

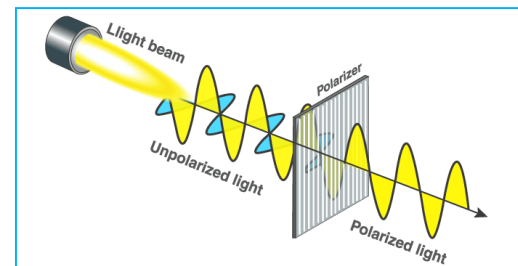
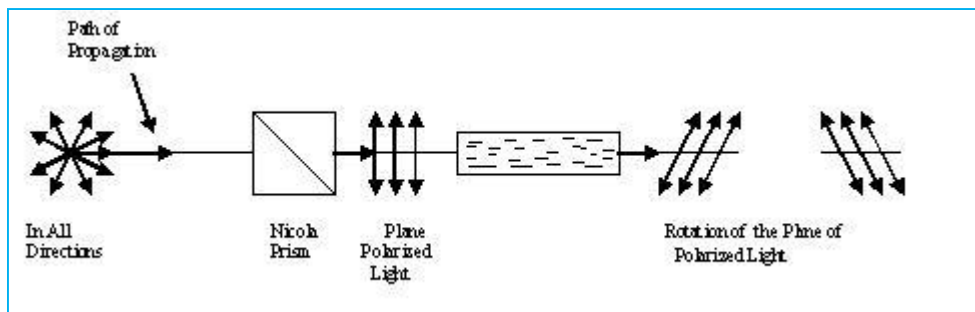
CYI101
Common CHEMISTRY(Organic)

**Stereochemistry: Concept of chirality,
Stereoisomers**

28th December 2021/Sec G & H

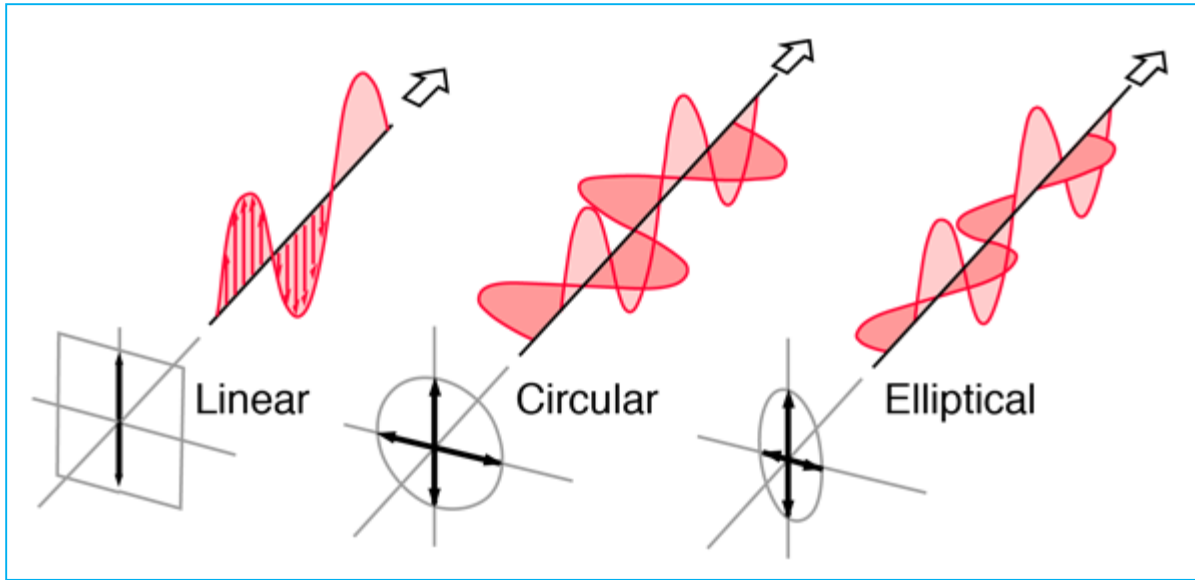
Optical Activity of Stereoisomers

- The chemical and physical properties of two enantiomers are identical except in their interaction with chiral substances. They have identical physical properties, except for how they interact with **plane-polarized light**.
- plane-polarized light** is light that has an electric vector that oscillates in a single plane. If a ray of light travels in any direction, it has vibrations in all directions at right angles to the path of propagation. If this light is passed through Nicola prism*, then the light which emerges out of the prism is found to have vibrations only in one plane. This light is called 'plane polarized light'. The Nicola prism thus used is called a polarizer.

