# **Stereochemistry**

#### 3<sup>rd</sup> year chemistry department /Academic Year 2022-2023

Asst. Prof. Dr. Media Noori Abdullah

Your teacher can open the door,

but you must enter by Yourself

**Chinese Proverb** 

### **STEREOCHEMISTRY**

The part of science that deals with structure in three dimension, that is how atoms in a molecule are arranged in space relative to one another

It has its own language and terms that need to be learned in order to fully communicate and understand the concepts.

**Properties of drugs depend on stereochemistry** 

# The Handiness of Life!

A right-hand glove is different than a left-hand glove.

The property is commonly called "handedness"

Organic molecules (including many drugs) have handedness that results from substitution patterns on  $sp^3$  hybridized carbon. The amino acids are all **left-handed**, meanwhile, all sugars are righthanded.

Handedness is important in **Organic** and **Biochemistry** 

# Stereochemistry

**Stereochemistry:** 

The study of the three-dimensional structure of molecules

### **Structural (constitutional) isomers:**

Same molecular formula but different bonding sequence

### **Stereoisomers:**

Same molecular formula, same bonding sequence, different spatial orientation

# **Types of Stereoisomers**

Two types of stereoisomers:
Enantiomers

two compounds that are nonsuperimposable mirror images of each other

#### Diastereomers

Two stereoisomers that are not mirror images of each other

**Geometric isomers** (cis-trans isomers) are one type of diastereomer.





There are two Fundamental types of isomerism: Constitutional isomerism and Stereoisomerism

# Isomers

Compounds of identical chemical content but differing in their *constitution* (constitutional isomers), *configurations* (enantiomers and diastereomers), or *conformers* (conformational isomers), and have different chemical and/or physical properties.

## **Constitutional isomers**

Constitutional isomer (Structural isomers) are molecules which have the same molecular formula, but can differ in the way their atoms are connected together!

Alkanes that contain three or fewer Carbon atoms have no isomers, why?

because there is only one possible way For the atoms to be arranged.

**Constitutional isomers** are also called **structural or positional isomers**.

## **Constitutional isomers have:**

- 1. different IUPAC names
- 2. different bonding connectivity.
- 3. the same or different functional groups.
- 4. different physical properties, so they are separable by physical techniques such as distillation.
- 5. different chemical properties.

They behave differently or give different products in chemical reactions

Constitutional isomers or Structural isomers can be split again into three main subgroups:

chain isomers, position isomers, and functional group isomers.

**Constitutional isomers (or structural isomer)** 



# So, different position of attachment of a functional group in a molecule lead to constitutional isomers

<u>Molecular Formula</u>	<b>Constitutional isomers</b>		
C2H6O	CH3CH2OH	and	CH3OCH3
	Ethanol		Dimethyl ether
	liq. at r.t b.p= 78	.5	gas at r.t b.p.= -23.6 use as refrigerante
C3H7Cl	CH3CH2CH2Cl 1-chloro propane	and	CH3-CHCl-CH3 2-chloro propane

#### These compounds have very different physical properties.

# **Newman Projections**

# and Conformational Isomers

# **Conformational isomers**

Conformational isomers are different by relative spatial arrangements of atoms that results from rotation about sigma bonds. Thus, unlike configurational isomers, conformers are interconverting stereoisomers of a single compound.

### CONFORMATION

### CONFORMATIONAL ISOMERS

 $\square \Rightarrow$  Conformations are different spatial arrangements of a molecule that are generated by <u>rotation about single bonds</u>.

- Different conformations of the same molecule are sometimes called conformers or rotamers or conformational isomers.



# **Newman Projections**

 Is a way to draw chemical conformations and views a carbon - carbon chemical bond from front to back, front carbon as a dot and back carbon as a circle. This type of representation makes it easy to assess the torsional angle between two bonds one at each carbon atom.

### **Conformational isomer**



# **Easy** to interconverted isomer can **not** be separated **Hard** to interconverted stereoisomers can be separated

# **Torsional Strain**

 Is caused by the electrons in the two bonds that are eclipsed. These electrons are closer together in the eclipsed form than in the staggered form, therefore the repulsions are greater. Recall that repulsion between similarly charged particles represent an increase in potential energy.

# Newman Projections

Newman Projections good for showing torsional(dihedral) angles.



Torsional or dihedral angle

# **Conformational Analysis of Ethane**





# Newman projections

A Newman projection, useful in alkane stereochemistry, visualizes the conformation of a chemical bond from front to back, with the front atom represented by a dot and the back atom as a circle.



#### CONFORMATION

#### CONFORMATIONS OF ETHANE

 Ethane has two conformations called the staggered and eclipsed conformations.



# Why is the eclipsed conformation higher in energy than the staggered conformation?

- there is some steric repulsion between the hydrogen atoms in the eclipsed conformation that is reduced in the staggered conformation.

 in eclipsed conformation the electron cloud of C-H bonds are most nearer and thus their <u>repulsion</u> increases.

- These repulsive forces creates torsional strain in molecule
- the more strain, the more will be internal energy of conformer

Q) What are the different possible conformations of 1,2-dibromoethane? Which one is more stable? Why?



#### **Conformational Energy Profile for 1,2-Dibromoethane**

of conf: that 1 Likewise, the barrier that separates conf: 2 from conf: 3 is larger than the barriers separating every conformation other This is because the size of bromine is larger than hydrogen, and the transition from conf: 2 to conf: 3 requires that these two atoms come in close proximity of one another.

