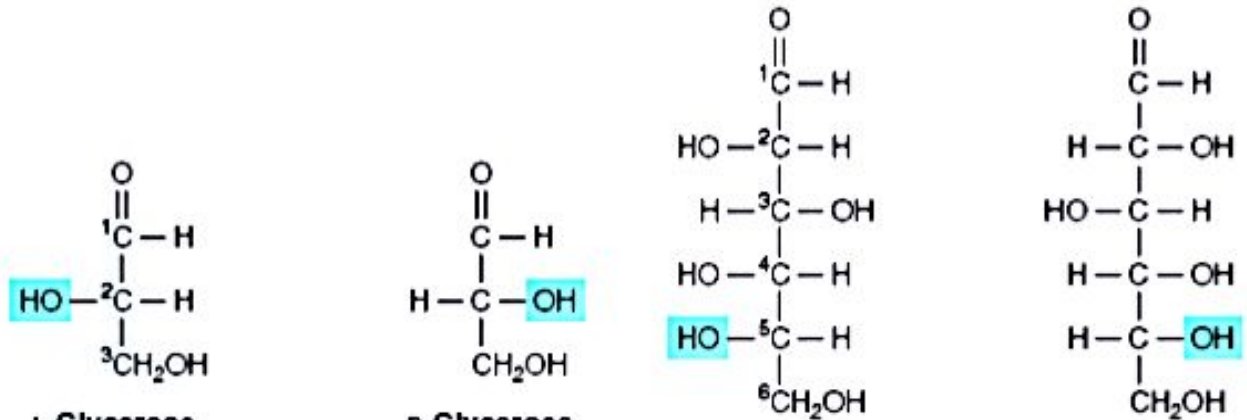
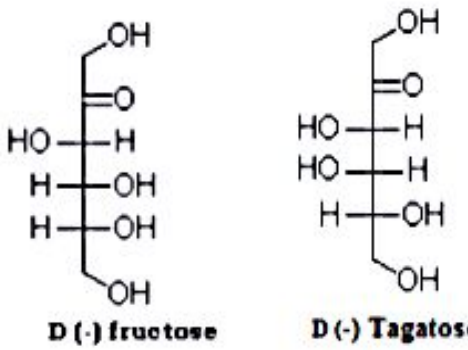
❖ D & L-System

- The **D & L** convention, not to be confused with the **d (dextro)** and **l (levo)** descriptors used to designate the direction of specific rotation of chiral compounds, is a convention used to distinguish between enantiomers of chiral monosaccharides and chiral alpha-amino acids, based on the molecule drawn as a ***Fischer projection*** in a specific orientation.
- The **L** and **D** forms of the sugar depends on the orientation of the **-H** and **-OH** groups around the carbon atom adjacent to the **terminal primary alcohol carbon** (carbon 5 in glucose) determines whether the sugar belongs to the **D** or **L** series.
- The **D-** and **L- notation** is based on **glyceraldehyde.**
- When the **-OH** group on this carbon is on the **right**, then sugar is the ***D-isomer***; when it is on the **left**, then it is the ***L-isomer***.



D- and L-isomerism of glycerose and glucose

- Most of the monosaccharide occurring in mammals is **D sugars**, and the enzymes responsible for their metabolism are specific for this configuration. In solution, glucose is dextrorotatory-hence the alternative name **dextrose.**
- The presence of asymmetric carbon atoms also confers **optical activity** on the compound. When a beam of plane-polarized light is passed through a solution of an **optical isomer,** it will be rotated either to the right, dextrorotatory (+); or to the left, levorotatory (-). The direction of rotation is independent of the stereochemistry of the sugar, so it may be designated D (-), D (+), L (-), or L (+). For example, the naturally occurring formof fructose is the D (-) isomer.

