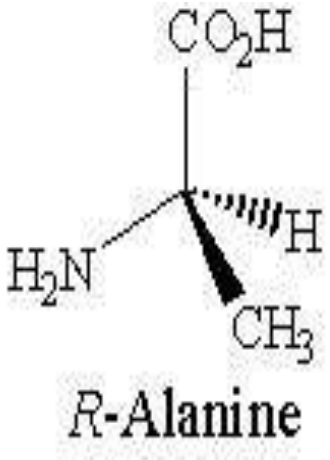
$[\alpha]^t_D = -13.5$

ENANT: Absolute config vs Optical Rotation

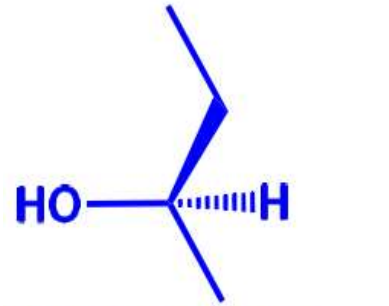
- Each enantiomer is identifiable by its absolute config (R/S) in its name
- Any of the Isomers can be (+) or (-) rotatory in terms of optical activity
- Hence you could have R-(+) or R-(-) or S-(+) or S-(-)



S-Alanine

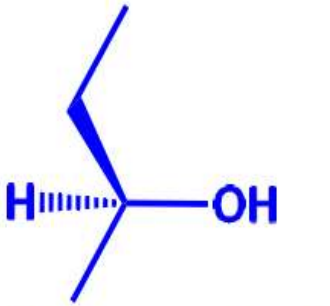


R-Alanine



(R)-Butan-2-ol

$[\alpha]_D^t = +13.5$



(S)-Butan-2-ol

$[\alpha]_D^t = -13.5$

QUESTIONS???

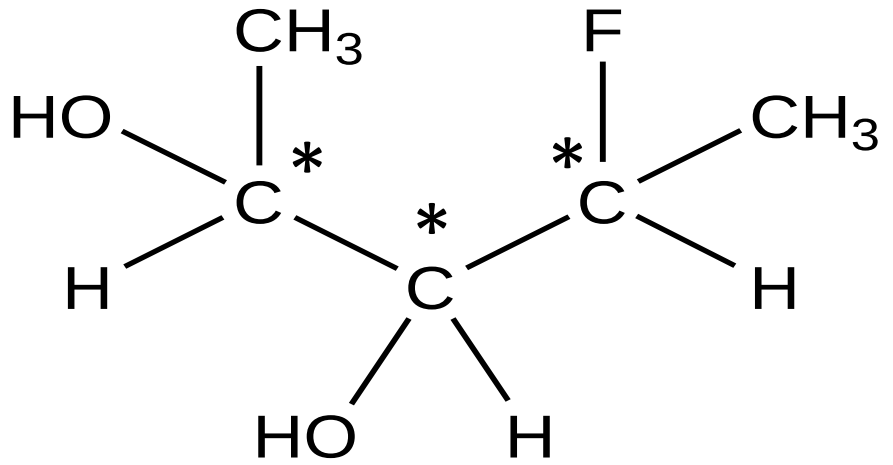
DIASTEREOMERISM

- Simply put; they are stereoisomers that are ***not enantiomers***
- Can only exists in ***molecules with multiple chiral centers***
- i.e. Compounds with **multiple chiral centres** can exhibit both **enantiomerism and diastereomerism**
- But compounds with a **single chiral centre can only exhibit Enantiomerism**
- Unlike Enantiomers, each diastereomer would have different physical & chemical properties from the others

DIASTEREOMERISM

Given a molecule with multiple chiral centres, how do you know..

- Which stereoisomers are diastereomers?
- Which ones are just enantiomers?



