

Stereochemistry

Dr. Ahmed Mutanabbi Abdula

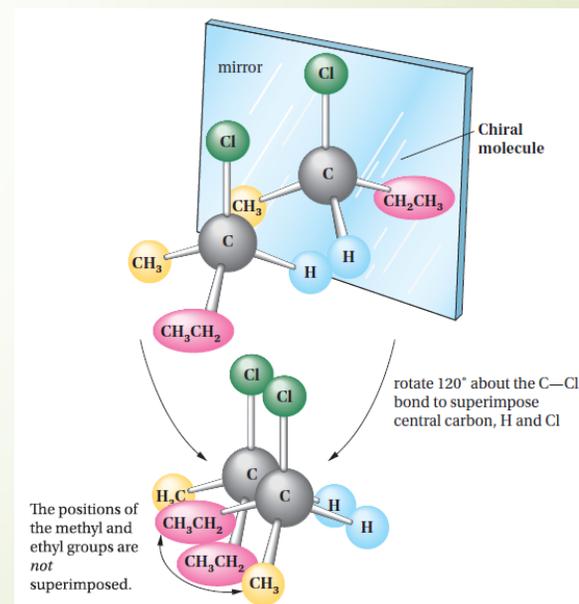
Stereoisomerism

Compounds that have the same order of attachment of the atoms, but different arrangements of the atoms in space.



1

Dr. Ahmed Mutanabbi Abdula



Chirality and Enantiomers

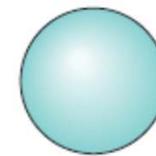
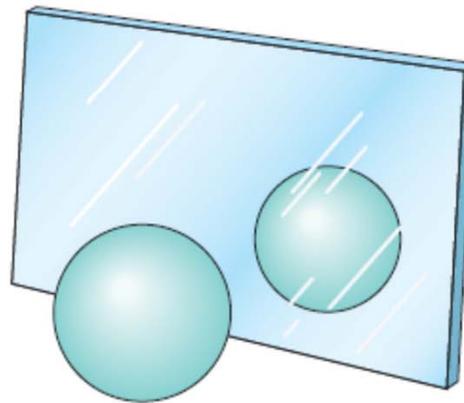
- ▶ **Chiral** molecules possess the property of handedness, whereas
- ▶ **achiral** molecules do not.
- ▶ *The mirror image of a chiral molecule cannot be superimposed on the molecule itself.*
- ▶ *The mirror image of an achiral molecule, however, is identical to or superimposable on the molecule itself.*

The mirror image of a left hand is not a left hand, but a right hand.



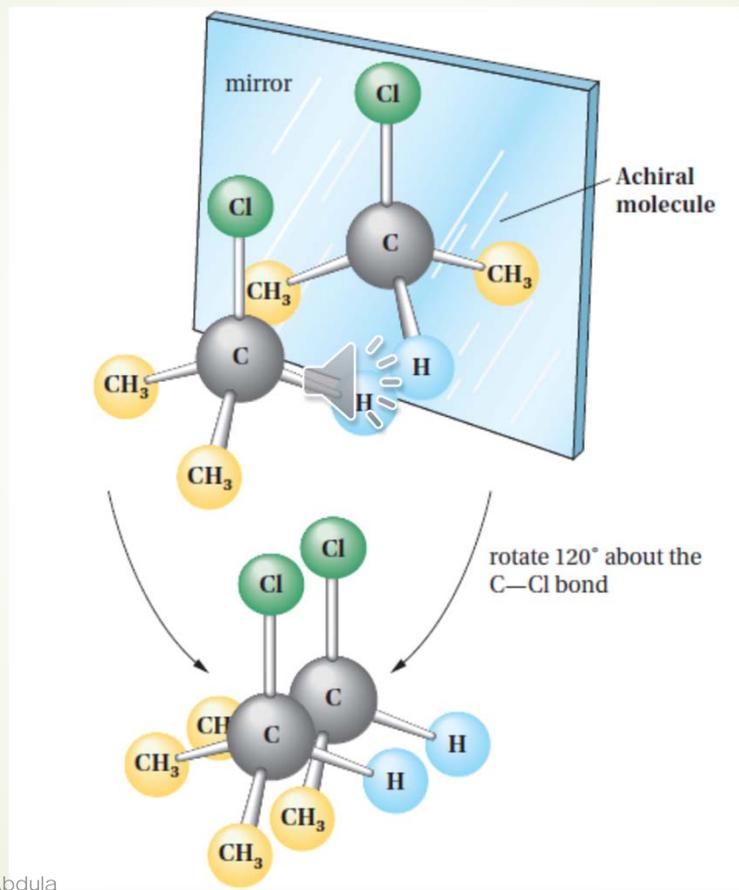
Chiral object

The mirror image of a ball is identical with the object itself.



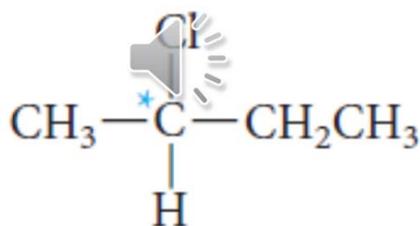
Achiral object

Model of 2-chloropropane and its mirror image. The mirror image is superimposable on the original molecule.



