Ministry of Higher Education and Scientific Researc

University Of Thi-Qar

College Of Sciences

Department of Chemistry

Asst .prof. Dr. Athraa hameed mekky

MSC 1st attemp

2020-2021

Stereochemistry

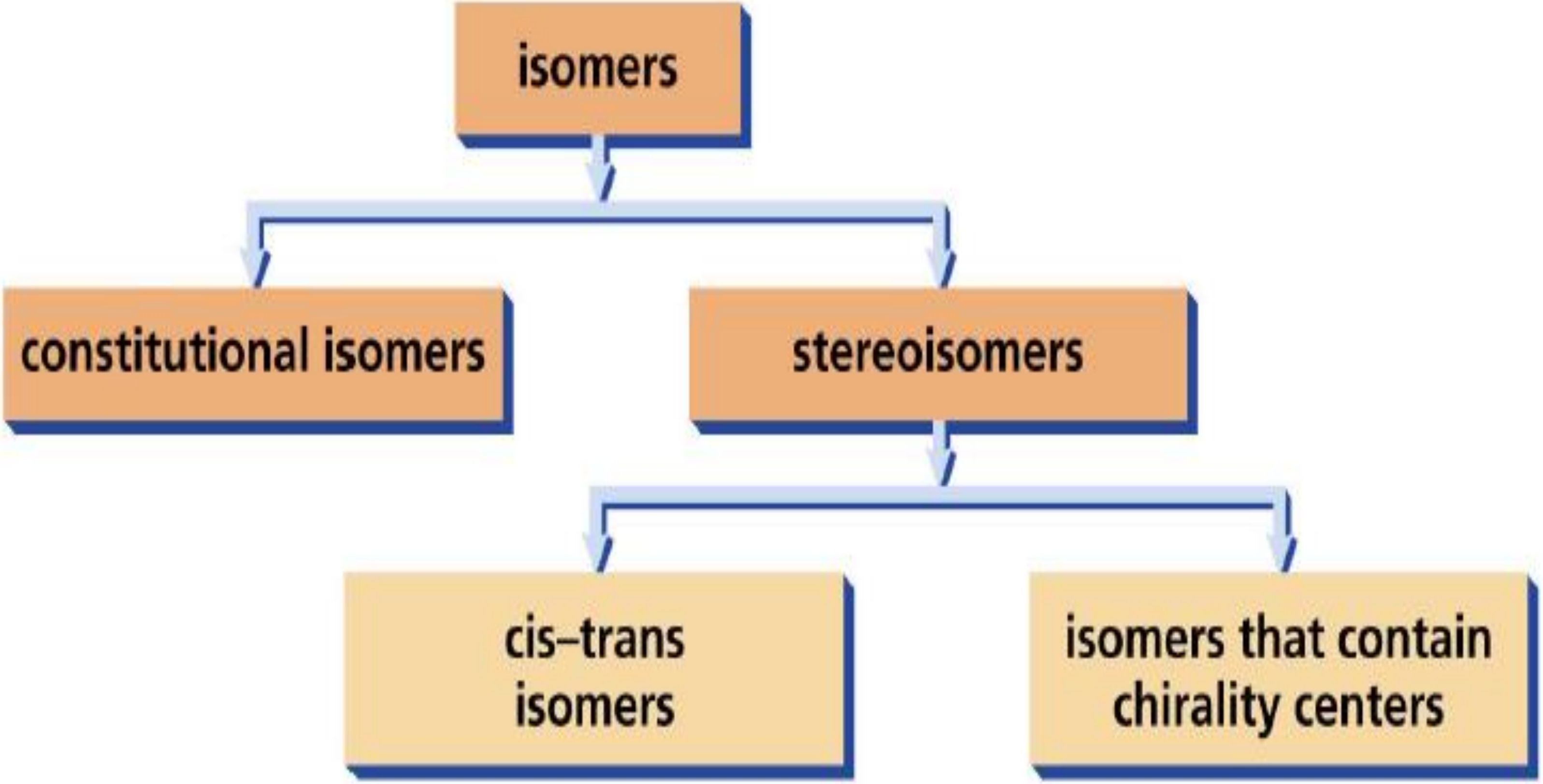
Stereochemistry.

Stereochemistry **of** an organic compound can be defined as the chemistry of that compound in space and as a function of molecular geometry **or study of the 3 dimensional arrangement in space of molecules or studies the properties of stereoisomers.**

Generally isomerism can be divided in to two categories;

a. Structural (constitutional) Isomerism.

b. Stereo (Configurational) Isomerism .



