CYI101
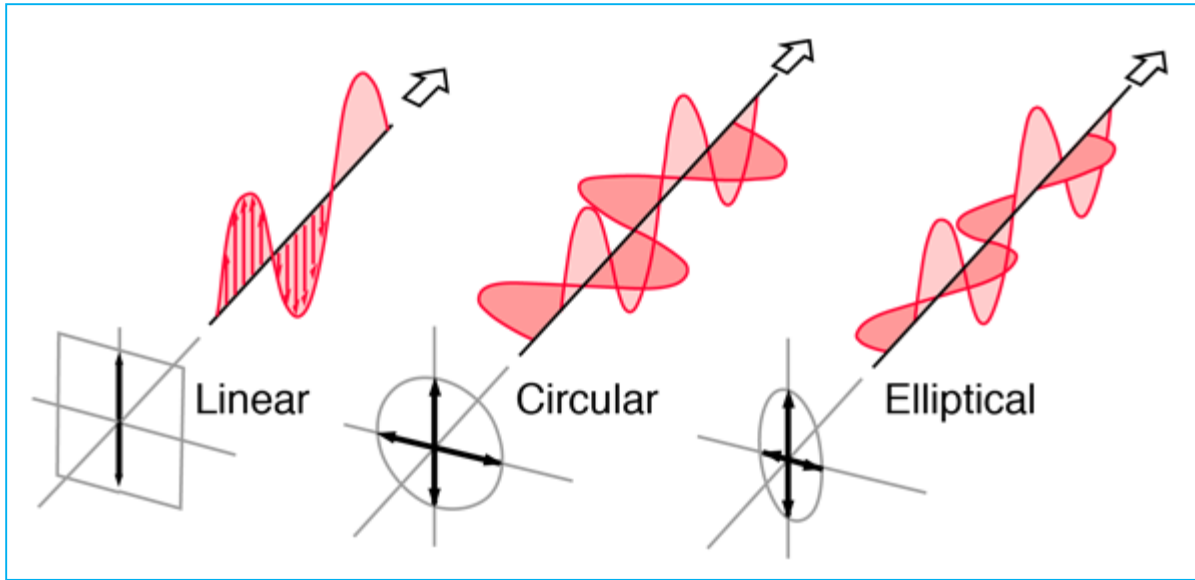# Common CHEMISTRY(Organic)

Stereochemistry: Concept of chirality, Stereoisomers

Polarization of Light

Linear   Circular   Elliptical

Classification of Polarization

Electric field

Magnetic field
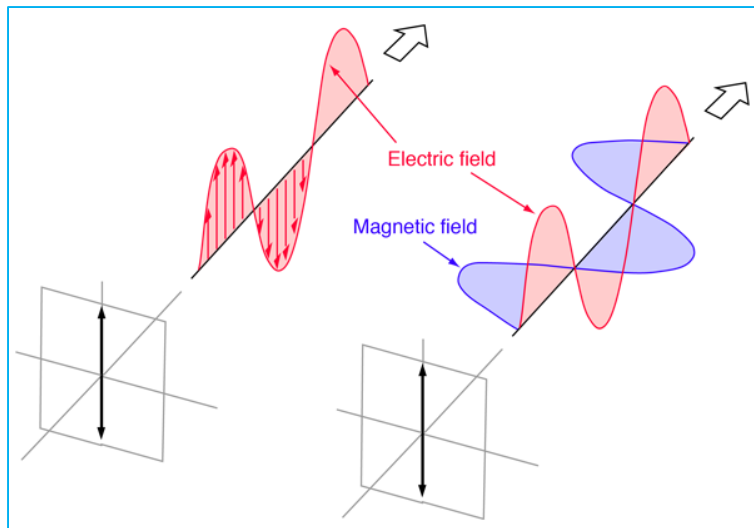
Linear Polarization

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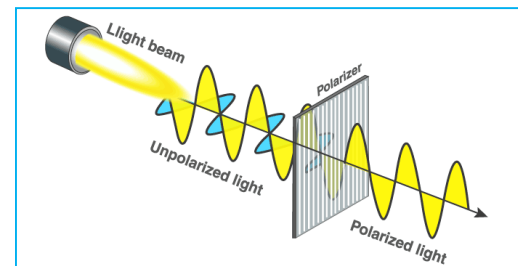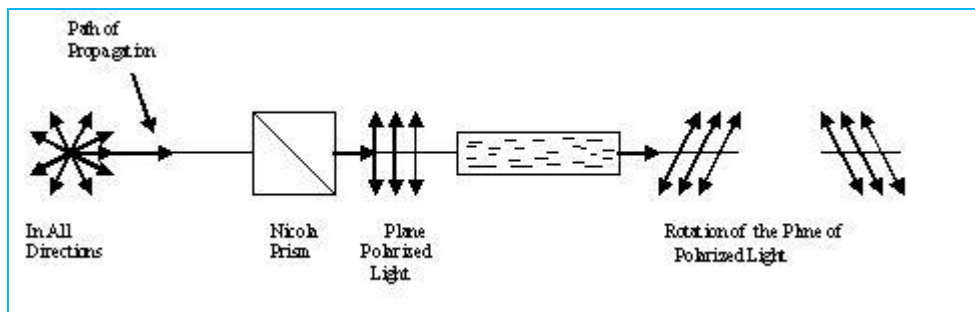
- **A polarimeter** is an instrument that allows polarized light to travel through a sample tube containing an organic compound. It permits the measurement of the degree to which an organic compound rotates plane-polarized light.