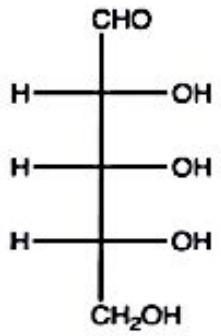


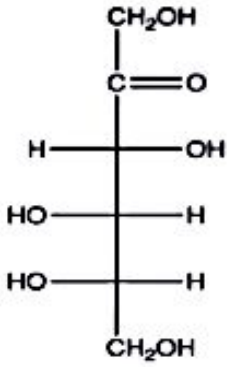
D-Tagatose is an epimer of D-fructose inverted at C-4

- **Application of D,L convention to monosaccharides:**

One enantiomer of a chiral monosaccharide is labeled **D** and the other **L**. To determine whether a given enantiomer of a chiral monosaccharide is **D** or **L**, use the following procedure.

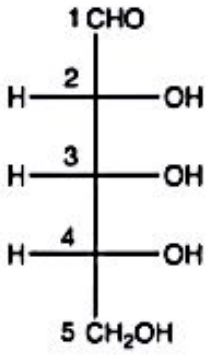
✓ **Step 1:** Make sure the acyclic form of the molecule is drawn as a Fischer projection. If the monosaccharide is an aldose, the aldehyde group must be on top; if it is a ketose, the carbonyl carbon must be the second carbon from the top.

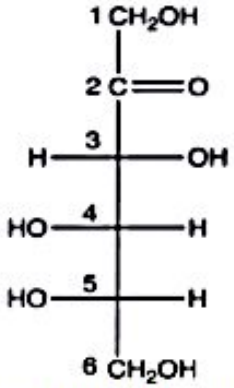




Aldose Sugar (Glucose) ***Ketose Sugar (Fructose)***

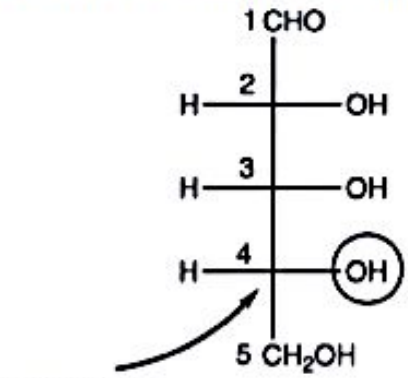
✓ **Step 2:** Number the carbon atoms starting at the top.





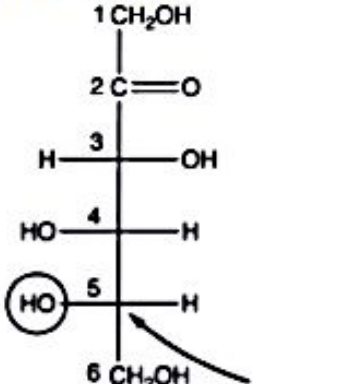
Aldose Sugar (Glucose) ***Ketose Sugar (Fructose)***

✓ **Step 3:** Locate the carbon atom that bears the second highest number, which is known as the **penultimate carbon**. If the **hydroxy group** on the **penultimate carbon** is on the right of the carbon chain, assign the label **D** to the compound; if it is on the left of the carbon chain, assign the label **L**.



D

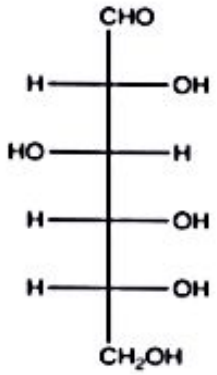
D-Glucose



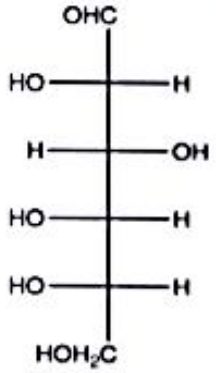
L

L-Fructose

✓ *The enantiomer of a given chiral monosaccharide, simply draw its mirror image.*



D-glucose

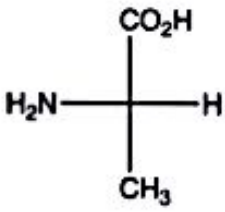


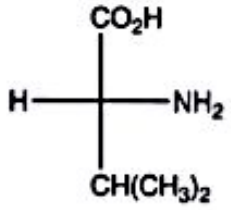
mirror image of D-glucose
(L-glucose)

- **Application of D,L convention to alpha-amino acids:**

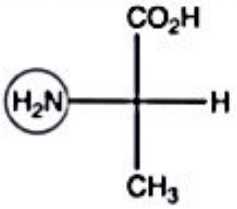
One enantiomer of a chiral alpha-amino acid is labeled **D** and the other **L**. To determine whether a given enantiomer of a chiral alpha-amino acid is **D** or **L**, use the following procedure.

