CHEM 261 Fall 2025 October 14, 2025

Recall:

Labelling Stereocentres

R/S Nomenclature:

R and S designation of stereoisomers

- R = Rectus (right-handed, clockwise)
- S = Sinister (left-handed, counterclockwise)

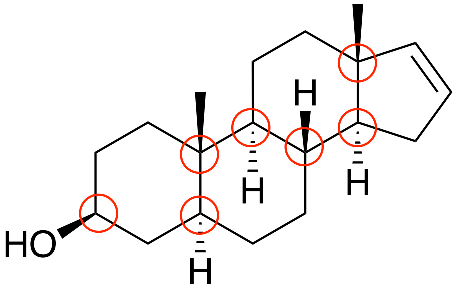
Labelling a stereogenic center as R or S:

- Identify all stereogenic centers (i.e. 4 different substituents)
- Look at atomic number of atoms attached to the stereogenic center
- Assign priority based on atomic number. If you cannot decide, go to the next set of atoms.
- Number from highest to lowest priority, then with the lowest priority group pointing back, count 1, 2, 3:
  - Clockwise → R configuration
  - Counterclockwise → S configuration

Each stereogenic center in a molecule is analyzed separately

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

Male Pheromone:



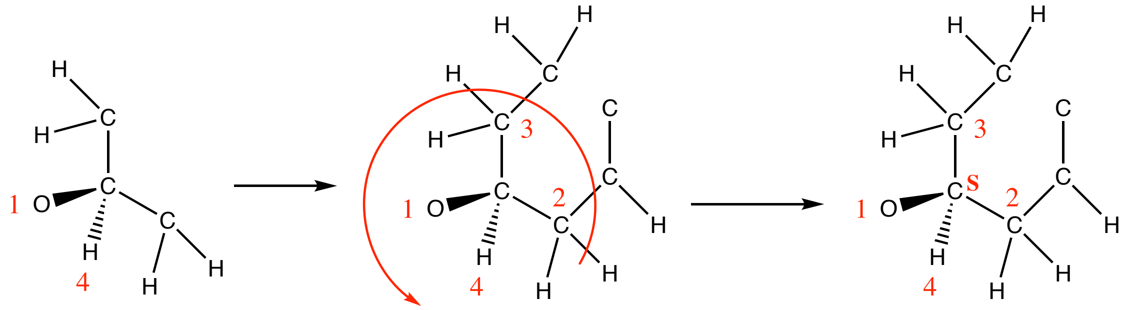
Androstenol

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.

Contains 7 stereogenic centers, circled in red above.
2^7 possible diastereomers
1 single enantiomer