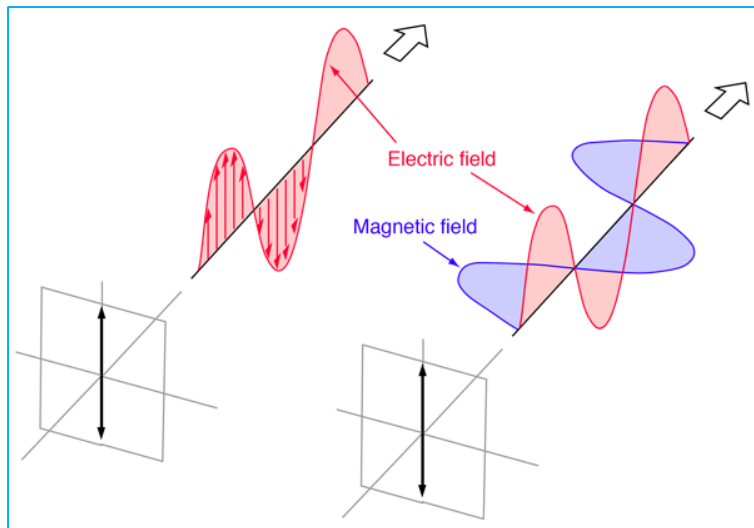


- A **polarimeter** is an instrument that allows polarized light to travel through a sample tube containing an organic compound. It permits the measurement of the degree to which an organic compound rotates plane-polarized light.

