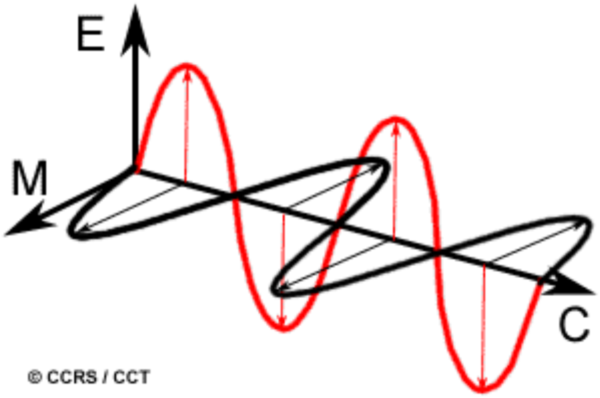
CHEM 261 Winter 2026 Feb 26, 2026

Physical Properties of Enantiomers

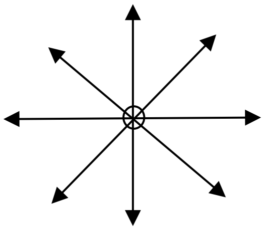
- Same physical properties with achiral agents or procedures
  - Melting point, boiling point, solubility in achiral solvents
- Separation of enantiomers (resolution) require a chiral agent

- **Diastereomers** have different physical properties (m.p, b.p, density, solubility)

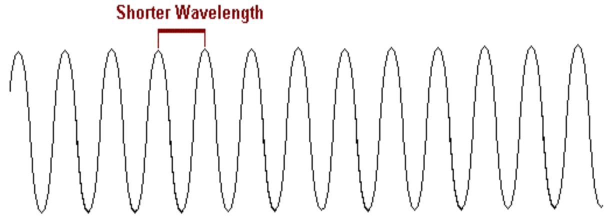
Light and Optical Rotation



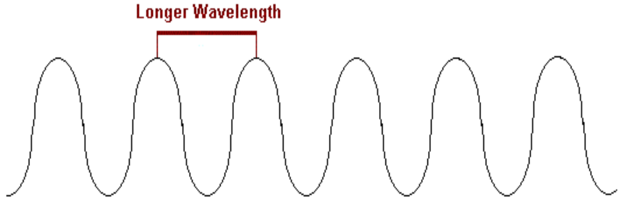
Light has an oscillating electric field (red) intersecting with a magnetic field (black)



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



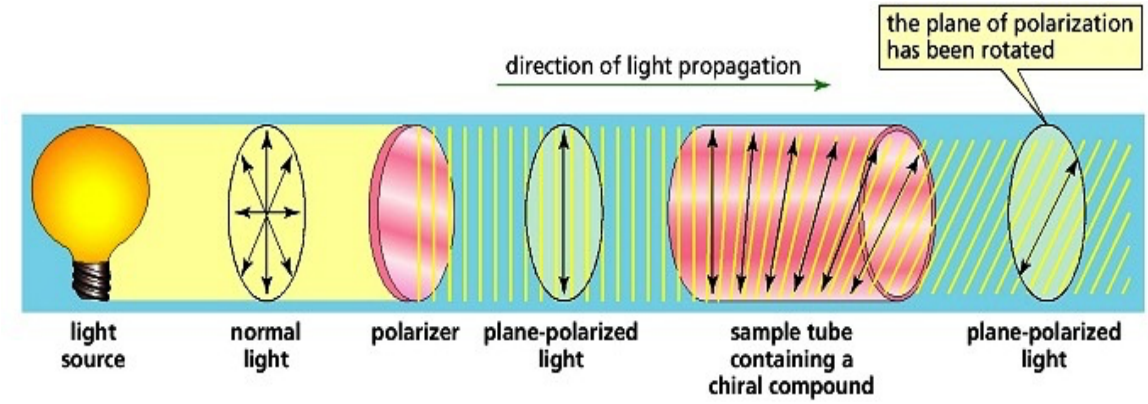
- ➢ Shorter Wavelength
- ➢ Higher Energy
- ➢ Higher Frequency