4-Fluoropentan-2,3-diol

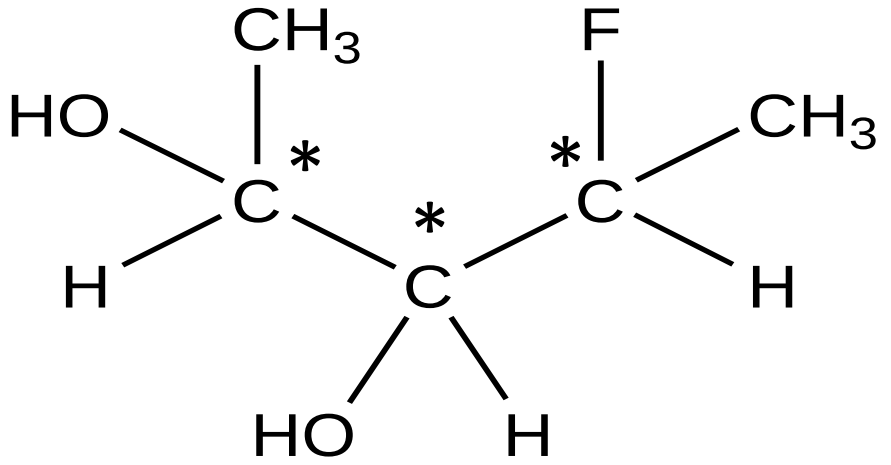
- It would be cumbersome to start checking for superimposability non-superimposability, mirror images or non-mirror images, etc

DIASTEREOMERISM

Simple: LOOK AT THEIR CHIRAL CENTRES IN THE TWO MOLECULES…

- If **all** chiral centres are **reversed** == **Enantiomers**

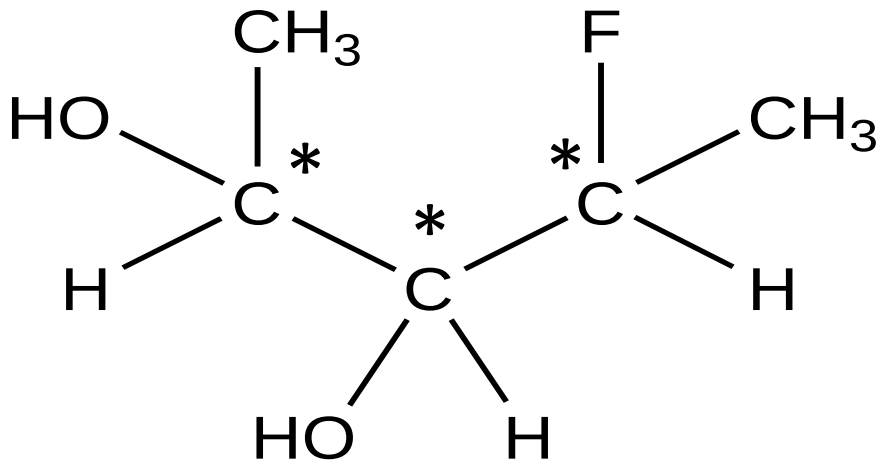
- If **some** chiral centres are reversed and some **retained** == **Diastereomers**