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



S configuration of stereogenic center

Morphine

- Is an alkaloid, meaning it contains nitrogen, can be isolated from a plant (or bacteria) and is considered a natural product.
- From Morpheus, Greek god of sleep
- Opium: Sap from the seed pod of opium poppy (*Papaver somniferum*)
    - (poppy sleep-carrying)
- ~10% of opium is morphine
- Morphine is used as an analgesic
- Heroin (diacetylmorphine) is even more potent (and more addictive)
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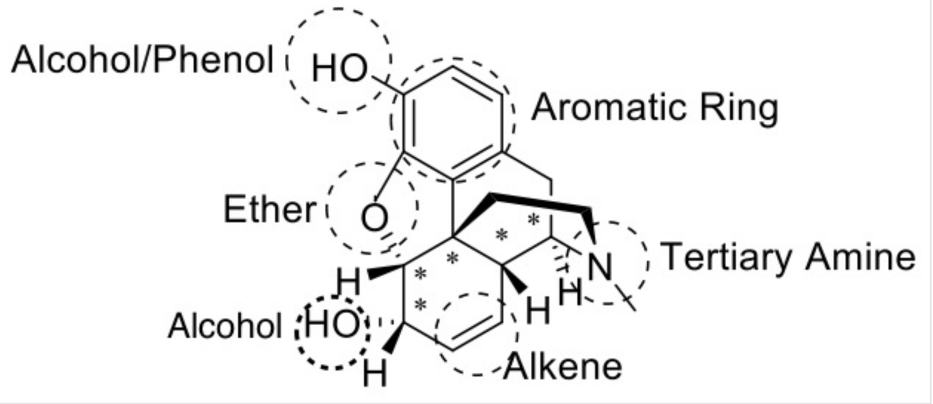
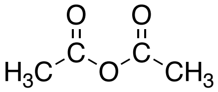
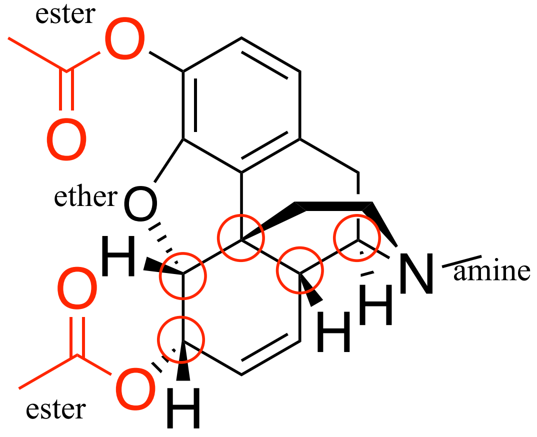
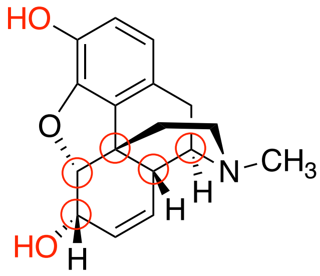


If you substitute CH_3COO for the two alcohol residues in morphine by reacting with

acetic anhydride ( $H_3C-C(=O)-O-C(=O)-CH_3$), you then create **HEROIN.**



1000x stronger as analgesic and more addictive than morphine

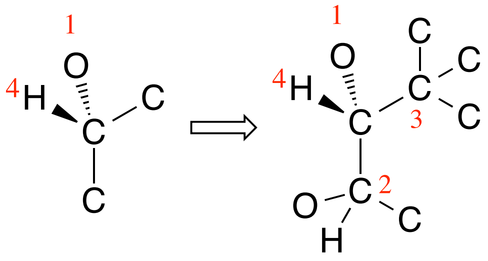


-5 stereogenic centers in morphine (represented by *) – Nitrogen is NOT a stereogenic centre because the methyl group can move up or down

- $2^5 = 32$ stereoisomers possible, where:
- 1 morphine (itself)
- 1 enantiomer
- 30 diastereoisomers

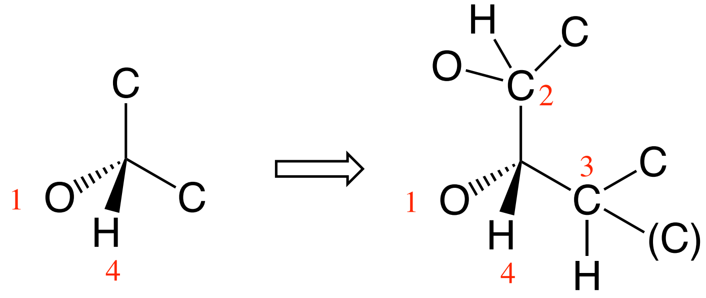
Examples of Configuration in Stereocenters of Morphine

Configuration at the **ether** stereocenter:



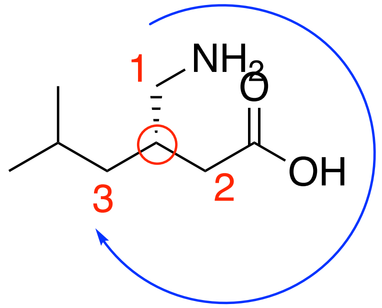
- Cannot assign 2, 3 at first try
- At the second atoms in the chain, there is a difference. The alcohol carbon is attached to one oxygen, one carbon, and one hydrogen. It has a higher priority than the other carbon which is attached to three carbons.
- Count 1, 2, 3: Counterclockwise
- This center is *R* and not *S* because the lowest priority group (the hydrogen) is pointing toward the front, not to the back.