- ➢ Longer Wavelength
- ➢ Low Energy
- ➢ Low Frequency

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

E = energy
H = Planck's Constant (6.6 x 10^{-34} Joules•sec
ν = frequency
λ = wavelength



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Optical Activity/Rotation

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

Pure enantiomers show equal but opposite rotation

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

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

α = measured rotation (°) c = concentration (g/cm^3) 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

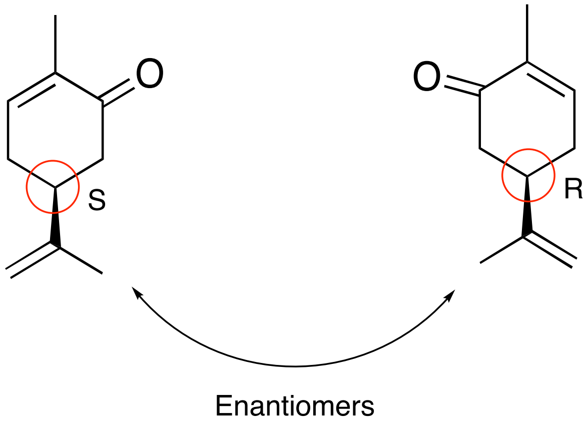
Optical Rotation

Factors affecting optical rotation:

- Concentration of compound, g/cm^3 (c)
- Path length that light travels through the solution, cm (l)

Example: Carvone

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



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 (°)**	**Optical Purity (%)**
100 %	0 %	+ 60 °	100 %
75 %	25 %	+ 30 °	50 %
50 %	50 %	0 °	0 %
25 %	75 %	–30 °	50 %
0 %	100 %	–60 °	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: defined as the separation of enantiomers

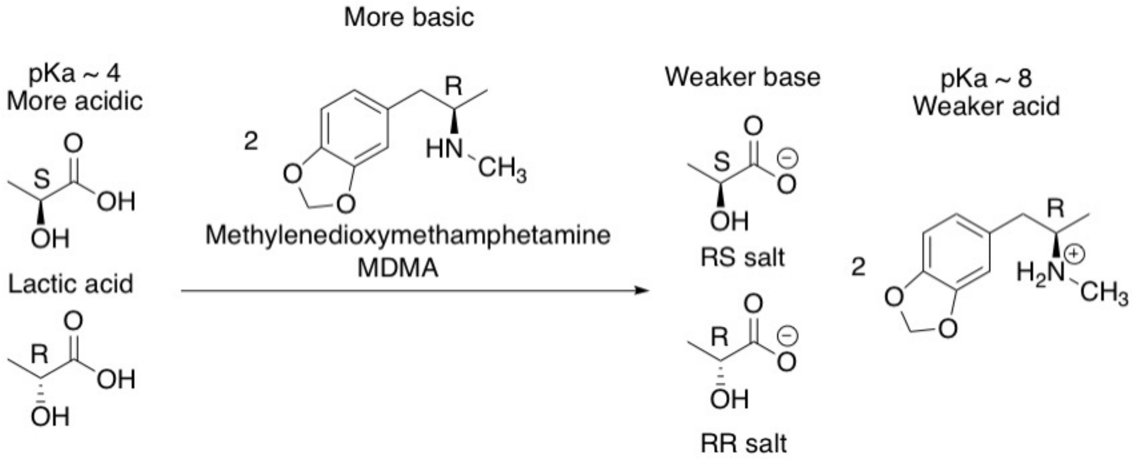
Resolution of Enantiomers

Definition: separation of two enantiomers

- Requires a chiral reagent to convert enantiomers to diastereomeric salts

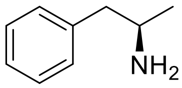
Racemic mixture: 1:1 ratio of enantiomers in a mixture