✓ **Step 1:** Make sure that the molecule is drawn as the Fischer projection in which the **carboxylic acid** group is on top and the **side chain** on bottom.

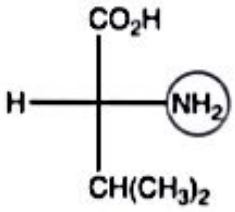




✓ **Step 2:** If the **amine group** is on the right of the carbon chain, assign the label **D** to the compound; if it is on the left of the carbon chain, assign the label **L**.

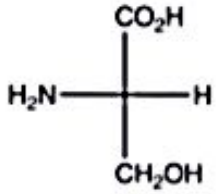


L

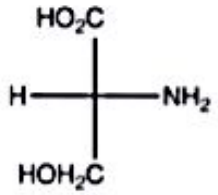


D

✓ *To draw the enantiomer of a given chiral alpha-amino acid, simply draw its mirror image.*



L-serine

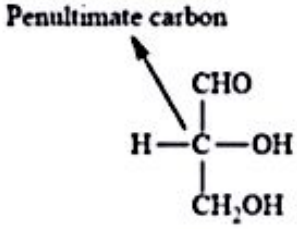


mirror image of L-serine
(D-serine)

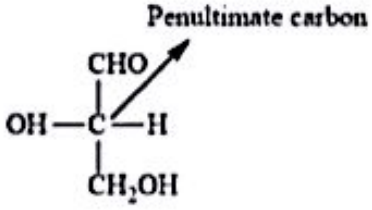
- **Note By: What is the PENULTIMATE CARBON?**

Penultimate means next to last.

The penultimate (second to last carbon) carbon is the last chiral carbon of the chain.



D-glyceraldehyde

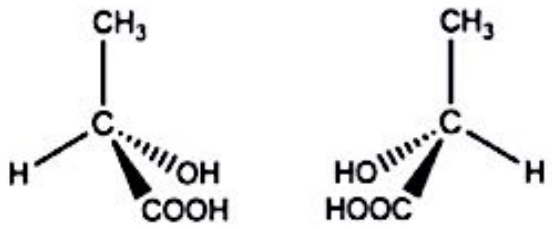


L-glyceraldehyde

❖ Racemic Mixture & Racemization

• RACEMIC MIXTURE

- A racemic mixture is a 1:1 mix of two enantiomers (Each of a pair of molecules that are mirror images of each other).
- No matter how many molecules are in a mixture, it is racemic if there are equal numbers of the two enantiomers.
- The racemic mixture produces a net optical rotation - of plane polarized light - of zero degrees. This is because the mixture contains equal amounts - **equimolar mixture** - of both enantiomers that have opposite rotations.
- **A racemic mixture** is a solution containing equal amounts of **a pair of enantiomers.**



(R) - Lactic Acid 50% + (S) - Lactic Acid 50%

Racemic Mixture

- **Note By:**

***(S)*-2-butanol** ***(R)*-2-butanol**

- A solution containing equal amounts of **(R)-2-butanol** and **(S)-2-butanol** is a **racemic mixture.**
- A solution containing an excess of either the **(R)-enantiomer** or the **(S)-enantiomer** would be **ENANTIOENRICHED.**
- A solution containing only the **(R)-enantiomer** or the **(S)-enantiomer** will be **ENANTIOMERICALLY PURE.**

• RESOLUTION OF RACEMIC MIXTURES

- The separation of a racemic mixture into the individual enantiomerically pure enantiomers is called resolution.
- Since enantiomers have identical physical properties, such as solubility, boiling point and melting point, they cannot be resolved by common physical techniques such as direct crystallization, distillation or basic chromatography.
- The main difficulty in a process of resolution is that **d** or **(+)** and **l** or **(–)** forms have identical physical and chemical properties, so they cannot be separated by ordinary methods. However, the following methods can be used for this purpose.