Polarization of Light

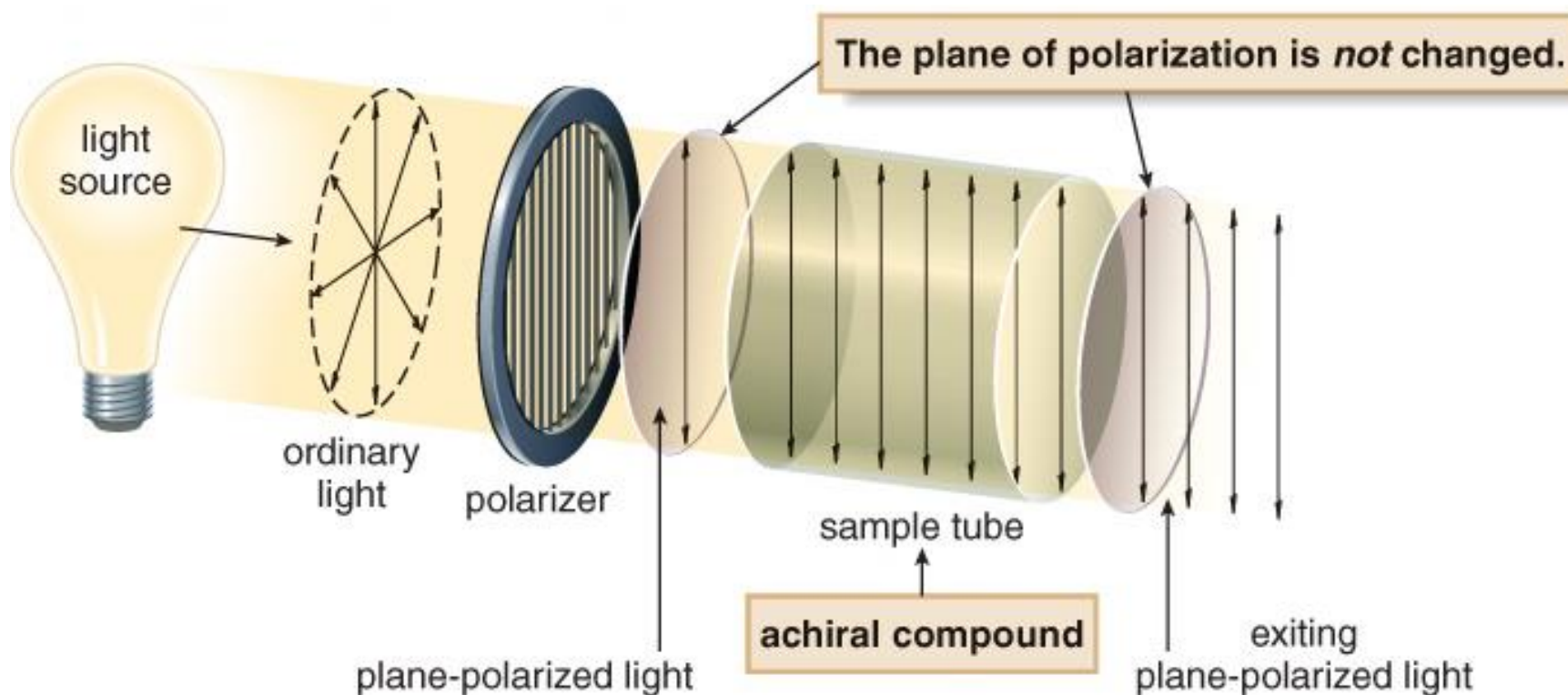


Classification of Polarization

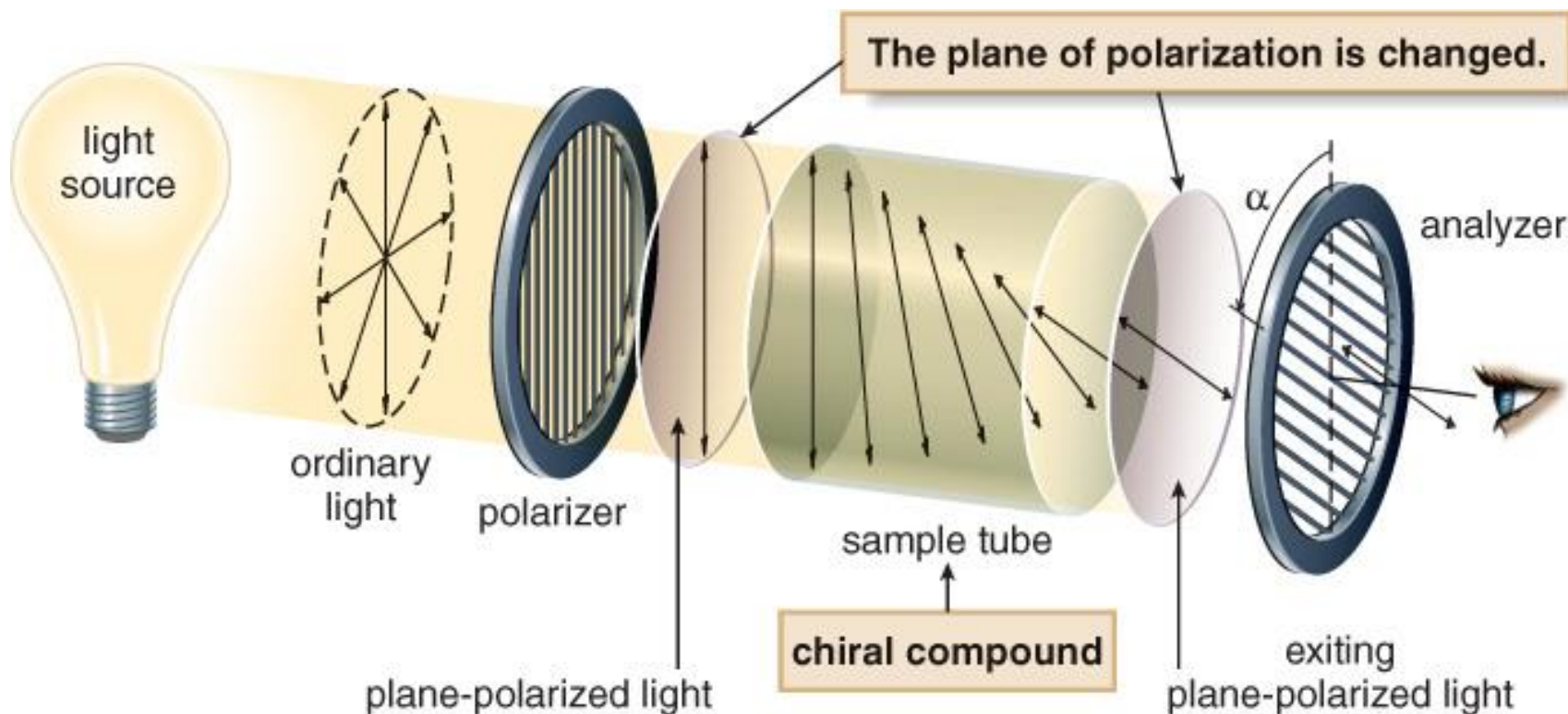


Linear Polarization

- With achiral compounds, the light that exits the sample tube remains unchanged. A compound that does not change the plane of polarized light is said to be **optically inactive**.

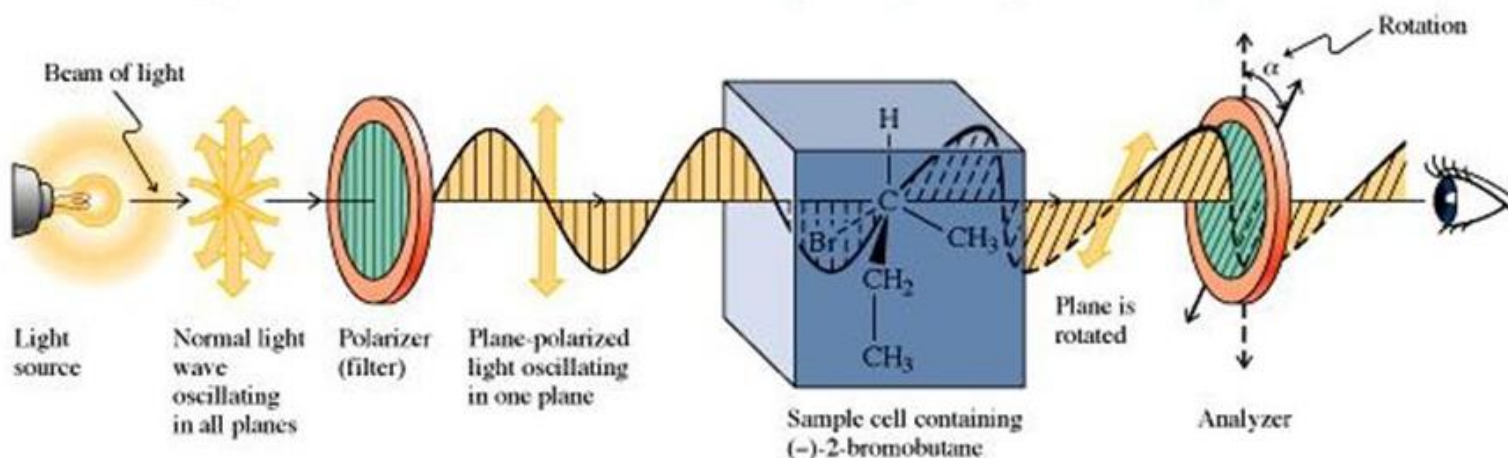


- With chiral compounds, the plane of the polarized light is rotated through an angle α . The angle α is measured in degrees ($^{\circ}$), and is called the **observed rotation**. A compound that rotates polarized light is said to be **optically active**.



