

# STEREOCHEMISTRY



## UNIT-VI

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# PTU-SYLLABUS

Unit VI Stereochemistry Representations of 3 dimensional structures, structural isomers and stereoisomers, configurations and symmetry and chirality, enantiomers, diastereomers, optical activity, absolute configurations, determination of R/S configuration, conformational analysis (ethane, propane & butane molecules).

## *Selected Historical Landmarks in the Development of the Field of Stereochemistry:*

- 1848 *Pasteur* achieves the *first optical resolution* of the (+)- and (-)-enantiomers of tartaric acid.
- 1874 *van't Hoff* and *Le Bel* independently suggest that tetravalent carbon is tetrahedral.
- 1900 *Fischer* develops the first systematic method for depicting stereochemistry (*Fischer projections*) and a notation for designating configuration (*D/L notation*).
- 1905 *Rosanoff* arbitrarily assigns the configuration of the structure corresponding to (+)-glyceraldehyde as being D-glyceraldehyde.
- 1951 *Bijvoet* determines the *absolute configuration* of the sodium rubidium double salt of (+)-tartaric acid using anomalous dispersion X-ray crystallography.
- 1969 *Hassell* and *Barton* (Imperial College) jointly awarded the Nobel prize in Chemistry for their work on the *conformational analysis* of cyclohexane.

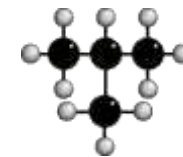
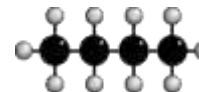
# STEREOCHEMISTRY

- Isomers are different compounds with the same molecular formula.
- The two major classes of isomers are **constitutional isomers** and **stereoisomers**.
  - ➡ **Constitutional/structural isomers** have different IUPAC names, the same or different functional groups, different physical properties and different chemical properties.
  - ➡ **Stereoisomers** differ only in the way the atoms are oriented in space. They have identical IUPAC names (except for a prefix like *cis* or *trans*). They always have the same functional group(s).
- A particular three-dimensional arrangement is called a **configuration**.
- Stereoisomers differ in configuration.

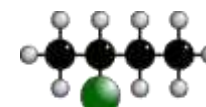
## STRUCTURAL ISOMERISM

Same molecular formula but different structural formulae

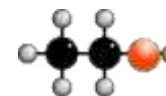
### CHAIN ISOMERISM



### POSITION ISOMERISM



### FUNCTIONAL GROUP ISOMERISM

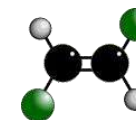
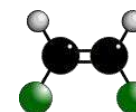


## STEREOISOMERISM

Same molecular formula but atoms occupy different positions in space.

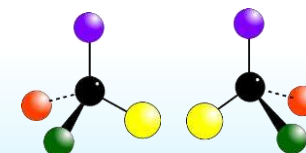
### GEOMETRICAL ISOMERISM

Occurs due to the restricted rotation of C=C double bonds... two forms... **CIS** and **TRANS**



### OPTICAL ISOMERISM

Occurs when molecules have a chiral centre. Get two non-superimposable mirror images.



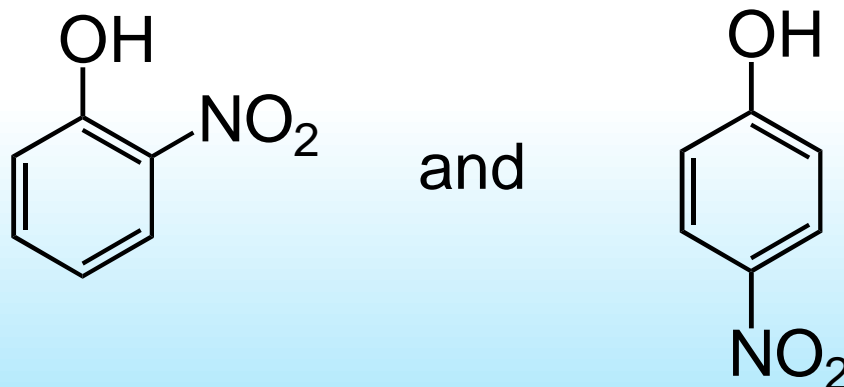
# CONSTITUTIONAL ISOMERS

Constitutional isomers (also known as structural isomers) have the same molecular formula but differ in the sequence in which the individual atoms are bonded (connectivity).

- skeletal isomerism



- positional isomerism

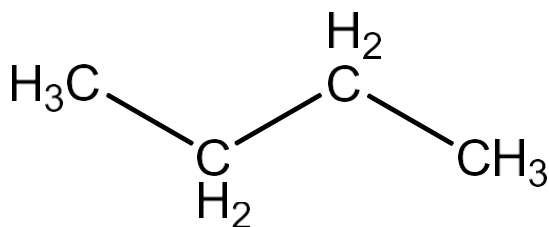


# CONSTITUTIONAL ISOMERS

- Functional isomers: - compounds of identical molecular formula but which have different functional groups.

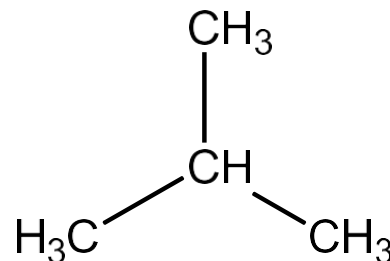
e.g.  $C_2H_5OH$  and  $CH_3OCH_3$

**Constitutional isomers** are isomers which have the same molecular formula but differ in the way their atoms are connected.



butane

Chemical Formula: C<sub>4</sub>H<sub>10</sub>



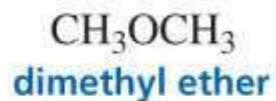
2-methylpropane

Chemical Formula: C<sub>4</sub>H<sub>10</sub>

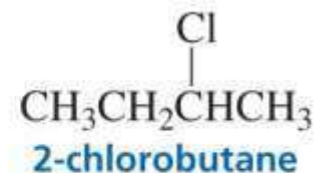
constitutional isomers



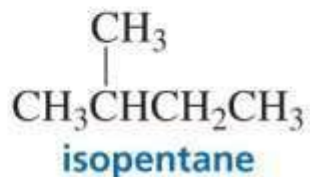
and



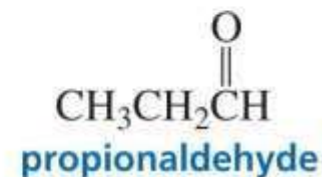
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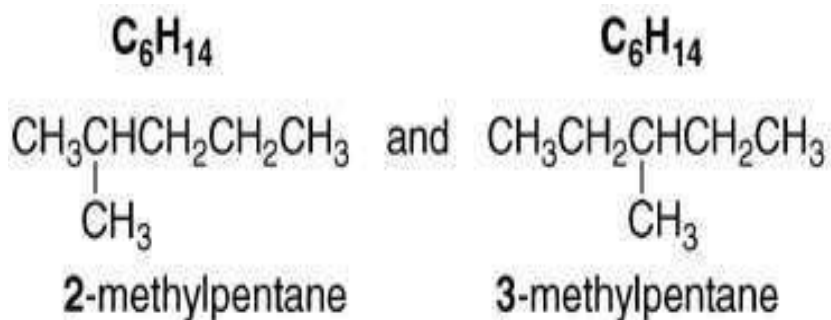


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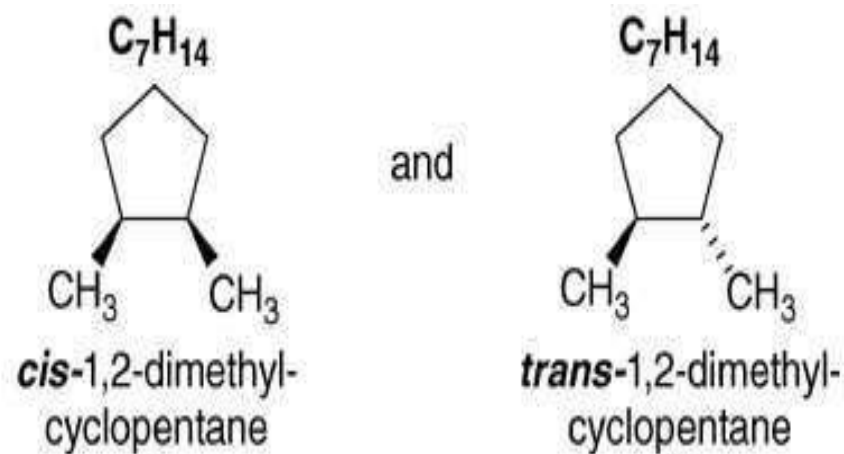


