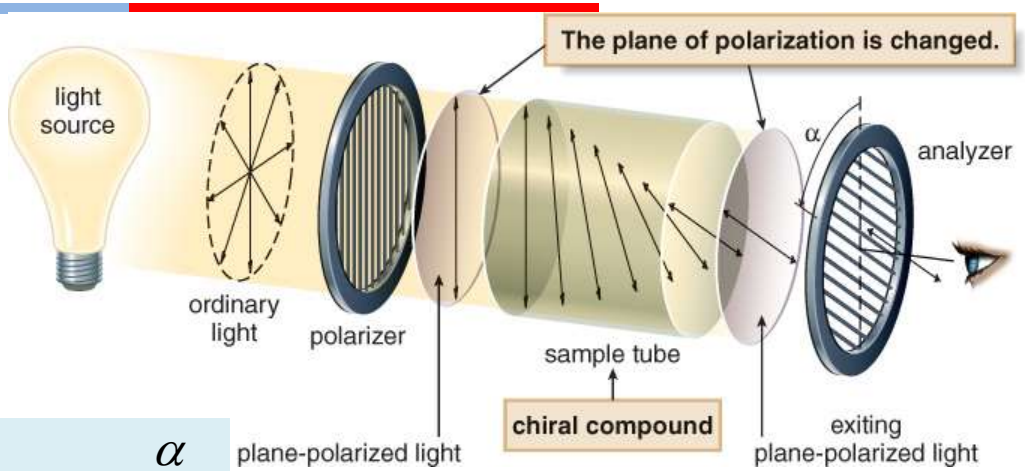
CHEM F111 : General Chemistry

Semester II: AY 2017-18

Lecture 34 (13-04-2018)

Summary of Lecture 35

The angle of rotation of plane polarized light by an optically active substance is proportional to the number of atoms in the path of the light.



$$[\alpha]_D = \frac{(\text{observed rotation in degrees})}{(\text{pathlength in dm})(\text{concentration in g/ml})} = \frac{\alpha}{l \times C}$$

$$\text{\% Enantiomeric excess (\% ee) (Optical purity)} = \frac{\text{Observed rotation}}{\text{Rotation of pure enantimer}} \times 100$$

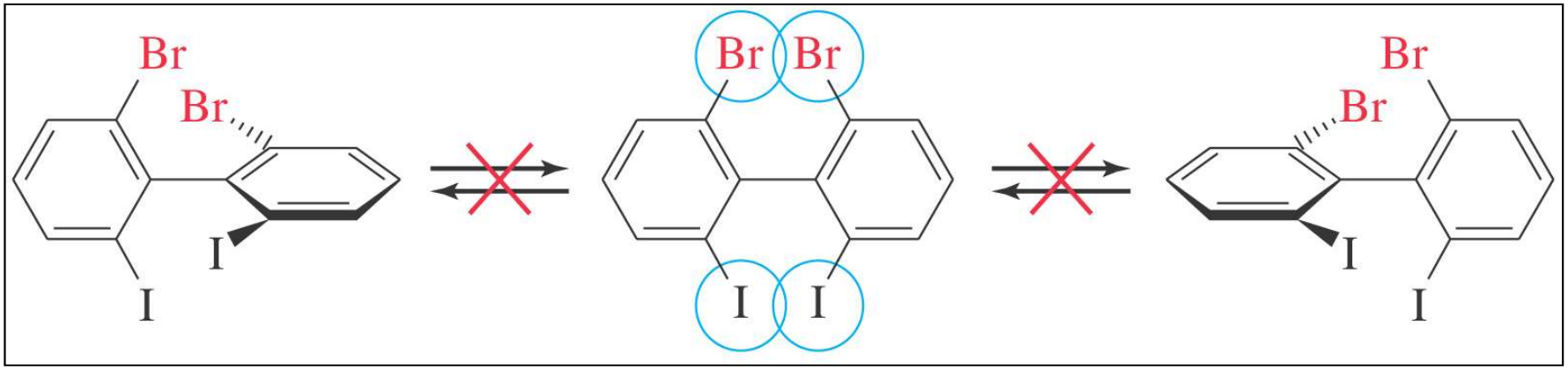
If the mixture contain one of the enantiomer in excess to other, the mixture will show optical activity. If a substance contain exclusively one enantiomers, the substance is called optically pure substance

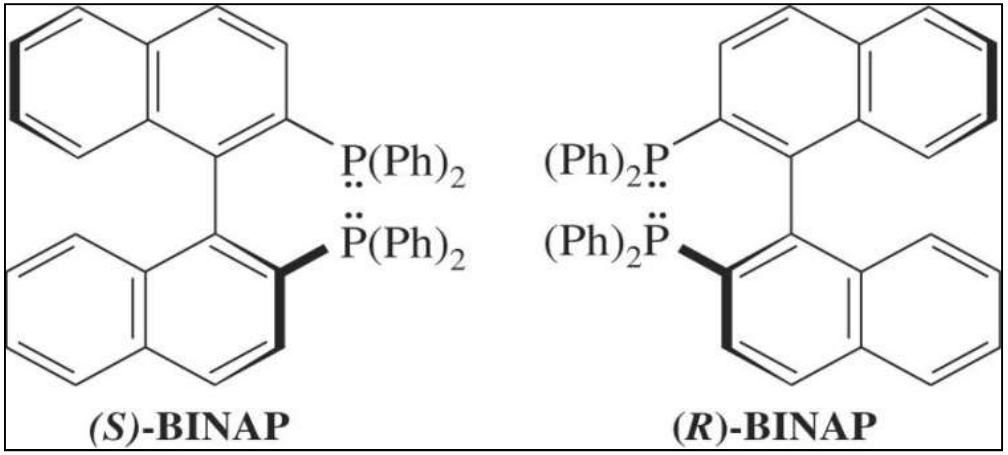
Molecular Symmetry: Plane of symmetry and center of symmetry

They have diastereomeric relationship. Stereoisomers that are not enantiomers (non-superimosable mirror images) are called diastereoisomers. Diastereoisomers have different physical and chemical property. For *n* chiral centers = 2^n maximum stereoisomers

Chirality without chiral center (Chiral axis)

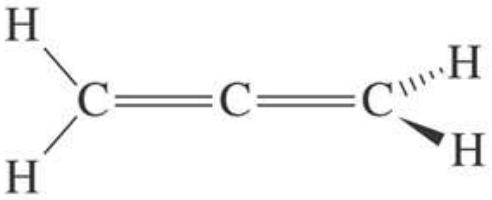
Atropisomers: If a molecule is bulky or highly strained and can not easily convert from its original conformation to the mirror image conformation. The molecule becomes conformationally locked and enantiomers generated so are called atropisomers.