Optical Activity of Enantiomers

- 1) Most Physical Properties are identical: mp, bp, density, etc...
- 2) Enantiomers interact differently with plane polarized light



- 3) Each enantiomer of a pair rotates the light in a different direction
 - a) Dextrorotatory = clockwise rotation (+)
 - b) Levorotatory = counterclockwise rotation (-)
- 4) Descriptions: Optical Activity, Optically Active, Optical Isomers

Specific Rotation $[\alpha]_D$: a standardized value for the optical rotation

$$[\alpha]_{\lambda}^T = \frac{[\alpha]_{\text{obs}}}{l \times c}$$

α = observed rotation in **degrees**

l = path length in **dm**

c = concentration of sample in **g/mL**

T = temperature in **°C**

λ = wavelength of light, usually D for the D-line of a sodium lamp (589 nm)

Unit: $\text{deg} \cdot \text{mL} \cdot \text{g}^{-1} \cdot \text{dm}^{-1}$

The specific rotation is a physical constant of a chiral molecule
The $[\alpha]_D$ may also depend upon solvent, therefore the solvent is usually specified.

temperature

Specific rotation

wavelength of monochromatic light
D = Na 'D' line 589 nm

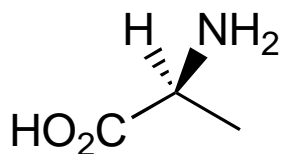
$$[\alpha]_D^t (\text{Solvent}) = \frac{\alpha}{lc}$$

observed rotation (degrees)

concentration (g mL)⁻¹

length of sample tube (decimeters)

Solvent used must be quoted: rotation is solvent dependent



for alanine:

$$[\alpha]_D^{20} = +14.5^\circ (c\ 10, 6N\ HCl)$$

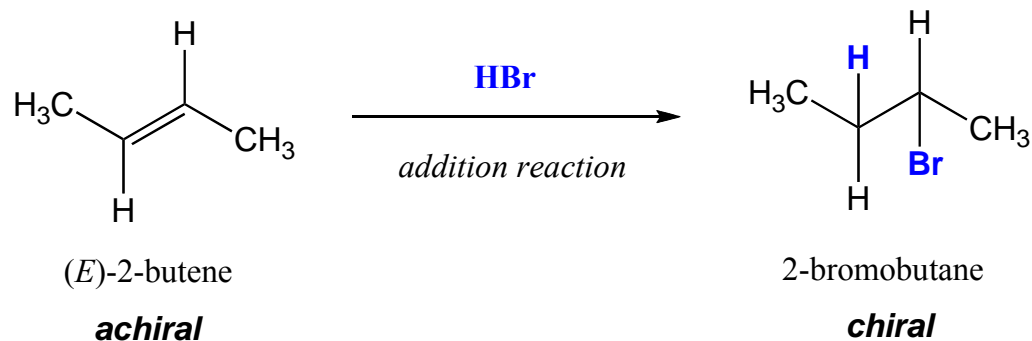
- **Enantiomeric excess, ee OR (optical purity)** is a measurement of how much one enantiomer is present in excess of the racemic mixture. It is denoted by the symbol *ee*.

$$ee = \% \text{ of one enantiomer} - \% \text{ of the other enantiomer.}$$

- **Consider the following example—**If a mixture contains 75% of one enantiomer and 25% of the other, the enantiomeric excess is $75\% - 25\% = 50\%$. Thus, there is a 50% excess of one enantiomer over the racemic mixture.
- **The enantiomeric excess can also be calculated if the specific rotation $[\alpha]$ of a mixture and the specific rotation $[\alpha]$ of a pure enantiomer are known.**

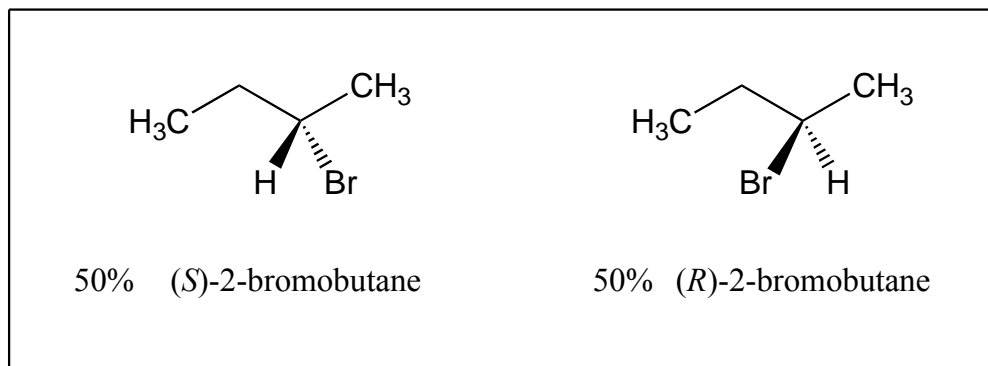
$$ee = ([\alpha] \text{ mixture} / [\alpha] \text{ pure enantiomer}) \times 100.$$

Racemic Mixtures



But do we get (*R*) or (*S*)?

