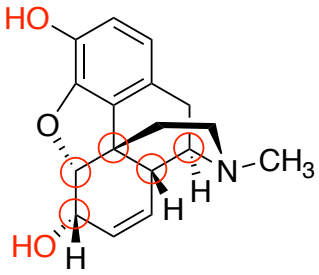
Recall:

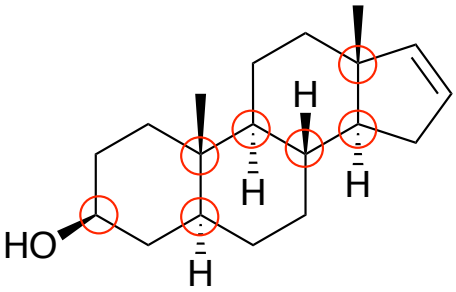
Morphine



-contains 5 stereogenic centres (marked with red circles)

Pheromones: from Greek "pherein horman" meaning to carry excitement. Discovered by Adolf Butenandt.

Male Pheromone:



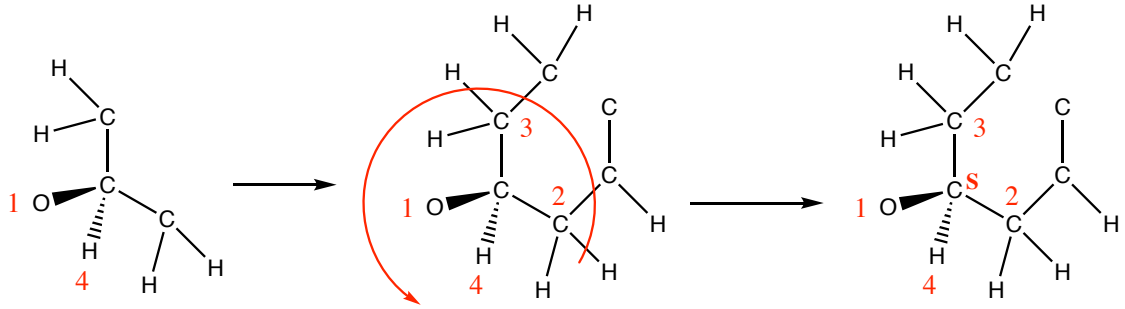
Androstenol

Only about 50 % of the population can smell this compound, which is genetically determined. About half find the smell disgusting while the other half find it tolerable or pleasant.

Some pheromones can be detected by insects at concentrations of 10^{-17} molar.

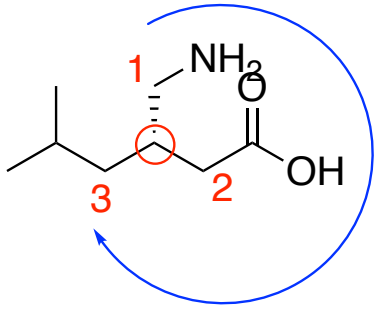
Contain 7 stereogenic centers, circled in red above.

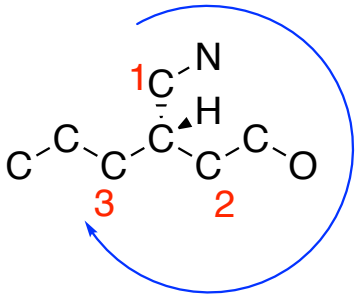
What is the R/S configuration of the carbon attached to OH?



S configuration of stereogenic center

Lyrica Pregabalin- An analgesic developed by Richard Silverman

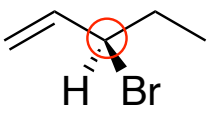


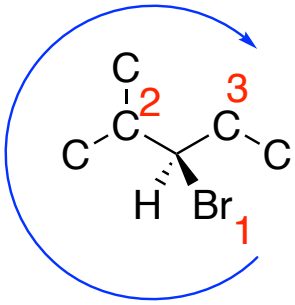


Note: The priority numbers are rotating clockwise however the lowest priority (H) is pointing towards you, hence it is S.