# A COMPARISON OF CONSTITUTIONAL ISOMERS AND STEREOISOMERS.....



same molecular formula  
different names

**constitutional isomers**

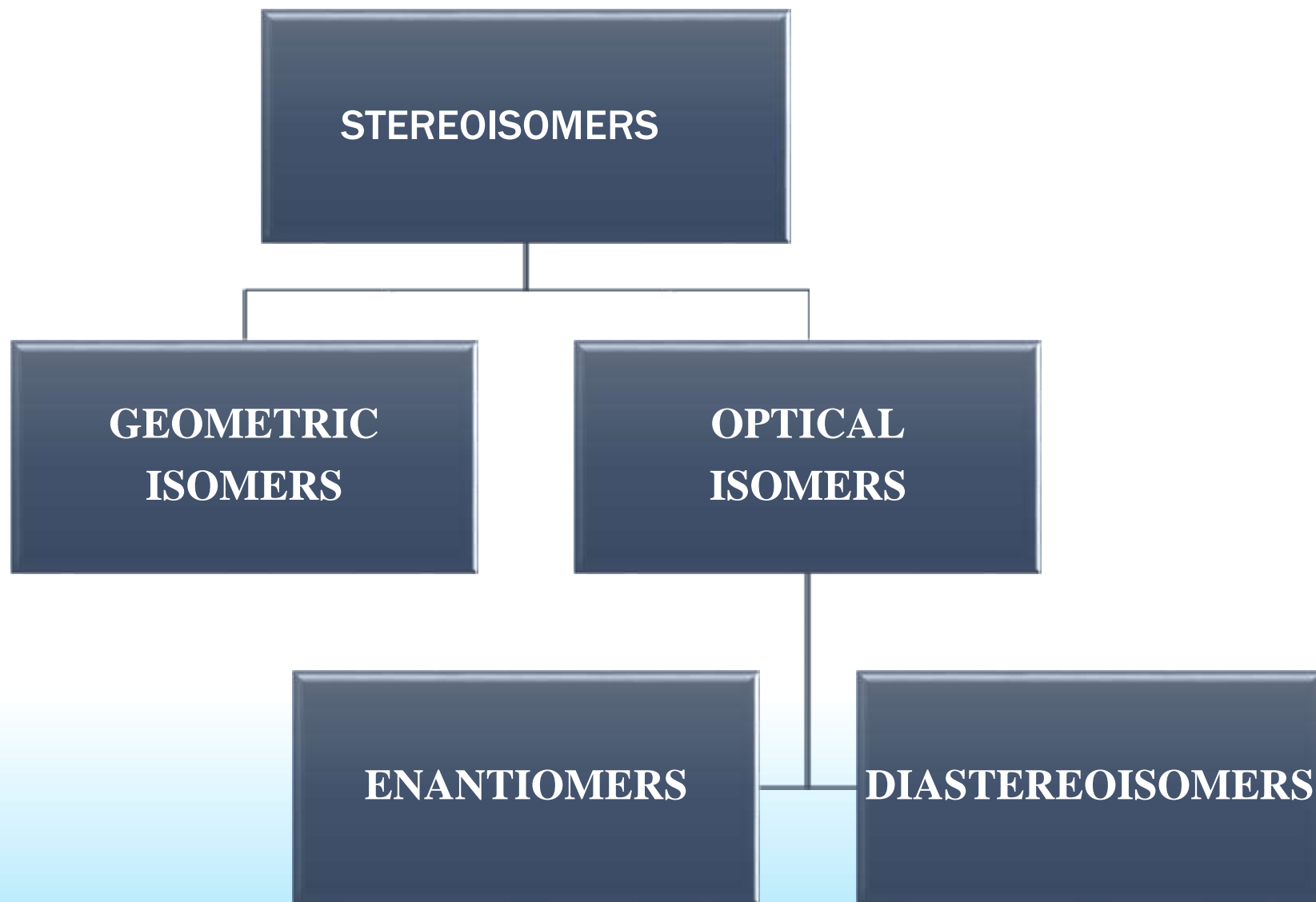


same molecular formula  
same name except for the **prefix**

**stereoisomers**

# STEREISOOMERS

- Stereoisomers are molecules with one or more “chiral” centres that allow the possibility of forms with the **same chemical formula** but **differing spatial arrangements**.



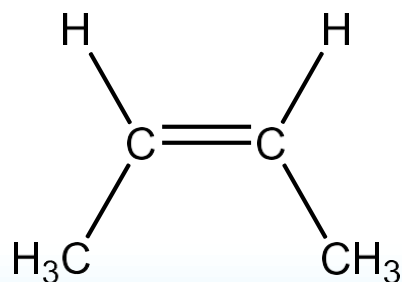
## GEOMETRICAL ISOMERS

THE  $\pi$ -BOND IN AN ALKENE DOES NOT PERMIT ROTATION, THUS ALL OF THE ATOMS ATTACHED DIRECTLY TO THE ALKENE LIE IN A PLANE.

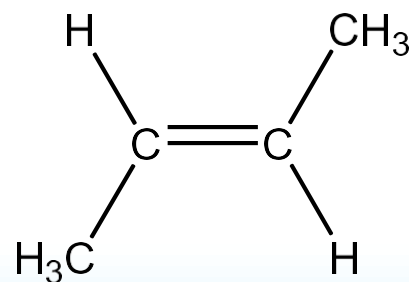
GROUPS ATTACHED TO THE ALKENE COULD BE POSITIONED ON THE SAME SIDE OF THE ALKENE (OR) ON OPPOSITE SIDES OF THE ALKENE. SUCH COMPOUNDS ARE DIFFERENT IN CHEMICAL AND PHYSICAL PROPERTIES AS WELL AS IN THEIR GEOMETRY, AND ARE CALLED GEOMETRICAL ISOMERS.

**Ex:**

In 2-butene the methyl groups can be located on the same side or on the opposite side of the double bond, giving rise to two geometrical isomers.



*cis*-2-butene

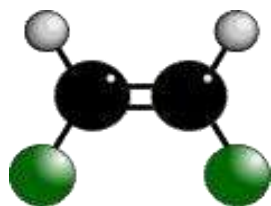


*trans*-2-butene

The isomer with the groups on the same side is called the **Cis isomer**, while the isomer with the groups located on opposite sides is called the **Trans isomer**.

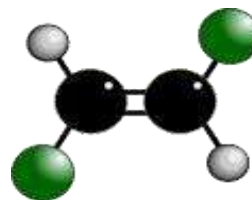
**Trans isomers of compounds are usually more stable than Cis isomers.**

# In alkenes



**CIS**

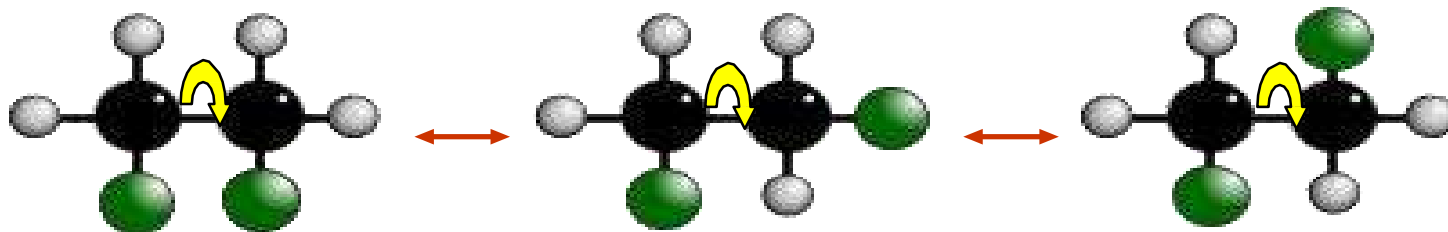
Groups/atoms are on the **SAME SIDE** of the double bond



**TRANS**

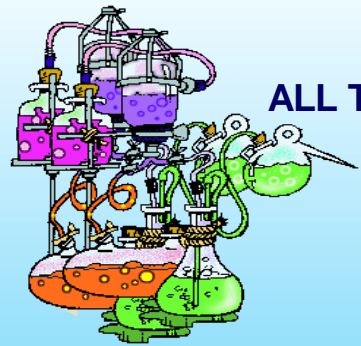
Groups/atoms are on **OPPOSITE SIDES** across the double bond

## RESTRICTED ROTATION OF C=C BONDS



**Single covalent bonds can easily rotate.** What appears to be a different structure is not. It looks like it but, due to the way structures are written out, they are the same.

**ALL THESE STRUCTURES ARE THE SAME BECAUSE C-C BONDS HAVE 'FREE' ROTATION**



GEOMETRIC (CIS AND TRANS) ISOMERS RESULT FROM RESTRICTION ROTATION.

### COMPOUNDS WITH DOUBLE BONDS:

*Cis* isomer – have same substituents on the same side of the double bond (*Z-zusammen (together)* with more complex molecules having high priority groups on the same side).

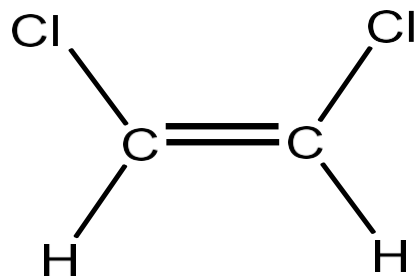
*Trans* isomer – have the same substituents on the opposite side of the double bond (*E - entgegen (opposite)* with more complex molecules having high priority groups on opposite sides).

### Compounds with bonds in a ring:

*Cis* isomer – have the same substituents on the same side of the ring.

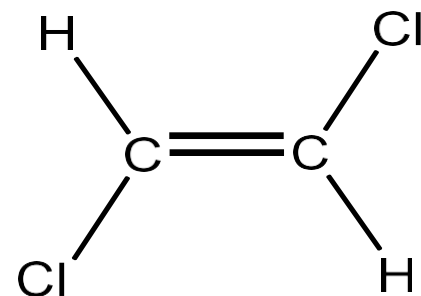
*Trans* isomer - have the same substituents on the opposite side of the ring.

# CIS-TRANS (GEOMETRIC) ISOMERISM IN ALKENES



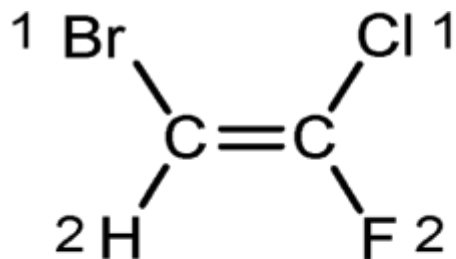
*cis*-1,2-dichloroethene

(*Z*)-1,2-dichloroethene



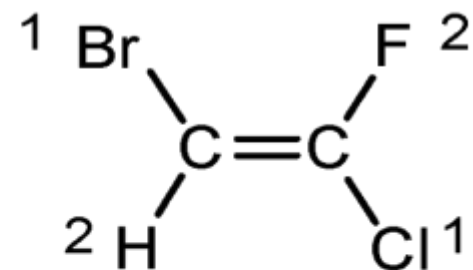
*trans*-1,2-dichloroethene

(*E*)-1,2-dichloroethene



groups with higher priority  
on the same side

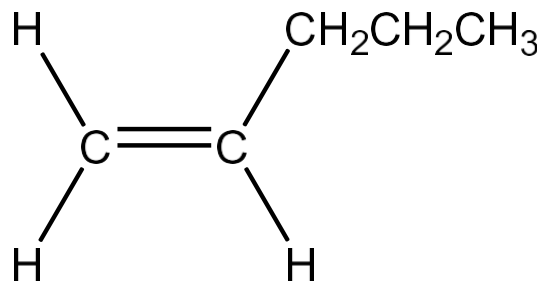
**Z-isomer**



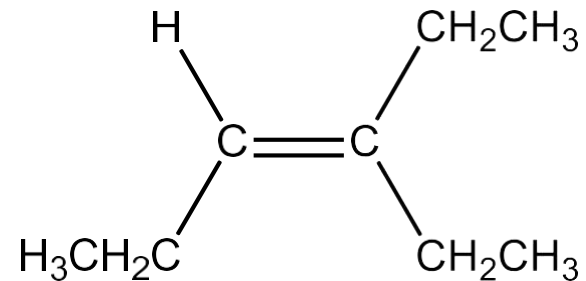
groups with higher priority  
on opposite side