We get both!



A 50:50 mixture of 2 enantiomers is called a racemic mixture or a racemate.

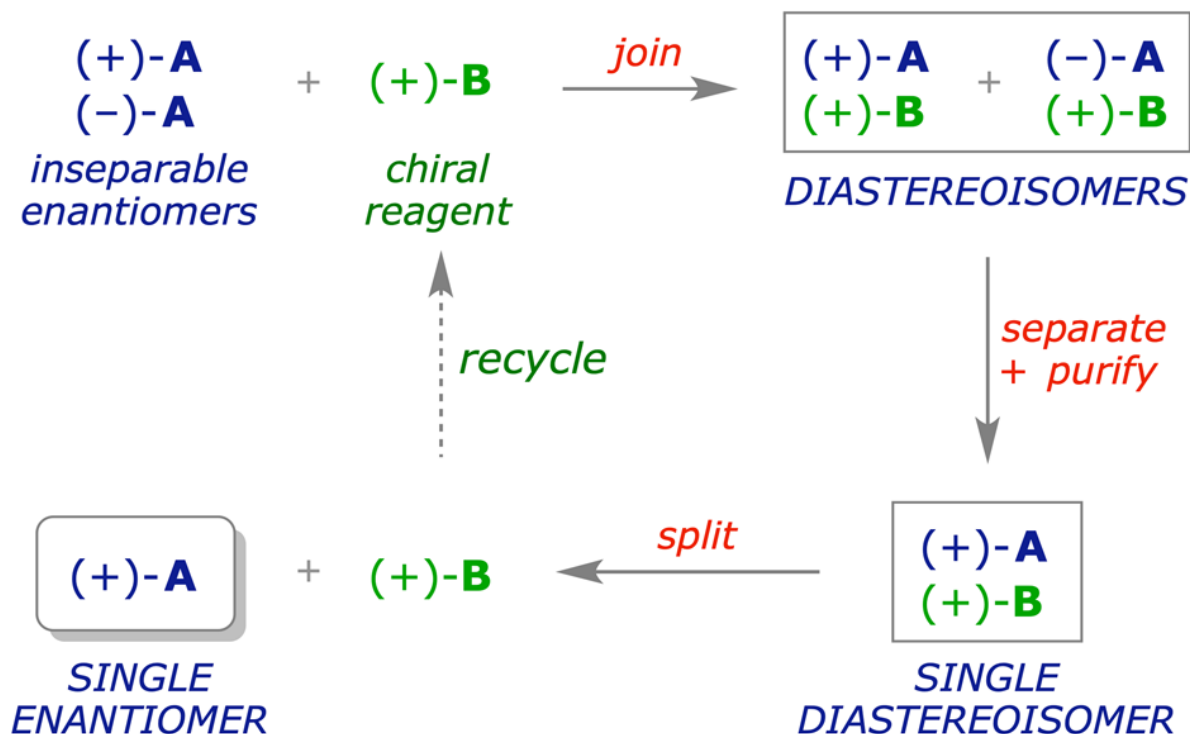
Resolution of Enantiomers

Strategy:

The **enantiomeric** relationship \longrightarrow converted into a **diastereoisomeric** one.

This requires another source of chirality, e.g. an enantiomerically pure chiral reagent, and a procedure that can be applied on a preparative scale. The overall strategy for this process, called **resolution**.