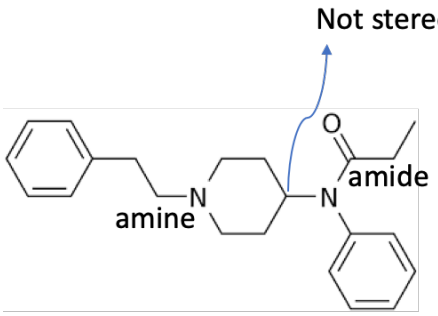
S-pregabalin

More example

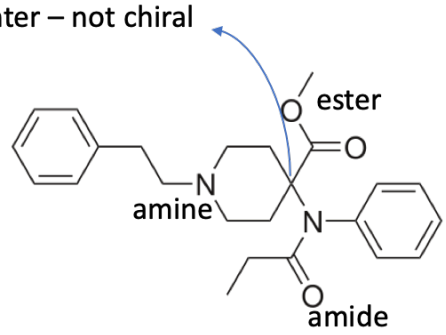




Priorities are rotating clockwise, hence this is **R**



Fentanyl

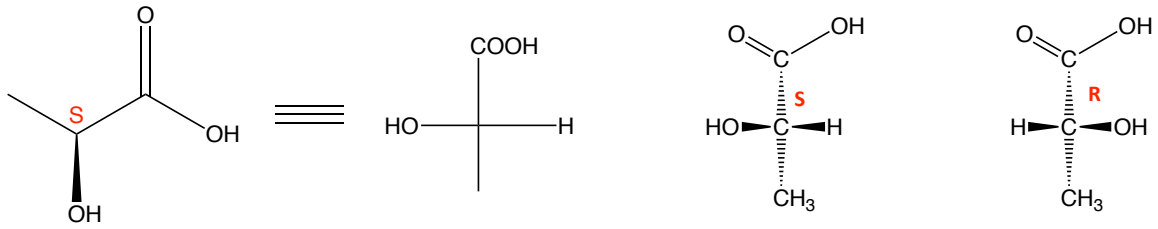


Carfentanil

Fischer Projections

A method of drawing chemical structures, where the horizontal components are coming towards you and the vertical ones are going back.

Example #1: Lactic Acid



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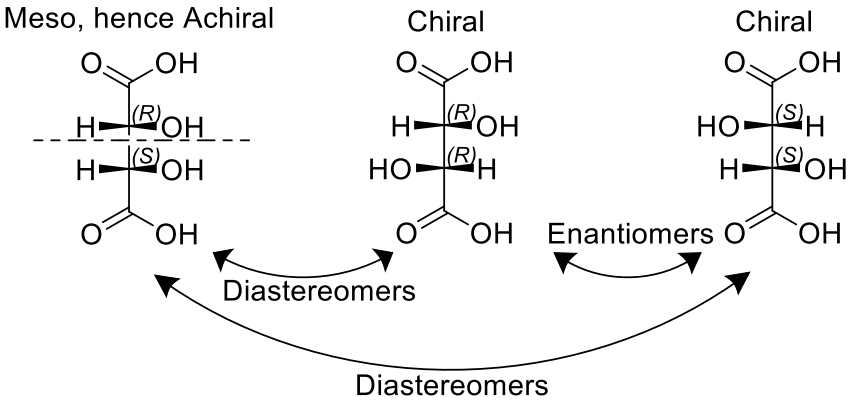
Example #2: Tartaric acid



Meso compounds have stereogenic centers but contain a plane of symmetry and are achiral

Racemic mixtures (or racemate) contain a 1:1 ratio of each enantiomer

Physical Properties of Enantiomers

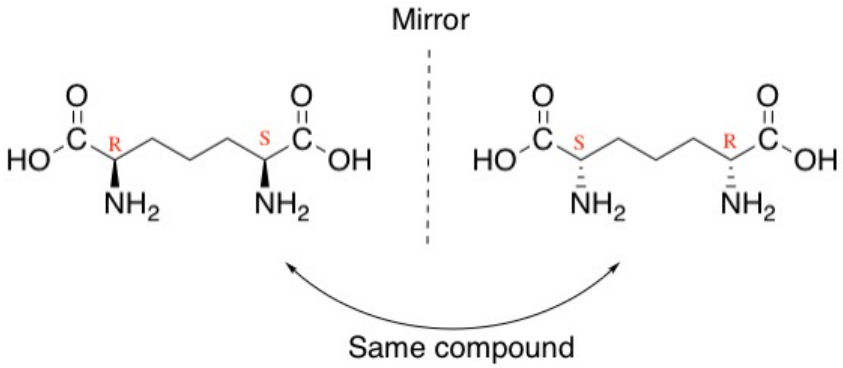
- Same physical properties with achiral agents or procedures
  - Melting point, boiling point, solubility in achiral solvents
- Separation of enantiomers (resolution) require a chiral agent