**E-isomer**

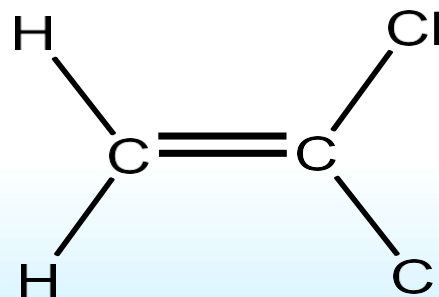
\*If one of the two carbon atoms of the double bond has **two identical substituents**, there are **no cis-trans isomers** for that molecule



1-pentene



3-ethyl-3-hexene

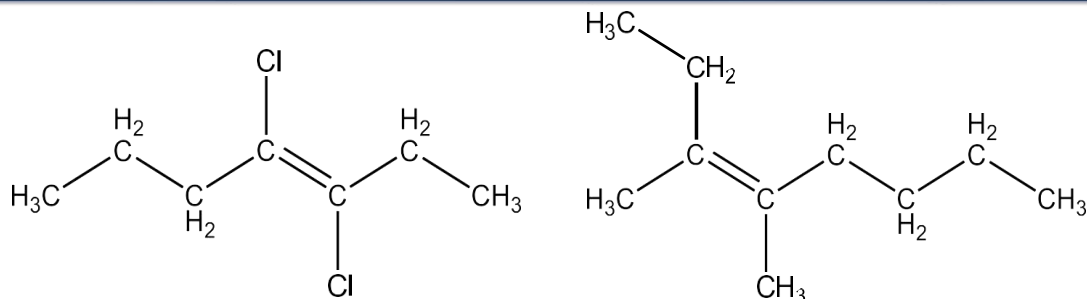


1,1-dichloroethene



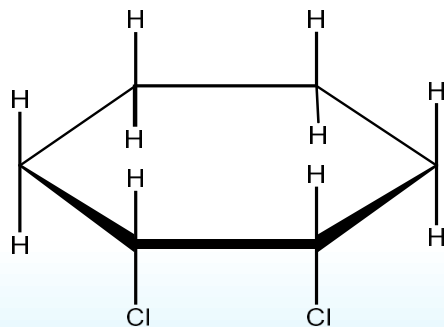
# IDENTIFYING CIS AND TRANS ISOMERS OF ALKENES

Example: Name the following geometric isomers.

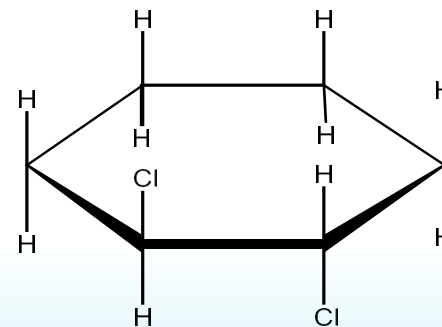


*trans*-3,4-dichloro-3-heptene *cis*-3,4-dimethyl-3-octene

Cis-trans isomers are molecules having the same arrangement of atoms but differ in the spatial orientation of their substituents.



*cis*-1,2-  
dichlorocyclohexane

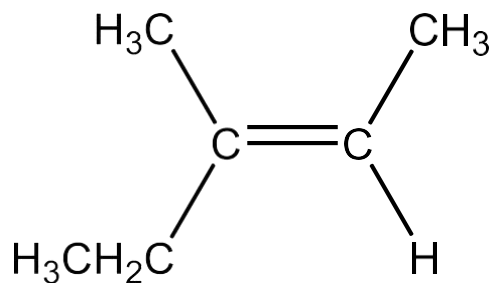


*trans*-1,2-  
dichlorocyclohexane

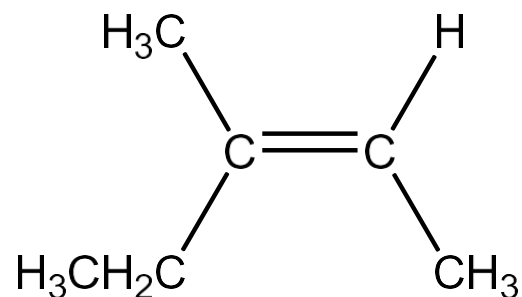
Example:3

Determine whether each of the following molecules can exist as cis-trans isomers:

(1) 3-methyl-2-pentene



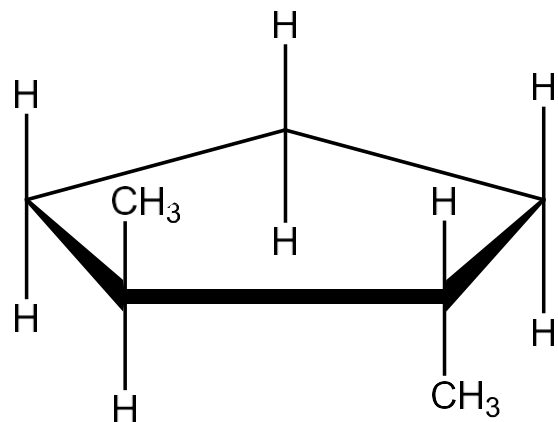
*cis*-3-methyl-2-pentene



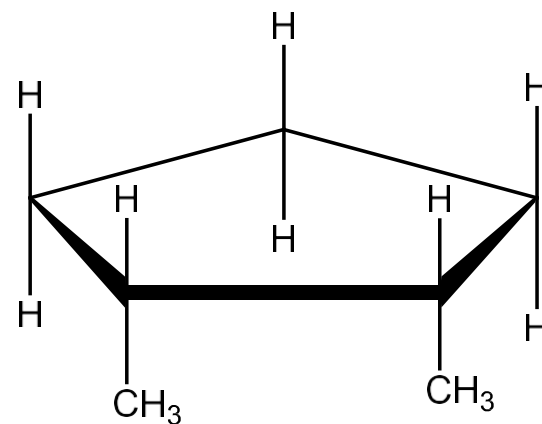
*trans*-3-methyl-2-pentene

## Example:3

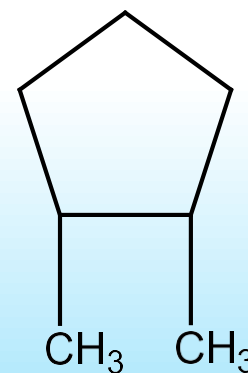
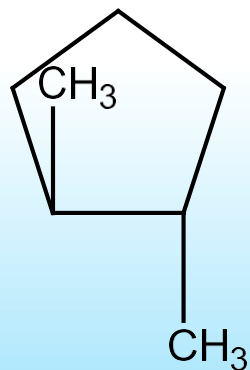
Determine whether the following substituted cycloalkanes are *cis* or *trans* isomers.



*trans*-1,2-dimethylcyclopentane



*cis*-1,2-dimethylcyclopentane



# CHIRALITY

Molecules that can exist as enantiomers are said to be chiral; they are non-superimposable on their mirror images.

Chirality is a necessary and sufficient condition for the existence of enantiomers.

“cheir” - Greek meaning “hand”

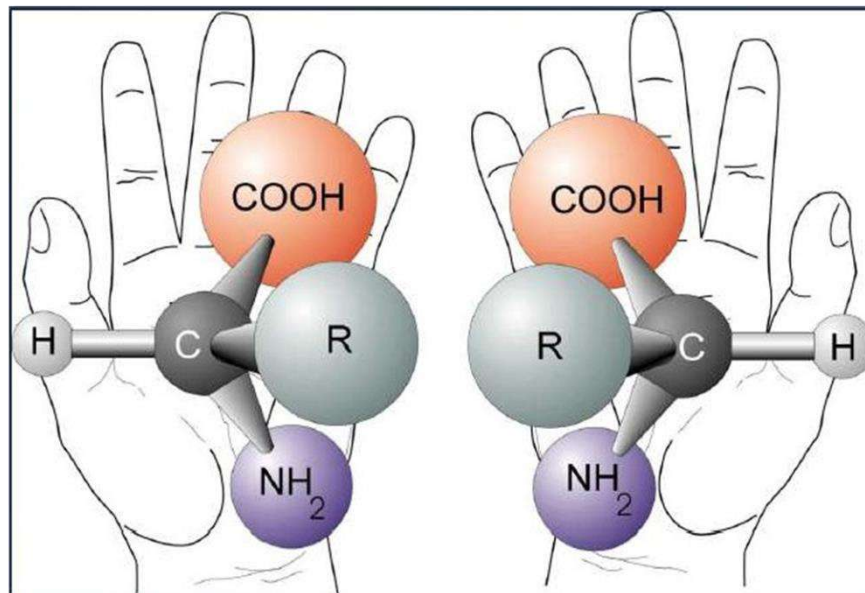
Molecules that are superimposable on their mirror images are said to be achiral.

# CHIRALITY

Which of the following objects are chiral?