4-Fluoropentan-2,3-diol

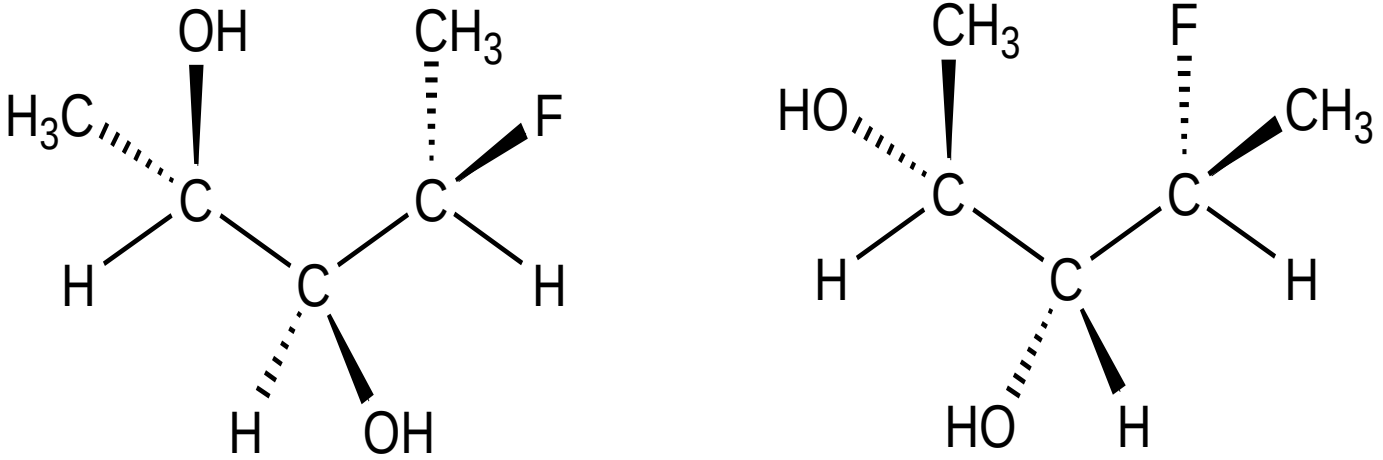
DIASTEREOMERISM

- If **all** chiral centres are **reversed** == **Enantiomer**
- If **some** chiral centres are reversed and some **retained** == **Diastereomer**