RESOLUTION: A GENERALISED SCHEME

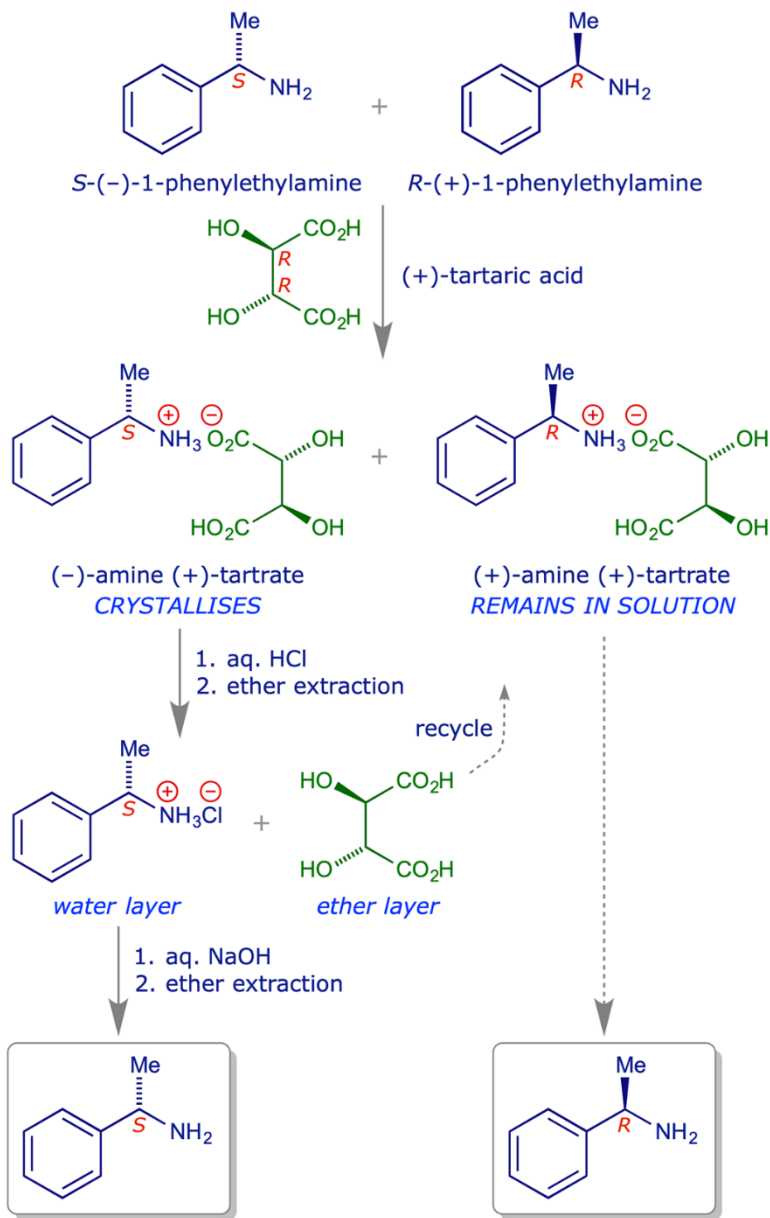


Diastereoisomeric intermediates resulting from any type of interaction between **A** and **B** might be useful, including:

- *Ionic bonding*
- *Covalent bonding*
- *Weak coordinate bonding* (H-bonding, dp-dp interactions, pi/pi interactions, etc.)

Resolution *via* Salt Formation: Amines

RESOLUTION OF 1-PHENYLETHYLAMINE



Strategy:

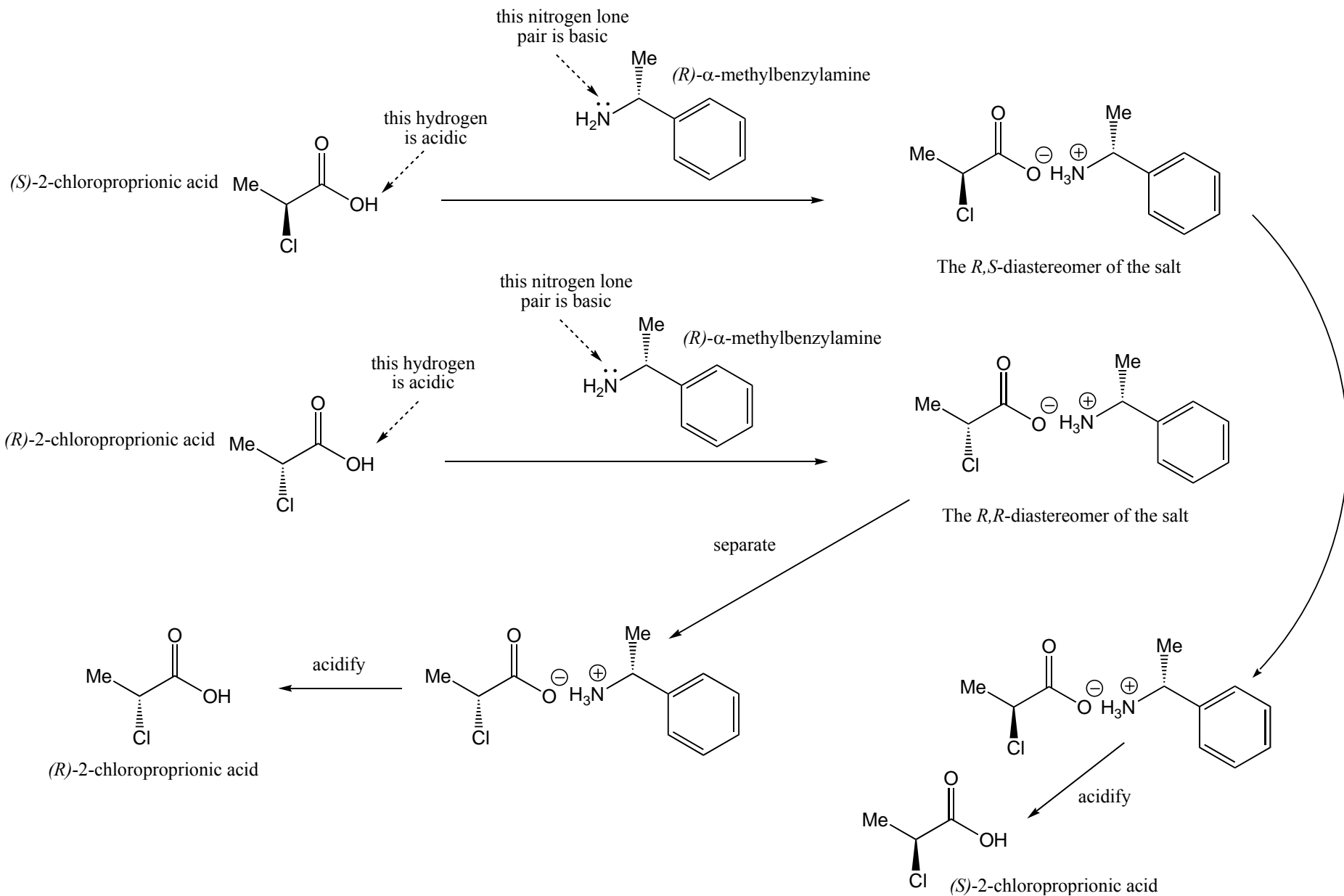
Resolution involves the neutralisation of **acids** or **bases** in order to convert them into a separable pair of diastereoisomeric **salts**.