- a screw
- a screwdriver
- a golf club
- an ear
- a shoe

CHEIR MEANS “HAND” IN GREEK



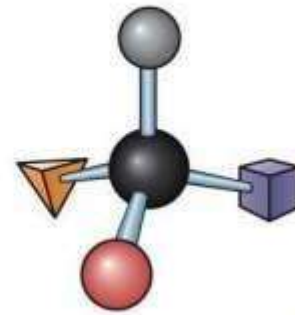
(A)



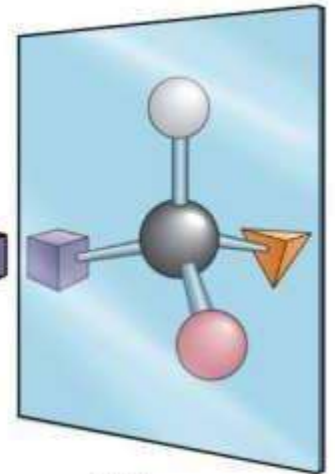
Hand



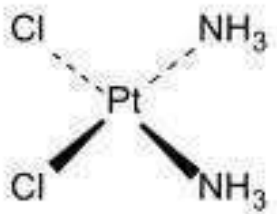
Mirror image



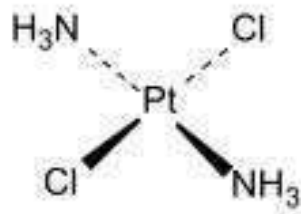
Molecule



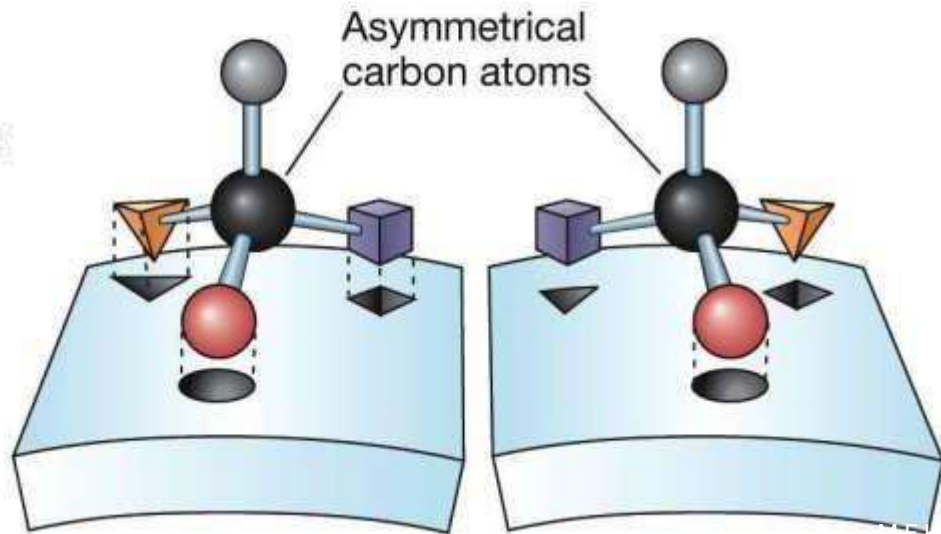
Mirror image



Cisplatin

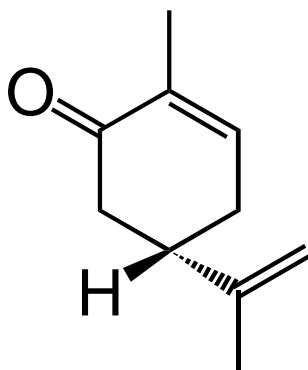


Transplatin



# TETRAHEDRAL STEREOGENIC CENTRES

A carbon atom bonded to four different groups is called a tetrahedral stereogenic centre, asymmetric centre, or chirality centre.

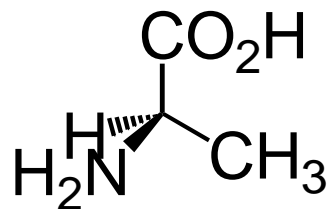
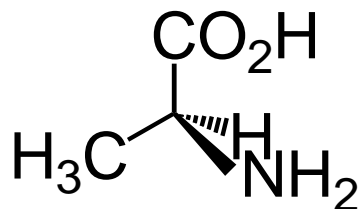
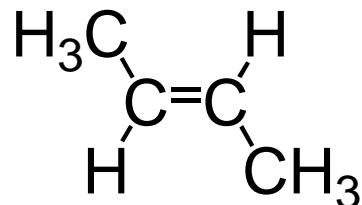
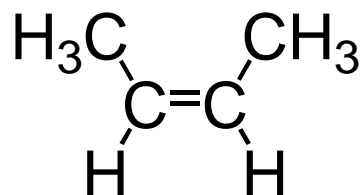


(+)-carvone

(+)-Carvone is responsible for the odour of caraway seed oil.

# STEREOGENIC CENTRES

A centre where a swapping of groups leads to a stereoisomer:

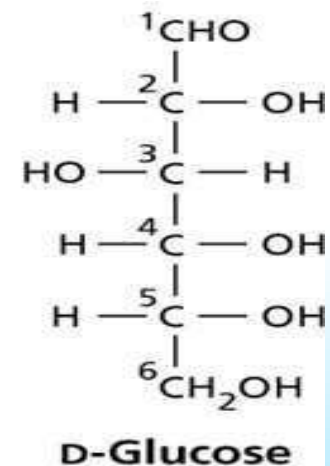
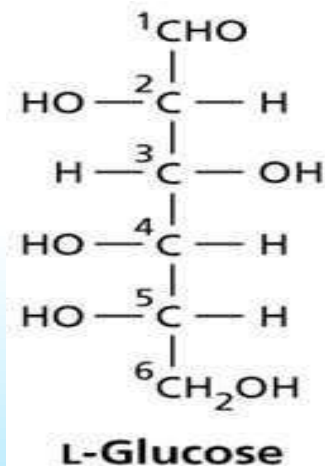
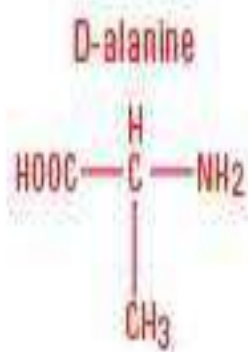
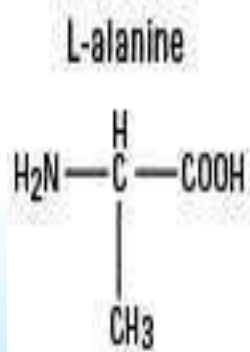


alanine



# ENANTIOMERS

- ✓ Enantiomers are **non-superimposable mirror image** isomers.
- ✓ Enantiomers are related to each other much like a right hand is related to a left hand.
- ✓ Enantiomers are said to be *Chiral*.
- ✓ sometimes the terms right-handed and left-handed are used describe compounds with an asymmetric carbon.



## Characteristic features of enantiomers:

❖ Enantiomers have identical physical properties (bp, mp, density, solubility and refractive index) but there is a difference in direction of rotation of plane polarized light.

Property	(+)-Lactic acid	(-)-Lactic acid
Specific rotation	+2.24°	-2.24°
Melting Point	26°C	26°C

❖ They have identical chemical properties except in chemical reactions with other optically active compounds.

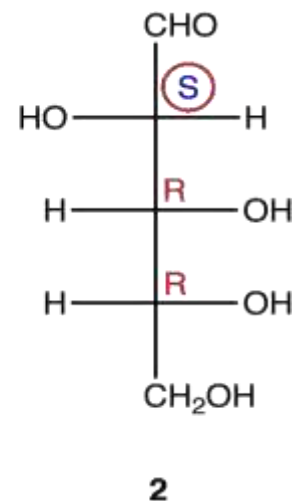
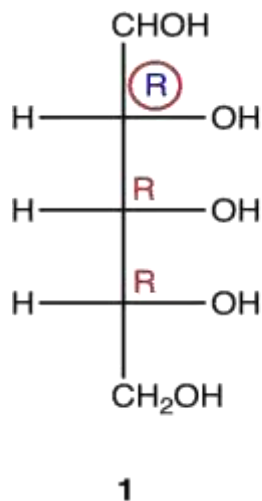
❖ They have different biological properties

E.g. (+)-Dextrose plays an important role in animal metabolism, where as (-)-Dextrose is not metabolized.

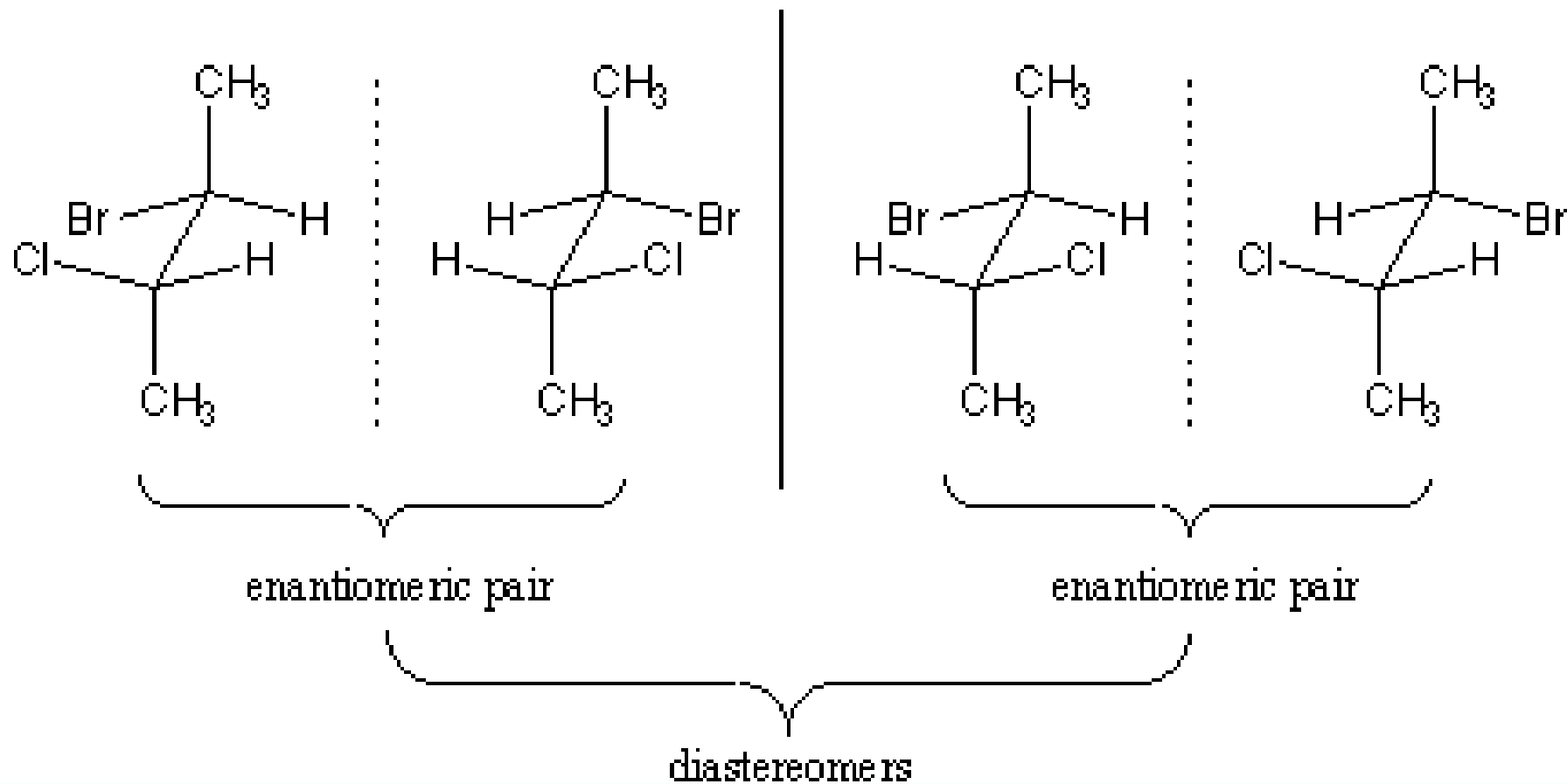
❖ When equal quantities of enantiomers are mixed an optically inactive compound racemic mixture is formed.