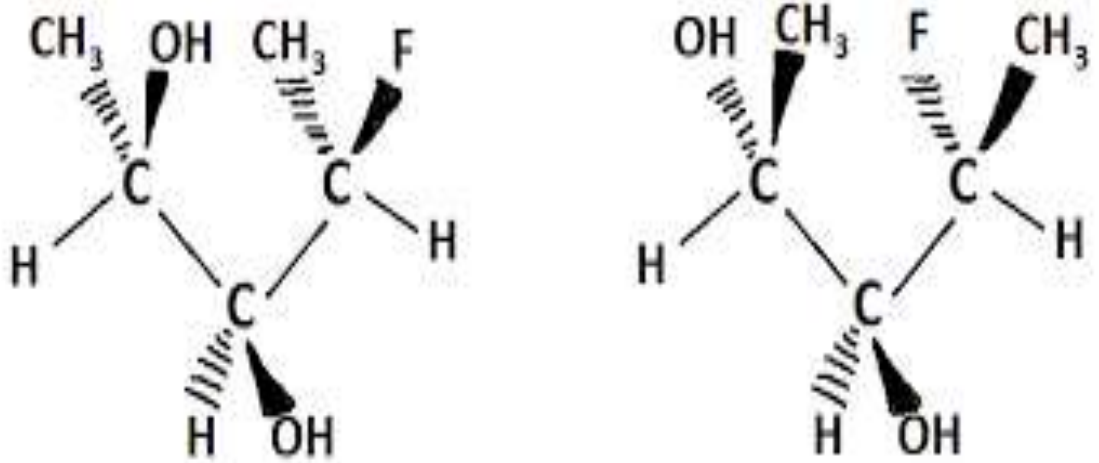


4-Fluoropentan-2,3-diol

Enantiomers



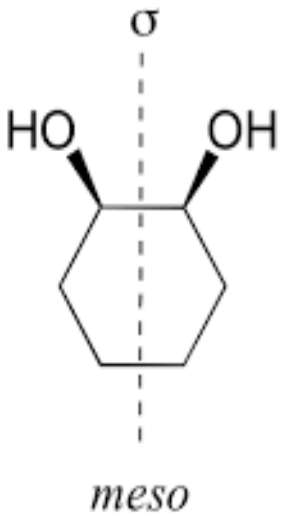
Diastereomers

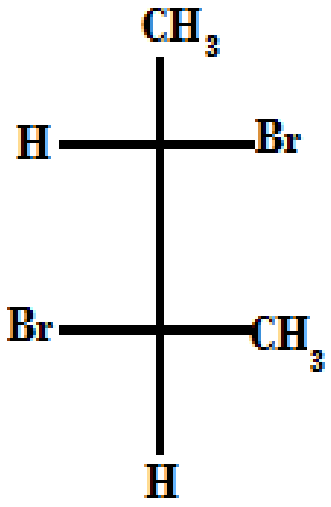


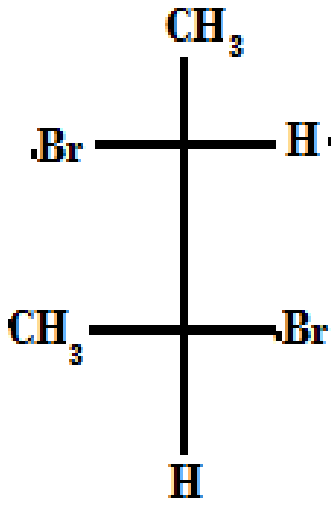
QUESTIONS???

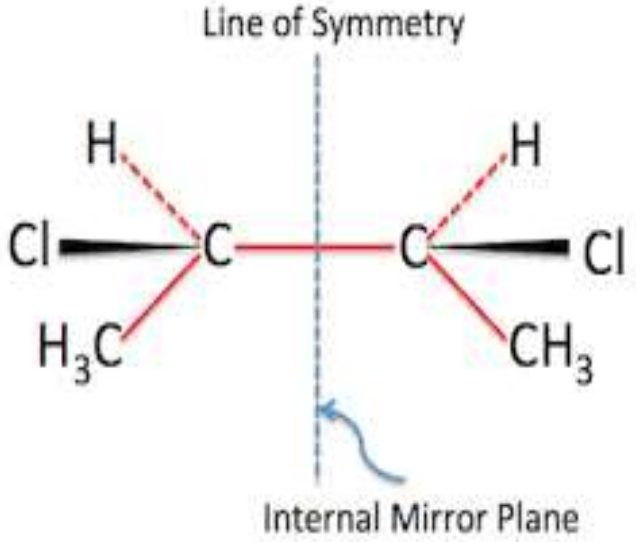
MESOMERS

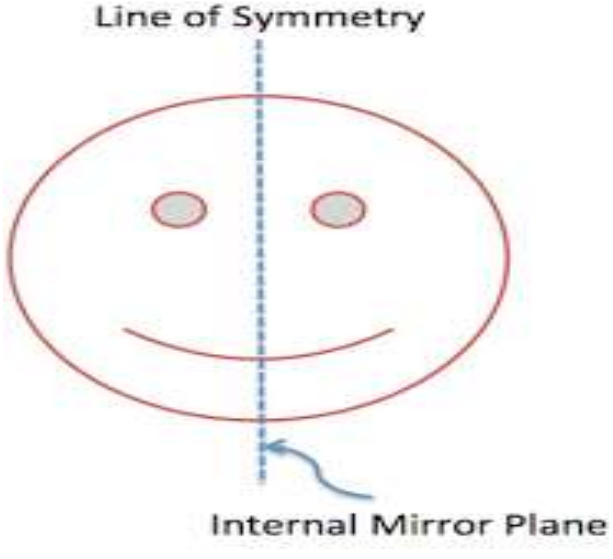
- Mesomers are compounds which have chiral centres but DO NOT exhibit optical activity
  - Due to the presence of an internal plane of symmetry in molecule
  - In such case the optical activities of the 2 chiral centres cancel out