The energy levels of

# Minimum Energy Conformations of 1,2-Dibromoethane

For 1,2-dibromoethane, MarvinSketch finds three staggered conformations, as shown. Each structure has been oriented in order to present a view comparable to a Newman projection. The energy is listed above each conformation. The lowest energy conformation is assigned a value of 0.75 kcal/mole while the other two conformations have values of 0.95 kcal/mol each. Conformations labeled 2 and 3 look similar, but in fact they cannot be superimposed one on the other; instead they have a mirror image relationship as shown below.

#### **Conformer 1 is Anti**



Conformer 2 and 3 are called Gauche. The word gauche means not planer



#### **Conformers of Butane**

Generally, Butane has four conformation isomers which are fully eclipsed, gauche, eclipsed, and anti butane conformational isomers.





degrees of rotation about the C2-C3 bond

### **Ranking of Conformation Isomers**

The ranking of the conformational isomers is given below taking into account the energy levels from lowest to highest. It is given as;

• anti

- gauche
- eclipsed
- fully eclipsed

This can also be visualized using an energy diagram.

• **Stereoisomers:** are the particular kind of isomers that are different from each

other **only** in the way the atoms are oriented in space

- **Optical isomers**: isomers arising from chiralty (enantiomers and diastereomers).
- Enantiomers: are stereoisomers whose molecules are nonsuperposable mirror images of each other.
- **Diastereomers:** are stereoisomers whose molecules are **not** mirror images of each other.
- **Geometric isomers**: (cis and trans) (Z and E) in alkenes and cyclo compounds

## Stereoisomers

• In stereochemistry, stereoisomerism, is a form of isomerism in which molecules have the same molecular formula and sequence of bonded atoms (bonding connectivity), but **differ in the three dimensional orientations of their atoms in space.** 

• Stereoisomers have identical IUPAC names (except for a prefix like cis or trans, because they differ only in the three dimensional arrangement of atoms, **stereoisomers always have the same functional group(s)**.

• There are two main types of stereoisomerism Geometric isomerism, and Optical isomerism.

## **Geometrical Isomers**

• This type of isomerism most frequently involves in compounds containing carbon-

carbon double bonds with suitable substituents. Rotation of these bonds is

restricted, compared to single bonds, which can rotate freely.

• If there are two different atoms, or groups of atoms, attached to each carbon of the

carbon carbon double bond, they can be arranged in different ways to give different molecules.

#### Alkenes

#### Geometric isomers (*cis*, *trans*), (*E*, *Z*)

The particular kind of diastereomers that owe their existence to hindered rotation about double bonds are called G.I.

If we take 2-Butene, *cis-trans* isomers are not mirror images, so they are **diastereomers** 



-They are not mirror image of each other

- and hence are not Enantiomers
- They are Diastereomers

If the atoms on each double bond carbon are different, **priority** is based on the **atomic number** of the **single atom directly attached to the double-bond carbons**. **The atom with higher atomic number receives a higher priority** 

F CI Br I 9 17 35 53 atomic no. increasing priority Z= in the same side  $\begin{array}{c|c} Br & F \\ I \text{ higher priority} \\ than Br & F \\ \end{array} C = C & Cl \text{ higher priority} \\ than F \\ \end{array}$ (Z)-1-bromo-2-chloro-2-fluoro-1-iodo ethene

If the two groups with the **higher** priorities are on the same side of the double bond, that is described as the (Z)- isomer. So you would write it as (Z)-name of compound. The symbol Z comes from a German word (**zusammen**) which means **together** 



If the two groups with the higher priorities are on **opposite sides** of the double bond, then this is the (E)- isomer. E comes from the German **Entgegen** which means opposite

E-1-bromo-2-chloro-2-floro-1-lodo ethene





The two attached atoms are C and H, so since the atomic numbers C >H then the -CH<sub>3</sub> group is **higher priority**. Therefore the two high priority groups are on the **opposite side**, then this is (*E*)-**but-2-ene**. Or *trans*-2-butene

# Diastereomers

Diastereomers are stereoisomers that are not mirror images of each other – they are stereoisomers that are not enantiomers.



### **Geometric Isomers in Cyclic Systems**

Stereochemistry of cyclic compounds cis and trans -isomers









Configurational isomers (cis, trans isomers)



# Q) Why does the dry-cleaning solvent trichloroethene (Cl2C=CHCl) not have geometric isomers?

For geometric isomer to exist there must **be two different groups attacked to each carbon of the double bond**. Q) Why does the dry-cleaning solvent trichloroethene (Cl2C=CHCl) not have geometric isomers?

For geometric isomer to exist there must **be two different groups attacked to each carbon of the double bond**.

### E, Z will work, but may not agree with cis, trans, how? Consider the molecule shown



Q)

This is 2-bromo-2-butene -- ignoring the geometric isomerism for now. **Cis or trans?** This molecule is clearly cis. The two methyl groups are on the same side. More rigorously, the "parent chain" is cis.

The high priority groups are  $-CH_3$  (left) and -Br (right). Thus, the two priority groups are on opposite sides = entgegen = E.

#### This example should convince you that cis and Z are not synonyms

# Thank you for your attention