- **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.**
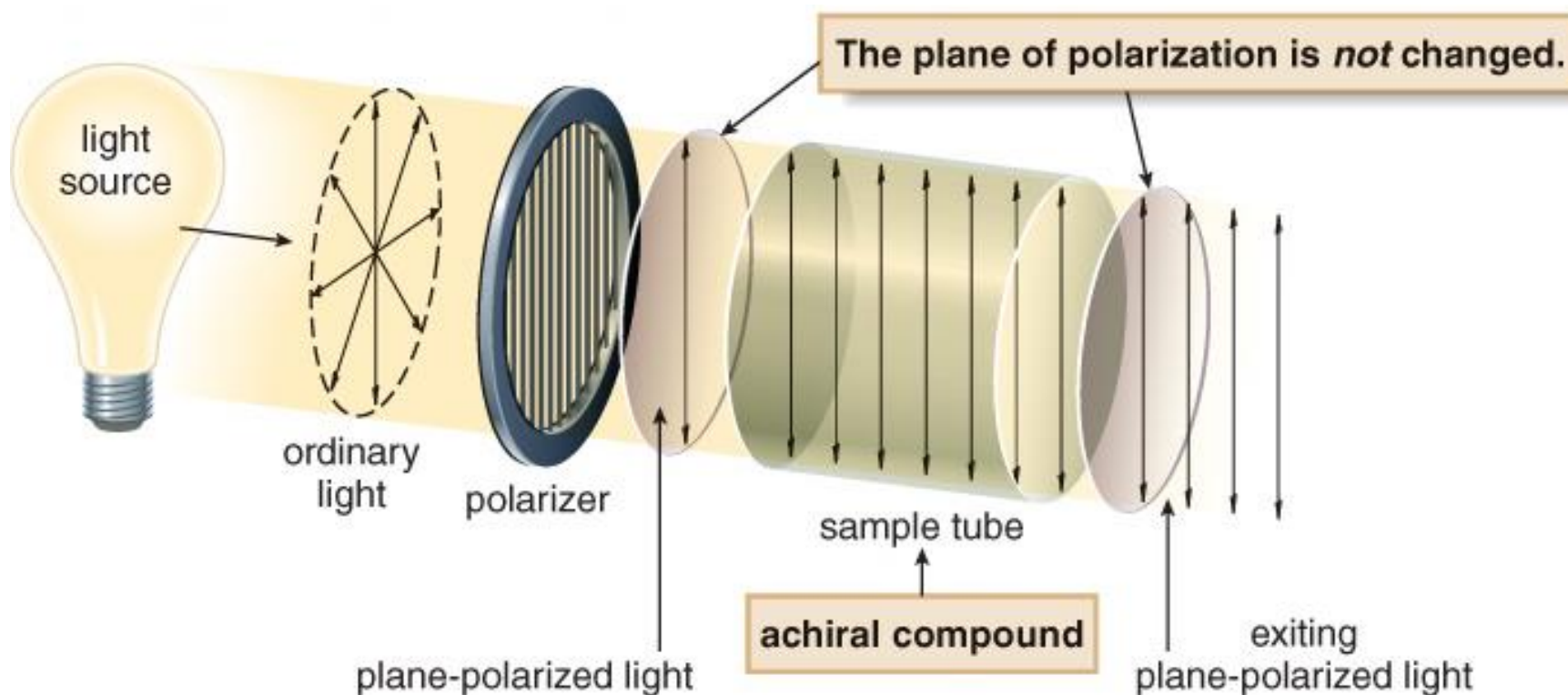
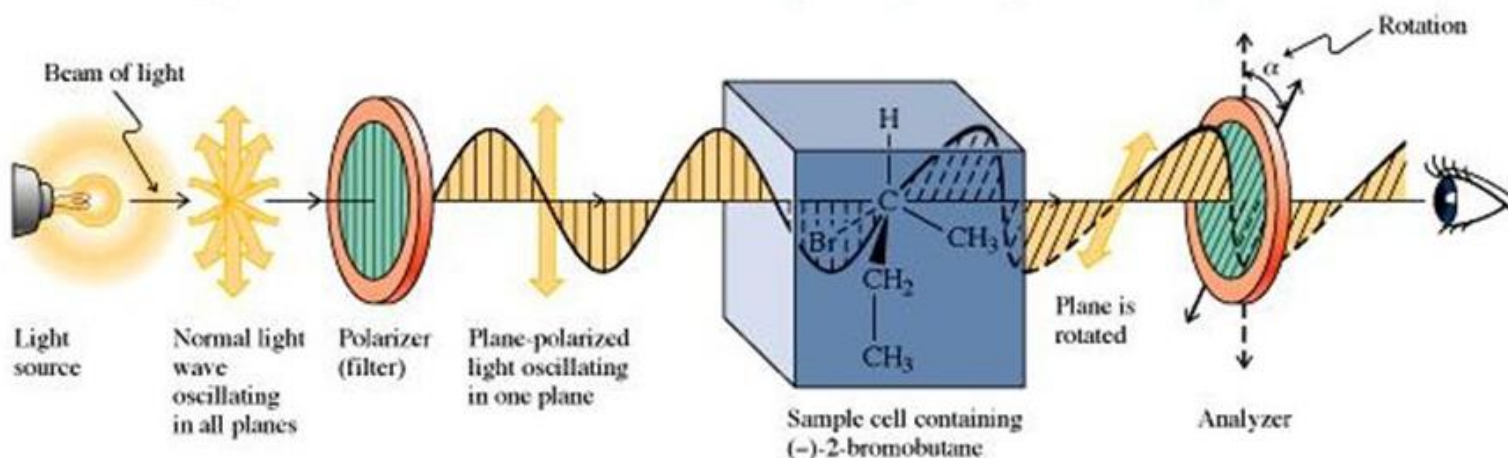- **With chiral compounds, the plane of the polarized light is rotated through an angle α. The angle α is measured in degrees (°), and is called the observed rotation. A compound that rotates polarized light is said to be optically active.**
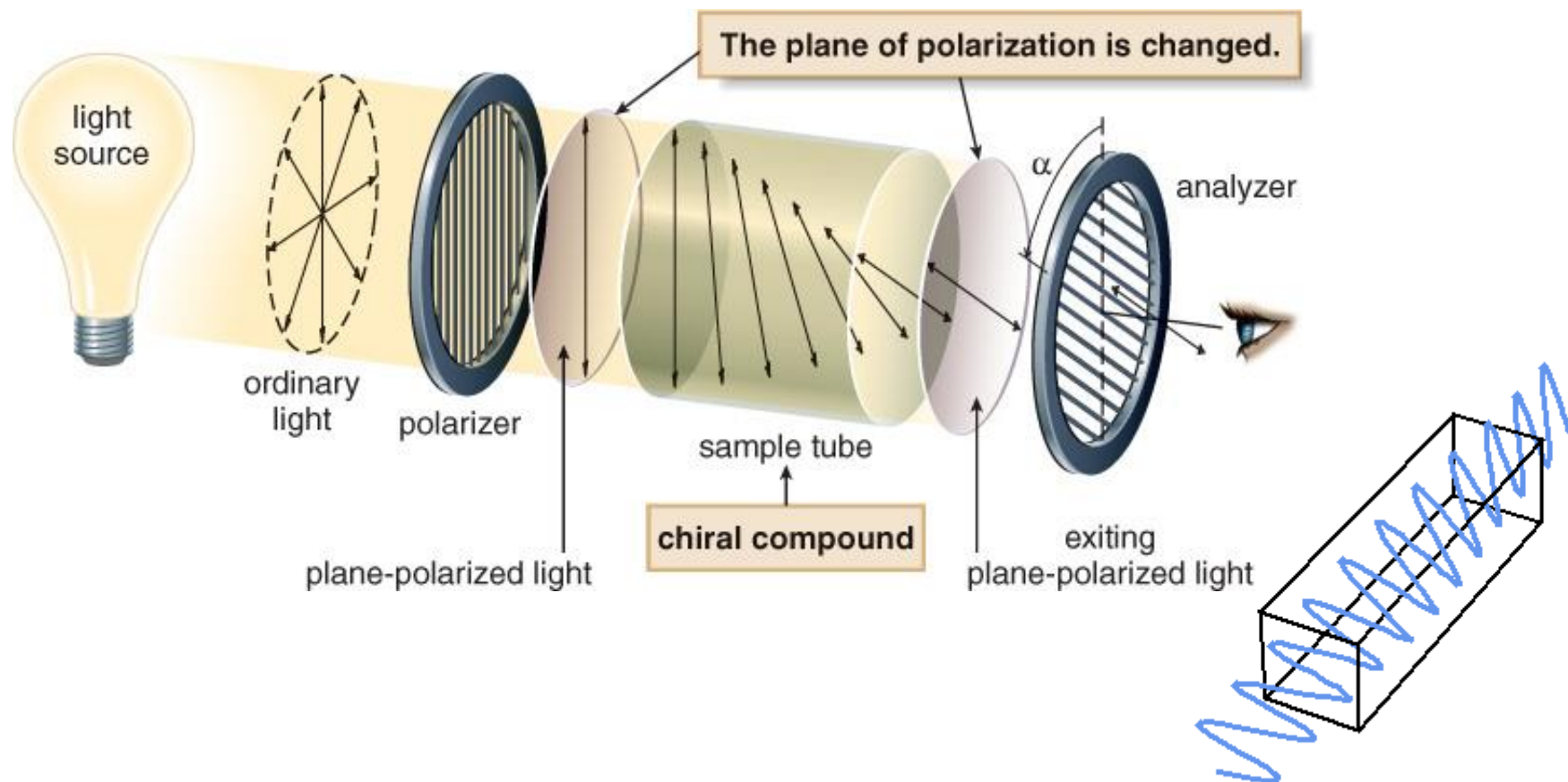
Optical Activity of Enantiomers

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

Beam of light

Rotation

Light source

Normal light wave oscillating in all planes

Polarizer (filter)

Plane-polarized light oscillating in one plane

H

C

Br

CH_3

CH_2

CH_3

Sample cell containing (−)-2-bromobutane

Plane is rotated

Analyzer

α

3) Each enantiomer of a pair rotates the light in a different direction
   a) Dextrorotatory = clockwise rotation (+) d
   b) Levorotatory = counterclockwise rotation (-) l

4) Descriptions: Optical Activity, Optically Active, Optical Isomers

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

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

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: deg.ml.g^{-1}.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.

Specific rotation

temperature

observed rotation (drgrees)

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

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

concentration (g ml)$^{-1}$

length of sample tube (decimeters)

Solvent used must be quoted:
rotation is solvent dependent
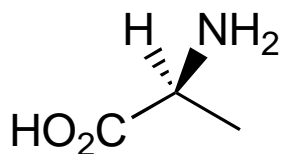
for alanine:

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

- **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 = % of one enantiomer - % 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 [α] of a mixture and the specific rotation [α] of a pure enantiomer are known.

  ee = ([α] mixture/[α] pure enantiomer) x 100.

What is the ee of the following racemic mixture?

95% A and 5% B

ee = % of A - % of B

= 95 – 5 = 90 ee

Given the ee value, what percent is there of each isomer, 60% ee

60% excess A, then 40% racemic mixture(so 20% A and 20% B)

So, 60% + 20% = 80% A and leaves 20% B

A pure compound has a specific rotation of +24, a solution of this compound has a rotation of +10, what is the ee?

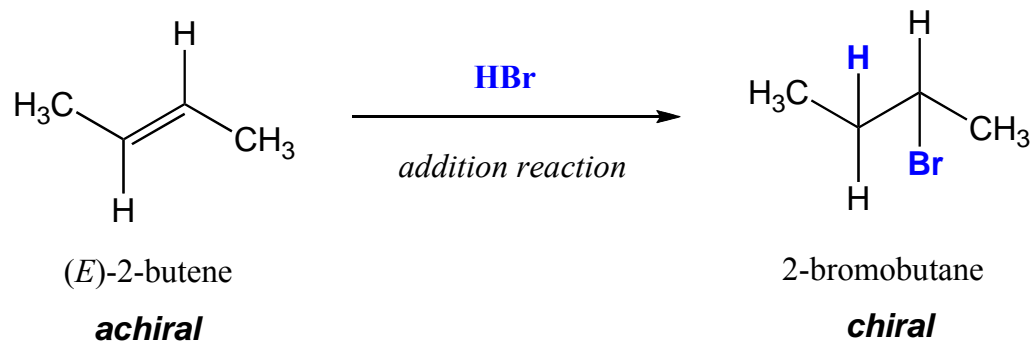**ee = [α] of mixture / [α] of pure x 100**

=+10/+24 x 100 = 42%

Enantiomeric Excess = **%Optical Purity** = how much more of one enantiomer than the other

$$\%\text{Optical Purity} = \left(\frac{[\alpha_{observed}]}{[\alpha]} x100 \right)$$

Exercise   75% optical purity, $[\alpha] = 23.1°$, what is $[\alpha]_{observed}$?

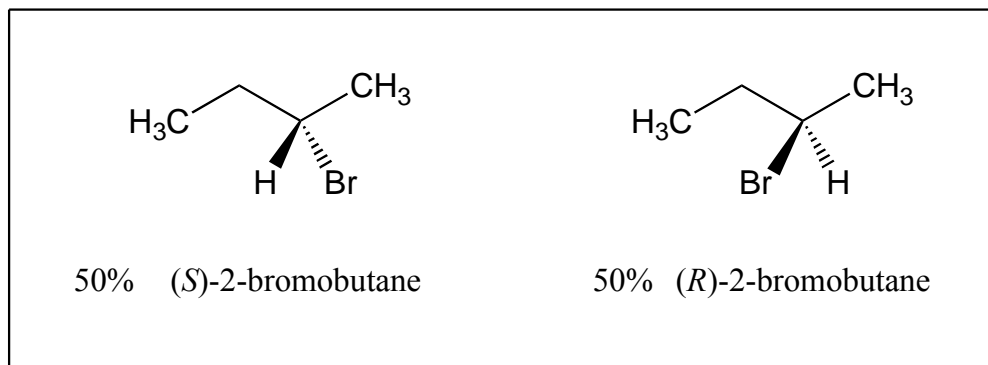$$0.75 = \frac{\alpha_o}{\alpha} \Rightarrow 0.75\alpha = \alpha_o = (0.75)(23.1°) = 17.33°$$

Racemic Mixtures

(E)-2-butene → HBr (addition reaction) → 2-bromobutane

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

(E)-2-butene
achiral

2-bromobutane
chiral

We get both!

50%   (S)-2-bromobutane

50%   (R)-2-bromobutane

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

Racemic Modifications: Thermodynamics

When equimolecular quantities of two enantiomers of a chiral molecule are mixed together or formed in a reaction, the resultant mixture is called a racemic modification/racemate/simply a (±) pair.

Entropy of mixing:

$$\Delta S = -Rx_1 lnx_1 - Rx_2 lnx_2 \; (x_1 \& x_2 \text{ are the mole fractions.})$$
$$= -Rln\frac{1}{2} = Rln2 \approx 6 \text{ J/mol/degree } (x_1 = x_2 = \frac{1}{2})$$

Change of Free Energy ΔG:

$$\Delta G = \Delta H - T\Delta S \; (\Delta H = \text{Enthalpy}; \Delta S = \text{entropy.})$$

At RT (300K), ΔG = 300 x 6 J = 1.8 kJ/ mol; assuming the enthalpy remains constant.

The conversion of pure enantiomers into the racemic modification – a process known as racemisation – *is thermodynamically favourable and a spontaneous process.*

Racemization: *Thermodynamically favored process*

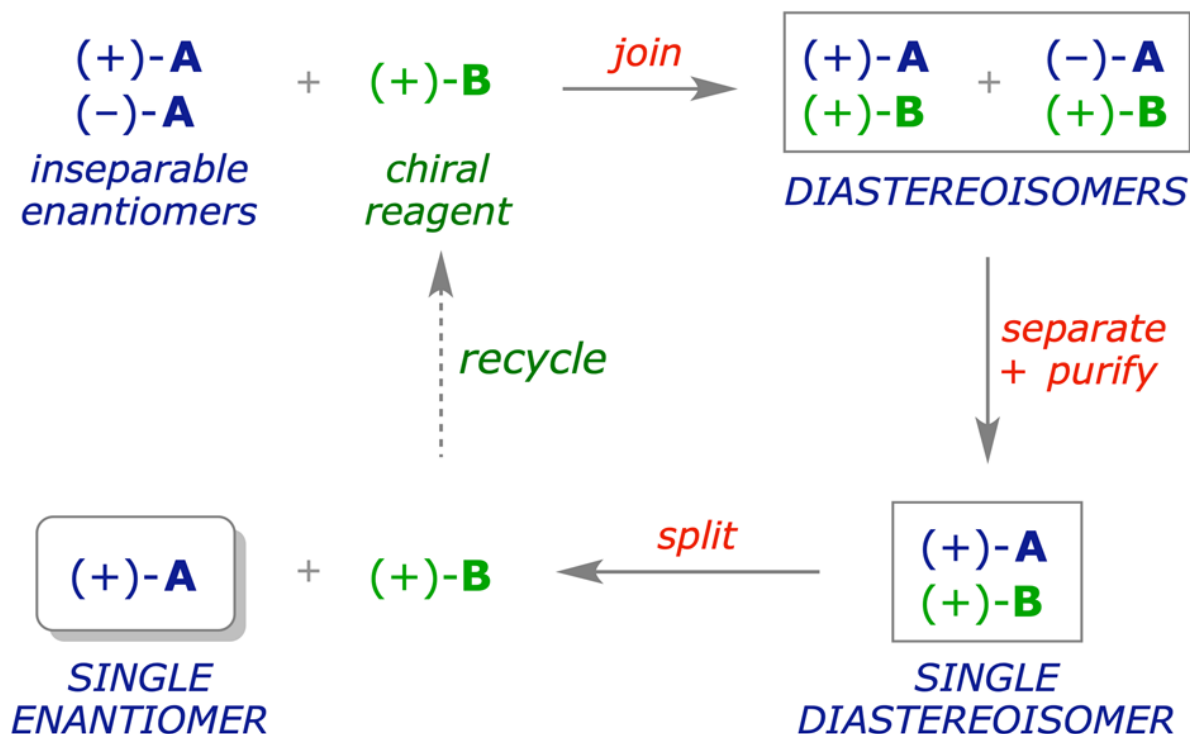

Room temperature racemization of Alanine

(L)-alanine   (rac)-alanine   (D)-alanine
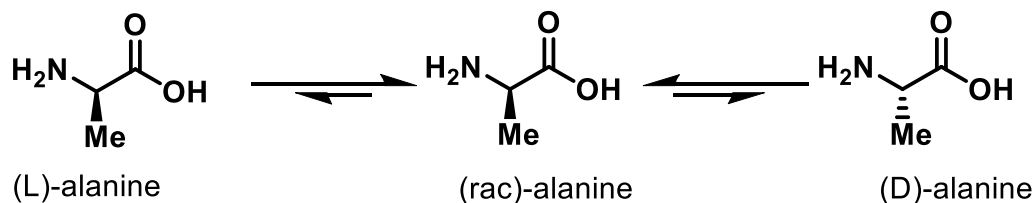
Resolution of Enantiomers

Strategy:

The **enantiomeric** relationship ⟶ 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

(+)-**A**
(−)-**A**   +   (+)-**B**   —*join*→ | (+)-**A**   +   (−)-**A** |
                                        | (+)-**B**   (+)-**B** |

inseparable enantiomers   *chiral reagent*   **DIASTEREOISOMERS**

recycle

separate + purify

(+)-**A**   +   (+)-**B**   ←*split*— | (+)-**A** |
                                          | (+)-**B** |

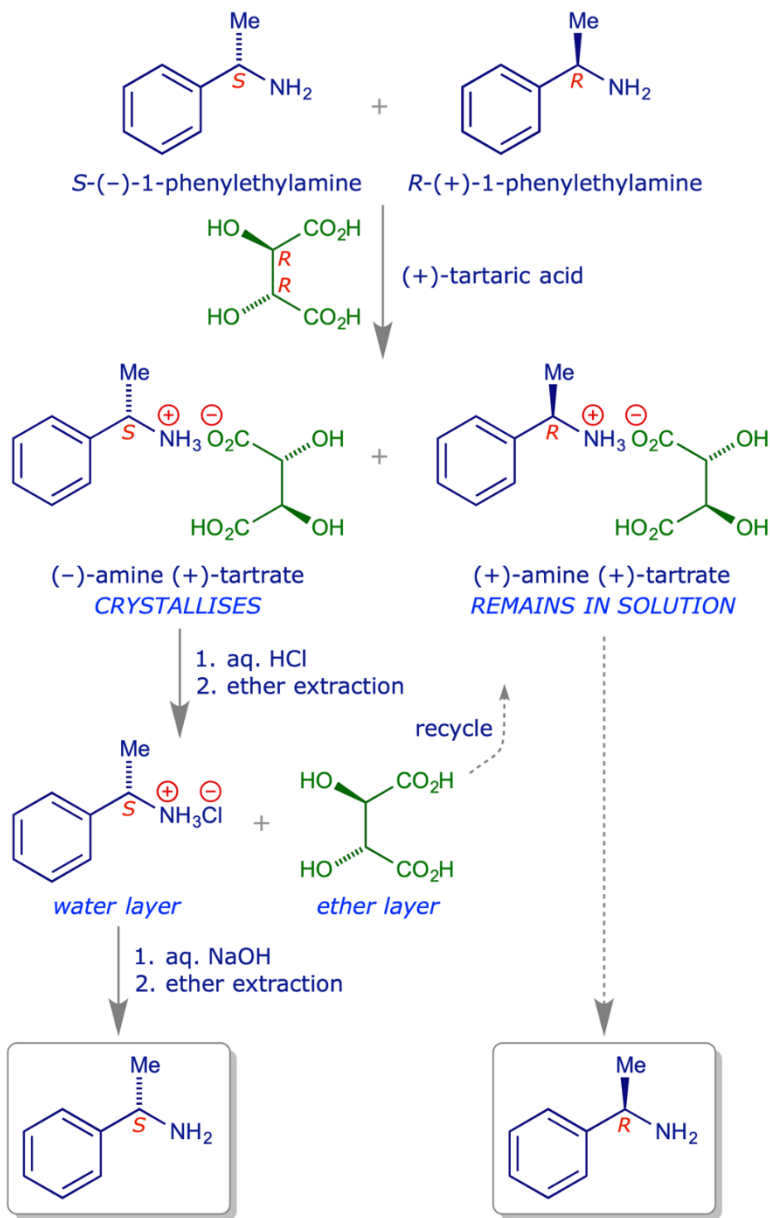**SINGLE ENANTIOMER**   **SINGLE DIASTEREOISOMER**

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
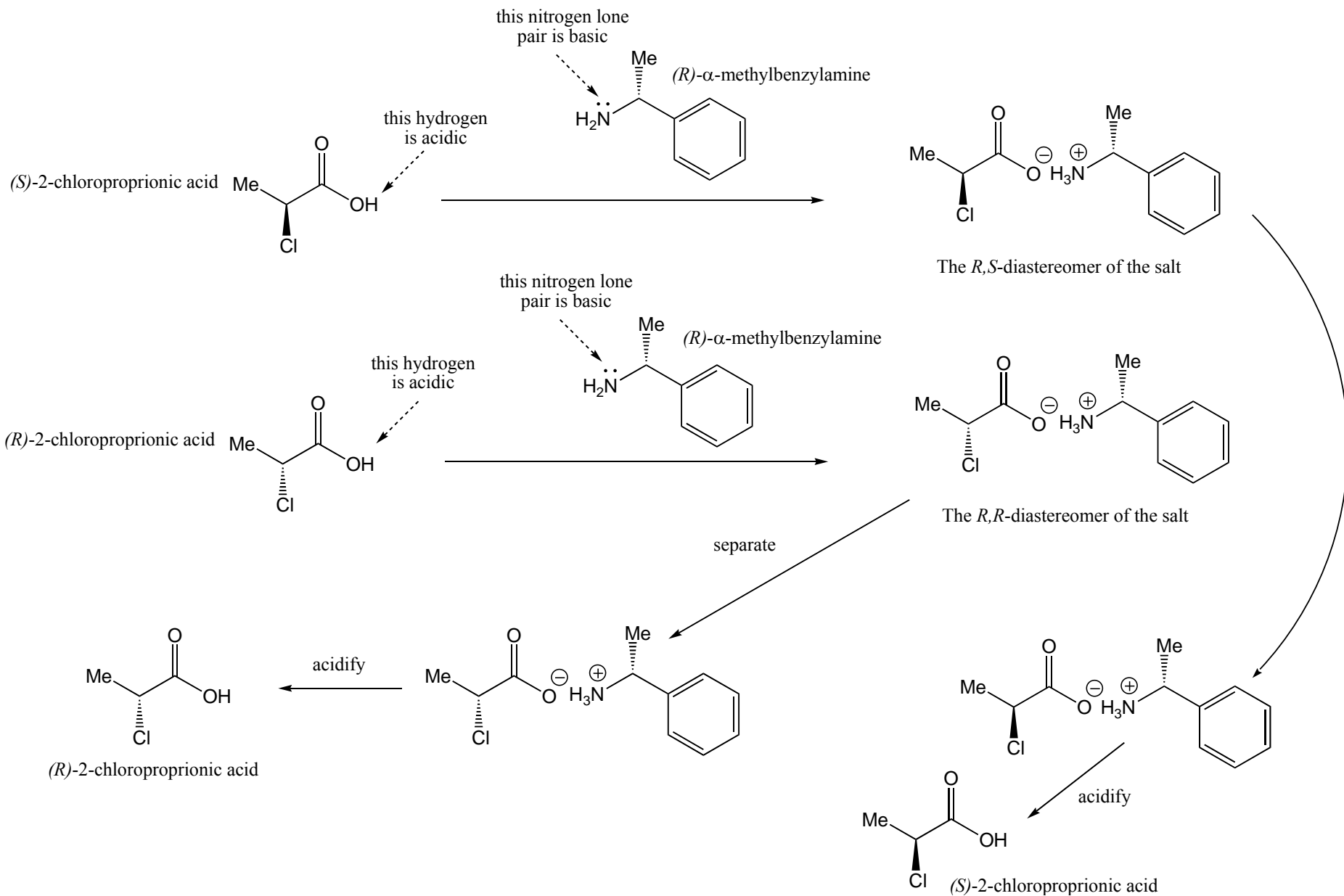

RESOLUTION OF 1-PHENYLETHYLAMINE

Strategy:
Resolution involve 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*).
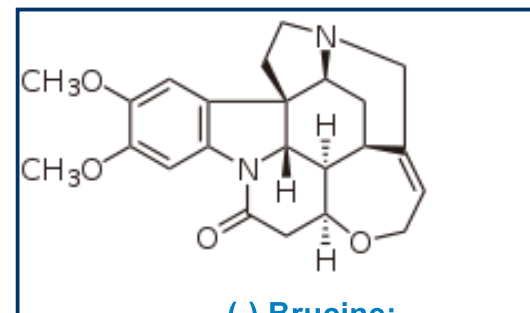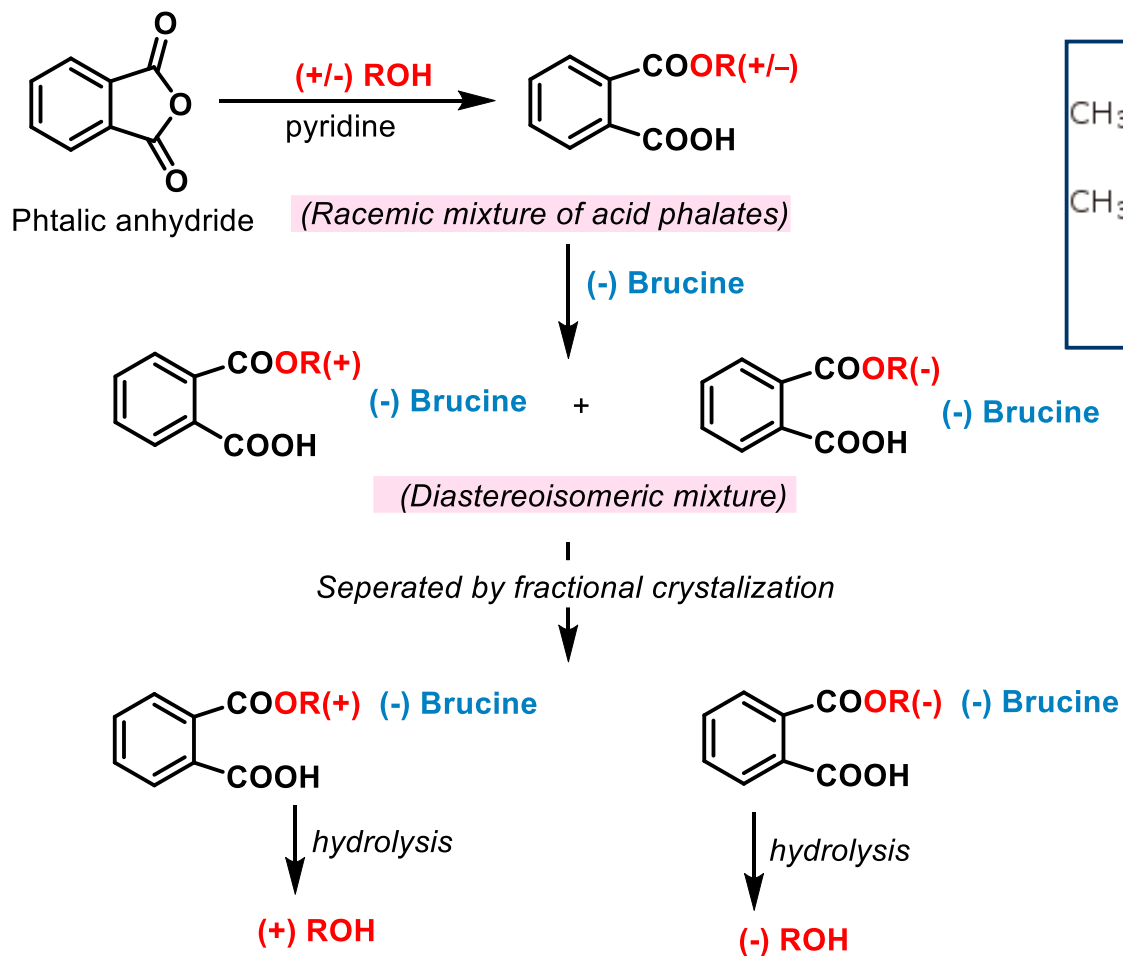
This type of resolution is generally efficient for the following reasons:

• 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
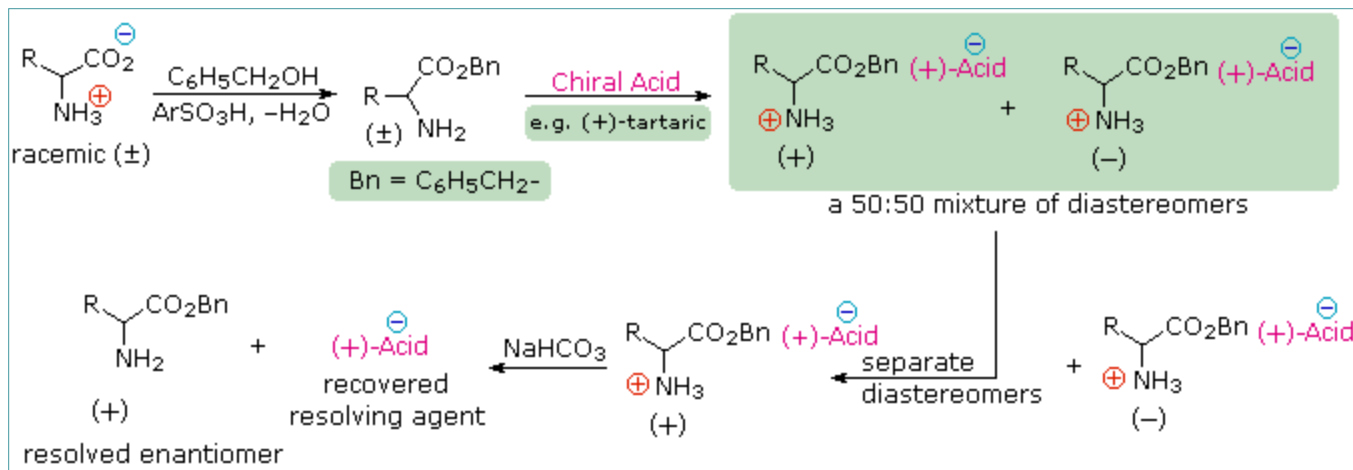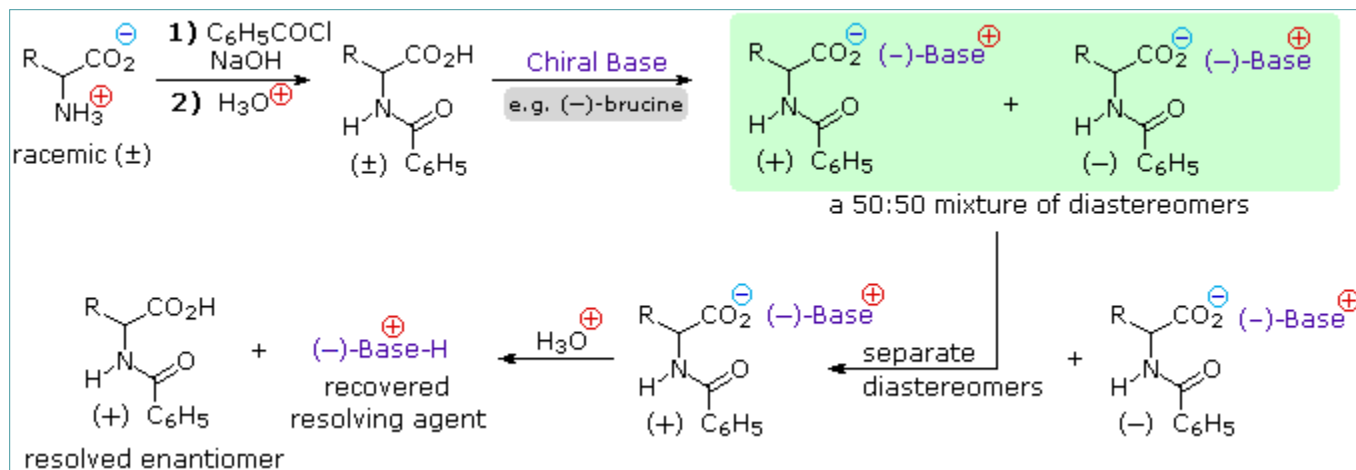
Resolution of Enantiomeric Alcohols

Phtalic anhydride → (+/–) ROH / pyridine → COOR(+/–), COOH *(Racemic mixture of acid phalates)*

(-) Brucine

COOR(+), COOH · (-) Brucine + COOR(-), COOH · (-) Brucine

(Diastereoisomeric mixture)

Seperated by fractional crystalization

COOR(+), COOH (-) Brucine → *hydrolysis* → (+) ROH

COOR(-), COOH (-) Brucine → *hydrolysis* → (-) ROH

(-) Brucine: Naturally avaiable 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