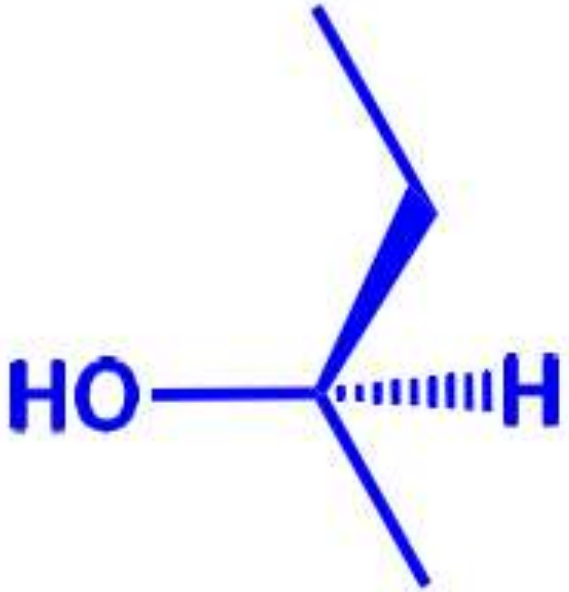


RACEMIC MIXTURES

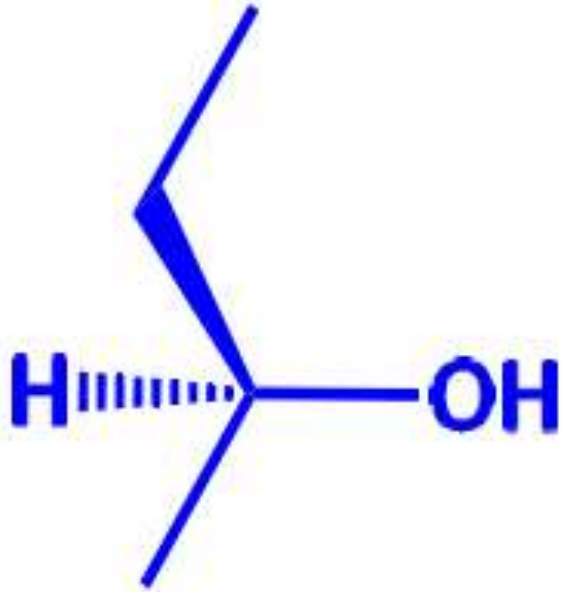
- A Racemic mixture is a 50/50 mixture of both ‘R’ and ‘S’ enantiomers of same molecule
- Hence **NO optical activity** will be exhibited by such a mixture
- This usually occurs after lab synthesis of chiral compounds

- **RACEMISATION**: The process of separating a racemic mixture
- An enantiomerically pure substance is one which contains only one enantiomer of the molecule

RACEMIC MIXTURES



(R)-Butan-2-ol



(S)-Butan-2-ol

Specific Rotation: $[\alpha]_D^t = +13.5$ $[\alpha]_D^t = -13.5$

STEREOCHEMISTRY: Importance

The thalidomide tragedy

Thalidomide

Thalidomide was hailed as a "wonder drug" that provided a "safe, sound sleep". It was a sedative that was found to be effective when given to pregnant women to combat many of the symptoms associated with morning sickness.

(S)-Thalidomide

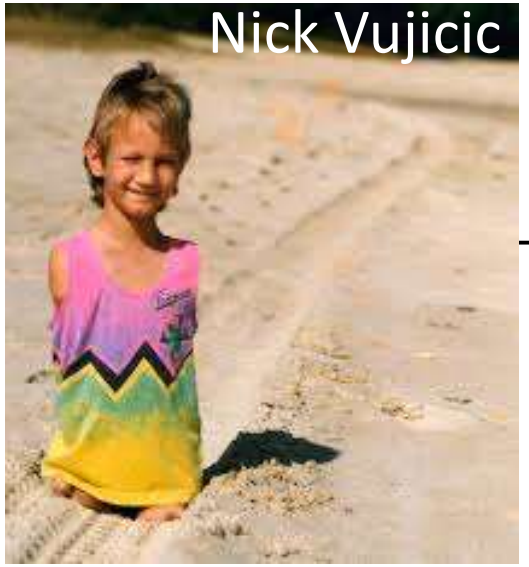
(R)-Thalidomide

Sedative

Teratogen

Agents that cause malformations in a developing embryo

THALIDOMIDE EFFECT




Question