# DIASTEREOMERS

Stereomers of a substance that are not mirror images of each other are termed as Diastereomers.

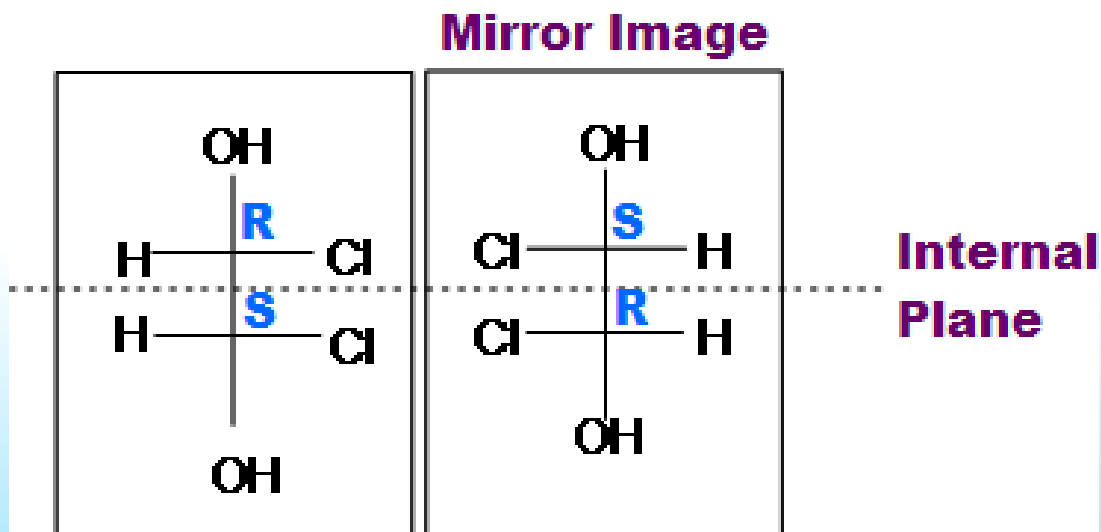


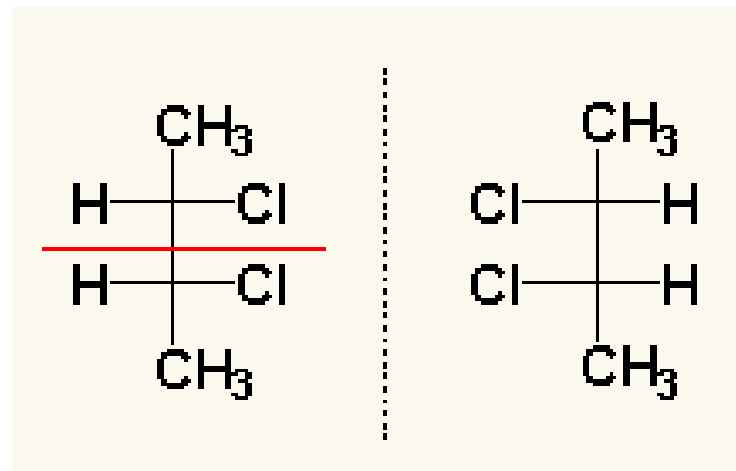
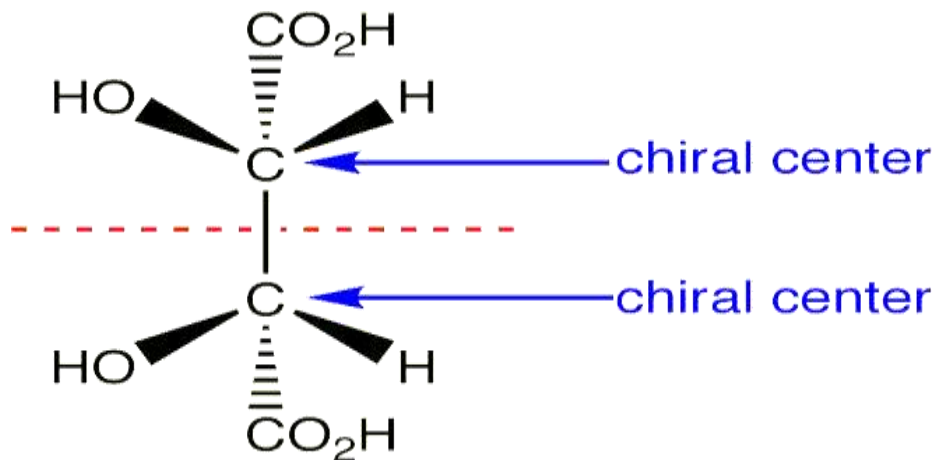
- ❖ They have different physical properties like m.p, b.p, solubility, density and refractive index, etc.
- ❖ Diastereomers have different specific rotation but they may have same or opposite sign of rotation.



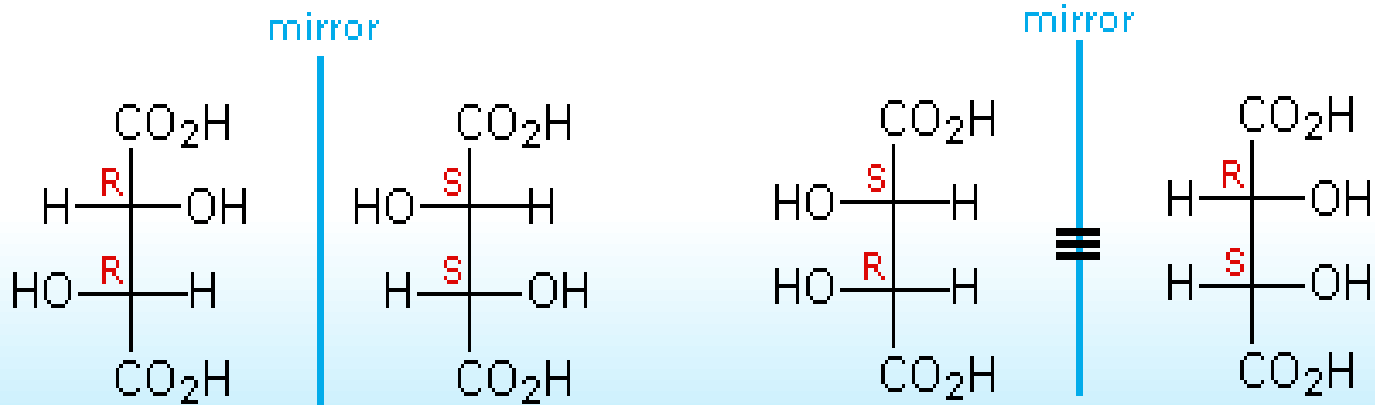
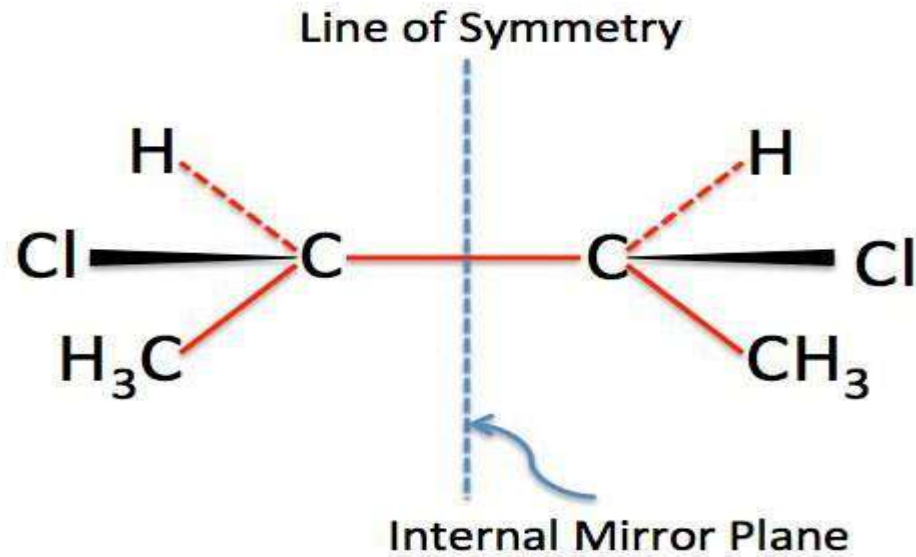
# MESO COMPOUND

- A meso compound is a molecule with multiple stereocenters that is superimposable on its mirror image.
- Meso compounds are **achiral compounds** that has multiple chiral centers.
- Meso compounds are **optically inactive**.
- It has an internal symmetry plane that divides the compound in half.





A meso compound should contain two or more identical substituted stereocenters. Also, it has an internal symmetry plane that divides the compound in half. These two halves reflect each other by the internal mirror. The stereochemistry of stereocenters should "cancel out". What it means here is that when we have an internal plane that splits the compound into two symmetrical sides, the stereochemistry of both left and right side should be opposite to each other, and therefore, result in **optically inactive**.

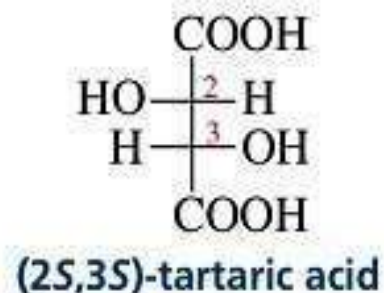
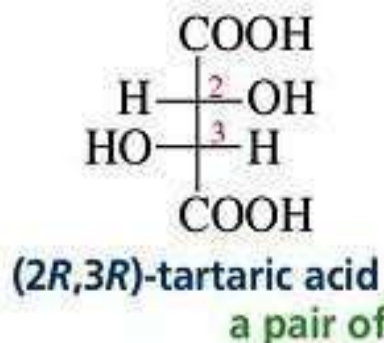
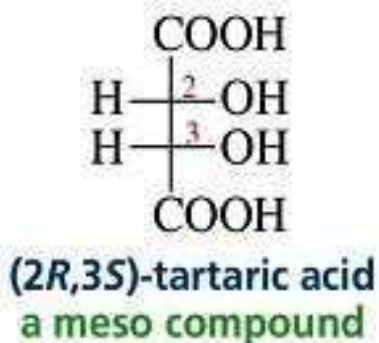


(+)-tartaric acid    (-)-tartaric acid

*meso*-tartaric acid

## RACEMIC MIXTURE

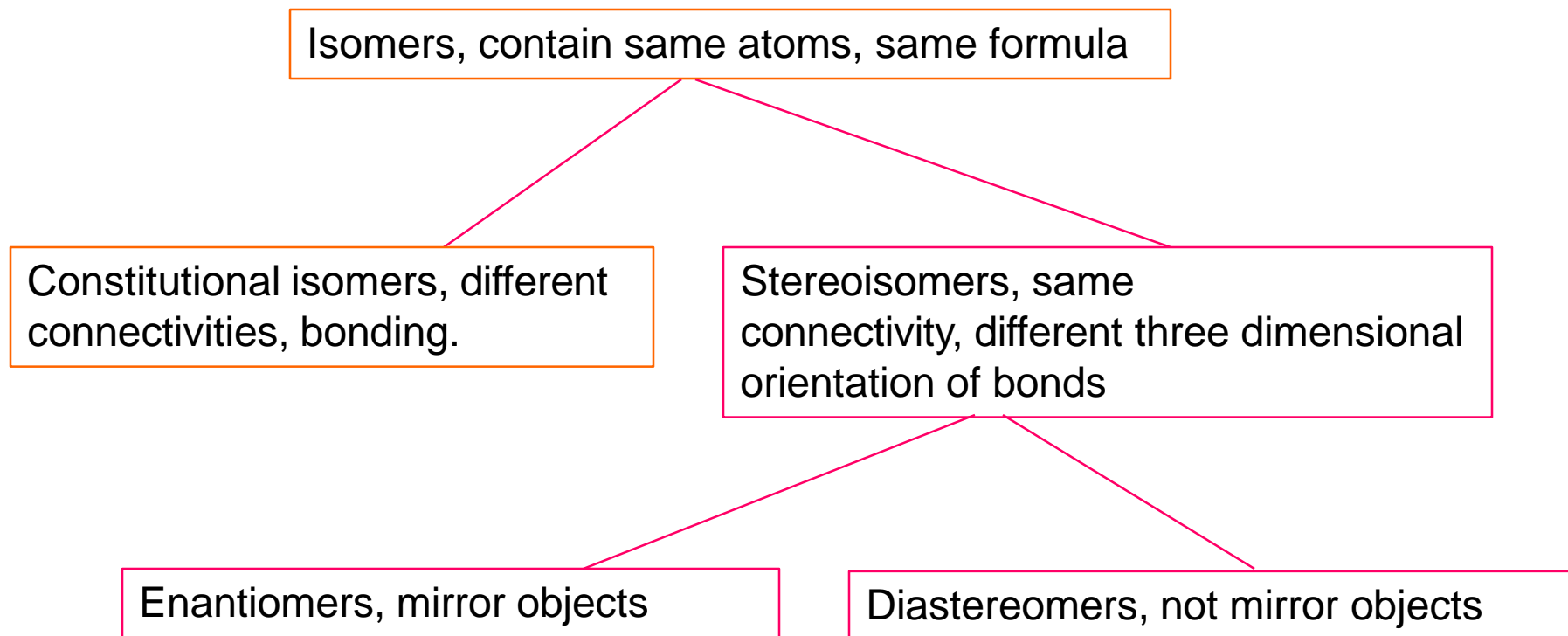
- A mixture having equal amounts of enantiomers is called **racemic mixture** or **racemic modification**.
- A **racemic mixture (or) racemate** is one that has equal amounts of left- and right-handed enantiomers of a chiral molecule. The first known racemic mixture was racemic acid, which Louis Pasteur found to be a mixture of the two enantiomeric isomers of tartaric acid.
- A racemic mixture is denoted by the prefix **(±)-** or **dl-** (for sugars the prefix **DL-** may be used), indicating an equal (1:1) mixture of dextro and levo isomers. Also the prefix symbols ***RS*** and ***SR*** (all in *italic* letters) are used.



Fischer projections of the stereoisomers of tartaric acid

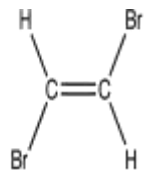
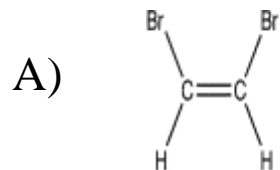


# SUMMARY OF ISOMERISM CONCEPTS

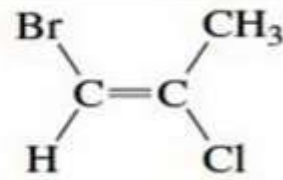
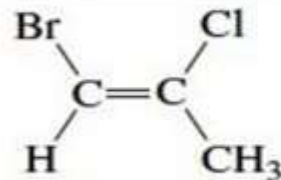


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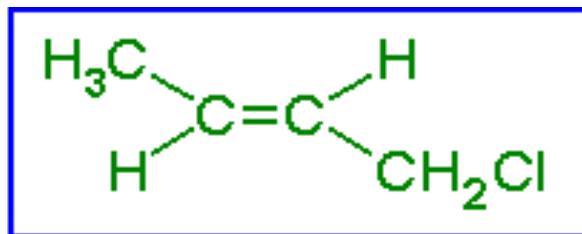
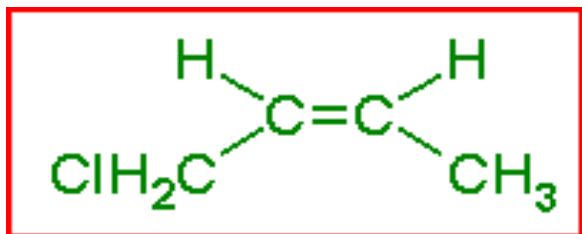
Which isomer is cis isomer and which is trans.....?



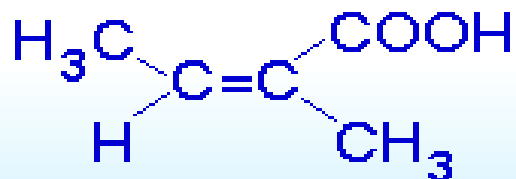
B)



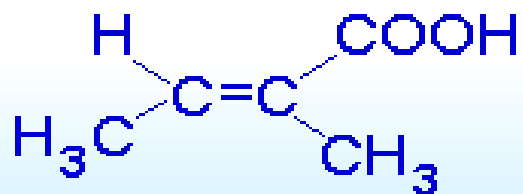
C)



D)



angelic acid



tiglic acid

# R AND S CONFIGURATION

## R Configuration:

- Definition:** If the sequence of priority of the substituents around a stereocenter is clockwise, the configuration is designated as R (from the Latin "rectus," meaning right).
- Representation:** The R configuration is denoted by the label R in square brackets.

## S Configuration:

- Definition:** If the sequence of priority of the substituents around a stereocenter is counterclockwise, the configuration is designated as S (from the Latin "sinister," meaning left).

# Rules for Assigning R and S Configuration:

## Assigning Priority:

Assign priority to the substituents based on the atomic numbers of the atoms directly attached to the stereocenter.

The atom with the highest atomic number gets the highest priority.

## Orienting the Molecule:

Orient the molecule so that the substituent with the lowest priority (usually hydrogen) is pointing away from you.

## Determining Configuration:

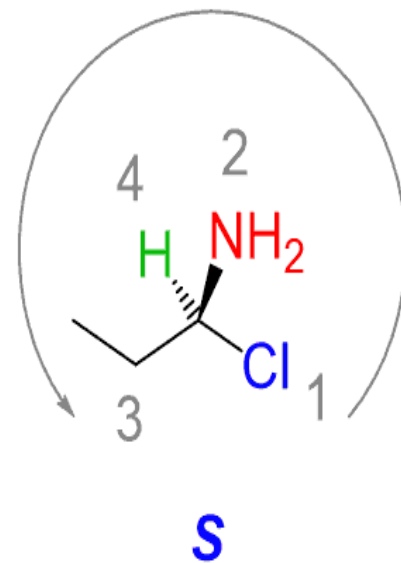
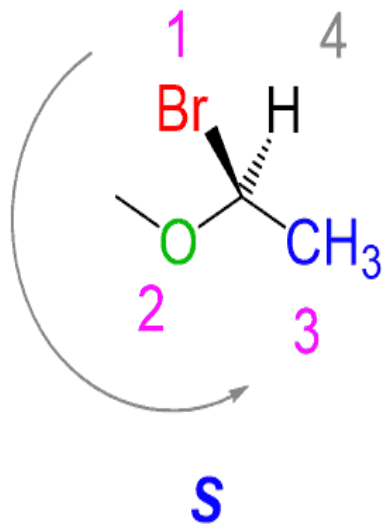
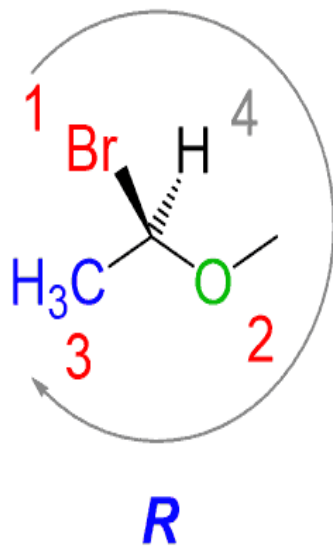
Observe the sequence of the remaining three substituents. If the sequence is clockwise, it is R; if it is counterclockwise, it is S.