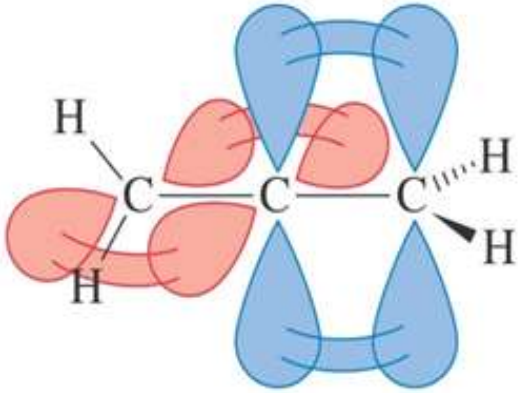


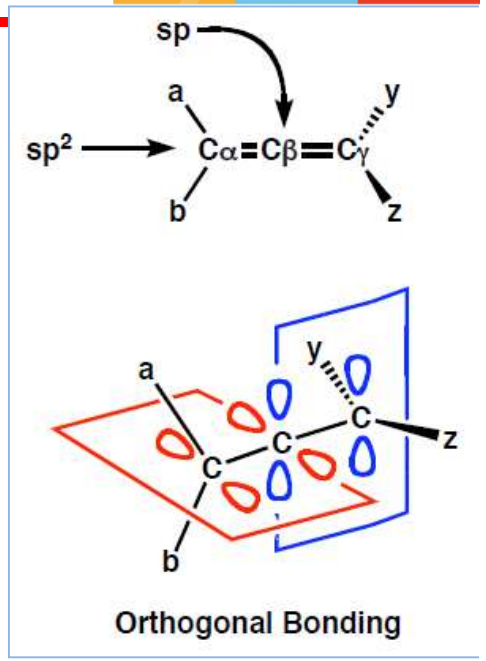


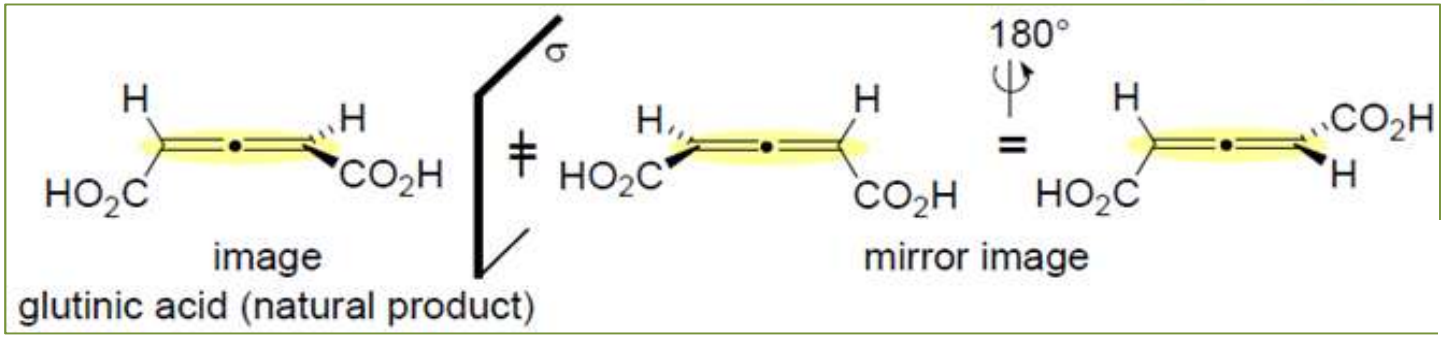
Chirality without Chiral center

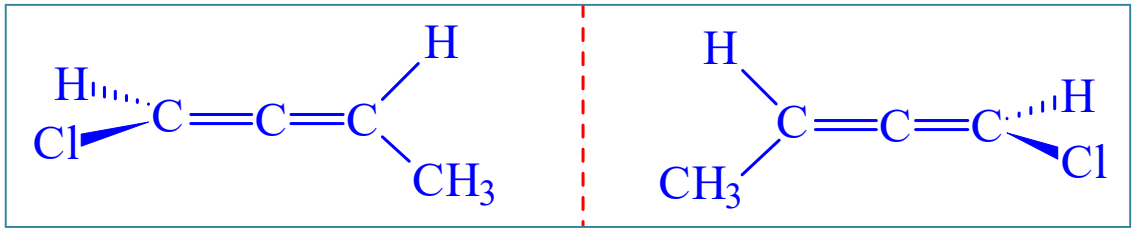
Allenes can be Chiral

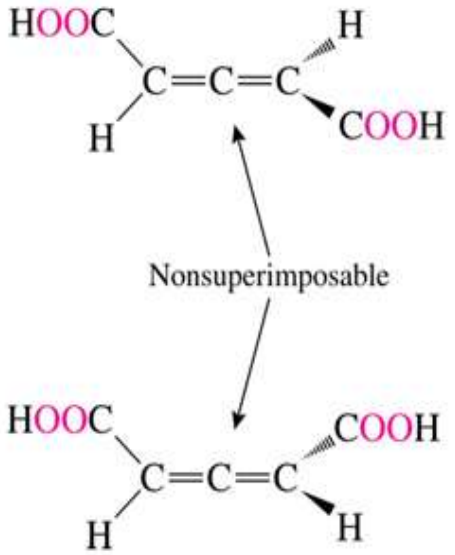












For allenes to be chiral, and carbons must have different groups.

