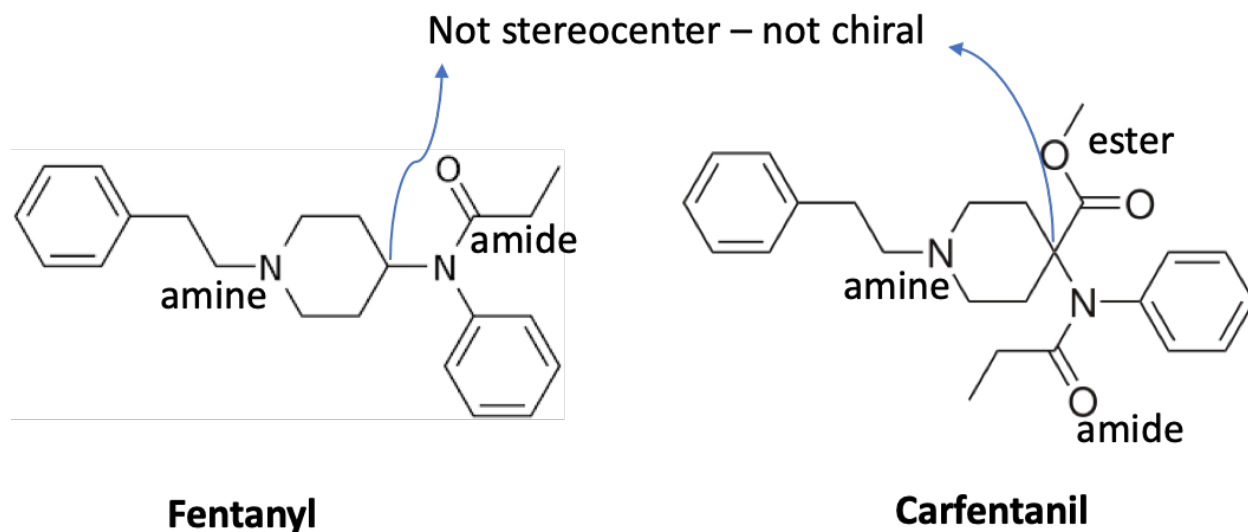


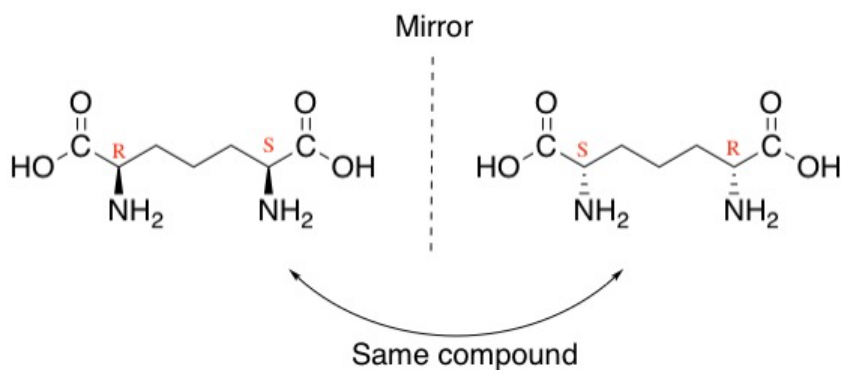
Recall:**Physical Properties of Enantiomers**

- Same physical properties with achiral agents or procedures
 - o Melting point, boiling point, solubility in achiral solvents
- Separation of enantiomers (resolution) require a chiral agent
- **Diastereomers** have different physical properties (m.p, b.p, density, solubility)

Resolution: defined as the separation of enantiomers

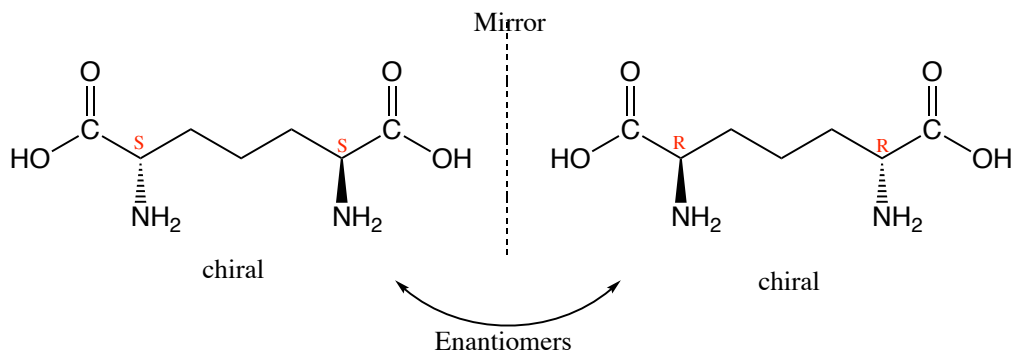
Identification of Chiral and Achiral (not chiral) compounds

Example: Diaminopimelic acid



- The above molecule is achiral even though there are stereogenic center (s), because there is symmetry within the molecule

- These kinds of molecules are called **meso compounds**, which are compounds that contain stereocenters yet because of their symmetry, have mirror images that can be superimposed.
- All achiral molecules, including meso compounds do not rotate polarized light (i.e. $[\alpha]_D = 0$)
- Diaminopimelic acid - a component of bacterial cell wall and biosynthetic precursor to the amino acid known as lysine
- this R,S diaminopimelic acid (above) is a diastereomer of the enantiomers (S,S or R,R diaminopimelic acid) below:

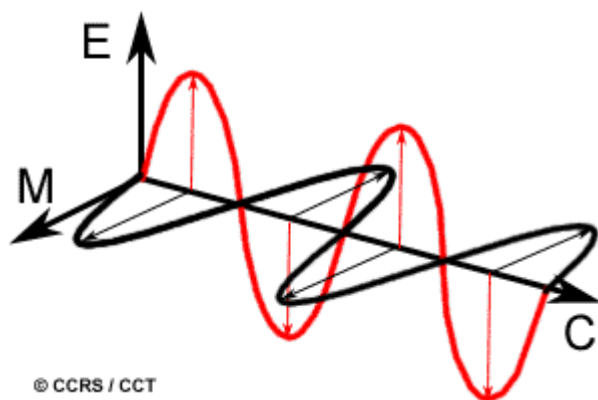


A racemic mixture (racemate) of two enantiomers in a 1:1 ratio also has an $[\alpha]_D = 0$

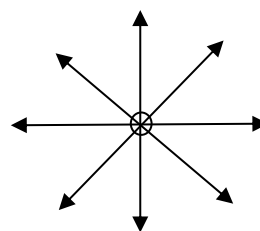
Optical Activity/Rotation

- Rotation of plane of polarized light
- α = measured rotation ($^\circ$)
- $[\alpha]_D$ = Absolute rotation
 - o (+) (clockwise = dextrorotatory)
 - o (-) (counter-clockwise = levorotatory)
- Absolute rotation is 0° for achiral molecules

Pure enantiomers show equal but opposite rotation

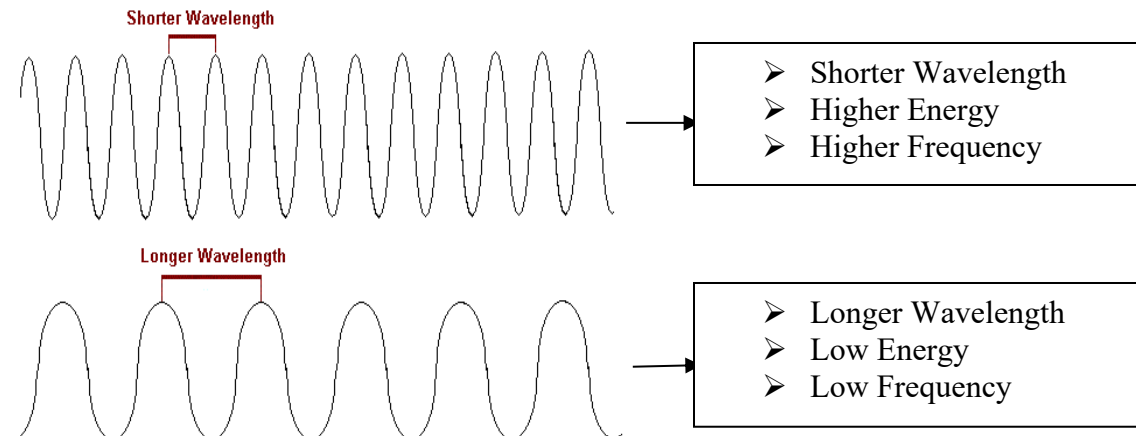


Light has an oscillating electric field (red)



End on view of vector components of normal light. It is possible to polarize light and remove some of those vectors.

intersecting with a magnetic field (black)



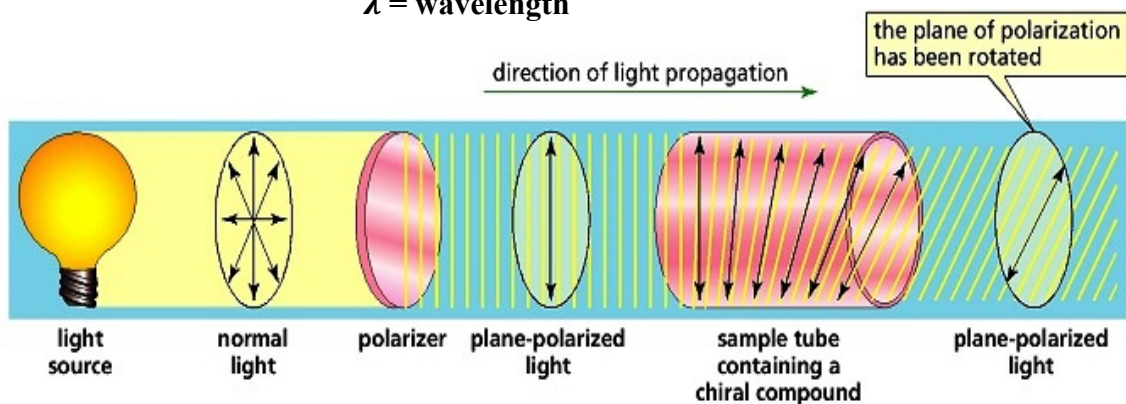
$$E = h\nu = \frac{hc}{\lambda}$$

E = energy

H = Planck's Constant (6.6×10^{-34} Joules•sec

ν = frequency

λ = wavelength



Optical Rotation

Factors affecting optical rotation:

- Concentration of compound, g/cm³ (c)
- Path length that light travels through the solution, cm (l)

$[\alpha]_D$ = Absolute rotation at the D line of sodium (589 nm or 5890 Å)

$$[\alpha]_D = \frac{\alpha}{c \cdot l}$$

α = measured rotation (°) c = concentration (g/cm³) l = path length (cm)

D = D-line of sodium light $[\alpha]$ = absolute rotation

Degrees (°) = + : Clockwise (dextrorotatory/D)

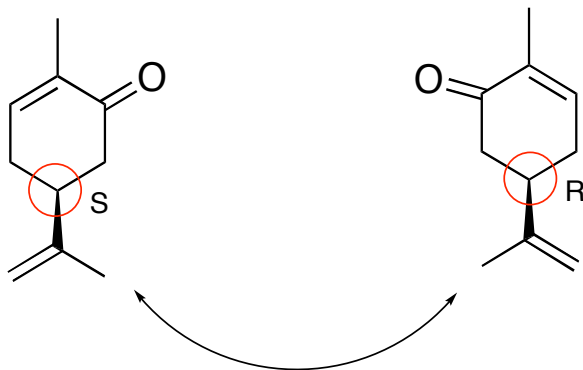
 - : Anticlockwise (levorotatory/L)

Note: not correlated with R/S configuration

Example: Carvone

$[\alpha]_D = -60^\circ$

$[\alpha]_D = +60^\circ$ (made up values, not real rotation)



Enantiomers

S-carvone (caraway)

R-carvone (spearmint)

Note: enantiomers will always have equal but opposite rotation, as such, they would cancel the rotation of the other when present as mixtures in solution.

Calculating Optical Purity

For this example for S-carvone, assume the pure S enantiomer has -60° rotation

R	S	Rotation ($^\circ$)	Optical Purity (%)
100 %	0 %	+ 60 $^\circ$	100 %
75 %	25 %	+ 30 $^\circ$	50 %
50 %	50 %	0 $^\circ$	0 %
25 %	75 %	-30 $^\circ$	50 %
0 %	100	-60 $^\circ$	100 %

If a solution is an equivalent mix of 1:1 R + S enantiomers, α measured = 0°

A 50:50 mixture of enantiomers is called a *racemic mixture* (or racemate)

Optical Purity (measured experimentally) = Enantiomeric Excess (ee) (Theoretical value)

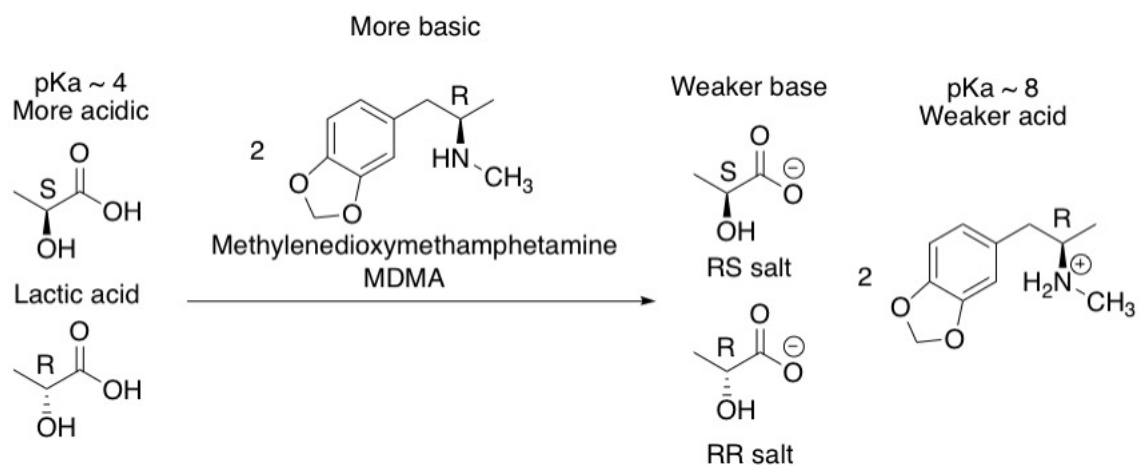
Resolution of Enantiomers

Definition: separation of two enantiomers

- Requires a chiral reagent to convert enantiomers to diastereomeric salts

Racemic mixture: 1:1 ratio of enantiomers in a mixture

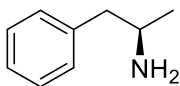
Example: Lactic Acid



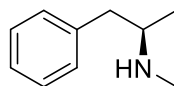
The starting material lactic acids are enantiomers of each other.

By reacting enantiomers to make a salt with an enantiomer of MDMA (another chiral molecule that is optically pure), also known as ecstasy, one can obtain salts which are now diastereomers of each other (RS and RR). The resulting diastereomers have different melting points, boiling points, solubilities, and can be separated by crystallization.

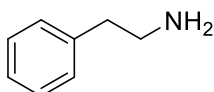
More examples of amines:



Amphetamine

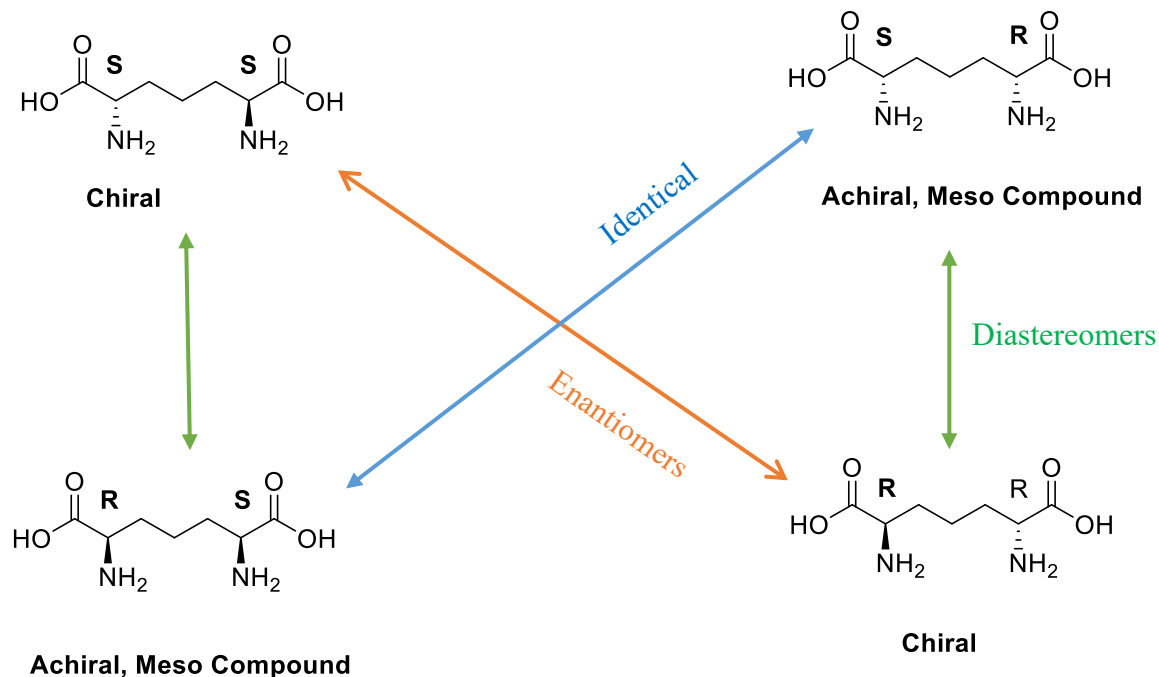


Methamphetamine



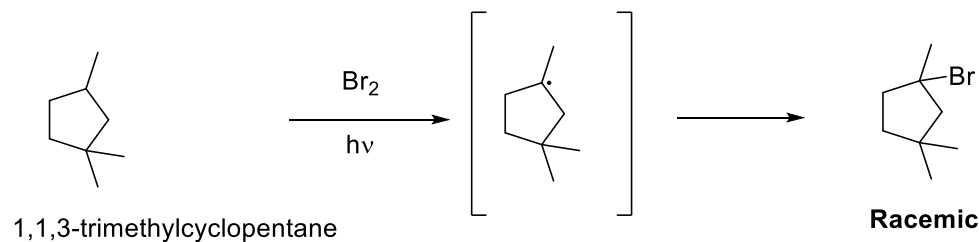
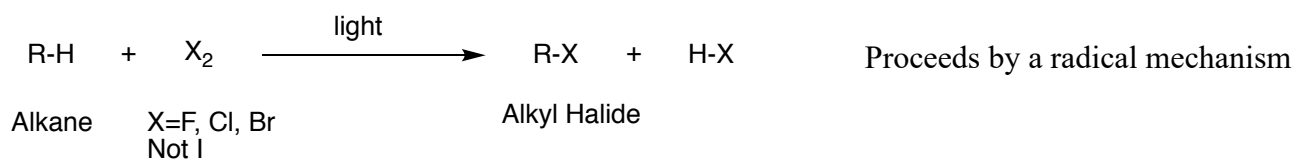
Cannot be used for resolution of enantiomers.
Need a stereogenic centre

Review of concepts:



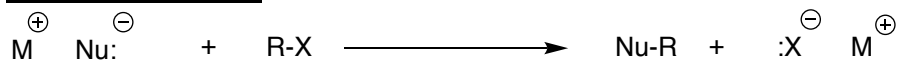
Substitution Reactions

Remember: Radical Substitution



Note: Although radicals are sp^3 hybridized, rapid inversion around the central C results in a loss of stereochemistry. Hence, the resulting product would be a racemic mixture.

Ionic Substitution:



Nucleophile
(Seeks positive charge)

Alkyl Halide

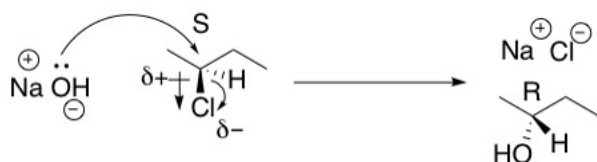
Nucleophile is a substance that seeks positive charge

Types of Nucleophilic Substitution (S_N)

S_N1 - rate depends on 1 concentration

S_N2 - The rate is dependent on the concentration of the nucleophile and the alkyl halide (2 concentrations)

S_N2 Mechanism



Reverse reaction will not occur.
 OH^- is a terrible leaving group

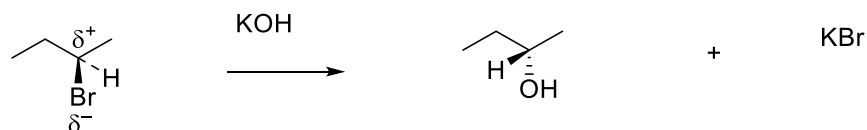
- **Rate:** Depends on concentration

- Inversion of configuration (**Walden inversion**)

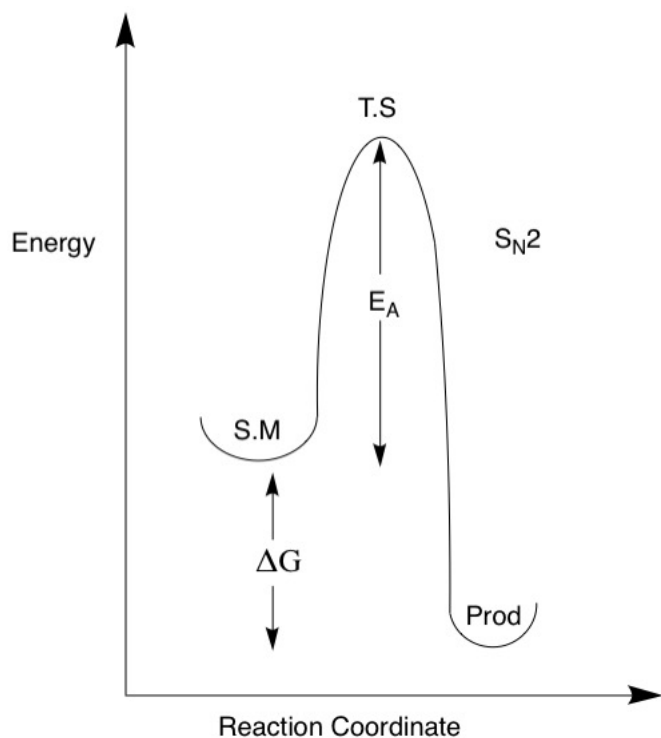
- **Concerted:** The bonds of the starting material break at the same time as the product bonds form.

- **Stereospecific:** stereochemistry of the starting material determines the stereochemistry of the product.

- Works for $\text{CH}_3\text{-X}$, $\text{R-CH}_2\text{X}$, $\text{R}_1\text{R}_2\text{CHX}$.



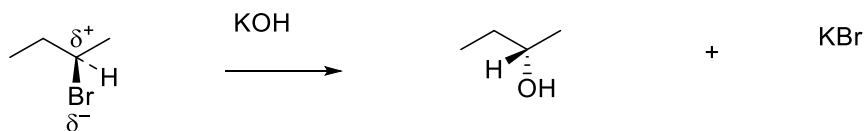
Energy Diagram of S_N2 Reaction



There is no intermediate in the S_N2 reaction, as it is concerted

Good Leaving Groups	Bad Leaving Groups
$\text{RSO}_3^- > \text{I}^- > \text{Br}^- > \text{Cl}^- \gg \text{F}^-$ (due to solvation)	H^+ , R^- (alkyl), NR_2^- , OR^- , OH^- , F^-

HOH, HOR are okay leaving groups, but need to protonate with acid before it can leave



Leaving groups must be connected to a primary or secondary carbon (carbon that has at least one hydrogen, preferably 2)