Resolution of racemic acids (using an **amine** as the *resolving agent*) and bases (using an **acid** as the *resolving agent*).

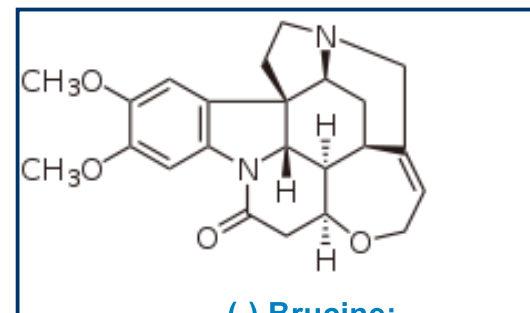
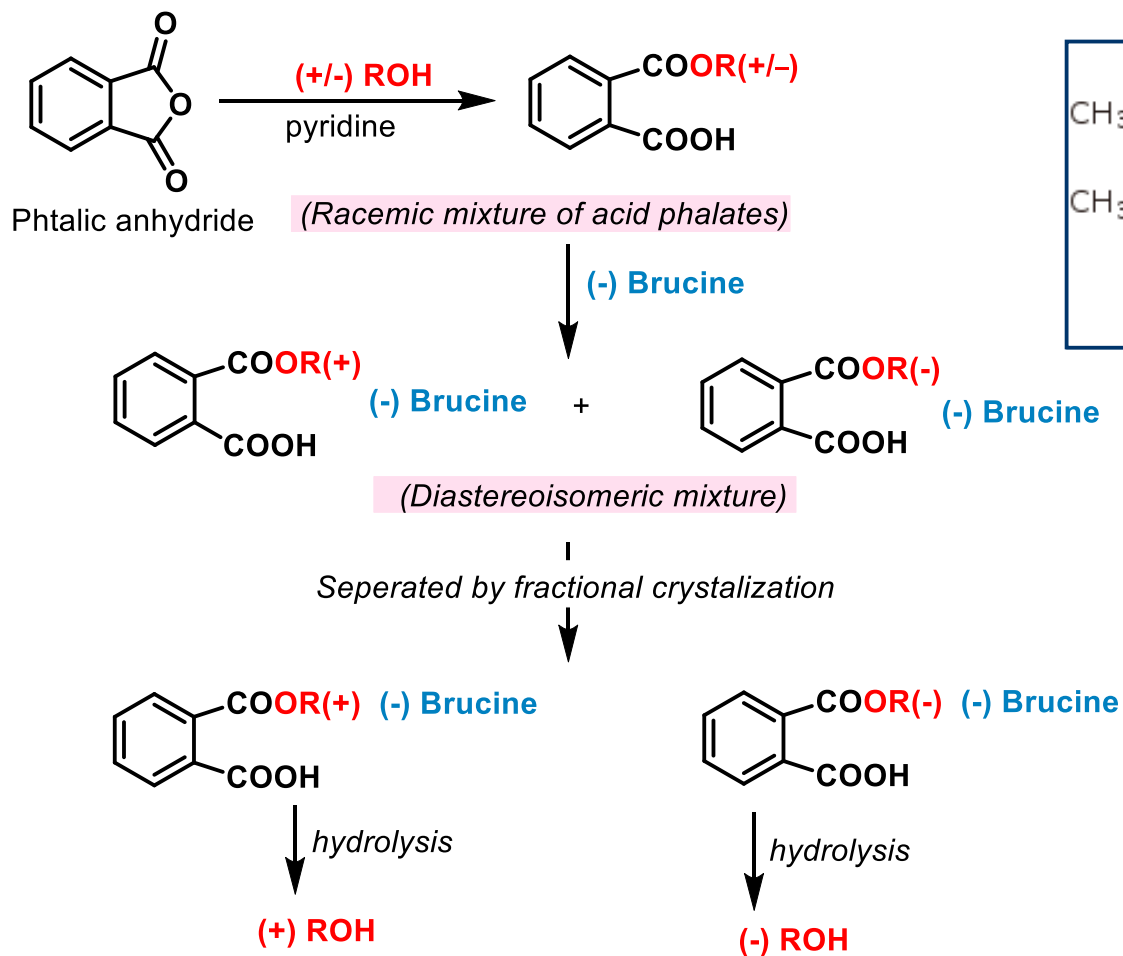
This type of resolution is generally efficient for the following reasons:

- Diastereoisomeric salts can often be separated by crystallisation. Recrystallisation gives high diastereoisomeric purity and the process is practical on a large scale.
- The pure enantiomers can easily be separated from the resolving agent at the end of the process by simple solvent (acid/base) extraction, which is again practical on a large scale.