Preparation of chiral compounds

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Strategy and classification of methods

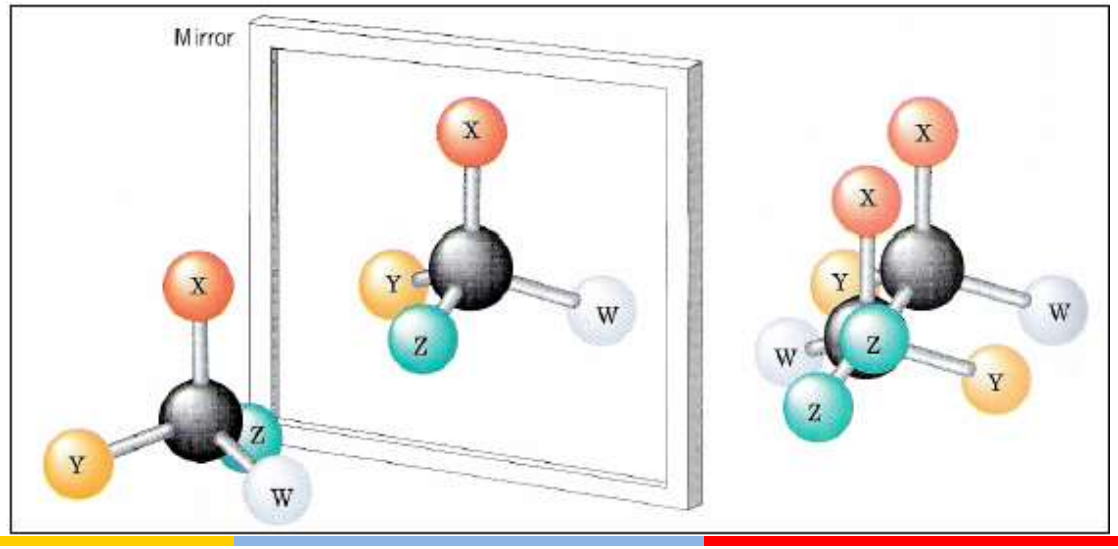
- Resolution methods: Using Chiral resolving agent
- The use of Chiral Pool method
- The use of Chiral auxiliaries method
- The use of Chiral reagents
- The use of Chiral catalyst

Resolution of Enantiomers

- **Since enantiomers have identical physical properties, they cannot be separated by conventional methods.**
  - **Distillation and recrystallization fail.**
- **The process of separating enantiomers is called resolution.**

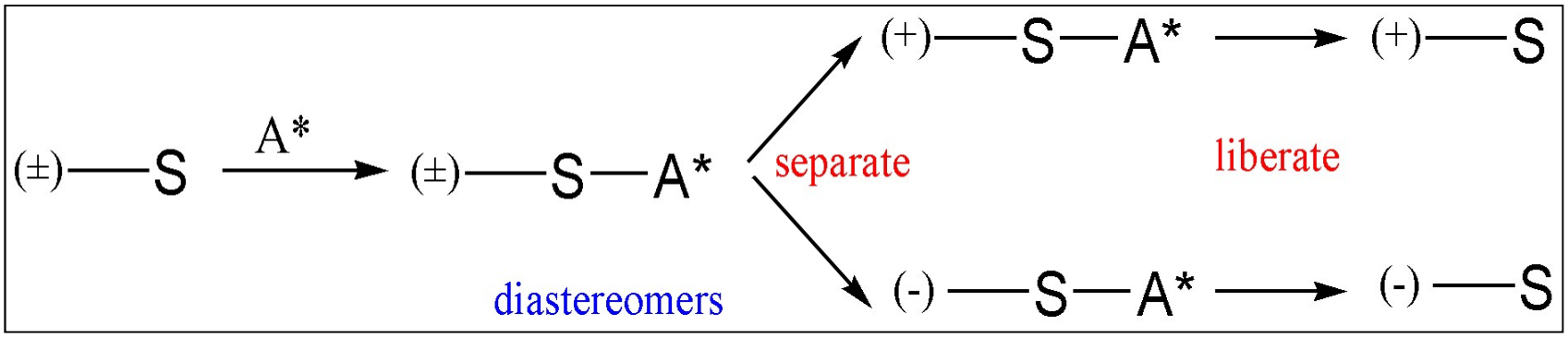
Resolution: A useful method for separation of enantiomeric compounds by preparation of diastereomeric molecules.

- **Two methods:**
  - **Chemical resolution**
  - **Chromatographic resolution**



Resolution of Enantiomers

- **Chemical resolution of enantiomers:**
  - temporarily convert both enantiomers into diastereomers
  - react with an enantiomerically pure (natural) product
  - separate the diastereomers based on differences in physical properties
  - convert each diastereomer back into the original enantiomer



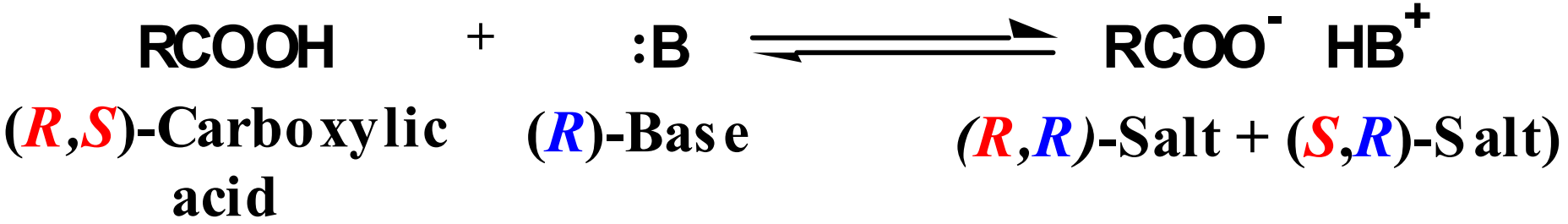
They are diastereomers, have different physical and chemical properties. Can be separated easily.