isomers

constitutional isomers

stereoisomers

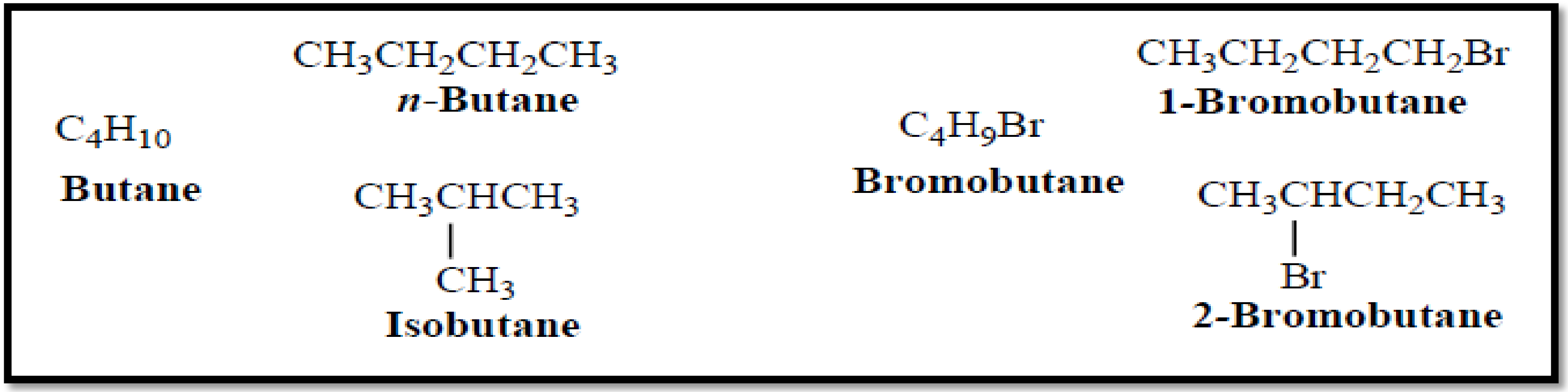
cis–trans isomers

isomers that contain chirality centers

STRUCTURAL (CONSTITUTIONAL) ISOMERISM

Structural isomerism is also known as '**constitutional isomerism**'. Structural isomerism arises when a molecule can be represented in to two or more than two different structures. The difference in structure is due to the difference in the arrangement of atoms within the molecules, irrespective of their position in space. In other words, structural isomers are compounds those have identical molecular formulae but different structural formulae; and the phenomenon is called **structural isomerism.**

Examples 1: Structural isomer of Butane (C_4H_{10}) and Bromo butane (C_4H_9Br)



C_4H_{10}

Butane

$CH_3CH_2CH_2CH_3$

***n*-Butane**

$CH_3\underset{\underset{\displaystyle CH_3}{|}}{C}HCH_3$

Isobutane

C_4H_9Br

Bromobutane

$CH_3CH_2CH_2CH_2Br$

1-Bromobutane

$CH_3\underset{\underset{\displaystyle Br}{|}}{C}HCH_2CH_3$

2-Bromobutane

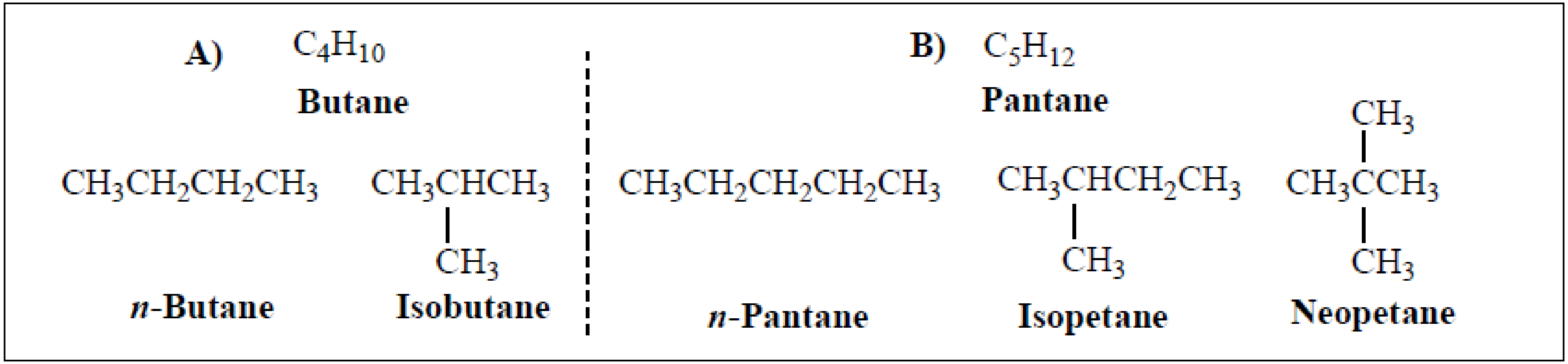
Structural isomerism can also be subdivided in to five types.

1) Chain Isomerism
2) Functional Isomerism
3) Position Isomerism
4) Metameric
5) Taotomeric

1) Chain Isomerism:

Chain isomers are those isomers having difference in the order in which the carbon atoms are bonded to each other. In other words chain isomers have variable amounts of branching along the hydrocarbon chain.

If you observe two or more than two molecules having similar molecular formulae, but difference in their hydrocarbon chain length, you should recognize them as chain isomers of each other.



