### 3.9. Asymmetric Synthesis

# 3.9.1. Definition and example

- The direct synthesis of an chiral/optically active compound or molecule from an optically inactive/achiral molecule with or without the help of chiral agent is known as asymmetric synthesis.
- Example: The conversion of 2-butanone to (+) or (-) 2-butanol in presence of a chiral reagent. However, which steroisomer will be formed, decided by the use of the chiral reagent.

- Asymmetric synthesis is two types (1) Partial asymmetric synthesis, (2) Absolute asymmetric synthesis.
- (1) Partial asymmetric synthesis: It is the synthesis of an optically active compound from an optically inactive compound by the intermediate use of some optically active reagent.
- e.g. Optically active lactic acid is obtained by the reduction pyruvic acid in presence of *l*-menthol.
- (2) **Absolute asymmetric synthesis**: The formation of an optically active compound from an optically inactive compound without the intermediate use of any optically active reagent.

### 3.9.2. Asymmetric Induction.

- It is nothing but the use of chiral reagent or catalyst for converting an achiral reactant top chiral product having one enantiomer in excess or only one enantiomer.
- In biochemistry, the chiral catalyst used is coenzyme.

• **Homotopic atoms or groups**: These can be interconverted by rotation about an axis of symmetry. e.g. all the H-atoms in methane, methyl group of any compound and methylene group of methylene dichloride.

• **Enantiotopic atoms or groups**: These can be interchanged by a rotation-reflection operation.

The two H-atoms of chlorobromomethane are enatiotopic. This is due to the fact that the replacement of one H –atom with any group X gives one enantiomer, whereas the replacement of other H-atoms with X will give the other enantiomer.

# 3.9.3. Chiral synthesis catalyzed by optically active substances

Addition of HCN to cinnamaldehyde is catalyzed by the alkaloids like quinine, cinchonine predominantly affords one enantiomer.

$$H_2C = C - CHO$$
  $\xrightarrow{HCN, Quinine}$   $H_2C = C - C CN$ 
60% optically pure

## 3.9.4. Chiral Auxiliaries

The temporarily incorporation of a chemical compound or unit into an organic synthesis resulting the formation of one enantiomer of the two enantiomer is called chiral auxiliary.

Chiral auxiliary was introduced by E.J. Corey in 1978 with chiral 8-phenyl menthol and by B.M. Trost in 1980 with chiral mandelic acid.

#### 3.9.5. Resolution

The separation of racemic mixture into its enantiomorphs (dextro and laevo components) is called resolution.

• Chemical Resolution of a Racemic Mixture

Pure enantiomers are obtained

- Other methods for resolution
- Mechanical method: This is applicable rarely to those organic compounds which differ in their crystal shapes.
- Bio-chemical method: In this method one of the isomer is completely destroyed and the other isomer is recovered and in this method enzyme or microorganism is used.
- Chemical method: Racemic acid can be resolved bu forming salt using an optically active base.