Resolution of Enantiomers

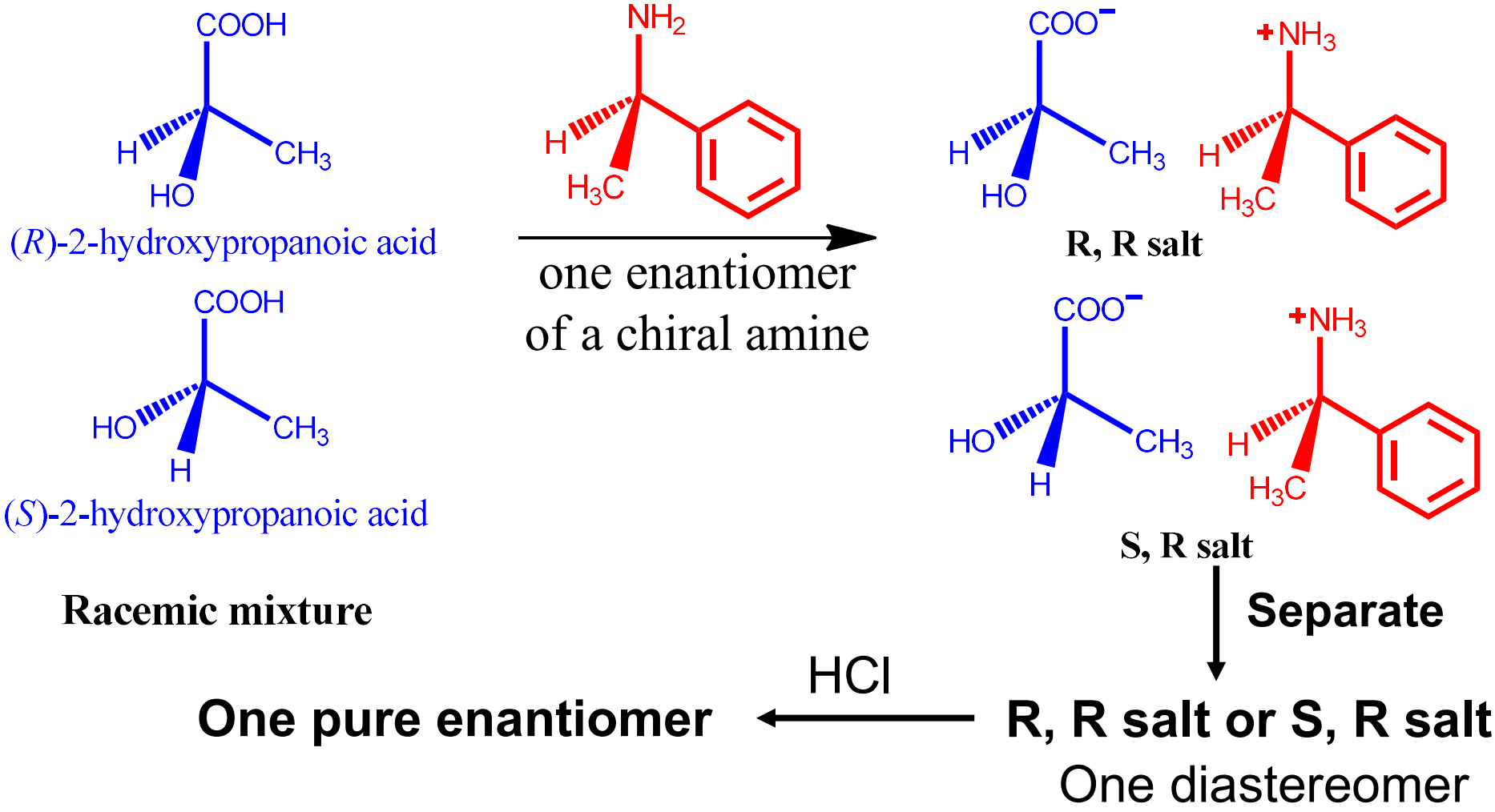
Resolution: Separating enantiomers by make environment chiral so that enantiomers have different properties.

- A chiral compound react with mixture of enantiomers to form diastereomers that can be separated easily.
- A common reaction for chemical resolution is salt formation. After separation of the diastereomers, the enantiomerically pure compounds are recovered.

- **Chiral resolving agents method was introduced (again) by Louis Pasteur in 1853 by resolving racemic tartaric acid with optically active (+)-cinchotoxine.**