Resolution of Enantiomeric Acids



Resolution of Enantiomeric Alcohols

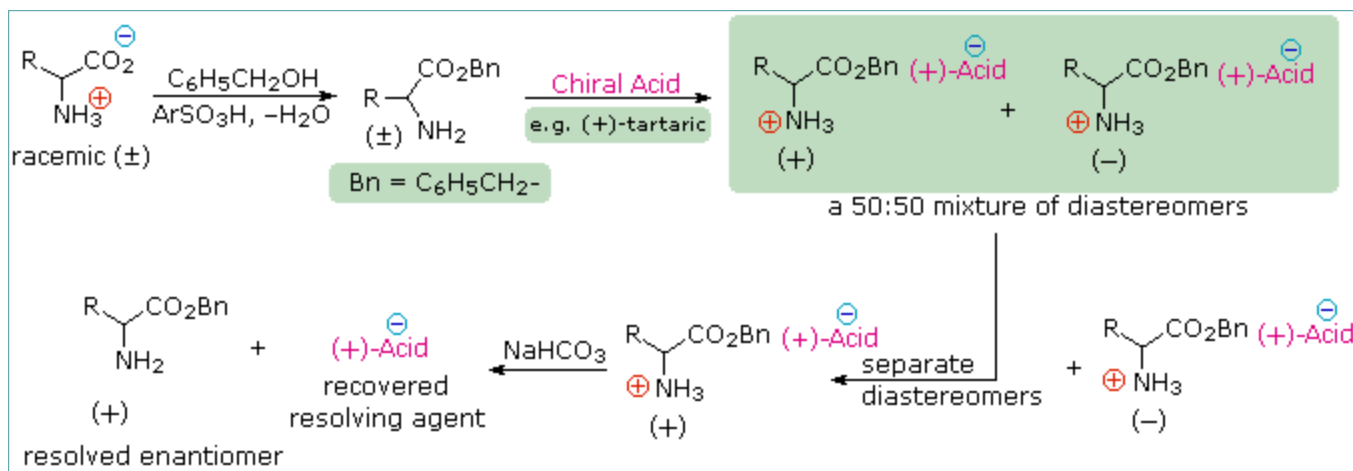
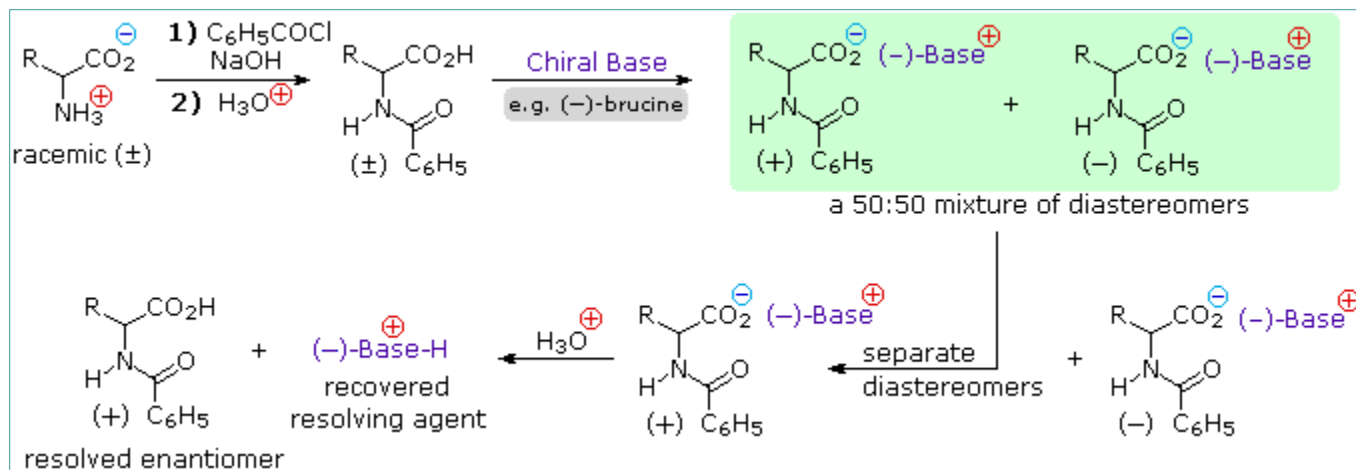


(-) Brucine:
Naturally available
chiral alkaloid

Resolution of Amino acids

Since amino acids are amphoteric, resolution could be achieved by using the basic character of the amine function or acidic character of the acid function

Chiral Base as resolving agent



Chiral Acid as resolving agent