Configuration at the **alcohol** stereocenter:

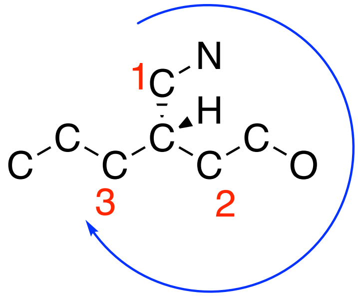


- Cannot assign 2, 3 at first try
- At the second atoms in the chain, the eth carbon is attached to one oxygen, one carl and one hydrogen. It has a higher priority the alkene carbon which is attached to tw carbons and one hydrogen
- Count 1, 2, 3: Clockwise
- This center is *S* and not *R* because the lo priority group (the hydrogen) is pointing toward the front, not the back

Lyrica Pregabalin- An analgesic developed by Richard Silverman

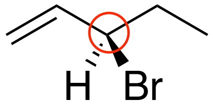


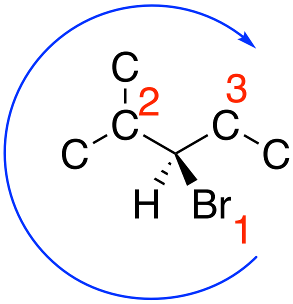
S-pregabalin



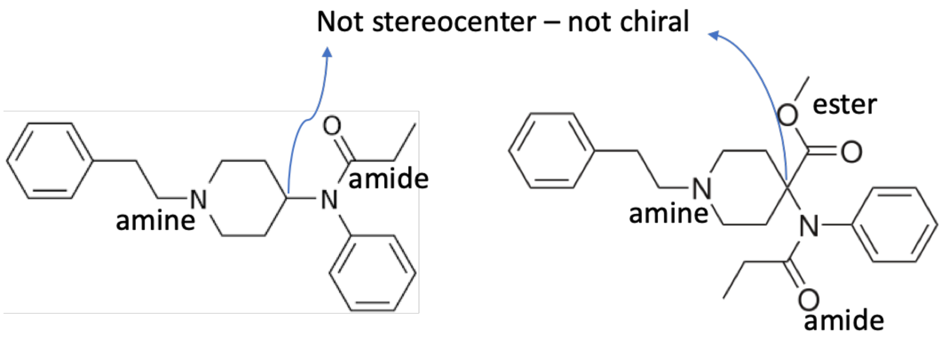
Note: The priority numbers are rotating clockwise however the lowest priority (H) is pointing towards you, hence it is S.

More examples





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



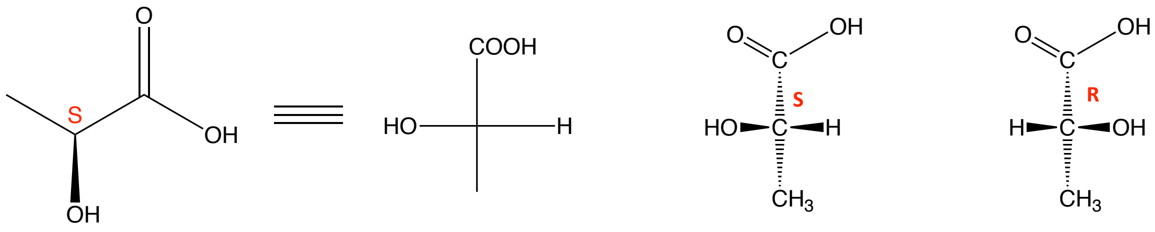
Fentanyl

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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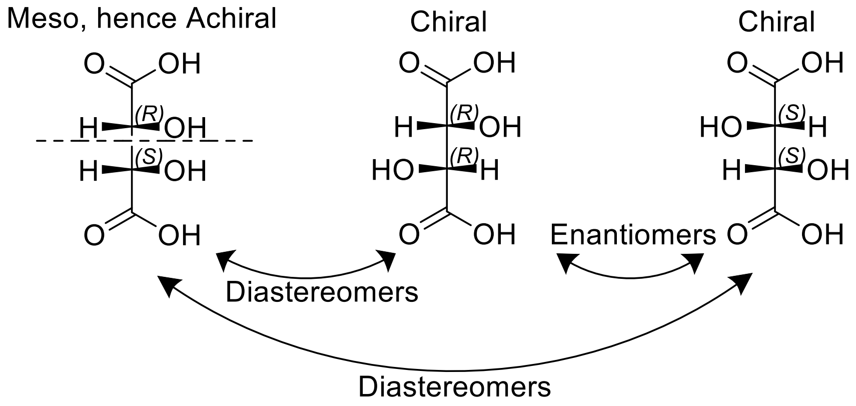
Example #2: Tartaric acid