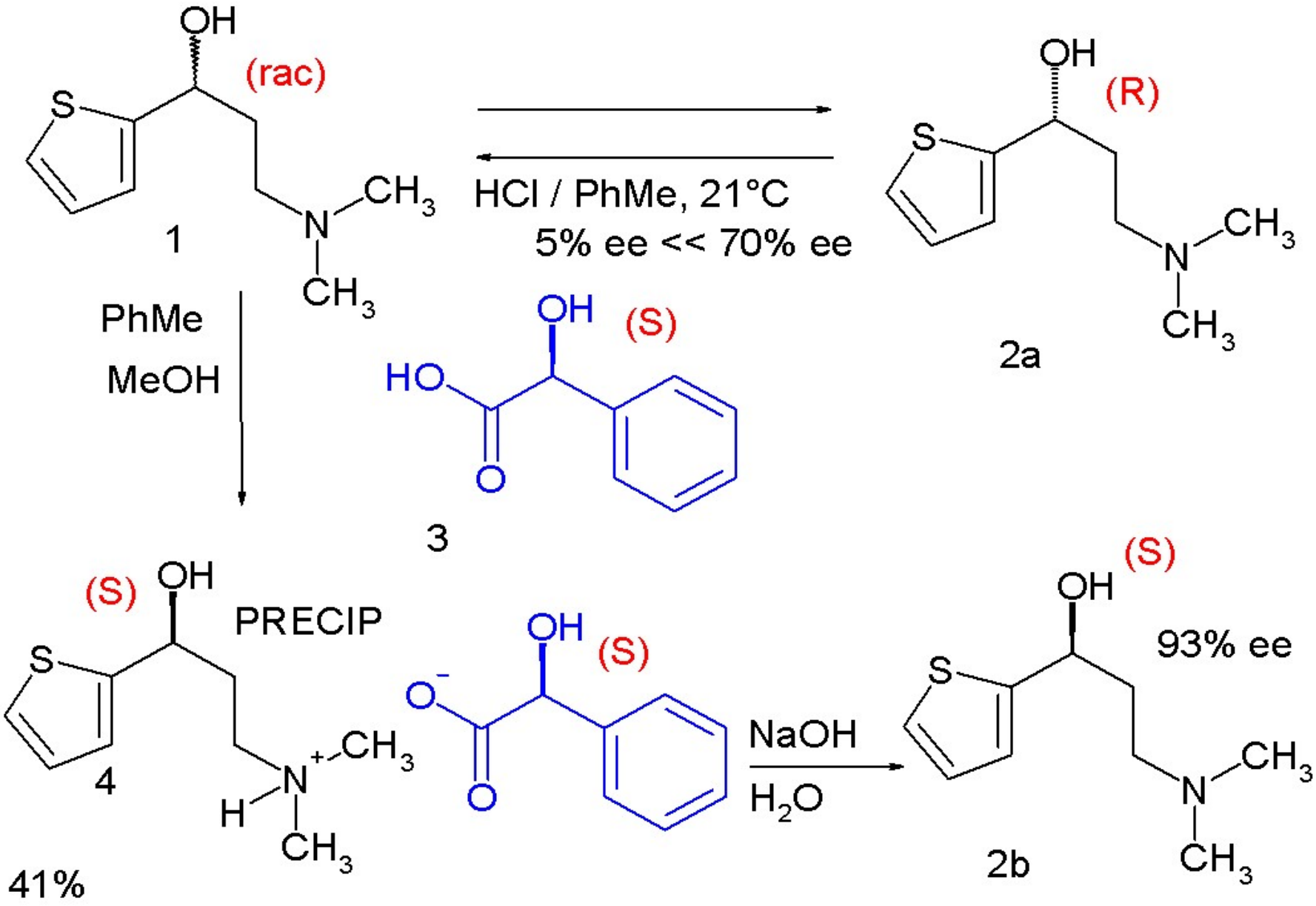


Resolution by Chiral Chromatography



Derivatization is possible by salt formation between an amine and a carboxylic acid (either one could be chiral)

Resolution of Enantiomers by crystallization



Resolution by Chiral Chromatography

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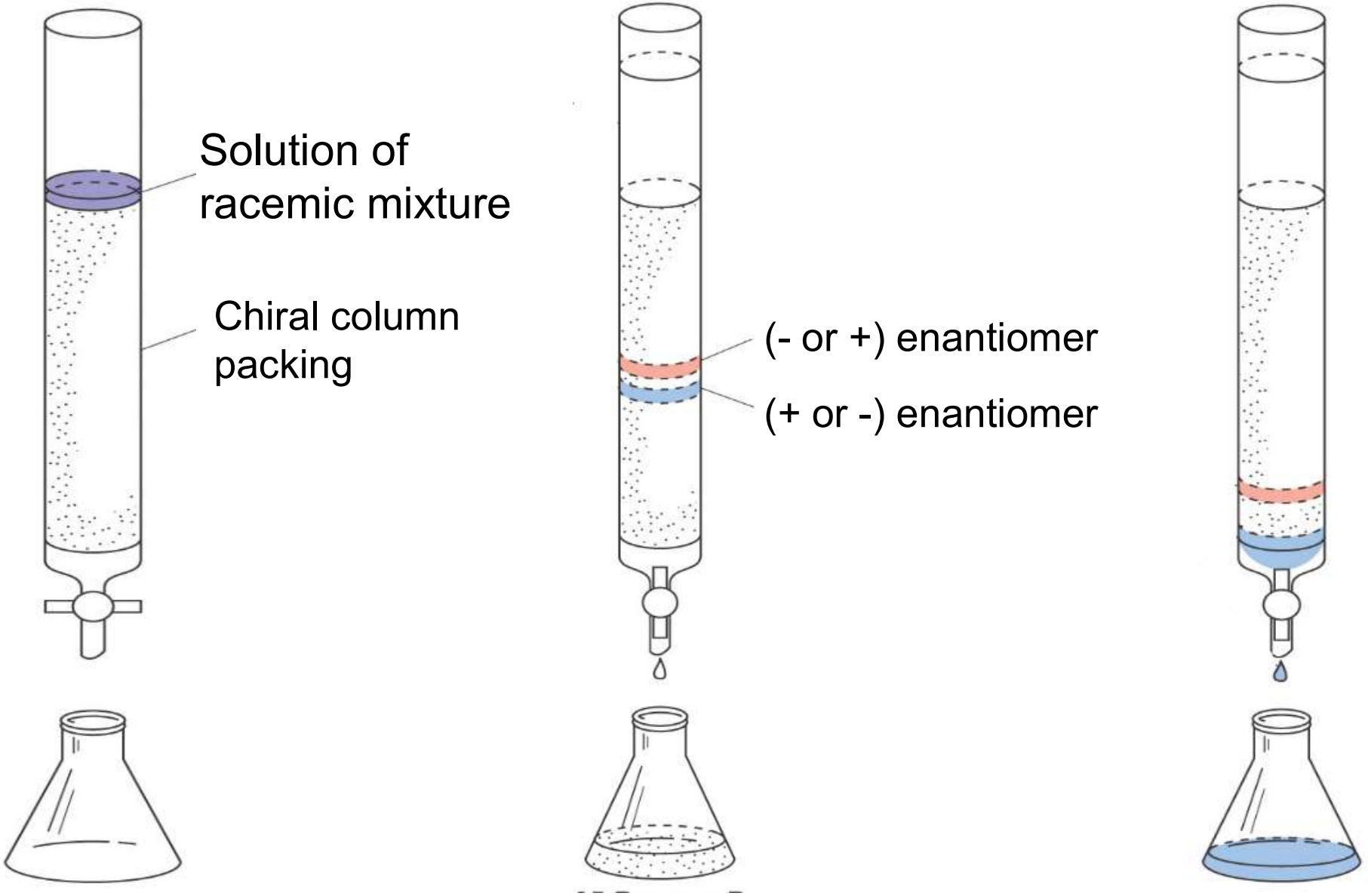
❑ Chromatographic resolution of enantiomers:

- **Prepare column containing chiral stationary phase**
- **Enantiomers form diastereomeric complexes with the chiral stationary phase**
- **Diastereomeric complexes separated out based on differences in affinity for stationary phase**
  - **strongly complexed: elutes slowly**
  - **weakly complexed: elutes more quickly**

Chromatography with a chiral stationary phase

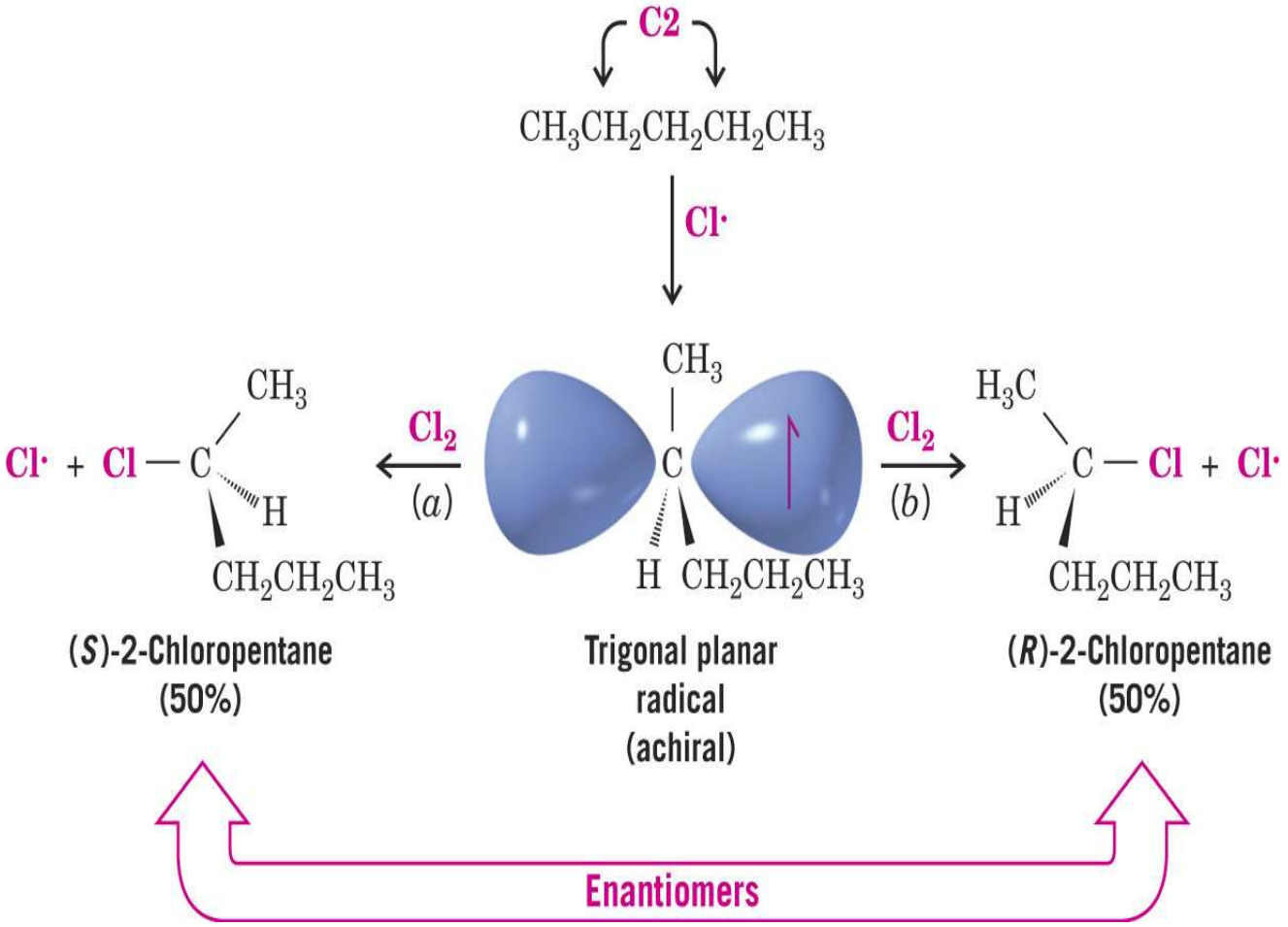
Resolution by Chiral Chromatography



Reactions creating stereoisomers

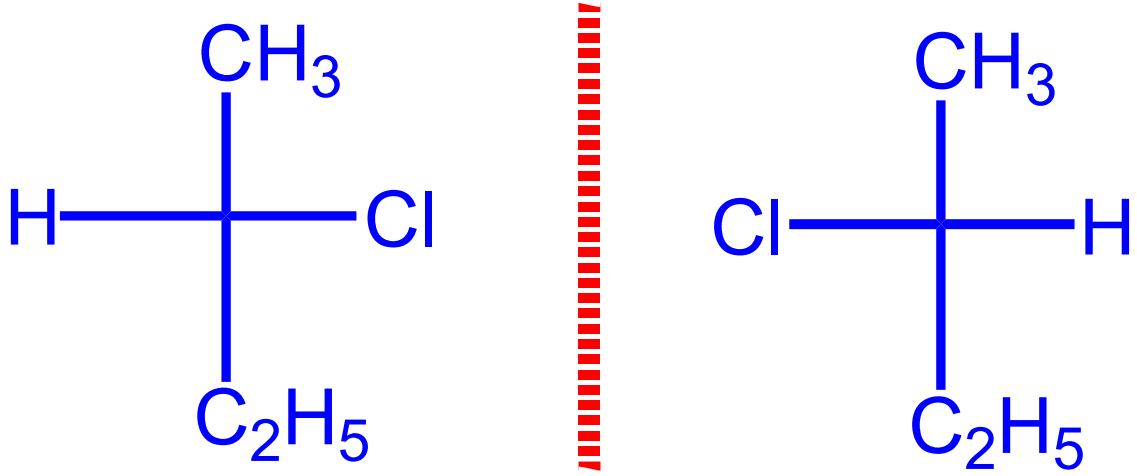
Conversion of an achiral molecule into a chiral molecule, with the generation of a chiral center.