A) C_4H_{10} **Butane**

$CH_3CH_2CH_2CH_3$ ***n*-Butane**

$CH_3CH(CH_3)CH_3$ **Isobutane**

B) C_5H_{12} **Pantane**

$CH_3CH_2CH_2CH_2CH_3$ ***n*-Pantane**

$CH_3CH(CH_3)CH_2CH_3$ **Isopetane**

$CH_3C(CH_3)_2CH_3$ **Neopetane**

2) Functional Isomerism:

Two or more than two molecules those having the same molecular formulae but have different functional groups are called functional isomers and the phenomenon is termed as functional isomerism.

If you observe two or more than two molecules having same molecular formulae, but difference in their functional groups, you should understand that these are **functional isomers** of each other.

Example 3: Ethyl alcohol and Dimethyl ether

CH_3CH_2OH CH_3OCH_3 Ethyl alcohol Dimethyl ether

Example 4: *n*-Butyl alcohol and Diethyl ether

$CH_3CH_2CH_2CH_2OH$ n-Butayl alcohol $CH_3CH_2OCH_2CH_3$ Diethyl ether

3) Position Isomerism:

Two or more than two molecules those having same molecular formulae but having difference in the position of functional group on the carbon chain are called **position isomers** and the phenomenon is called as **position isomerism.**

If you observe two or more than two molecules having same molecular formulae, but difference in their functional groups, you should understand that these are functional isomers of each other .

Example 5: 1-Butene and 2-Butene

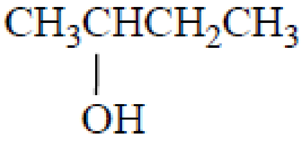
$CH_3CH_2CH{=}CH_2$ $CH_3CH{=}CHCH_3$

1-Butene **2-Butene**

Example 6: 1-Butyl alcohol, 2-Butyl alcohol and *t*-Butyl alcohol .

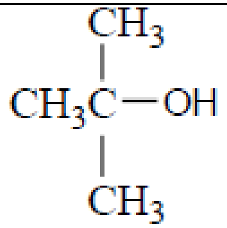
$CH_3CH_2CH_2CH_2OH$

1-Butyl alcohol



$CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_3$

2-Butyl alcohol



$CH_3\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle CH_3}{\underset{|}{C}}}}-OH$

***t*-Butyl alcohol**

4) Metameric:

Two or more than two molecules those having same molecular formulae and functional group but having difference in the distribution of carbon atoms on either side of functional group are called metamers and the phenomenon is called the metamerism.

When you see two or more than two molecule with identical molecular formulae but while structural representation you observe there is a difference in the alkyl group attached to same functional group you should understand these molecules are metamers of each other.

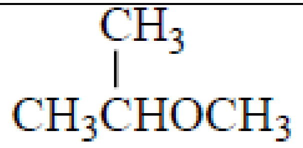
Example 7: Diethyl ether, Methyl propyl ether and isopropyl methyl ether .

$CH_3CH_2OCH_2CH_3$

Diethyl ether

$CH_3CH_2CH_2OCH_3$

Methyl propyl ether



$$\overset{\displaystyle CH_3\\|}{CH_3CHOCH_3}$$

Isopropyl methylether

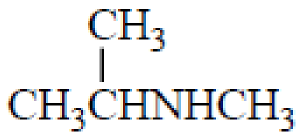
Example 8: Diethyl amine, Methylpropyl amine and isopropyl methyl amine

$CH_3CH_2NHCH_2CH_3$

Diethyl amine

$CH_3CH_2CH_2NHCH_3$

Methyl propyl amine



$$\overset{\displaystyle CH_3\\|}{CH_3CHNHCH_3}$$

Isopropyl methylamine

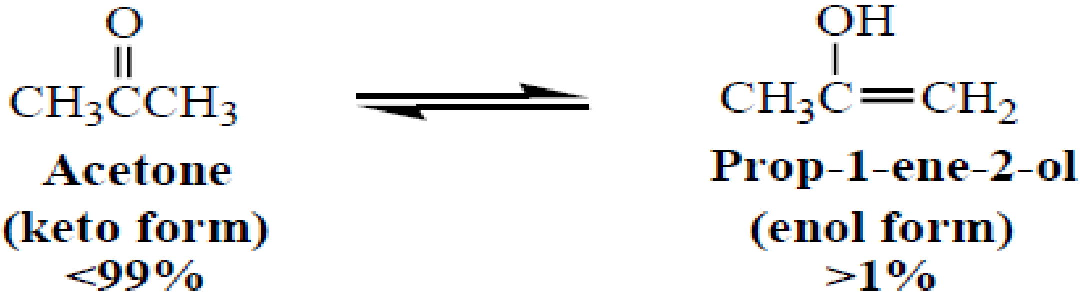
5) Tautomerism:

This is a special kind of isomerism where both the isomers are interconvertible and always exist in a dynamic equilibrium to each other. Due to their interconersion change in functional group takes place that gives two different isomers of an organic compound. This phenomenon is called Tautomerism .

When you observe two different isomeric forms of an organic compound are rapidly interconvertible to each other you should recognize them as tautomer of each other.