**Example:** Consider a stereocenter with substituents A, B, C, and D. If their priorities are assigned as follows:  $A > B > C > D$

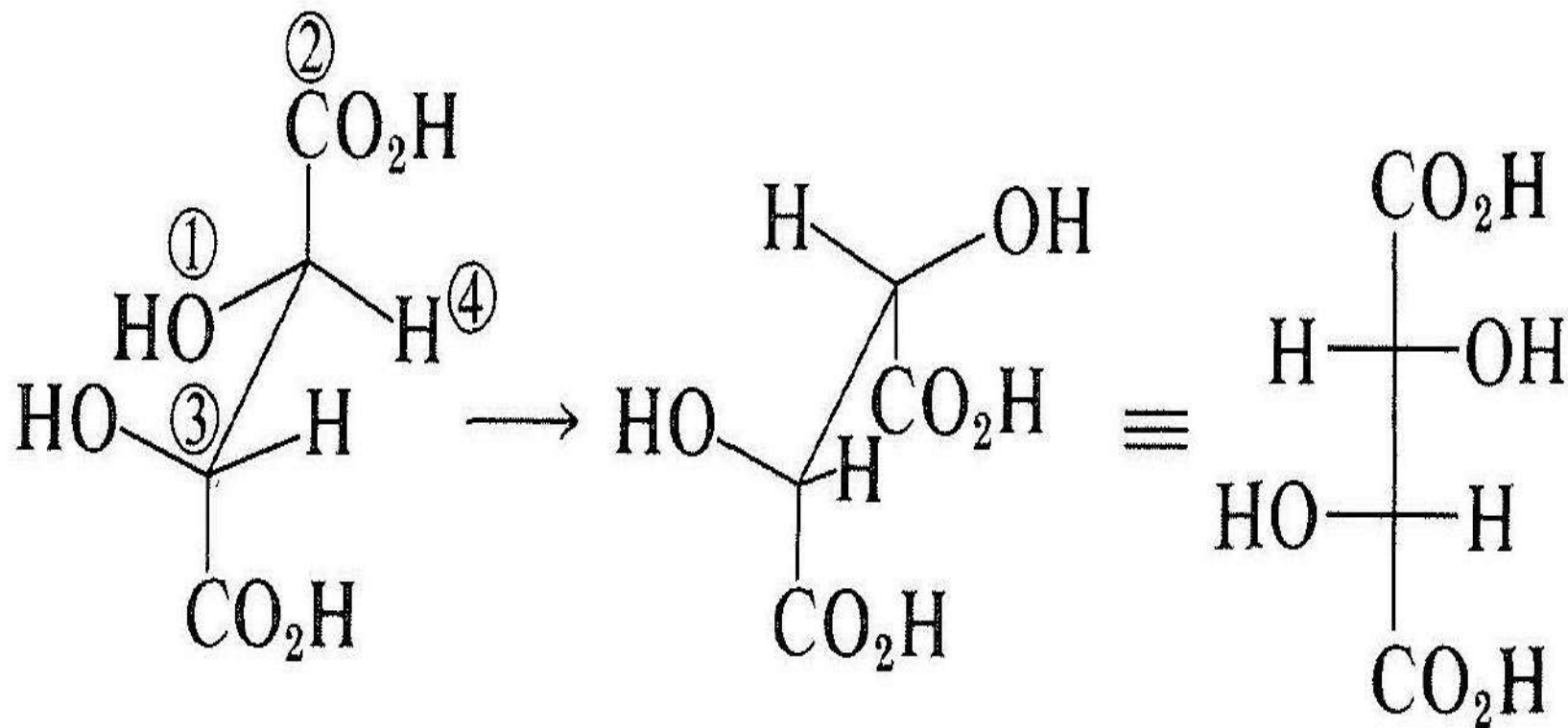
If the sequence ABC is clockwise, the configuration is R. If the sequence ABC is counterclockwise, the configuration is S.

# R AND S CONFIGURATION

The lowest priority (in this case the H) must be pointing back:



*There are, however, different ways to determine the configuration if the lowest priority is not pointing back.*



(2*R*,3*R*)-(+)-tartaric acid  
 or  
 D<sub>s</sub>-(+)-tartaric acid  
 or  
 L<sub>g</sub>-(+)-tartaric acid

# CONFORMATIONAL ISOMERISM

Conformation refers to the different spatial arrangements or shapes that a molecule can adopt by rotating around single bonds. In the case of alkanes, which are saturated hydrocarbons composed only of carbon-carbon single bonds, the most common conformational changes occur due to rotation around these single bonds. The most well-known example is the rotation around the carbon-carbon single bond in ethane.

## Ethane Conformation:

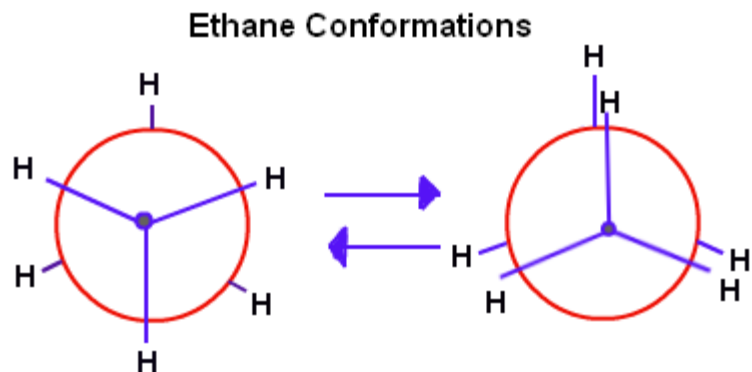
### 1. Eclipsed Conformation:

1. In the eclipsed conformation, the hydrogen atoms of one carbon are directly aligned with the hydrogen atoms of the adjacent carbon.
2. This conformation has higher energy due to steric hindrance, as the electron clouds of the hydrogen atoms come close to each other

# CONFORMATIONAL ISOMERISM

## Staggered Conformation:

In the staggered conformation, the hydrogen atoms of one carbon are positioned in the valleys between the hydrogen atoms of the adjacent carbon.



staggered

$E=0.0$  kcal/mol

eclipsed

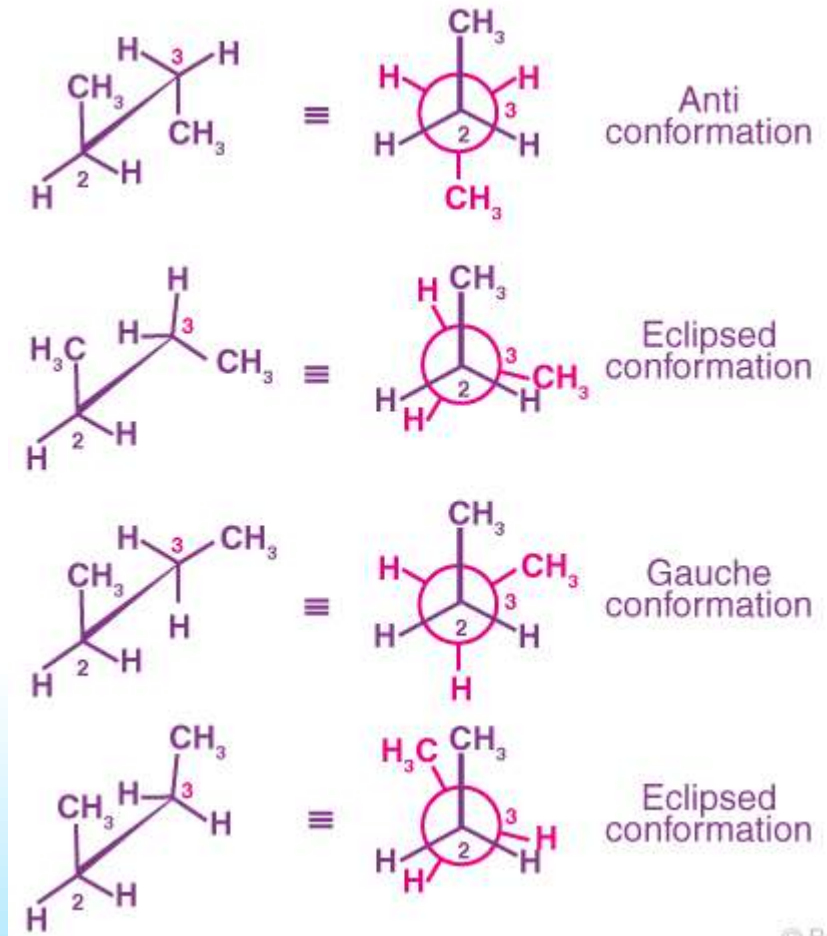
$E=2.9$  kcal/mol

**STAGGERED > Eclipsed**

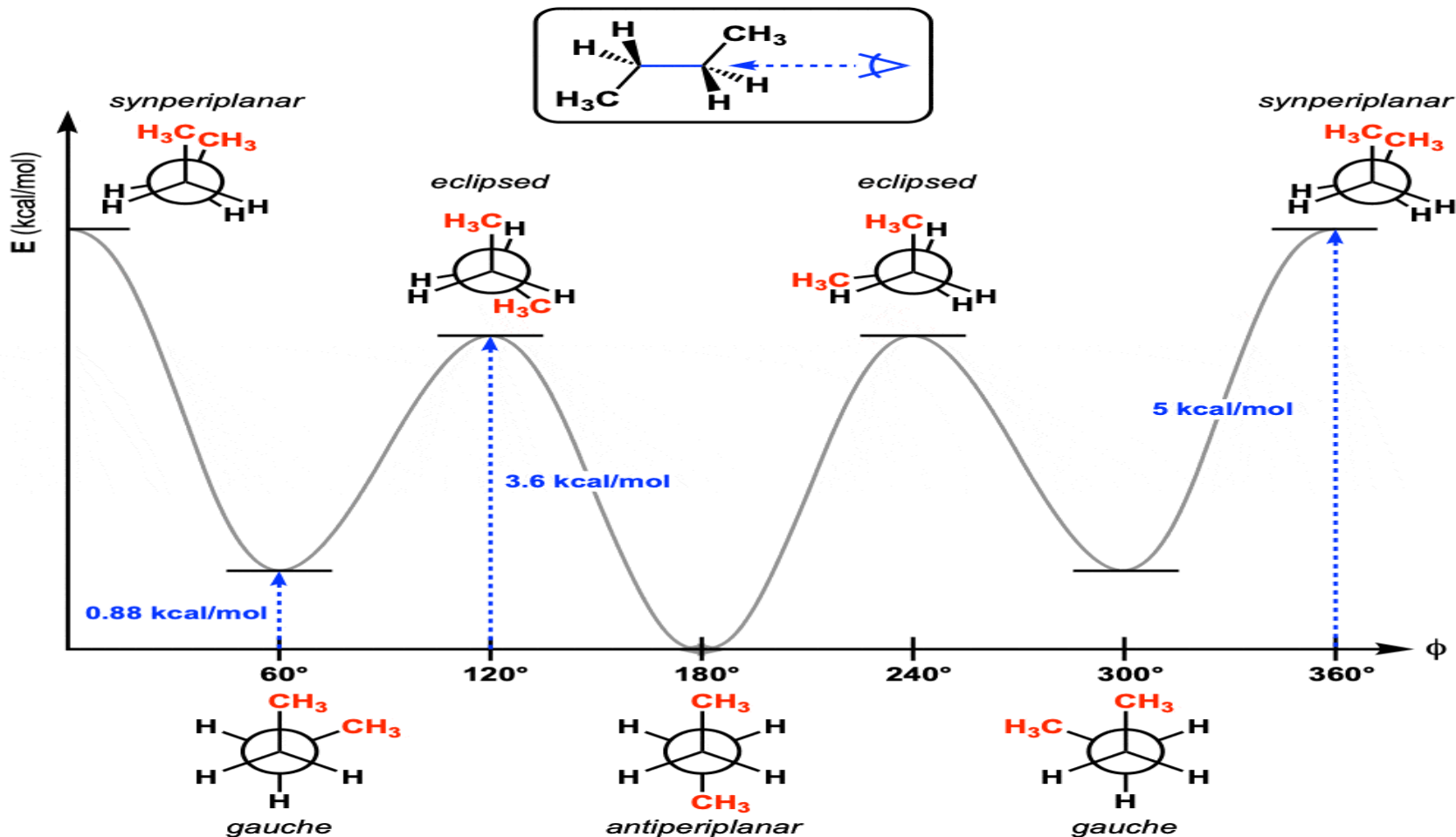


# CONFORMATIONAL ISOMERISM IN BUTANE

Butane is an organic compound which consists of an alkane with 4 carbon atoms.



# STABILITY OF CONFORMATIONS OF BUATNE

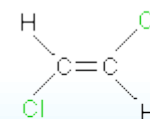
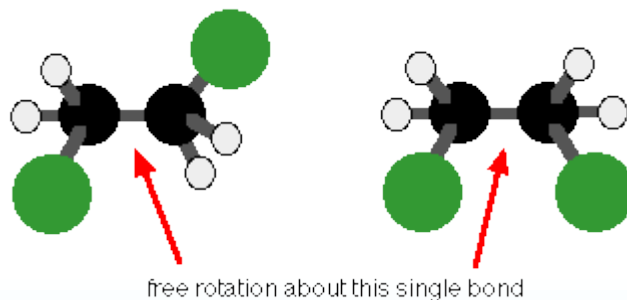


Anti > Skew or Gauche > Eclipsed > Fully eclipsed.

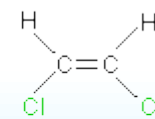
# GEOMETRICAL ISOMERISM

Geometric isomerism (also known as cis-trans isomerism or E-Z isomerism) is a form of stereoisomerism. This page explains what stereoisomers are and how you recognise the possibility of geometric isomers in a molecule.

These isomers occur where you have restricted rotation somewhere in a molecule.



*trans*-1,2-dichloroethene



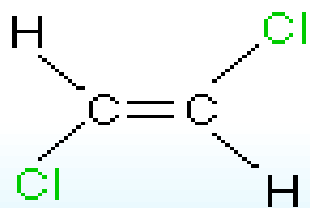
*cis*-1,2-dichloroethene

# GEOMETRICAL ISOMERISM

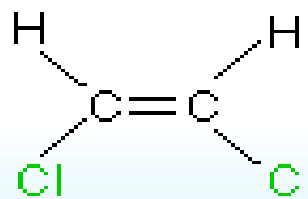
Drawing structural formulae for the last pair of models gives two possible isomers:

1. In one, the two chlorine atoms are locked on opposite sides of the double bond. This is known as the **trans** isomer. (trans : from latin meaning "across" - as in transatlantic).

2. In the other, the two chlorine atoms are locked on the same side of the double bond. This is known as the **cis** isomer. (cis : from latin meaning "on this side")

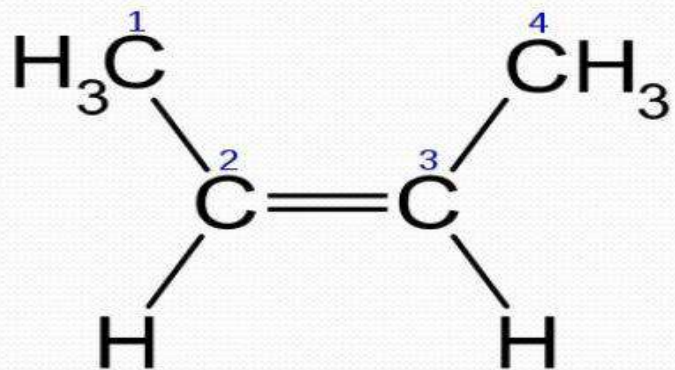


*trans*-1,2-dichloroethene

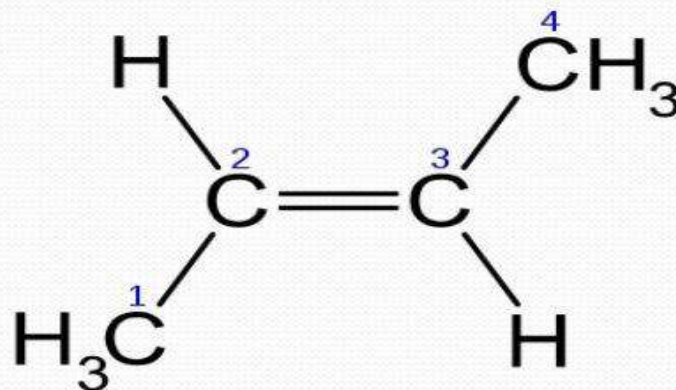


*cis*-1,2-dichloroethene

# Structures



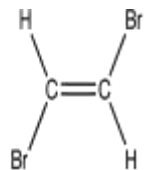
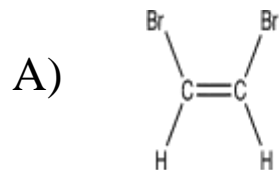
Cis-but-2-ene



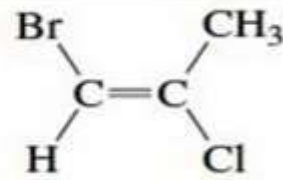
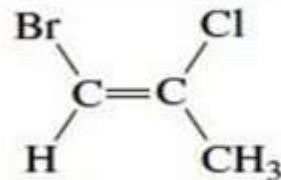
Trans-but-2-ene

## EXCERSIZE:

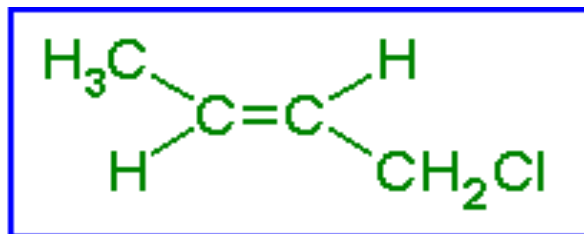
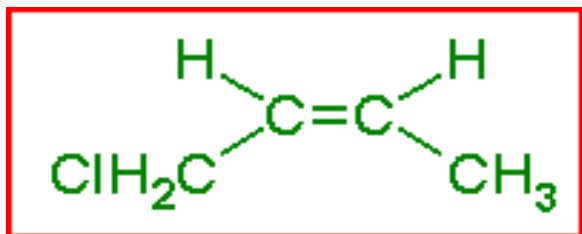
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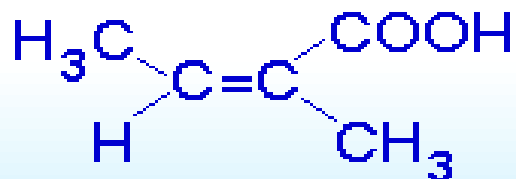
B)



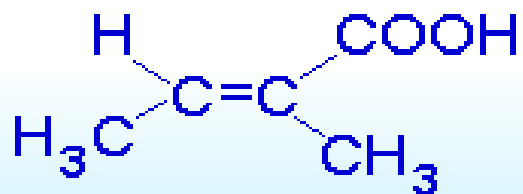
C)




D)



angelic acid



tiglic acid

A decorative card with floral patterns and flowers. The card is white with a colorful floral border in the top-left corner. The text is centered on the card. The background is a textured orange surface with various flowers including purple, yellow, and white ones.

Arise. Awake. And Stop Not  
till the Goal is reached....  
-Swami Vivekananda

THANK YOU