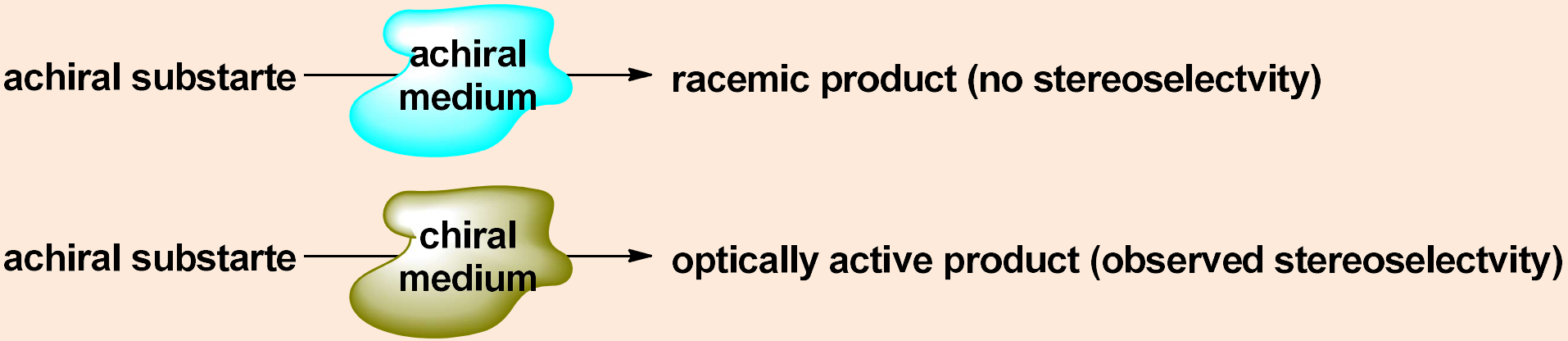
n-butane + Cl_2 $\xrightarrow{h\nu}$ *sec*-butylchloride + n-butylchloride



Reactions creating stereoisomers

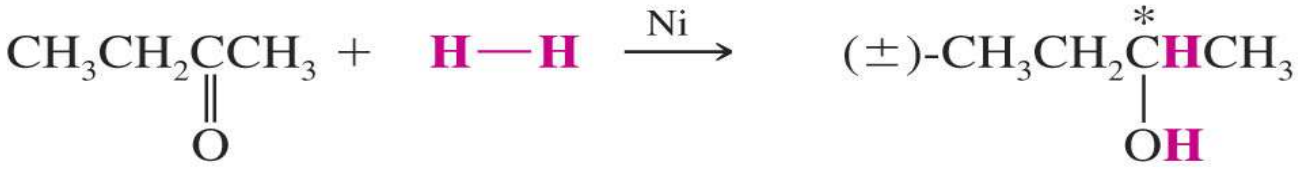
One of the products of chlorination of n-butane is sec-butylchloride which can exist as two enantiomers, as it has a stereocenter in it.