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

Tartaric acid has three NOT four stereoisomers. One meso isomer and RR and SS isomers. Racemic mixtures (or racemate) contain a 1:1 ratio of each enantiomer

Physical Properties of Enantiomers

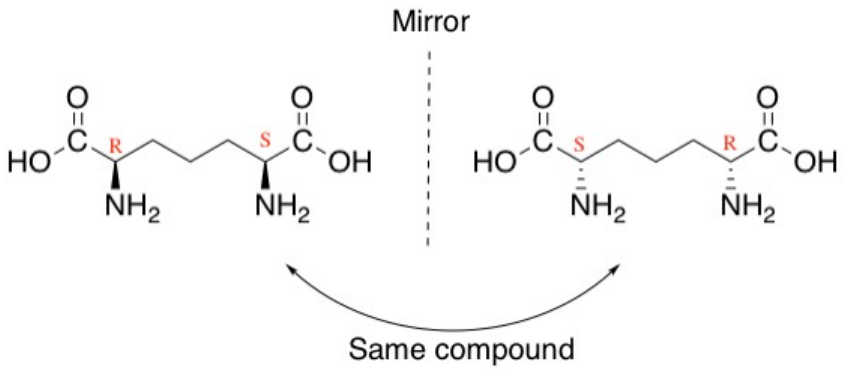
- Same physical properties with achiral agents or procedures
  - Melting point, boiling point, solubility in achiral solvents
- Separation of enantiomers (resolution) require a chiral agent

- **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

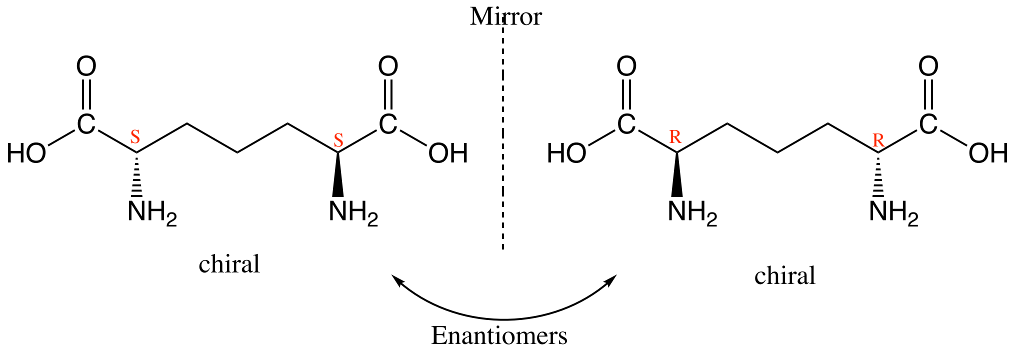
Example: Diaminopimelic acid



- 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:



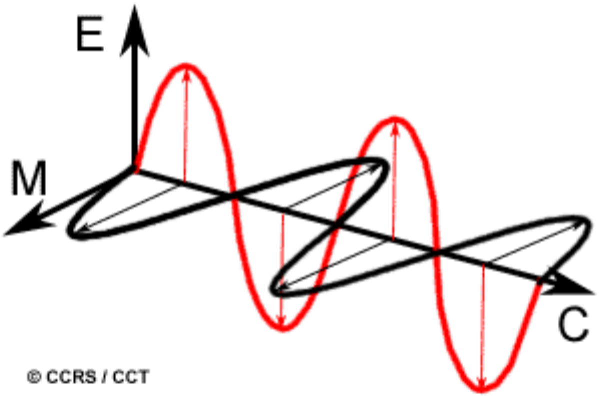
A racemic mixture (racemate) of two enantiomers in a 1:1 ratio also has an $[\alpha]_D = 0$