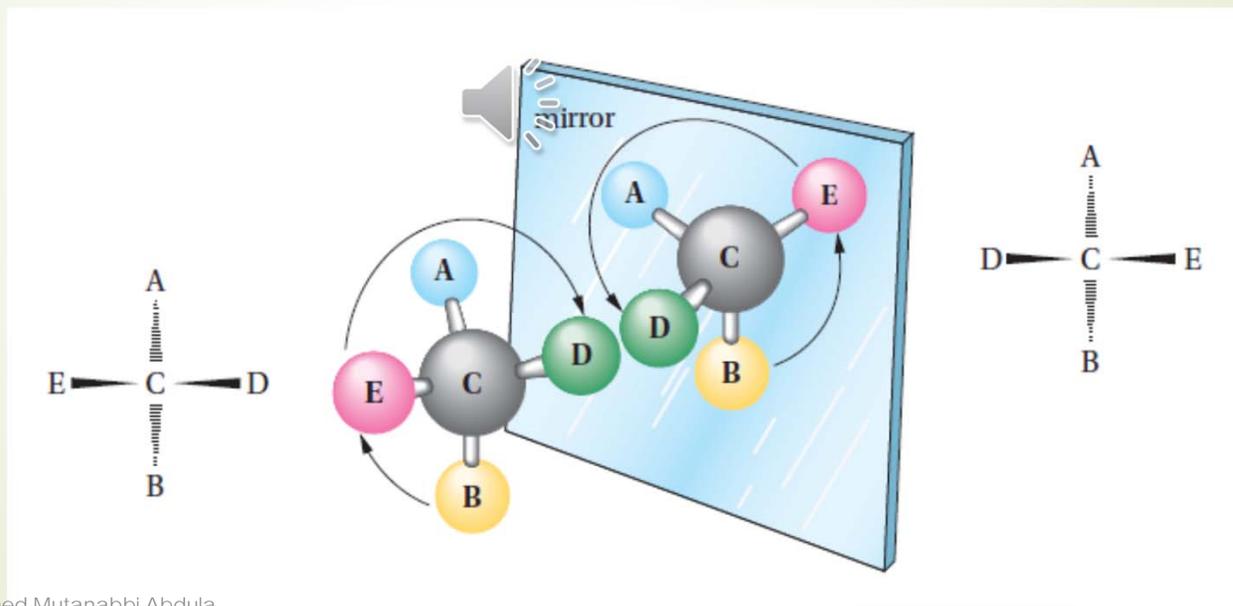
Stereogenic Centers; the Stereogenic Carbon Atom

- Carbon atom with four different groups attached to it.

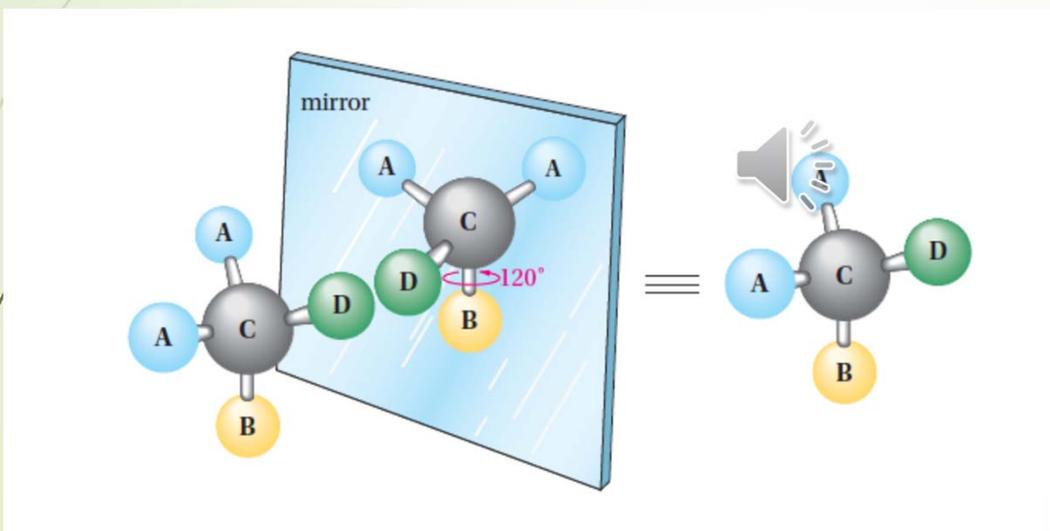


This type of carbon is also called a stereogenic center because it gives rise to stereoisomers.

- ▶ Chiral Molecules have carbon atom with four different groups.
- ▶ Molecules have carbon atom with four different groups are nonsuperimposable mirror images (enantiomers)



When all four of the groups attached to the central carbon atom are *not* different from one another, The molecule and its mirror image are now *identical*, and the molecule is achiral.



Notice that the molecule has a plane of symmetry. This plane passes through atoms B, C, and D and bisects the ACA angle.

On the other hand, the chiral molecule does *not* have a symmetry plane.

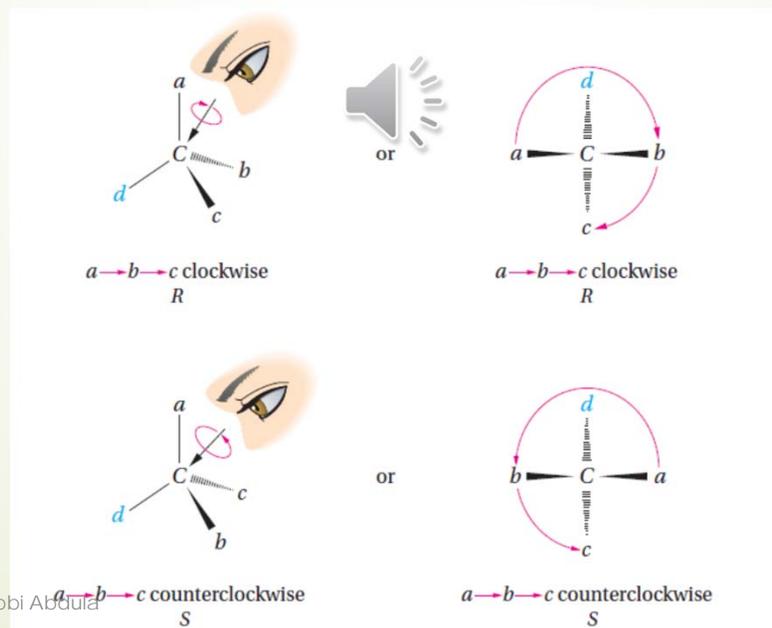
Configuration and the R-S Convention

9

- ▶ Enantiomers differ in the arrangement of the groups attached to the stereogenic center. This arrangement of groups is called the configuration of the stereogenic center.
- ▶ A convention for specify the configuration of stereogenic center is known as the R-S or Cahn–Ingold–Prelog* system.