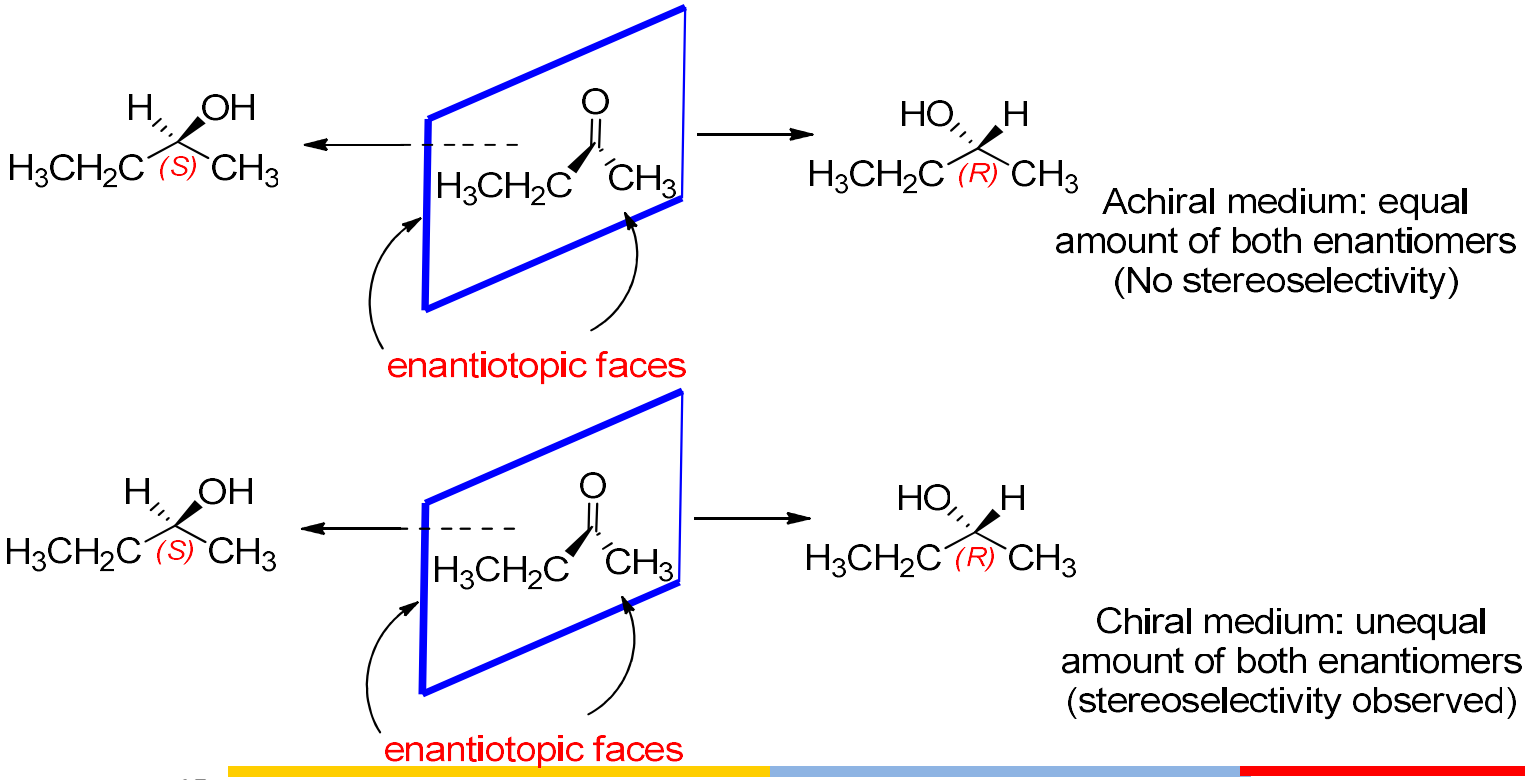


Reactions creating stereoisomers

- Synthesis of chiral compounds from achiral reactants always yields the racemate. **Optically inactive reactants yield optically inactive products.**

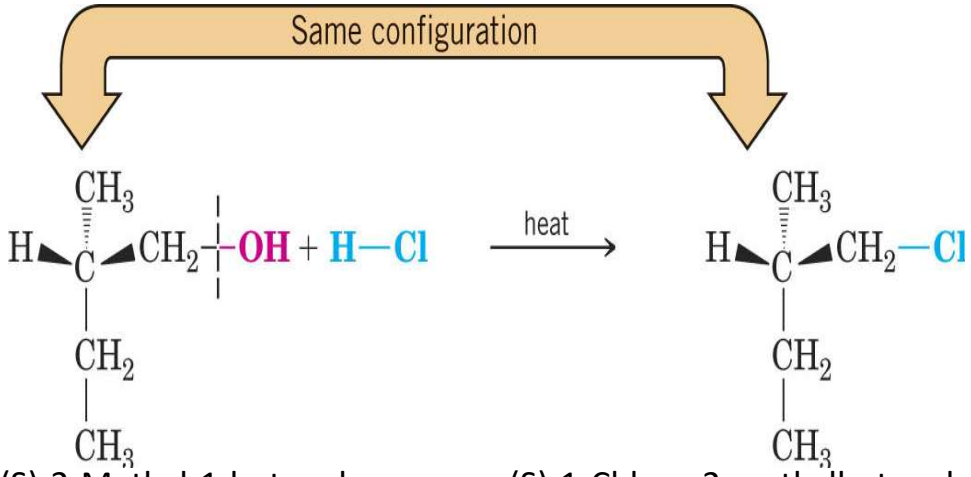


Butanone (achiral molecules) **Hydrogen (achiral molecules)** **(±)-2-Butanol [chiral molecules but 50 : 50 mixture (*R*) and (*S*)]**

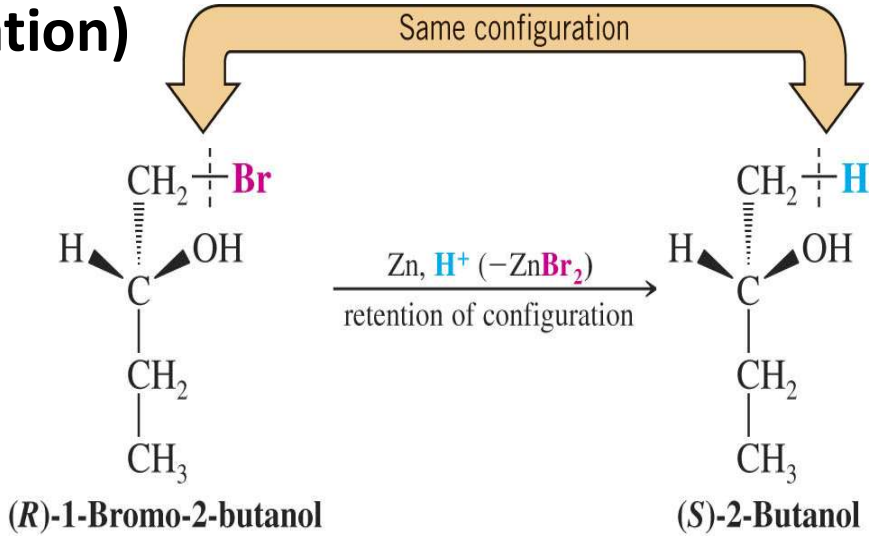


Relative and absolute configurations

A reaction that does not involve the breaking of a bond to a stereocenter proceeds with retention of configuration about that stereocenter. (Same relative configuration)

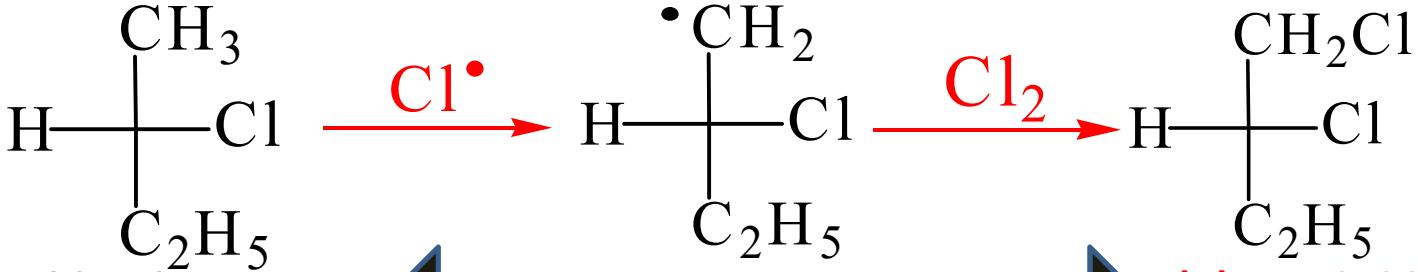


(S)-2-Methyl-1-butanol (S)-1-Chloro-2-methylbutanol



(*R*)-1-Bromo-2-butanol (*S*)-2-Butanol

- **Reaction of a chiral molecule where bonds to the chiral center are not broken. Chlorination of (S)-2-chlorobutane**



(S)-2-chlorobutane **(R)-1,2-dichlorobutane**