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



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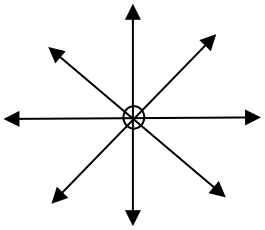
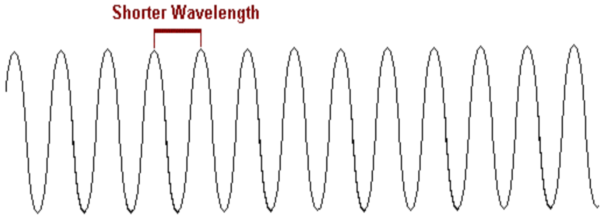
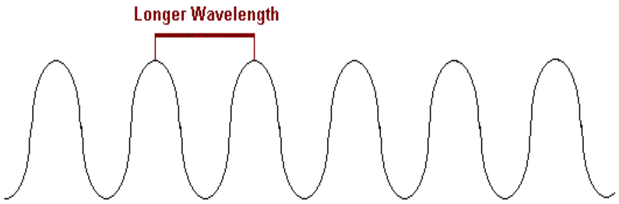
Light has an oscillating electric field (red) intersecting with a magnetic field (black)



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



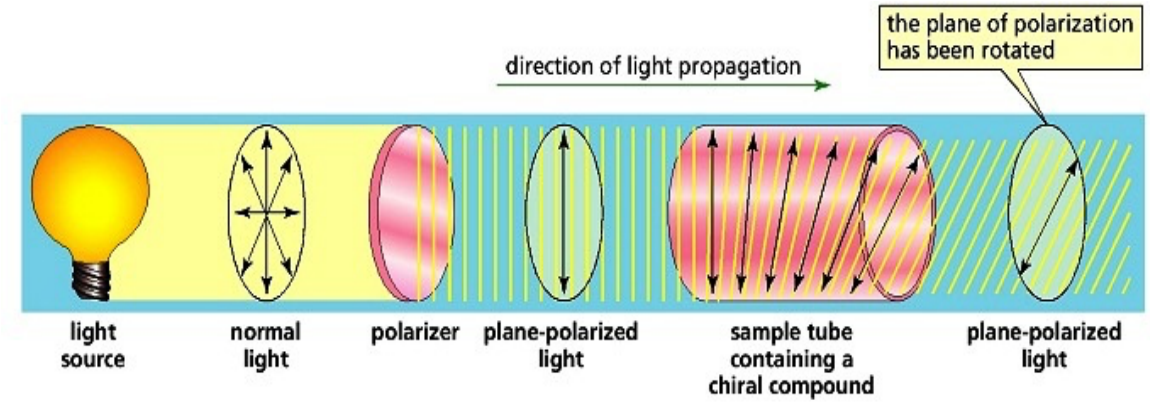
- ➢ Shorter Wavelength
- ➢ Higher Energy
- ➢ Higher Frequency



- ➢ 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)

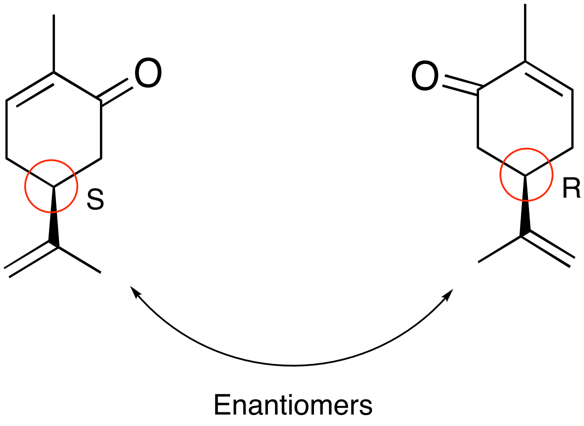
$$[\alpha]_D = \frac{\alpha}{c \bullet l}$$

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)