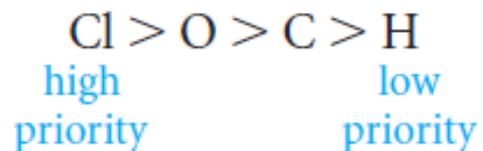
Cahn–Ingold–Prelog* system

The four groups attached to the stereogenic center are placed in a priority order $a : b : c : d$. The stereogenic center is then observed *from the side opposite the lowest priority group, d*. If the remaining three groups ($a : b : c$) form a clockwise array, the configuration is designated *R* (from the Latin *rectus*, right). If they form a *counterclockwise* array, the configuration is designated as *S* (from the Latin *sinister*, left).



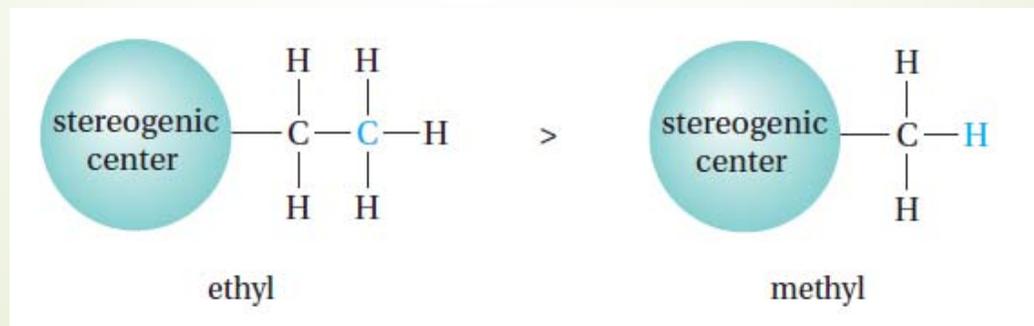
Cahn-Ingold-Prelog* system

- The priority order of the four groups is set in the following way:
- *Rule 1*
- The atoms directly attached to the stereogenic center are ranked according to *atomic number*: the higher the atomic number, the higher the priority



Cahn-Ingold-Prelog* system

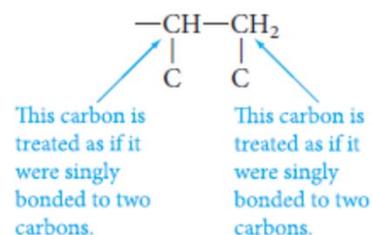
- ▶ *Rule 2*
- ▶ If a decision cannot be reached with rule 1 (that is, if two or more of the directly attached atoms are the same), work outward from the stereogenic center until a decision is reached. For example, the ethyl group has a higher priority than the methyl group, because at the first point of difference, working outward from the stereogenic center, we come to a *carbon* (higher priority) in the ethyl group and a *hydrogen* (lower priority) in the methyl group.



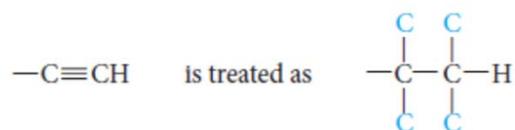
Cahn-Ingold-Prelog* system

Rule 3

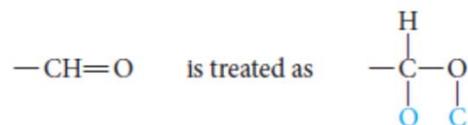
Multiple bonds are treated as if they were an equal number of single bonds. For example, the vinyl group $-\text{CH}=\text{CH}_2$ is counted as



Similarly,

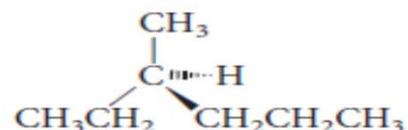


and



EXAMPLE

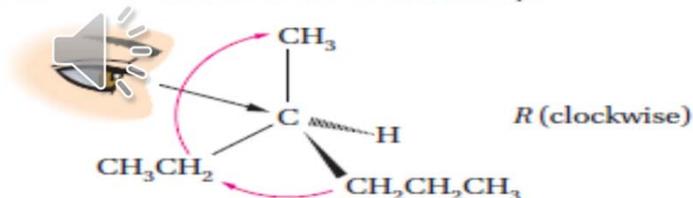
Assign the configuration (*R* or *S*) to the following enantiomer of 3-methyl-hexane (see Example 5.2).



Solution First assign the priority order to the four different groups attached to the stereogenic center.

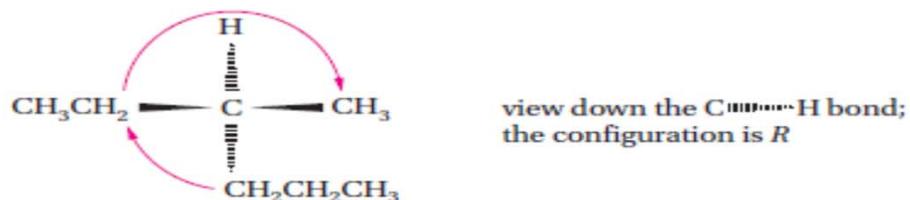


Now view the molecule *from the side opposite the lowest-priority group* ($-\text{H}$) and determine whether the remaining three groups, from high to low priority, form a clockwise (*R*) or counterclockwise (*S*) array.