(i) ***Mechanical separation:***

- If the **d** or **(+)** and **l** or **(–)** forms of a substance exits in well-defined crystalline forms, the separation can be done by hand picking with the help of magnifying lens and a pair of tweezers.
- For example, the d and l forms of sodium ammonium tartarate can be separated by this method.
- The method has very limited application and applies to only few crystalline constituents having different shape.

(ii) ***Biochemical separation:***

- In this method, the resolution is done by the use of microorganisms.
- When certain **bacteria** or **moulds** are added to a solution of a racemic mixture, they decompose one of the optically active forms more rapidly than the other.

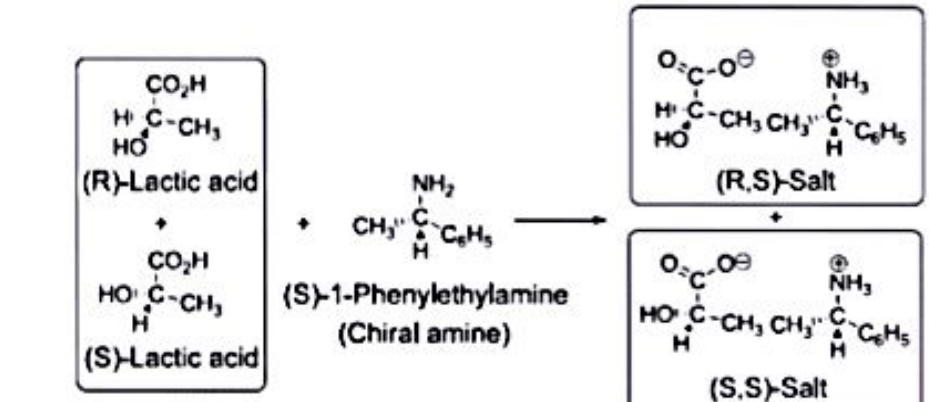
- For example, when the **mould, racemic ammonium tartarate**, the mould completely decomposes the **d** form white **l** form is left practically unaffected. The main drawback of the method is that half of the material is destroyed during resolution. The process is very slow and only small amounts of the materials can be separated.

(iii) ***Chemical separation:***

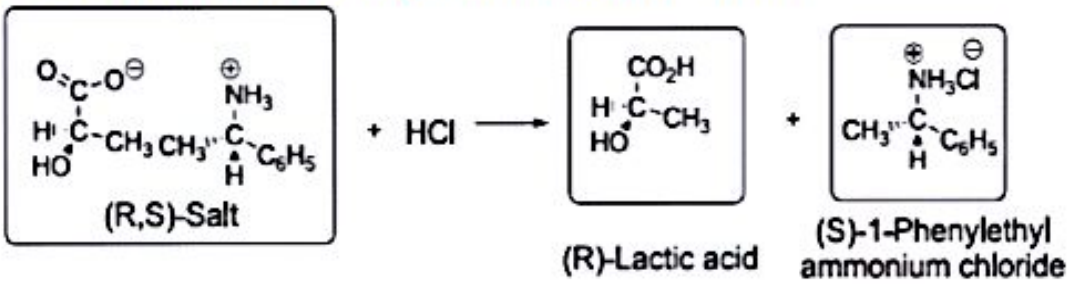
- This is probably the best method of resolution. The racemic mixture is made to combine with another optically active compound and the resulting solubility in various solvents.
- By fractional crystallization from a suitable solvent, they can be separated.
- For example, the racemic mixture of lactic acid is allowed to combine with the optically active base (-) strachnine or (+) brucine.

- ***Example of Resolution of Racemic Mixtures***

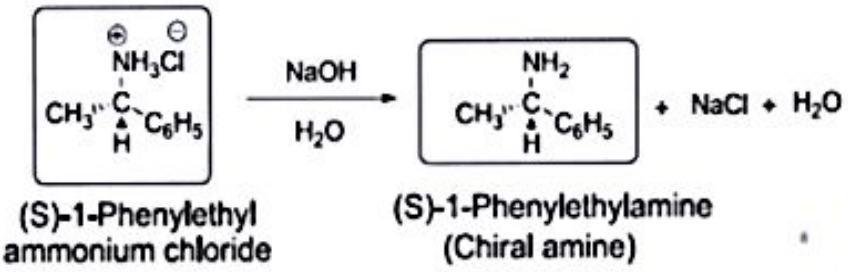
(i) ***(S)-1-Phenylethylamine*** combines with a racemic mixture of lactic acid to form **diastereomeric salts**. The diastereomers are separated by fractional crystallization.



- After the separation process, each of the diastereomers is subsequently treated with a strong acid such as hydrochloric acid to regenerate the corresponding enantiomer of lactic acid



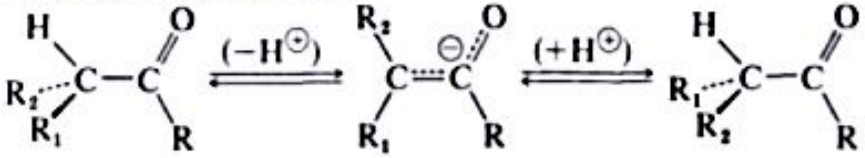
- Note that the lactic acid would be soluble in the organic layer, while the ammonium salt would be in the water layer.
- Since enantiomerically pure compounds are very expensive, it is usually necessary to recover and reuse the chiral amine. This is achieved by treating the (S)-1-phenylethyl ammonium chloride salt with a base such as sodium hydroxide to regenerate and recover the chiral amine.



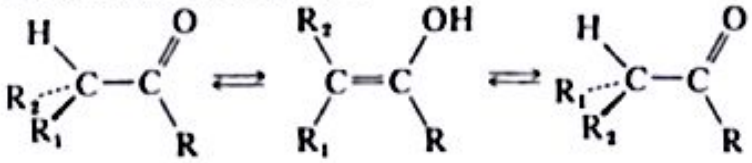
• RACEMIZATION

- **Racemization** is the conversion of an enantiomerically pure mixture (one where only one enantiomer is present) into a mixture where more than one of the enantiomers are present. (Or) Conversion of an optically active substance to a raceme.
- Optically active carbonyl compounds of the type **–CHC=O** , in which the **alpha** carbon is asymmetric, are racemized by both acids and bases

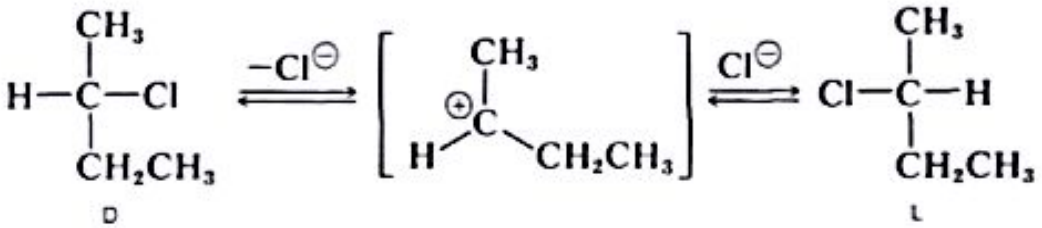
Base-catalyzed enolization



Acid-catalyzed enolization



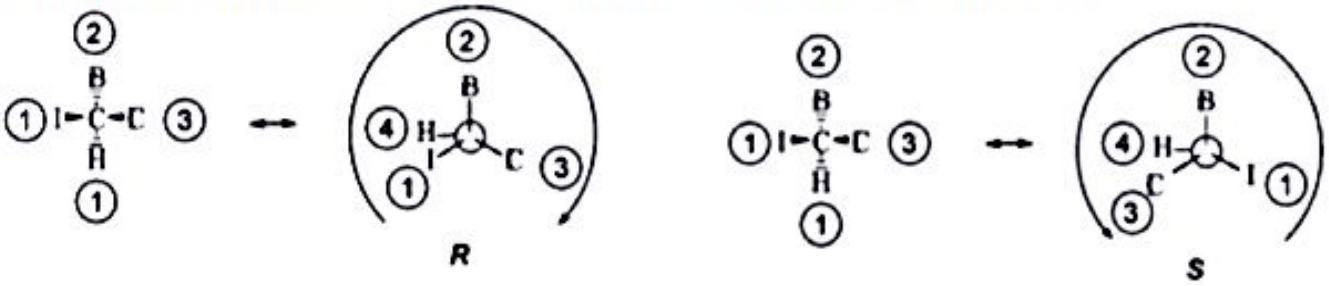
- The racemization of an optically active secondary halide with the chiral carbon carrying the halogen (e.g., 2-chlorobutane) may occur in the solution and, usually, the more polar and better ionizing the solvent is, the more readily the substance is racemized. Ionization of the halide by an **SN^1** process probably is responsible, and this certainly would be promoted by polar solvents. All indications are that an alkyl carbocation once dissociated from its accompanying anion is planar; and, when such an ion recombines with the anion, it has equal probability of forming the **D** and **L** enantiomers:



❖ Absolute configuration: R,S-System

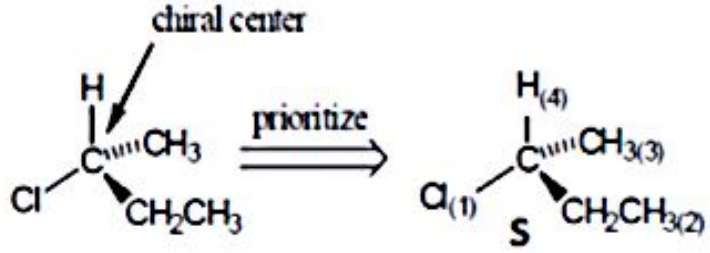
- An absolute configuration refers to the spatial arrangement of the atoms of a chiral molecular entity (or group) and its Stereochemical description e.g. **R** (***Rectus***) or **S** (***Sinister***).
- The arrangement of atoms in an optically active molecule, based on chemical interconversion from or to a known compound, is a **relative configuration**. Relative, because there is no way of knowing just by looking at a structure whether the assignment of (+) or (-) is correlated to a particular isomer, **R** or **S**.
- **R** and **S** notations are used only to describe asymmetric molecules following ***Cahn-Ingold-Prelog*** (CIP) sequence rules.

(a) Rule I: first we assign the priority numbers to the four atoms/groups attached to chiral centre according to CIP rules. For example in the case of **CHClBrI**, the four atoms attached to the chiral center are all different and priority will be given based on atomic weight, thus the priority follows as **I, Br, Cl, H**.

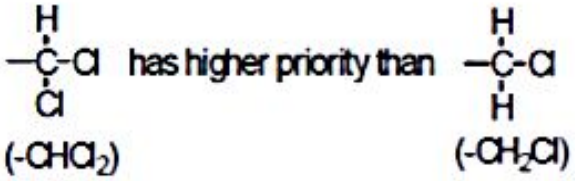


(b) Rule 2: If two or more of the atoms that are bonded directly to the chiral center are the same, then prioritize these groups based on the next set of atoms (i.e., atoms adjacent to the directly bonded atoms). Continue until priorities can be assigned. Priority is assigned at the first point of difference.

atomic numbers	
H	1
C	6
Cl	17



✓ *If two atoms have substituents of the same priority, higher priority is assigned to the atom with more of these substituents.*

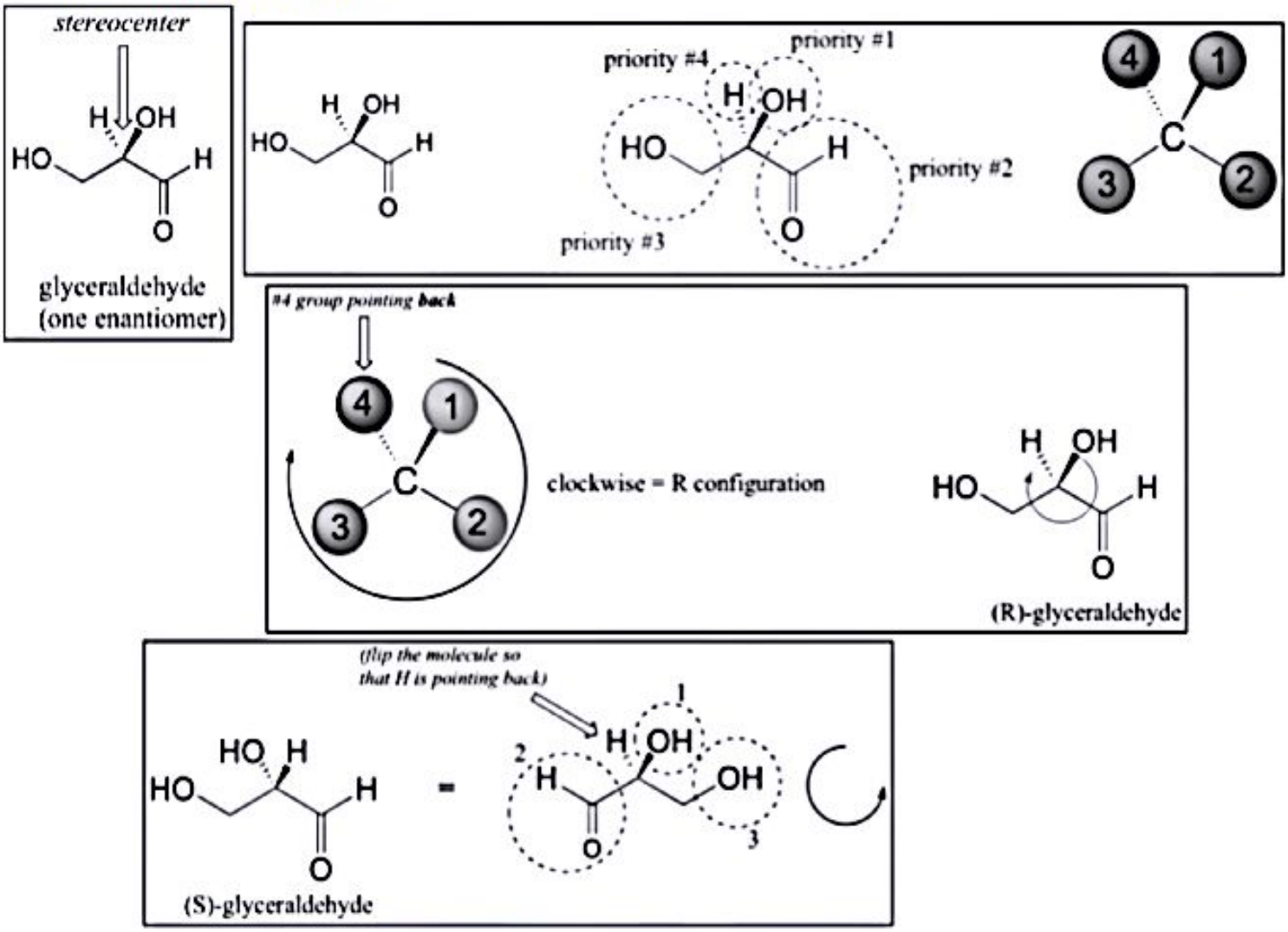


✓ *A larger group (i.e., more atoms) may not necessarily have a higher priority over another (smaller) group.*

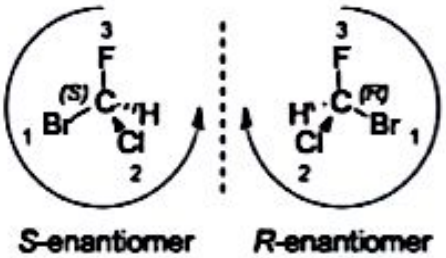
$-CH_2Cl$ has higher priority than $-CH_2CH_2CH_2CH_3$

(c) Rule 3: Atoms participating in double/triple bonds are considered to be bonded to an equivalent number of similar **"phantom"** atoms by single bonds. Note: **"phantom"** atoms are bonded to no other atoms.

(d) Rule 4: In Fischer projection representations orient the molecule so that the least priority group must be on lower end of vertical line. If the lower priority group on horizontal line or upper side on vertical line, then to bring the group on to vertical line do two mutual exchanges of groups so that the least priority group come to lower end of vertical line.



(e) Rule 5: After giving priority order for the groups at asymmetric centre, if priority direction is clockwise the configuration is specified **'R'** (*Latin*: **rectus,** right); if anticlockwise the configuration is specified **'S'** (*Latin*: ***sinister,*** left).



(f) Rule 6: Orient the molecule in space so that the lowest priority group **(#4)** is directed away from you. The three remaining groups then project toward you.