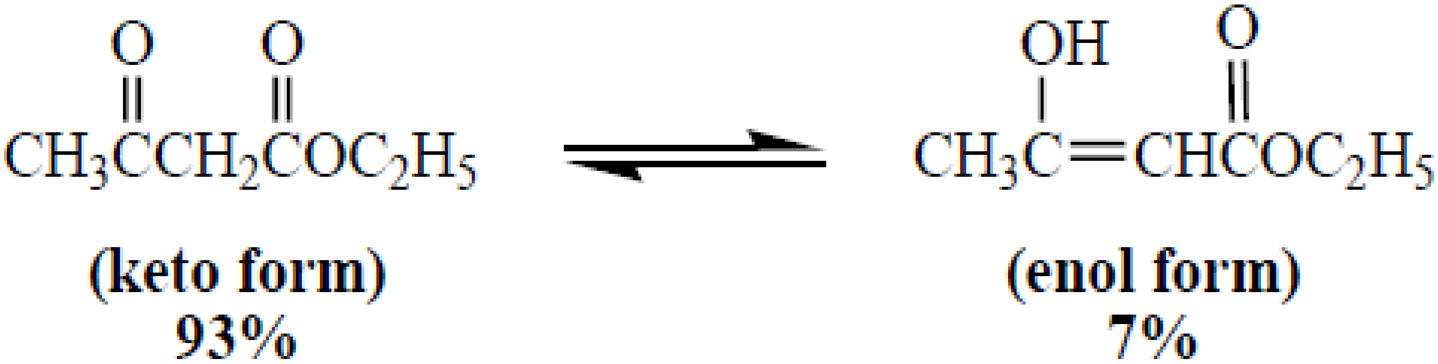
Remember: Tautomer's are not the resonance structure of same compound .

Example 9: Acetone exists in taotomeric equilibrium with Prop-1-en-2-ol



$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}CH_3 \rightleftharpoons CH_3\overset{\overset{\displaystyle OH}{|}}{C}{=}CH_2$$

Example 10: Tautomeric forms of Ethyl acetoacetate under taotomeric equilibrium .



$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}CH_2\overset{\overset{\displaystyle O}{\|}}{C}OC_2H_5 \rightleftharpoons CH_3\overset{\overset{\displaystyle OH}{|}}{C}{=}CH\overset{\overset{\displaystyle O}{\|}}{C}OC_2H_5$$

2- STEREO (or CONFIGURATIONAL) ISOMERISM .

Stereoisomerism is arises due to the difference in arrangement (configuration) of atoms or groups in space. When two or more than two isomers have the same structural formulae but having difference in the arrangement (configuration) of atoms in space are called stereo isomer and the phenomenon is called **stereo isomerism.** Stereo isomerism can be further classified as

i. Geometrical or *cis -trans* isomerism .

ii. Optical isomerism .

i- GEOMETRICAL ISOMERISM:

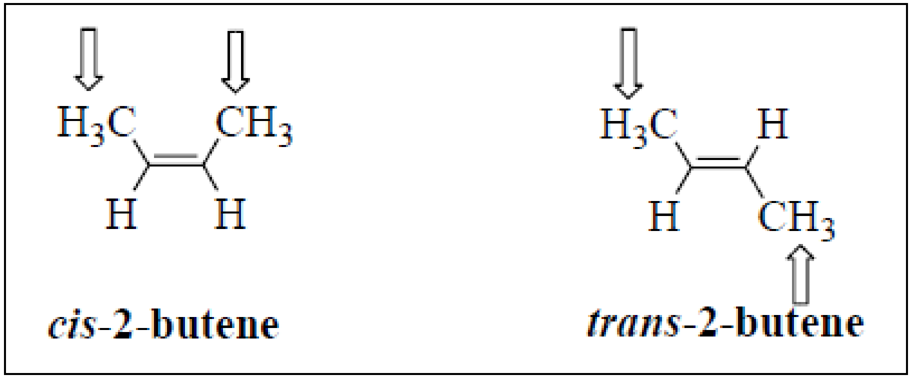
Geometrical isomerism is generally observed in alkenes and cyclic compounds due to their restricted rotation around carbon- carbon bond. The rotation about a double bond in alkene or about a single bond in a cyclic/ring like compound is restricted. Double bonded system consists of a σ (sigma) and a π (pi) bond perpendicular to each other. It is not possible to rotate the molecule about carbon-carbon bond. The rotation will break the π bond as a result the molecule will lose its identity. In some cased the rotation about single bond is also restricted due to steric hindrance. Geometrical isomerism is shown by various groups of compounds the major class of compounds that exhibit geometrical isomerism are classified as

i. Compounds having double bond; C=C, C=N, N=N

For example cis and trans 2-butene have same connection of bond and molecular formulae.

If you observe two similar groups are on the same side of C=C bond this is called cis- isomer; whereas, if two similar groups are on opposite side of C=C bond this is known as trans- isomer.

Example 1: cis- and trans- isomerism in 2-butene



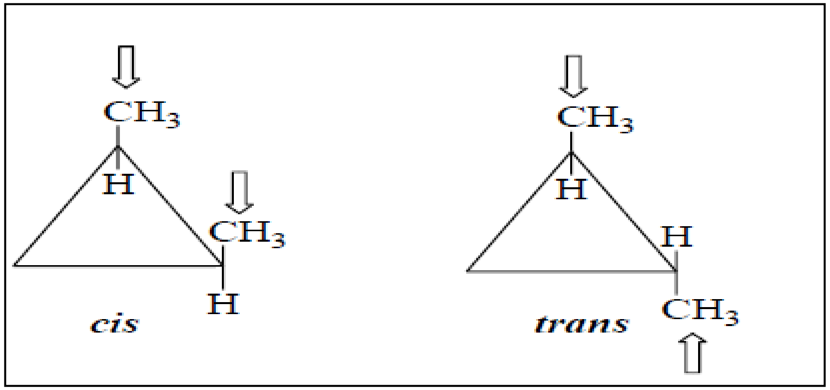
cis-2-butene *trans*-2-butene

You can understand that due to the presence of one σ (sigma) and one π (pi) bond in carbon–carbon double bond, rotation around C=C bond is not possible. The restricted rotation around C=C bond is responsible for geometrical isomerism in alkenes.

ii**. Cyclic compounds like homocyclic , heterocyclic and fused-ring systems**

You can easily observe that rotation around C-C bond is also not possible in cyclic compounds as the rotation would break the bonds and break the ring. Thus Geometrical isomerism is also possible in cyclic compounds.

Example 2: *cis* and *trans* isomers of 1,2-dimethylcyclopropane .



Conditions for geometrical isomerism:

Following two conditions are necessary for any compounds to show geometrical isomerism

a) There should be restricted (not allowed) rotation about a bond in a molecule.

b) Both substituent /atoms on each carbon about which rotation is not allowed should (restricted) be different.

Remember**:** Geometrical isomers are non-mirror image of each other hence they are called diastereomers . Therefore their physical and chemical properties are different.

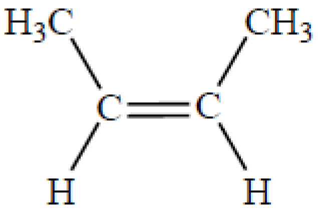
Triple bonded molecules do not exhibit any kind of stereoisomerism because such molecule shows cylindrical symmetry.

E & Z system of nomenclature for geometrical isomers:

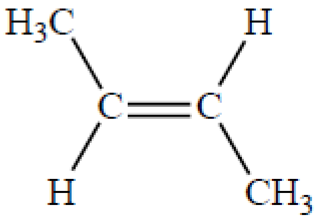
We have already discussed about the *cis* and *trans*- nomenclature of geometrical isomerism. The *cis* and *trans* nomenclature is the oldest and most fundamental nomenclature system for geometrical isomerism. The *cis* and *trans*- nomenclature system is applicable only for those geometrical isomers in which at least one identical atoms/groups is bonded with each double bonded carbon. If both the identical groups/atoms are on same side of double bond the isomer is called as *cis* isomer; whereas, if both identical groups/atoms are on opposite side of the double bond the isomer is called as *trans*- isomer (see example 1 of this unit). The *cis* and *trans*- nomenclature method is limited to the molecule in which identical groups/atoms are attached to double bonded carbon. If all the atoms/groups on double bonded carbon are different then the configuration of such molecule could not be assigned as *cis* and *trans*- nomenclature.

A more general nomenclature (*i.e.* E/Z nomenclature) was introduced which was based on *Cahn-In gold-Prelog* system. In E/Z system the configuration is specified by the relative positions of two highest priority groups/atoms on the two carbons of the double bond.

Let us understand the *E/Z* nomenclature system by considering an example which we have already discussed in the beginning of this Unit (example 1).



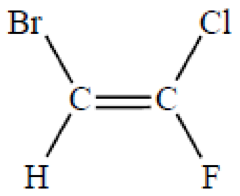
***cis*-2-butene**



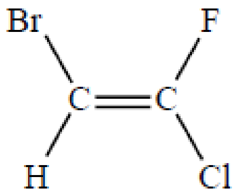
***trans*-2-butene**

You can easily identify which one is *cis*- isomer and which one is *trans*- just by looking the position of similar atoms/groups. It is a simple and visual way of telling the two isomers apart. *So why do we need an alternative system?*

Now consider one another example in which we will change all the atoms/groups in above example by replacing one CH_3- by Br, other CH_3- by Cl , and one H- by F. Now try to predict the nomenclature of these two isomers of **2-bromo-1-chloro-1-fluoroethene (I and II)**. ***Could you name these isomers using cis and trans-nomenclature?*** The simplest answer is ‘**NO**’.



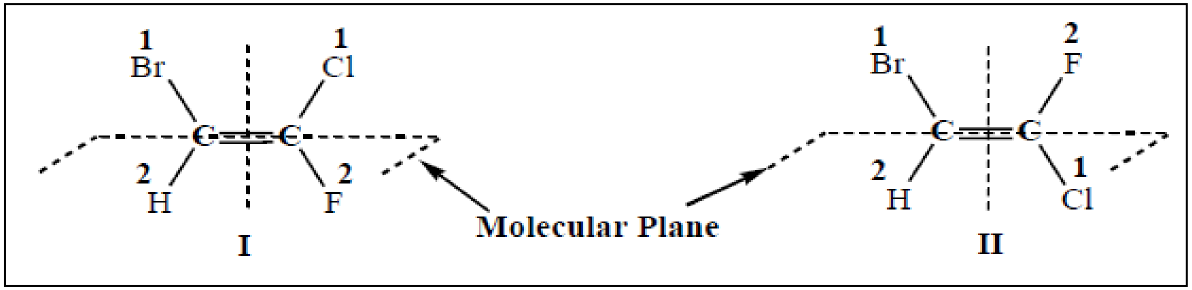
I



II

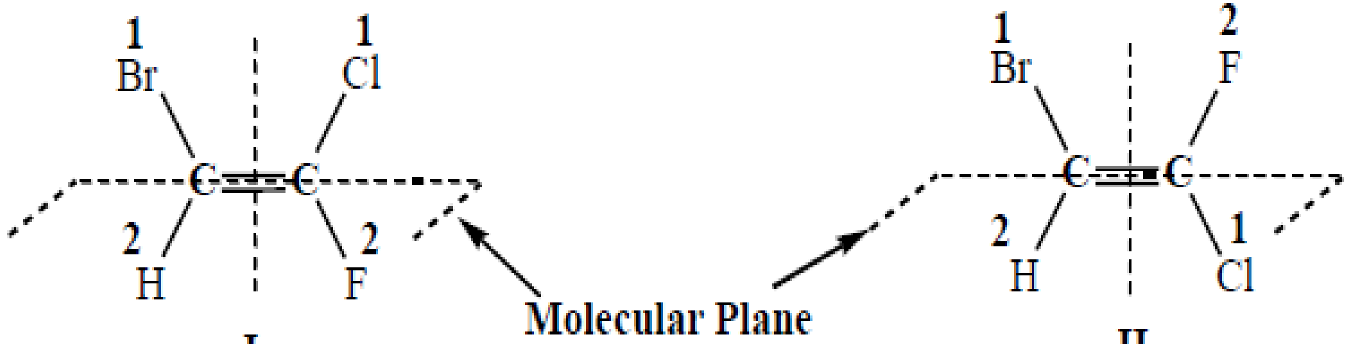
Because all four atoms attached to the carbon-carbon double bond are different, therefore it is not so simple that you can predict them as *cis*- and *trans*- to each other. The E/Z system of nomenclature provides the most appropriate solution to above problem.

This system is based on the priority of the attached atoms/groups on each double bonded carbon. The priority of the atoms/groups can be assigned as per the ‘Sequence Rule’ or ‘CIP Rule’ given by Cahn-In gold - Prelog. We have discussed the detail about ‘Sequence Rule’ in later part of this Unit. Now assign priority to atoms/groups attached to each double bonded carbon in above example



We can easily observe that the both higher priority atoms/groups on each double bonded carbon of isomer **I** are on same side; whereas, the higher priority atoms/groups on each double bonded carbon of isomer **II** are on opposite side. If the two groups with the higher priorities are on the same side of the double bond, such isomer is designated 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 such isomer is designated as (*E*)- isomer. *E* comes from the German ***ENTGEGEN***, which means opposite. Thus in given example the isomer **I** is having both higher priority groups/atoms are on same side of double bond, hence it is *Z*-isomer; whereas, the isomer **II** is having both higher priority groups/atoms are on opposite side of the double bond, hence it is *E*-isomer.



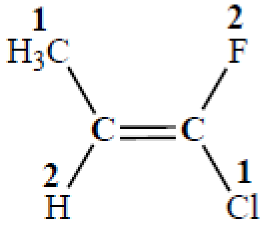
I

(*Z*)-2-bromo-1-chloro-1-fluoroethene

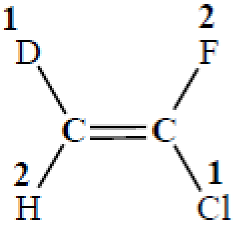
II

(*E*)-2-bromo-1-chloro-1-fluoroethene

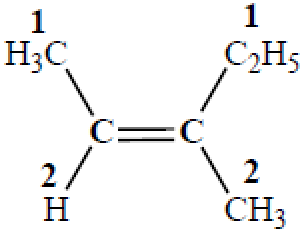
Example 10: Some other examples of geometrical isomers with *E* and *Z* configuration.



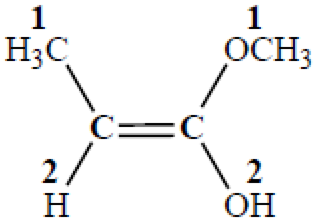
(*E*)-1-chloro-1-fluoroprop-1-ene



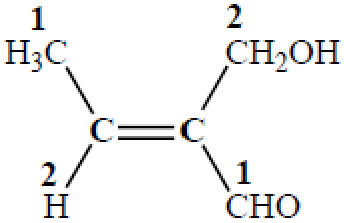
(*E*)-Deuterated1-chloro-1-fluoroprop-1-ene



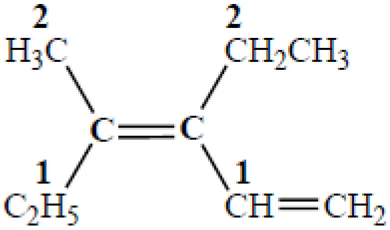
(*Z*)-3-methylpent-2-ene



(*Z*)-1-methoxyprop-1-en-1-ol



(*E*)-2-(hydroxymethyl)but-2-enal



(*Z*)-3-ethyl-4-methylhexa-1,3-diene

Geometrical isomerism in oximes and cyclic compounds:

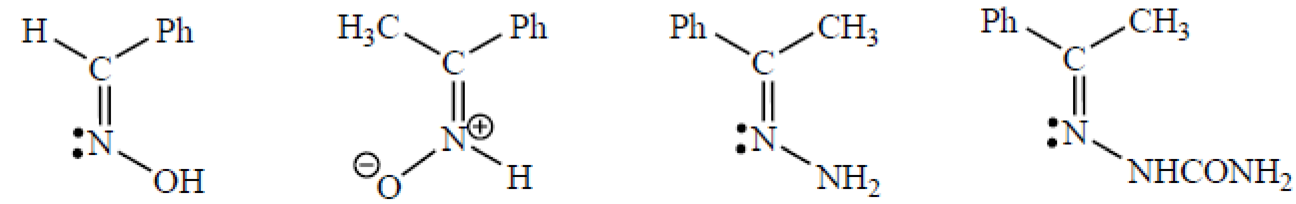
Nitrogen containing compounds like >C=N- as well as –N=N- bond also exhibit geometrical isomerism. The important classes of compounds that exhibit geometrical isomerism due to >C=N- bond are:

(a) Oximes

(b) Nitrones

(c) Semicarbazones

(d) Hydrazones



(*Z*)-benzaldehyde oxime

(*E*)-nitrone

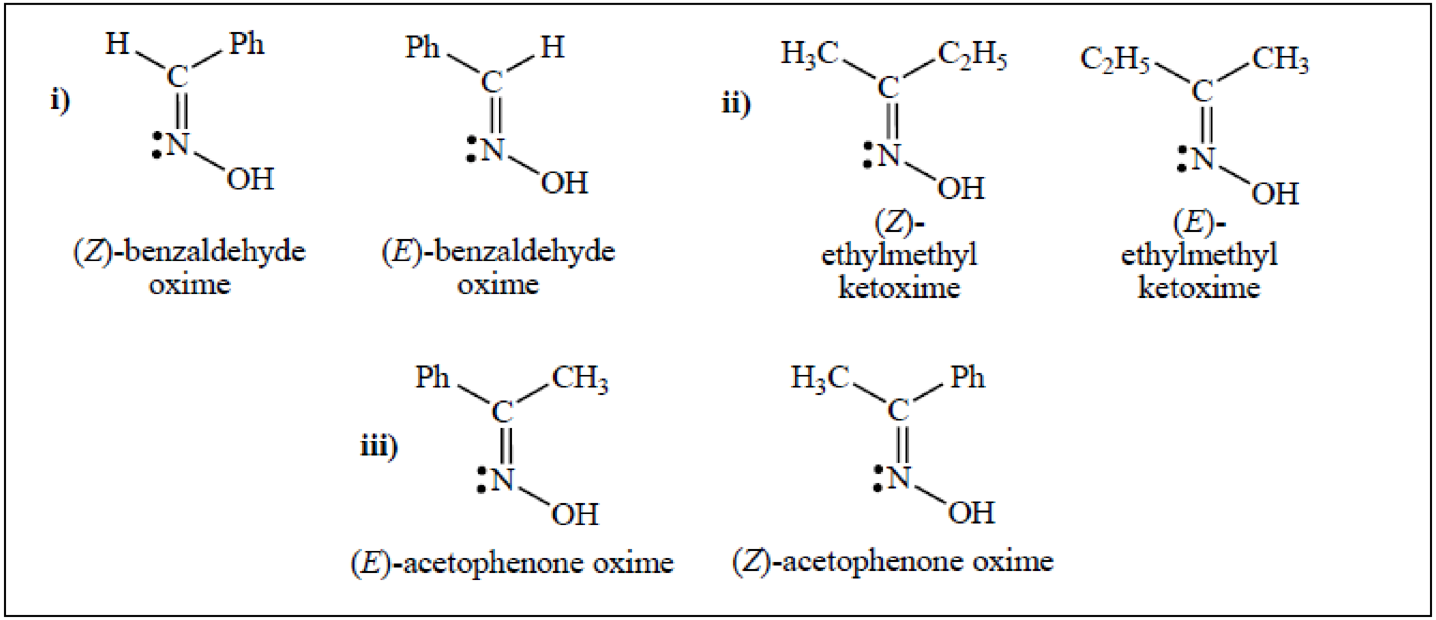
(*E*)-1-(1-phenylethylidene) hydrazine

(*E*)-1-(1-phenylethylidene) semicarbazide

Oximes are the most common compounds among all above classes. Both carbon and nitrogen atom in oxime are sp2 hybridized the C=N bond of oxime consists a sigma (σ) and a pi (π) bond. Therefore, there is no free rotation possible around C=N bond; hence, oximes of aldehyde and ketones (unsymmetrical) exhibit geometrical isomerism

The configuration of such compounds is also based on priority of the groups/atoms attached to the double bonded carbon and nitrogen. Lone pair of the nitrogen always considered to be the lowest priority group. The priority of the groups/atoms is assigned as per the sequence rule which we have already discussed in Unit 4. If the higher priority groups/atom on double bonded carbon and nitrogen are on same side of the double bond the isomer is considered as *Z*- isomer, whereas if the higher priority groups/atoms are on opposite side the isomer is considered as *E*- isomer.

Example 11: E/Z isomerism is shown by i) benzaldoxime, ii) ethylmethylketoxime and iii) methylphenylketoxime



(*Z*)-benzaldehyde oxime

(*E*)-benzaldehyde oxime

(*Z*)-ethylmethyl ketoxime

(*E*)-ethylmethyl ketoxime

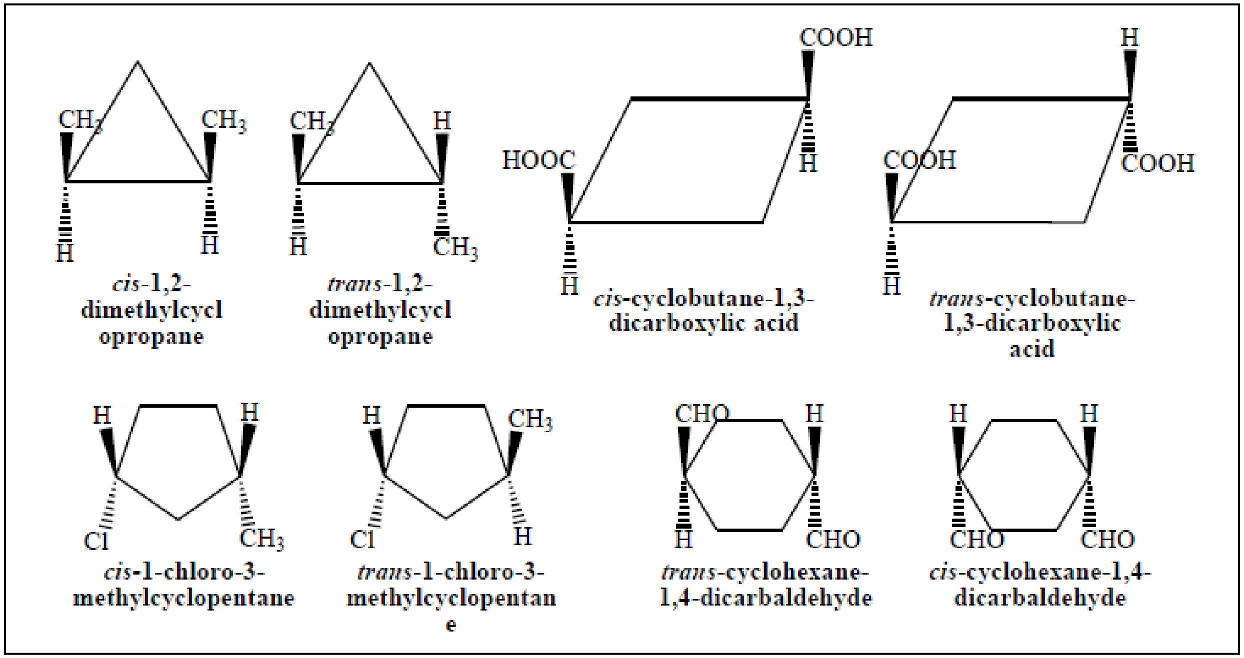
(*E*)-acetophenone oxime

(*Z*)-acetophenone oxime

We have already discussed that the geometrical isomerism is usually arises due to restricted rotation about a bond. Since, there is no rotation possible about the carbon-carbon bond in a cyclic compound or cycloalkanes like cyclopropane , cyclobutane , cyclopantane , cyclohexane, etc. Hence, such molecule also exhibit geometrical isomerism, and can be designated as *cis* and *trans*- isomer

. In a disubstituted cycloalkanes, where the two atoms/groups are bonded on different carbons, can be represented in to two geometrical isomers .The isomer in which the two atoms/groups are located on the same side of the ring is called *cis*-isomer; whereas, the isomer in which the two atoms/groups are located on the opposite side of the ring is called *trans*-isomer.

Example 12: Geometrical isomers of disubstituted cyclopropane, cyclobutane, cyclopantane and cyclohexane.



cis-1,2-dimethylcyclopropane

trans-1,2-dimethylcyclopropane

cis-cyclobutane-1,3-dicarboxylic acid

trans-cyclobutane-1,3-dicarboxylic acid

cis-1-chloro-3-methylcyclopentane

trans-1-chloro-3-methylcyclopentane

trans-cyclohexane-1,4-dicarbaldehyde

cis-cyclohexane-1,4-dicarbaldehyde