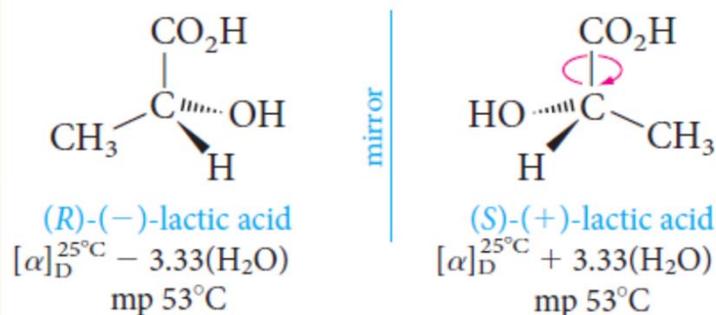
We write the name (*R*)-3-methylhexane.

If we view the other representation of this molecule shown in Example 5.2, we come to the same conclusion.



Properties of Enantiomers

- Enantiomers have identical achiral properties, such as melting point, boiling point, density, and various types of spectra. Their solubilities in an ordinary, achiral solvent are also identical. However, enantiomers have different chiral properties, one of which is the direction in which they rotate plane-polarized light (clockwise or counterclockwise). Although enantiomers rotate plane-polarized light in opposite directions, they have specific rotations of the same magnitude (but with opposite signs), because the *number of degrees* is not a chiral property.

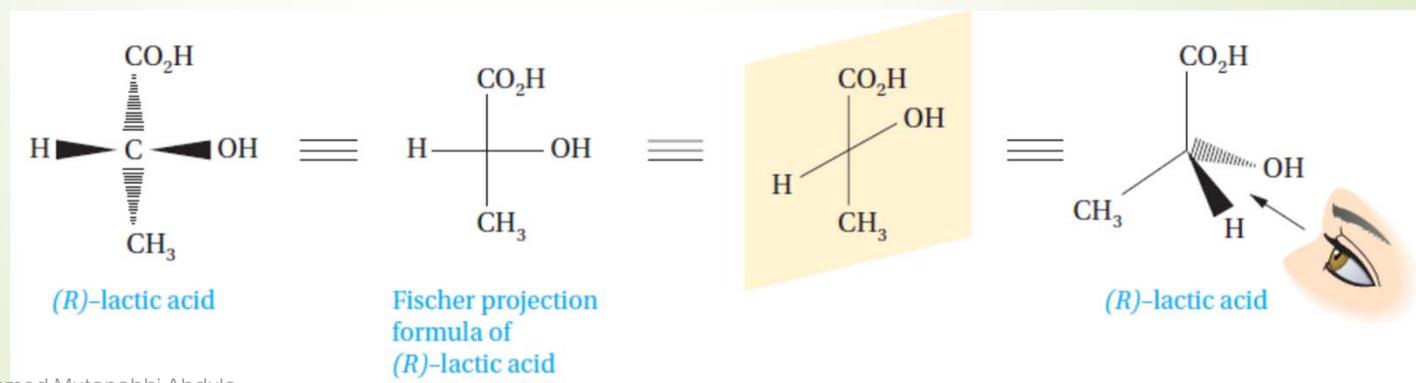


Dr. Ahmed Mutanabbi Abdula

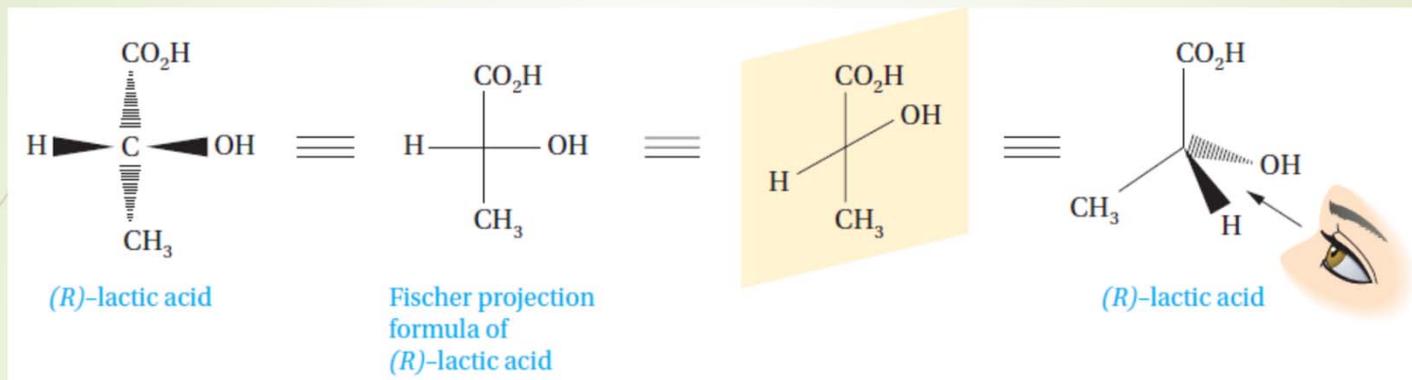
Enantiomers differ in many types of biological activity. One enantiomer may be a drug, whereas its enantiomer may be ineffective. For example, only (2)-adrenaline is a cardiac stimulant; (1)-adrenaline is ineffective.

Fischer Projection Formulas

- ▶ A Fischer projection is a type of two-dimensional formula of a molecule used to represent the three-dimensional configurations of stereogenic centers.
- ▶ Consider the formula for (R)-lactic acid, to the left of the mirror. If we project that three-dimensional formula onto a plane, we obtain the flattened Fischer projection formula.



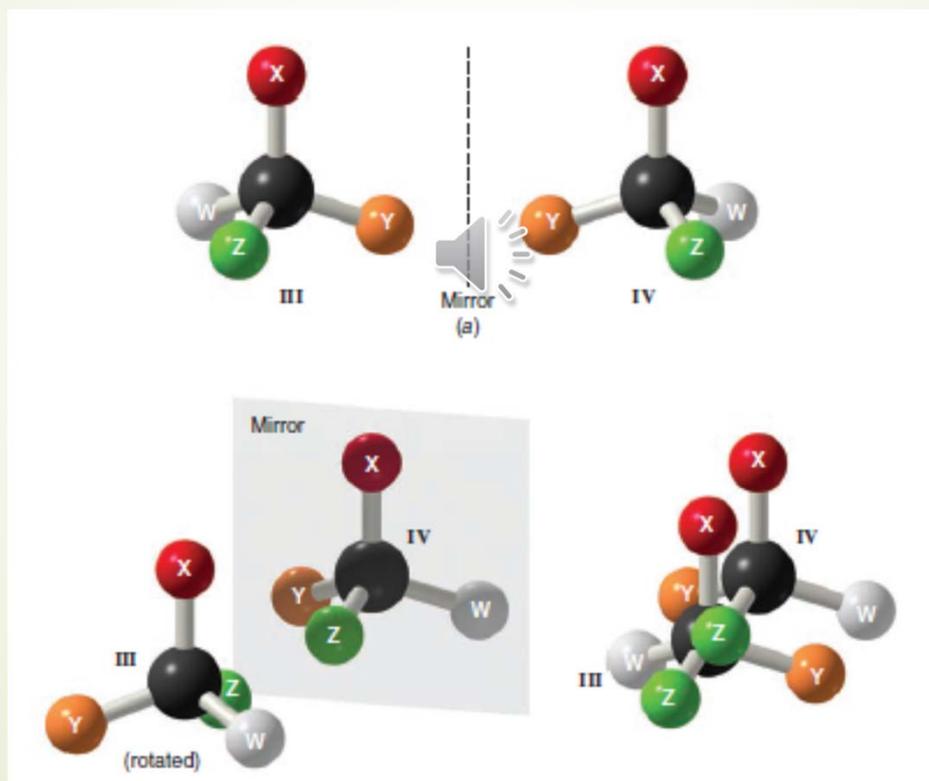
Fischer Projection Formulas



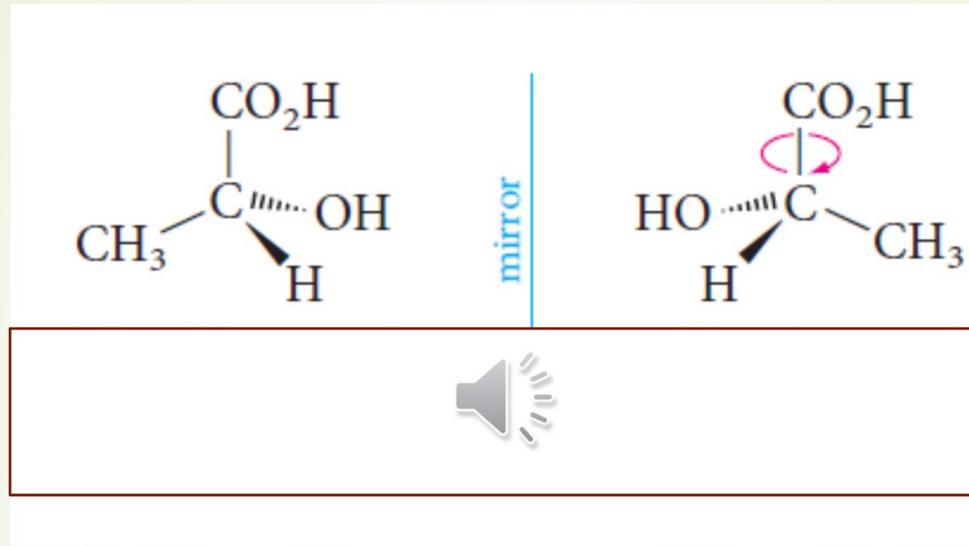
- The C for the stereogenic carbon atom is omitted and is represented simply as the crossing point of the horizontal and vertical lines.
- Horizontal lines connect the stereogenic center to groups that project *above* the plane of the page, *toward* the viewer; vertical lines lead to groups that project *below* the plane of the page, *away* from the viewer.

Enantiomers

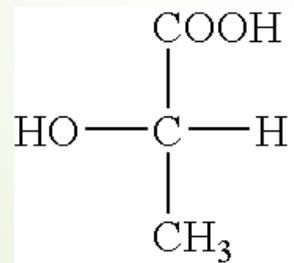
Enantiomers are stereoisomers whose molecules are nonsuperposable mirror images of each other.



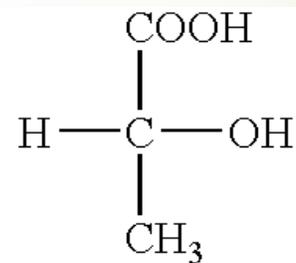
Enantiomers



2



L(+)-lactic acid



D(-)-lactic acid

Enantiomers

Enantiomers have identical achiral properties, such as melting point, boiling point, density, and various types of spectra. Their solubilities in an ordinary, achiral solvent are also identical.

Enantiomers have different chiral properties, one of which is the direction in which they rotate plane-polarized light (clockwise or counterclockwise).

Although enantiomers rotate plane-polarized light in opposite directions, they have specific rotations of the same magnitude (but with opposite signs), because the *number of degrees* is not a chiral property. Only the *direction* of rotation is a chiral property.

Diastereomers

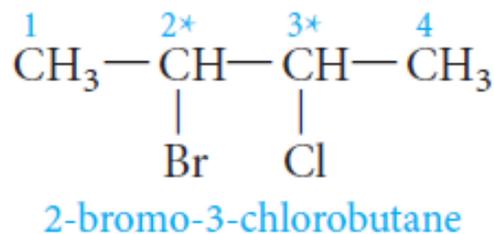


Compounds with More Than One Stereogenic Center

Solved Problem: Draw the Fischer projection formula for all the possible stereoisomers of 2-bromo-3-chlorobutane. Label pairs of enantiomers, diastereomers. Tell which isomers, if separated from all other stereoisomers, will be optically active.

1

Key



Diastereomers

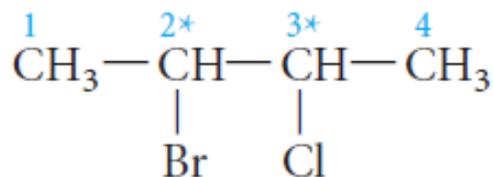


Compounds with More Than One Stereogenic Center

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2

Key



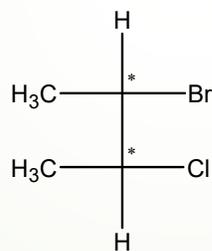
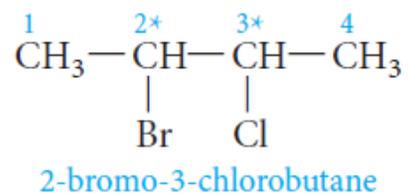
2-bromo-3-chlorobutane

$$\begin{aligned} \text{no. of stereoisomers} &= 2^n \\ &2^2 = 4 \end{aligned}$$

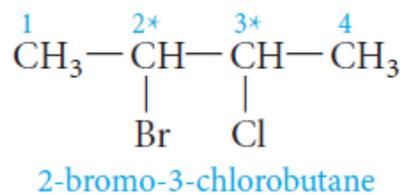
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Compounds with More Than One Stereogenic Center

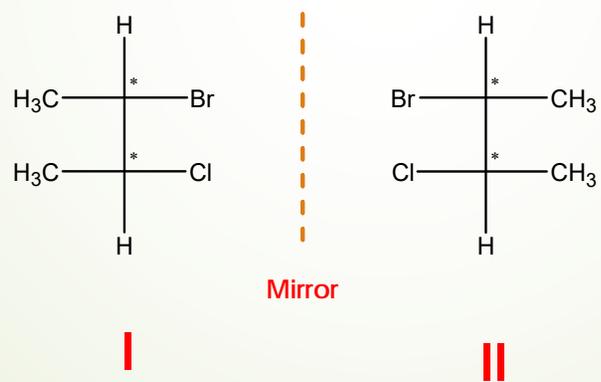
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Compounds with More Than One Stereogenic Center

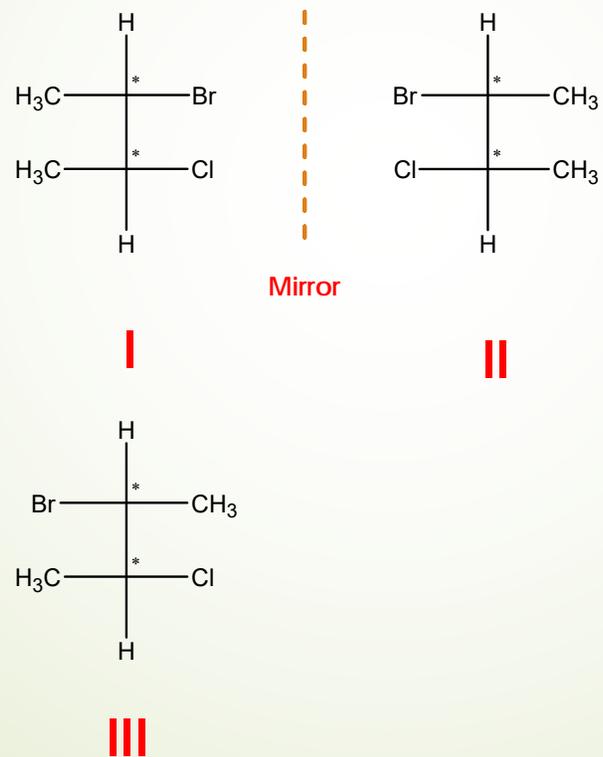
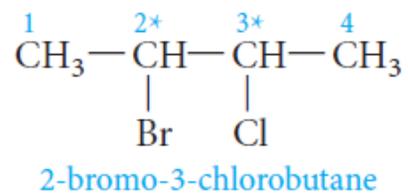


Key



Compounds with More Than One Stereogenic Center

Key

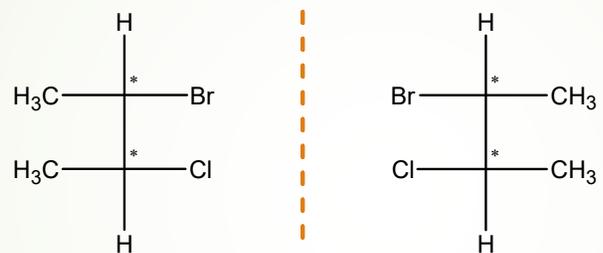
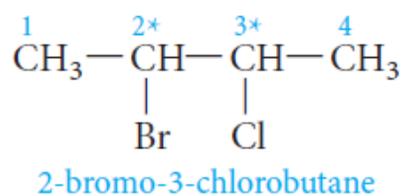


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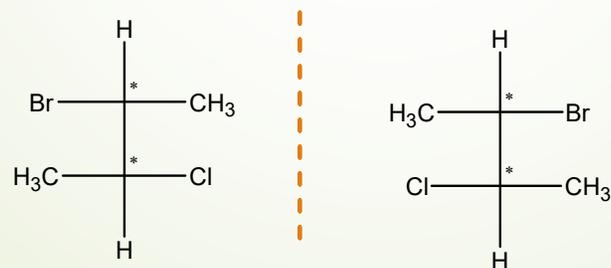
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Compounds with More Than One Stereogenic Center

Key



Mirror

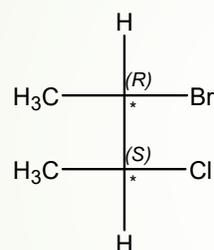
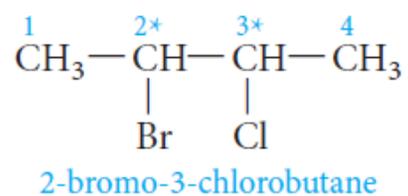


Mirror

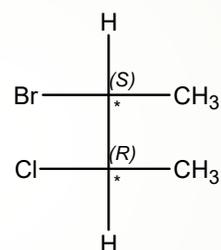
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Compounds with More Than One Stereogenic Center

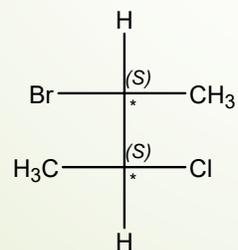
Key



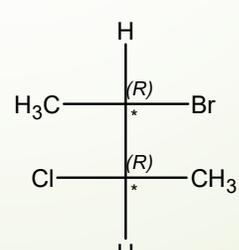
I



II



III



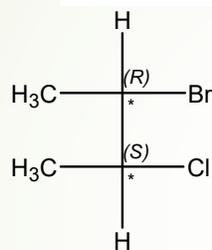
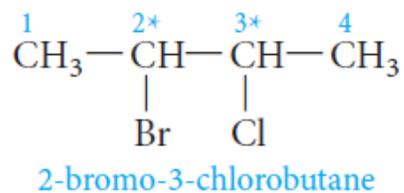
IV

7

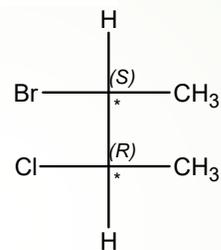
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Compounds with More Than One Stereogenic Center

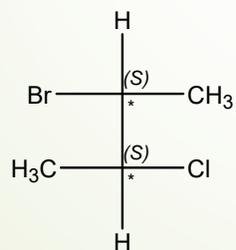
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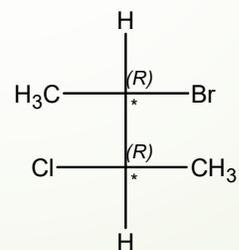
I
Optically Active



II
Optically Active



III
Optically Active



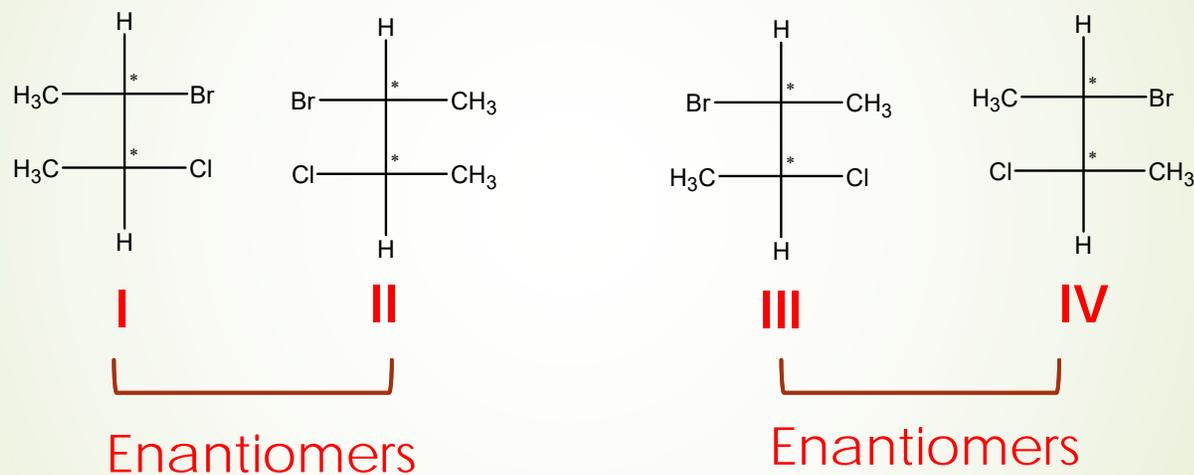
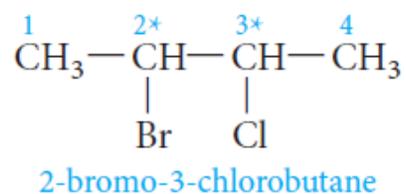
IV
Optically Active

8

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Compounds with More Than One Stereogenic Center

Key

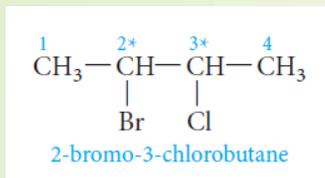


I and II
III and IV Enantiomers

د. أحمد متنبى عبدالله

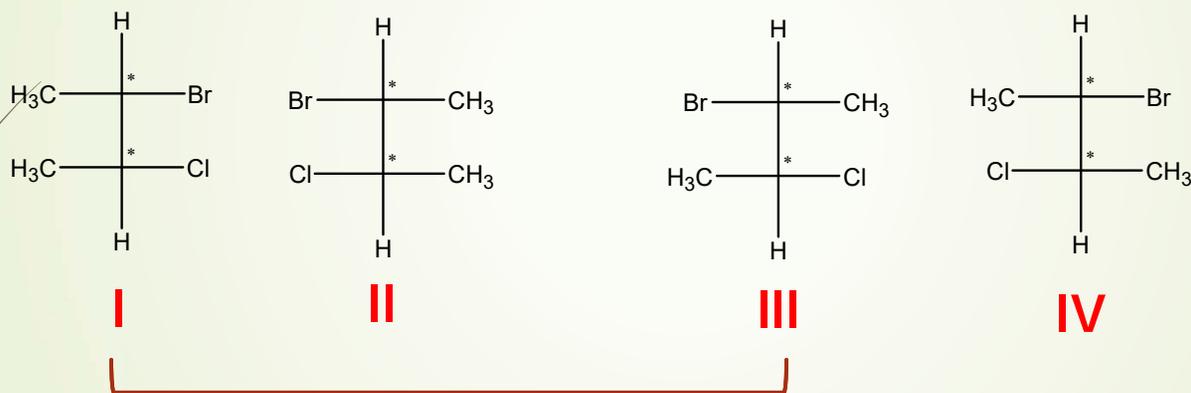
Compounds with More Than One Stereogenic Center

Key



10

Diastereomers



Diastereomers

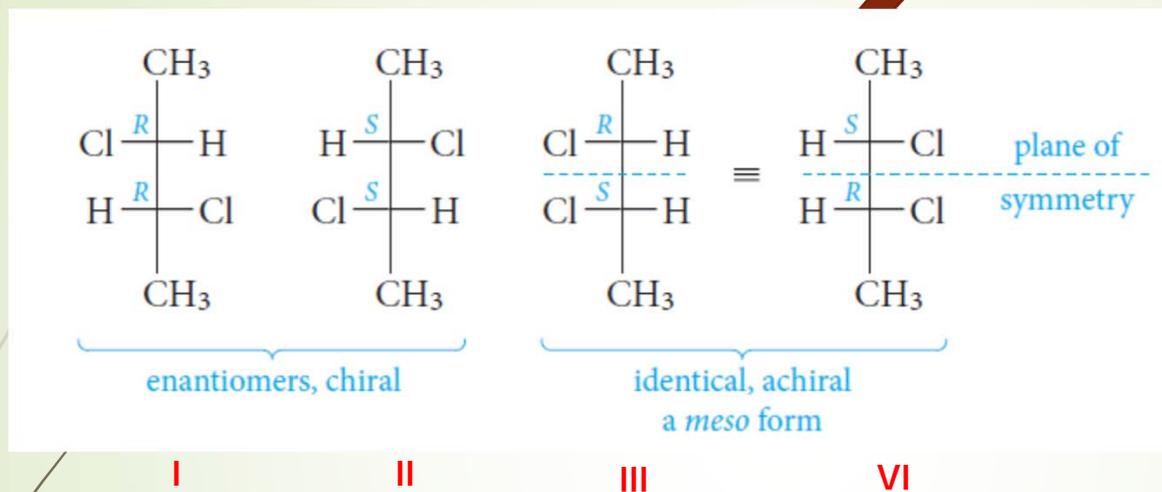
I and III
II and IV

Diastereomers

Diastereomers:
are stereoisomers
that are not mirror
images of each
other.

د. أحمد متنبی عبدالله

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The structures are identical, superimposable mirror images and therefore *achiral*.

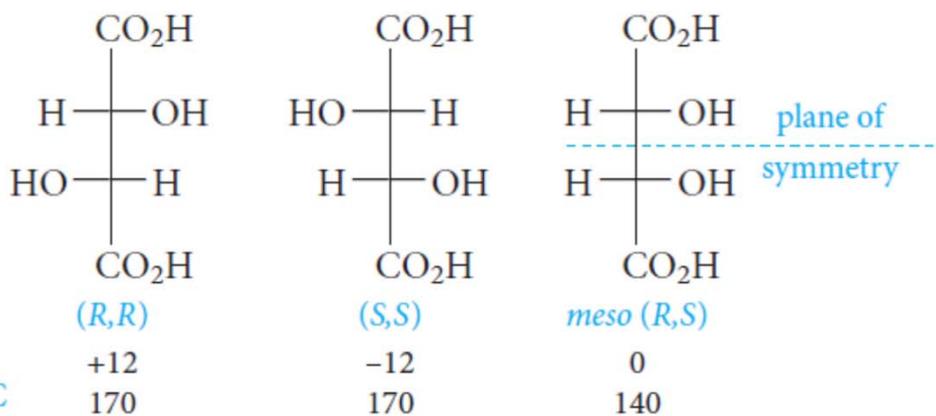
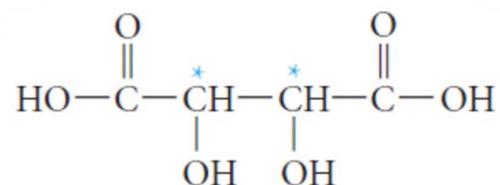
2

The other "two" structures, (R,S) and (S,R), in fact, now represent a single compound.

A meso compound is an achiral diastereomer of a compound with stereogenic centers.

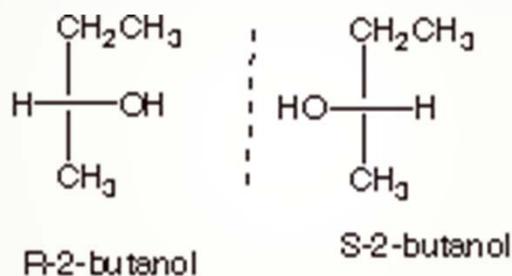
A meso compounds are optically inactive

Tartaric acid



Racemic Forms

An equimolar mixture of two enantiomers is called a **racemic mixture** (or **racemate** or **racemic form**). A racemic mixture causes no net rotation of plane polarized light.



1

The racemic form of a sample is often designated as being (\pm). A racemic mixture of (*R*)-(-)-2-butanol and (*S*)-(+)-2-butanol might be indicated as