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

Resolution: defined as the separation of enantiomers

Identification of Chiral and Achiral (not chiral) compounds

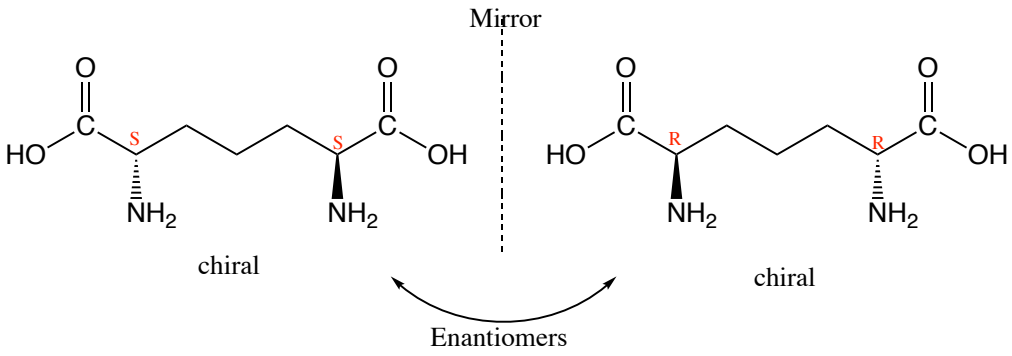
Example: Diaminopimelic acid



- 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 $[\alpha]_D = 0$

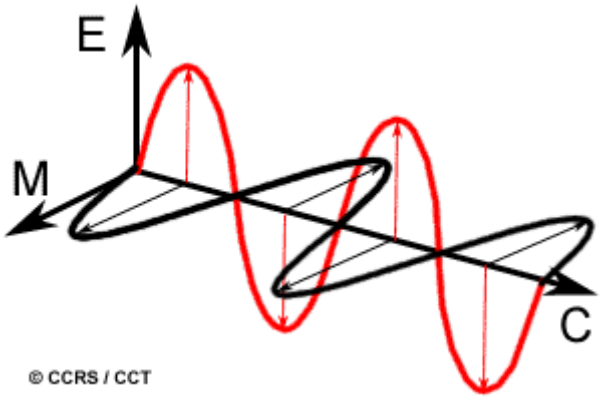
Optical Activity/Rotation

- Rotation of plane of polarized light
- α = measured rotation (°)
- $[\alpha]_D$ = Absolute rotation

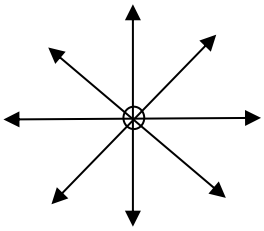
- (+) (clockwise = dextrorotatory)
- (-) (counter-clockwise = levorotatory)

- Absolute rotation is 0 ° for achiral molecules

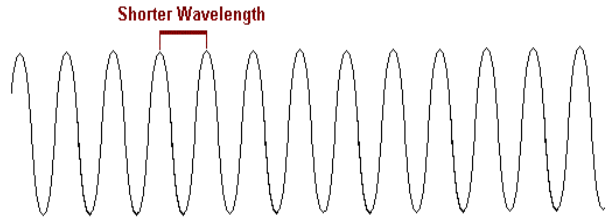
Pure enantiomers show equal but opposite rotation



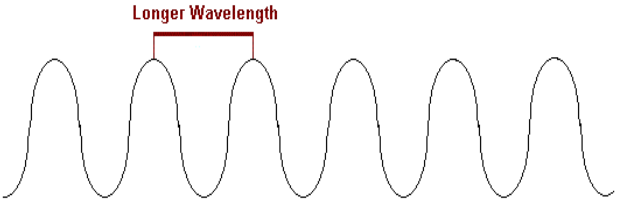
Light has an oscillating electric field (red) intersecting with a magnetic field (black)



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



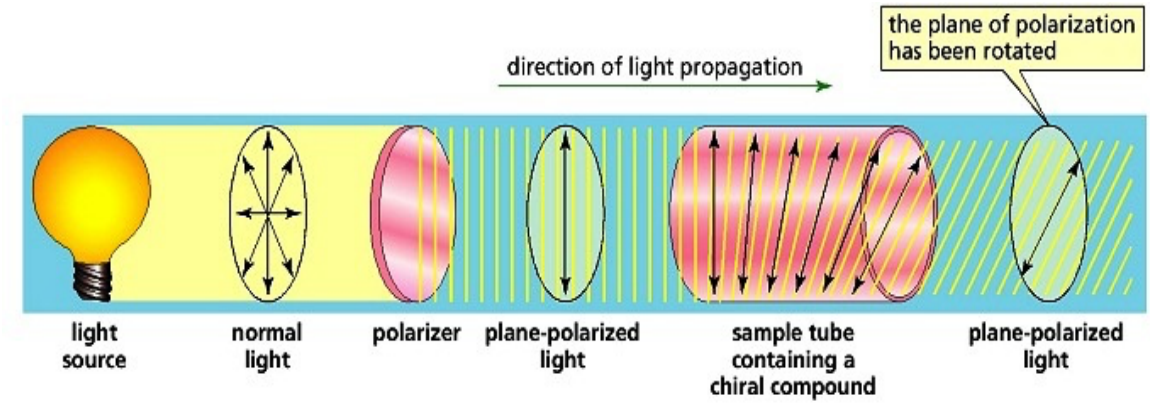
- Shorter Wavelength
- Higher Energy
- Higher Frequency



