# **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.



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2

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## **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.



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



5

Model of 2-chlorobutane and its mirror image. The mirror image is *not* superimposable on the original molecule. The two forms of 2-chlorobutane are enantiomers.



Enantiomers are a pair of molecules related as nonsuperimposable mirror images.

# 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.



Molecules have carbon atom with four different groups are nonsuperimposable mirror images (enantiomers)

8



9

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**

- 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.

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).



- 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

 $\begin{array}{c} Cl > O > C > H \\ high & low \\ priority & priority \end{array}$ 

#### 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 care of (higher priority) in the ethyl group and a hydrogen (lower priority) in the methyl group.



#### Rule 3

16

Multiple bonds are treated as if they were an equal number of single bonds. For example, the vinyl group ! CH"CH<sub>2</sub> is counted as



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.

$$-CH_2CH_2CH_3 > -CH_2CH_3 > -CH_3 > -H_3$$

Now view the molecule *from the side opposite the lowest-priority group* (--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.



view down the Comment bond; the configuration is R

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17

EXAMPLE

## **Polarized Light and Optical Activity**

- An ordinary light beam consists of waves that vibrate in all possible planes perpendicular to its path.
- Plane-polarized light is a light beam consisting of waves that vibrate in parallel planes.
- A polarimeter, or spectropolarimeter, is an instrument used to detect optical activity. An optically active substance rotates planepolarized light, whereas an optically inactive substance does not.



- An optically active substance that is **dextrorotatory** would rotate planepolarized light to the right (clockwise), while a **levorotatory** compound would rotate plane-polarized light to the left (counterclockwise).
  - The angle through which the analyzer prism must be rotated in this experiment is called a, the **observed rotation**. It is equal to the number of degrees that the optically active substance rotated the beam of plane-polarized light. If the analyzer must be rotated to the *right* (clockwise), the optically active substance is said to be **dextrorotatory**; if rotated to the *left* (counterclockwise), the substance is **levorotatory**



The observed rotation, a, of a sample of an optically active substance depends on its molecular structure and also on the number of molecules in the sample tube, the length of the tube, the wavele

All of these have to be standardized if we want to compare the optical activity of different substances. This is done using the **specific** rotation [a], defined as follows:

Specific rotation = 
$$[\alpha]_{\lambda}^{t} = \frac{\alpha}{l \times c}$$
 (solvent)

The **specific rotation** of an optically active substance (a standardized version of its **observed rotation**) is a characteristic physical property of the substance.

where *I* is the length of the sample tube in *decimeters, c* is the concentration in grams per milliliter, t is the temperature of the solution, and  $\lambda$  is the wavelength of light<sub>utanabbi</sub> Abdula

20

## **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.



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**

23



- 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.



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view down the Comment bond; the configuration is R

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6

EXAMPLE





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





# **Enantiomers**

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Enantiomers have different chiral properties, one of which is the direction in which they rotate plane-pole zed 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.

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3

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The observed rotation,  $\alpha$ , of a sample of an optically active substance depends on its molecular structure and also on the number of molecules in the sample tube, the length of the tube.

All of these have to be standardized if we want to compare the optical activity of different substances. This is done using the **specific rotation** [a], defined as follows:

Specific rotation = 
$$[\alpha]_{\lambda}^{t} = \frac{\alpha}{l \times c}$$
 (solvent)

The **specific rotation** of an optically active substance (a standardized version of its **observed rotation**) is a characteristic physical property of the substance.

where *I* is the length of the sample tube in *decimeters, c* is the concentration in grams per milliliter, *t* is the temperature of the solution, and  $\lambda$  is the wavelength of light.

**Problem :** A 1.50 g sample of coniine was dissolved in 10.0 mL of ethanol and placed in a sample cell with a 5.00 cm pathlength. The observed rotation at the sodium d line was  $11.21^{\circ}$ . Calculate [ $\alpha$ ]<sub>D</sub> for coniine.

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## **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.

Key

$$\begin{array}{c} 1 \\ CH_{3} \longrightarrow \begin{array}{c} 2^{\star} & 3^{\star} & 4 \\ CH \longrightarrow \begin{array}{c} CH \longrightarrow \begin{array}{c} CH \longrightarrow \begin{array}{c} CH \longrightarrow \begin{array}{c} CH \end{array} \\ & | \\ Br & Cl \end{array} \\ 2 \text{-bromo-3-chlorobutane} \end{array}$$

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2

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Key

no. of stereoisomers =  $2^n$  $2^2 = 4$ 

















## Meso Compounds

Consider the stereoisomers of 2,3-dichlorobutane. There are two stereogenic centers.



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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



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## **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.



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

( $\pm$ )-2-butanol or ( $\pm$ )-CH<sub>3</sub>CH<sub>2</sub>CHOHCH<sub>3</sub>

#### د. أحمد متنبي عبدالله Resolution or Separation of Racemic Forms

2

The process of separating the two enantiomers of a racemic (50:50) mixture is called resolution.

Since enantiomers have identical achiral properties, how can we resolve a racemic mixture into its components?

The answer is to convert them to diastereomers, separate the *diastereomers*, and then reconvert the now-separated diastereomers back to enantiomers.



## Resolution or Separation of Racemic Forms

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Reaction of racemic lactic acid with (R)-1-phenylethylamine yields a mixture of diastereometric ammonium salts, which have different properties and can be separated.



# **Fisher Projection**

#### Draw the two enantiomers of 3-methylhexane. Use fisher projection.









#### Determine the configuration (R or S) at the stereogenic center in