Example: Lactic Acid

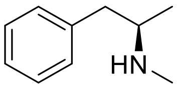


The starting material lactic acids are enantiomers of each other.
By reacting enantiomers to make a salt with an enantiomer of MDMA (another chiral molecule that is optically pure), also known as ecstasy, one can obtain salts which are now diastereomers of each other (RS and RR). The resulting diastereomers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

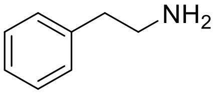
More examples of amines:



Amphetamine

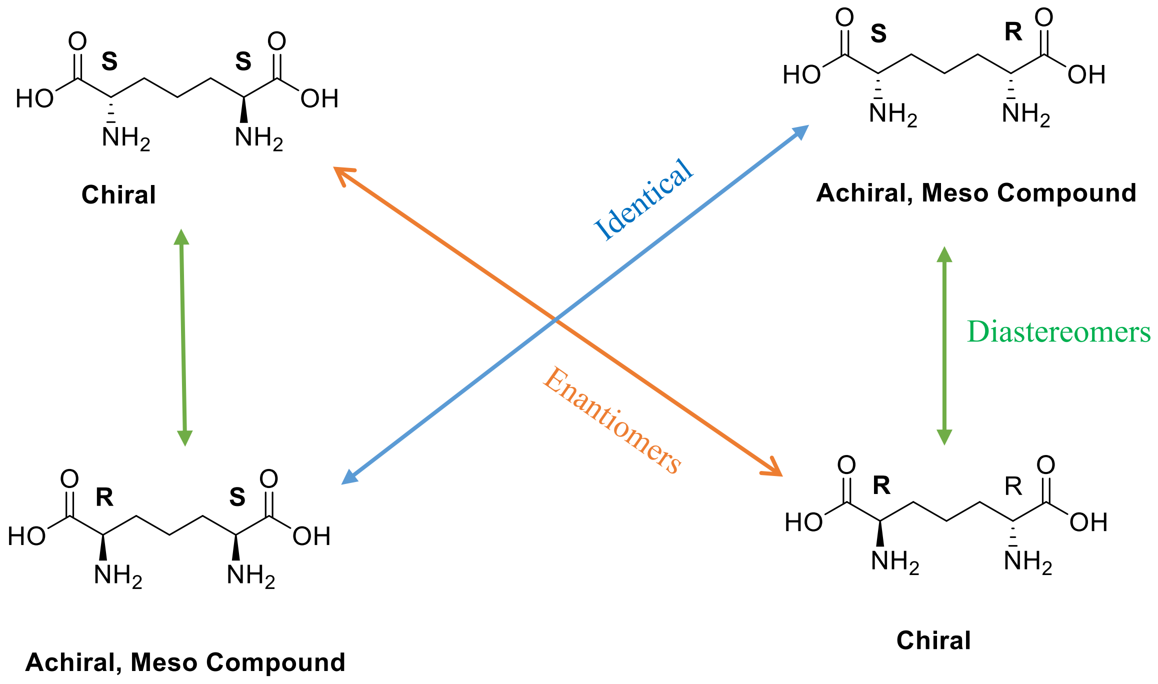


Methamphetamine
Methedrine= speed



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

Review of concepts:



Substitution Reactions

Remember: Radical Substitution

1) **Homolytic bond breaking**

$$\text{A}-\text{B} \longrightarrow \text{A}\cdot \quad \cdot\text{B}$$

Example:

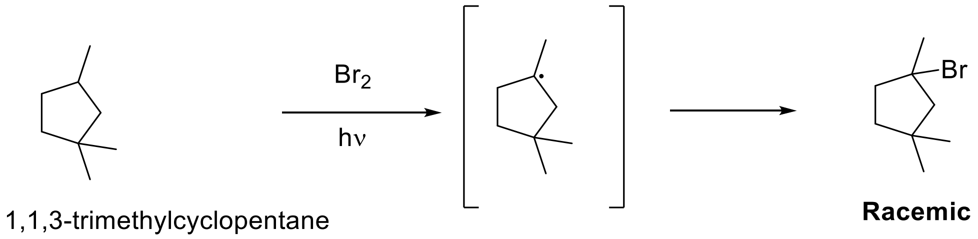
$$\text{R-H} + X_2 \xrightarrow{\text{light}} \text{R-X} + \text{H-X}$$

Proceeds by a radical mechanism

Alkane

X=F, Cl, Br
Not I

Alkyl Halide



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.

2) Heterolytic Bond Breaking (<u>Ionic Substitution)</u>

$$\overset{\oplus}{M}\ \ \overset{\ominus}{Nu:}\ +\ R\text{-}X \longrightarrow Nu\text{-}R\ +\ \overset{\ominus}{:X}\ \ \overset{\oplus}{M}$$

Nucleophile (Seeks positive charge)

Alkyl Halide

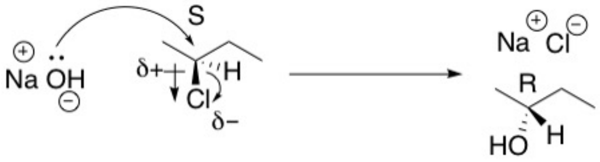
Nucleophile is a substance that seeks positive charge

Types of Nucleophilic Substitution (S_N)

S_N1 - rate depends on 1 concentration

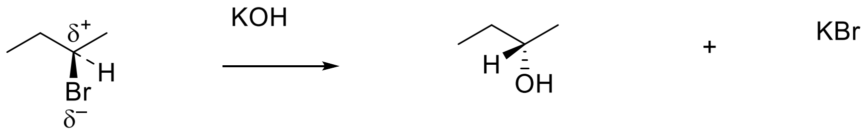
S_N2 - The rate is dependent on the concentration of the nucleophile and the electrophile (2 concentrations)

Sn2 Mechanism

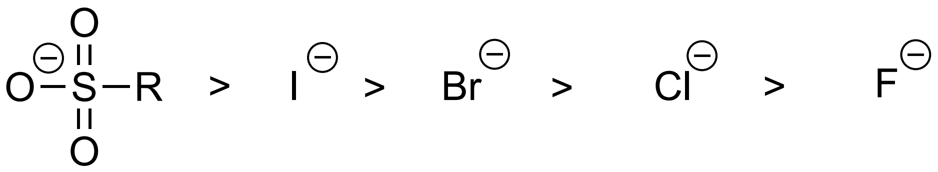


Reverse reaction will not occur.
OH^- is a terrible leaving group
- **Rate**: Depends on concentration

- 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 CH_3–X, R–CH_2X, R_1R_2CHX.



Good leaving groups:

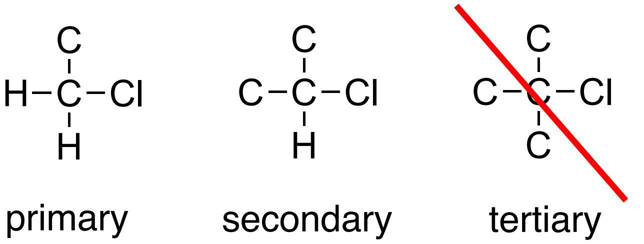


$^{-}O-SO_2-R > I^- > Br^- > Cl^- > F^-$

Bad leaving groups:

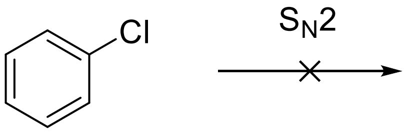
H^- R^- NR_2^- OR^- OH^-

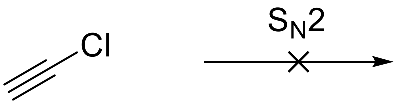
Leaving groups must be connected to a primary or secondary carbon (carbon that has at least one hydrogen, preferably 2)



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

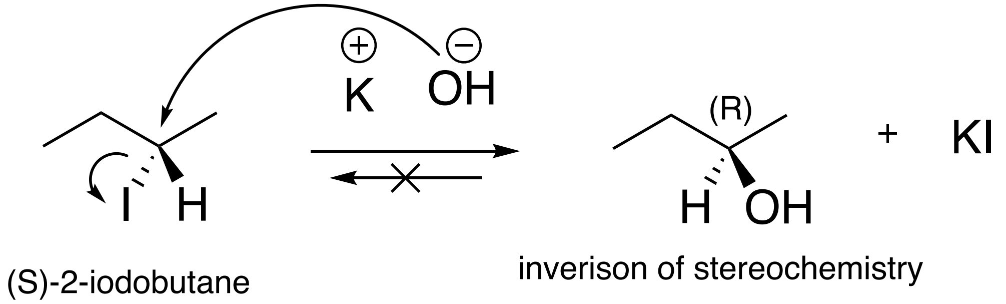
Examples of reactions that do not proceed via S_N2

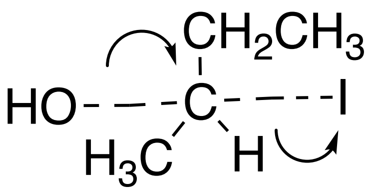




Another example of mechanism of S_N2 reaction

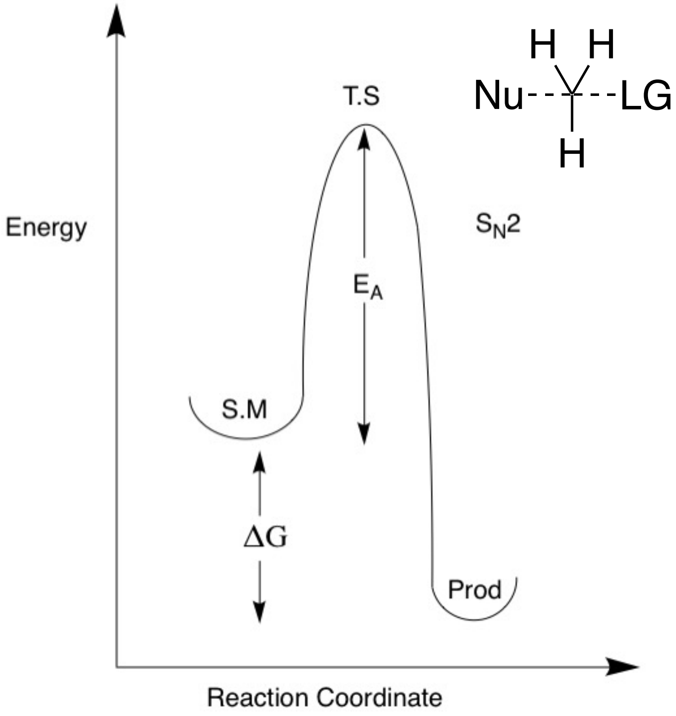
As such, the reaction below is not reversible:





S_N2 always inverts stereochemistry, (Walden inversion)
Favored conditions are with less steric bulk, primary best and secondary okay

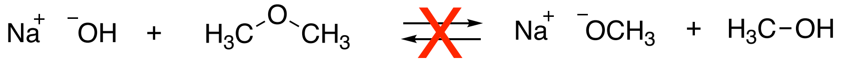
Energy Diagram of S_N2 Reaction



There is no intermediate in the S_N2 reaction, as it is concerted. S_N2 reactions are stereospecific.

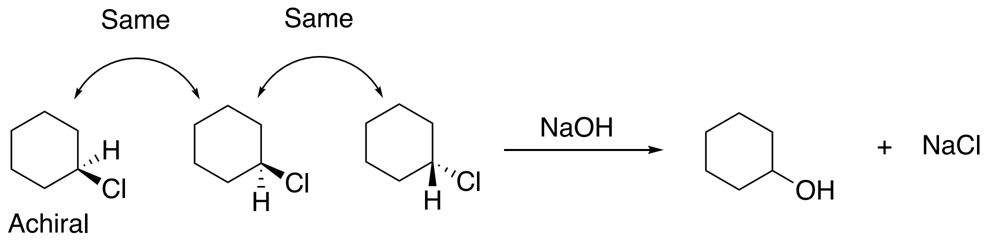
Example:

1)

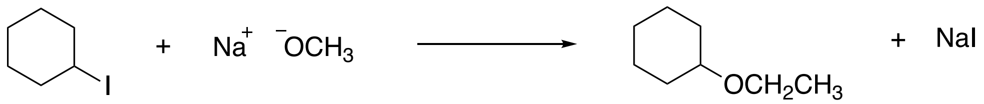


Note: Methoxide (CH_3O^-) and hydroxide (^-OH) are bad leaving groups

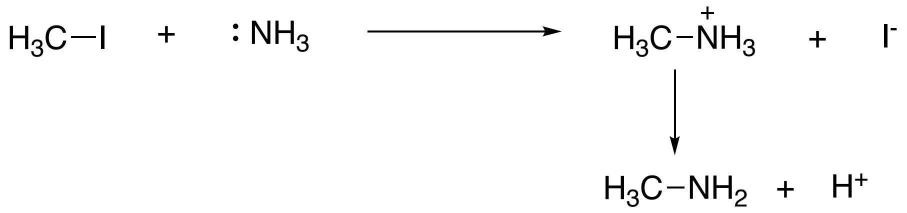
2)



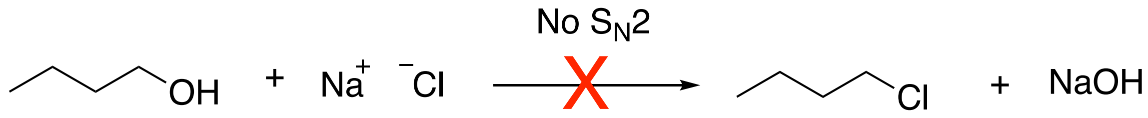
3)



4) Neutral leaving group containing lone pair

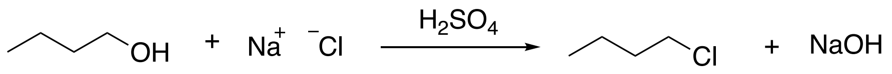


5)

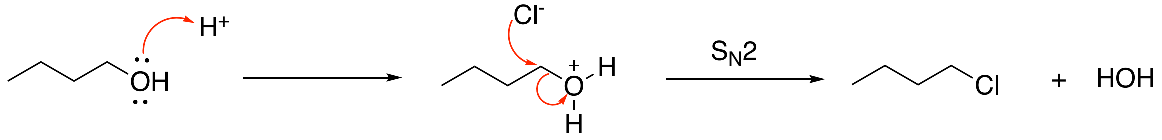


Note: OH is never a leaving group but if you add a strong acid or the reaction happen in a strongly acidic condition (see next example), the reaction will occur

6)

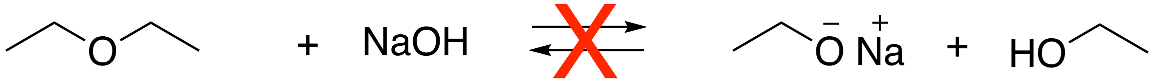


Mechanism:



Note: The leaving group in this reaction is now HOH

7)



Diethyl ether

Note: Alkoxide (⁻OR) or hydroxide (⁻OH) are bad leaving group therefore no Sn2 reaction will occur on either direction. However, if the reaction happens in strongly acidic condition the reaction will occur. (see mechanism below)

8)