- 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



Optical Rotation

Factors affecting optical rotation:

- Concentration of compound, g/cm^3 (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)

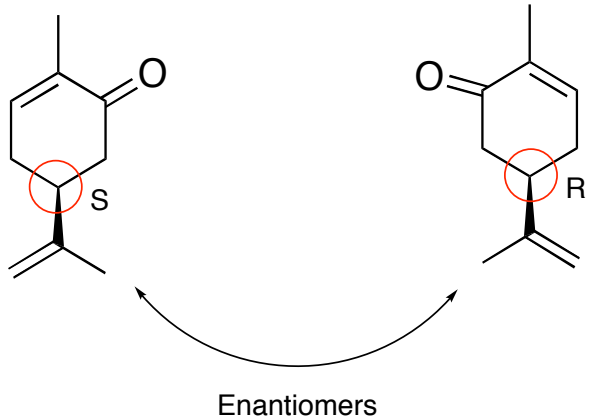
$$[\alpha]_D = \frac{\alpha}{c \bullet l}$$

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

Example: Carvone

$[\alpha]_D = -60°$ $[\alpha]_D = +60°$ (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)

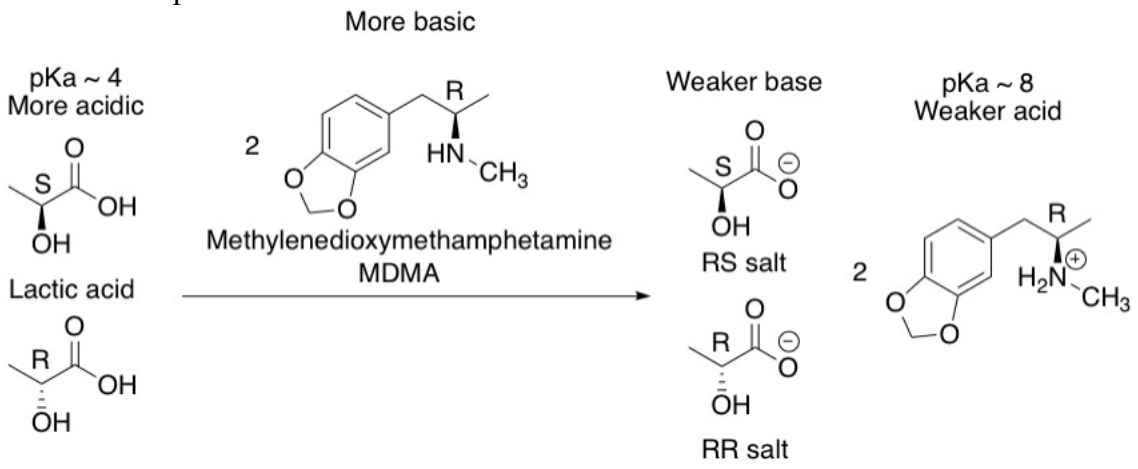
Resolution of Enantiomers

Definition: separation of two enantiomers

- Requires a chiral reagent to convert enantiomers to diastereomeric salts

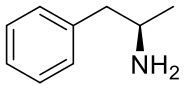
Racemic mixture: 1:1 ratio of enantiomers in a mixture

Example: Lactic Acid

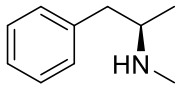


The starting material lactic acids are enantiomers of each other.
By reacting enantiomers to make a salt with an enantiomer of MDMA (another chiral molecule that is optically pure), also known as ecstasy, one can obtain salts which are now diastereomers of each other (RS and RR). The resulting diastereomers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

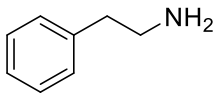
More examples of amines:



Amphetamine



Methamphetamine
Methedrine= speed



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

Review of concepts: