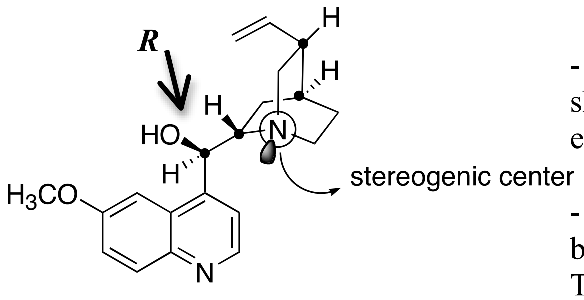
Review of Chiral Centers



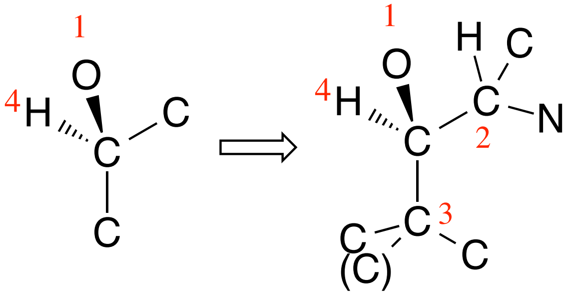
quinine - anti-malarial drug
from the bark of the tree
Cinchona officinalis

malaria is cause by *Plasmodium* species
transmitted by *Anopheles* mosquito

- Carbon stereocenters are shown with dots in this example.

- Nitrogen is a stereocenter here because it can't invert freely. The ring structure restricts its geometry.

Configuration at the alcohol center:



- Cannot assign 2, 3 at first try
- At the second atoms in the chain, there is a difference. The carbon attached to one nitrogen, one carbon, and one hydrogen has a higher priority than the carbon attached to three carbons.
- One nitrogen trumps three carbons.
- Count 1, 2, 3: Clockwise is *R*.

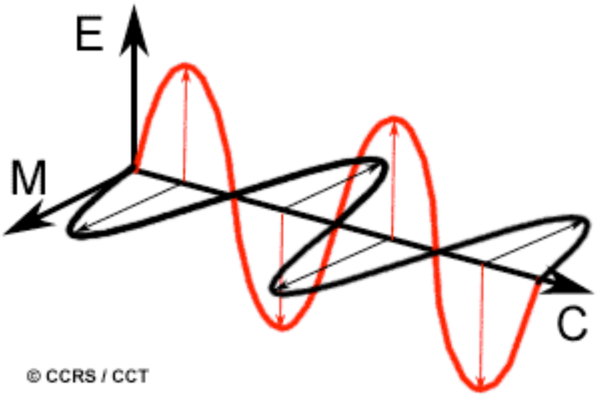
Physical Properties of Enantiomers

- Same physical properties with achiral agents or procedures
    - Melting point, boiling point, solubility in achiral solvents
- Enantiomers behave differently with chiral agents
- Diastereomers have different physical properties (m.p, b.p, density, solubility)

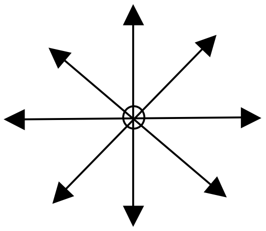
Light: Electromagnetic radiation

Light → $E = h\upsilon = \frac{hc}{\lambda}$

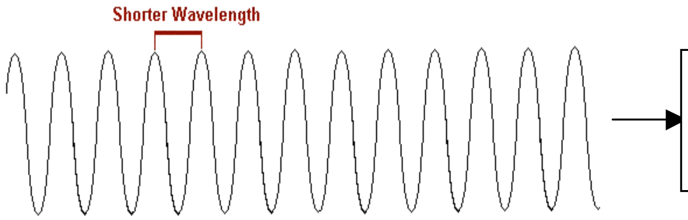
υ = frequency E = energy h = Planck's constant λ = wavelength
c = speed of light



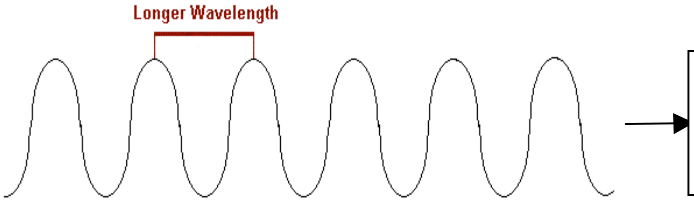
Light has an oscillating electric field (red) combined with a magnetic field (black)



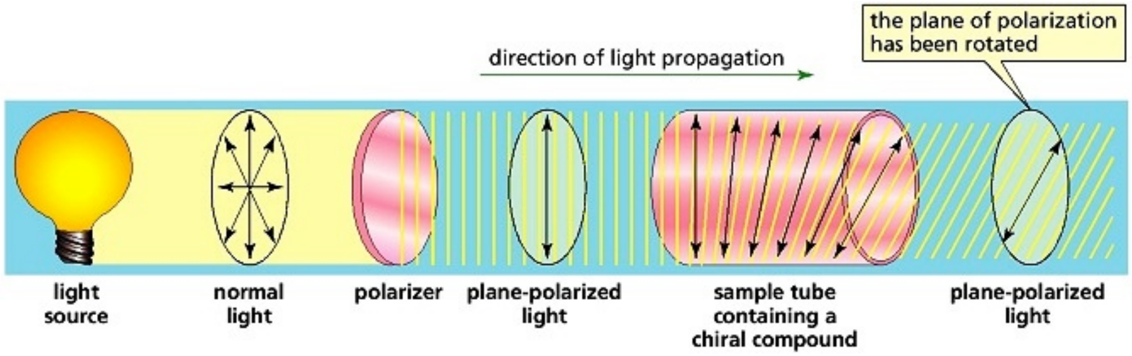
End on view of vector components of normal light. It is possible to polarize light and remove some of those vectors.



- Shorter Wavelength
- Higher Energy
- Higher Frequency



- Longer Wavelength
- Low Energy
- Low Frequency



Optical 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 (dm)

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

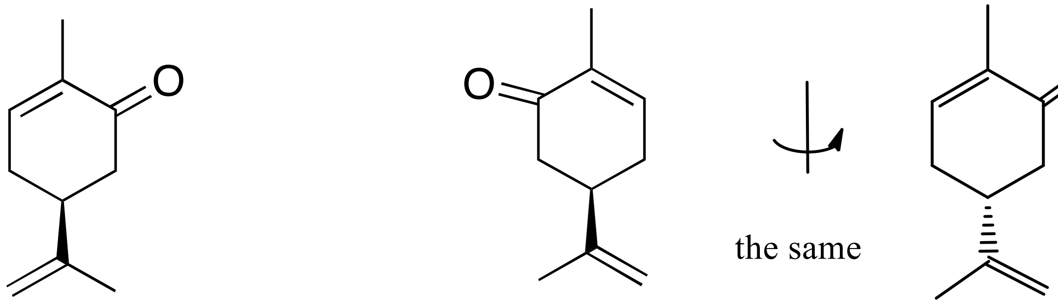
Degrees (°) = + : Clockwise
- : Anticlockwise

Optical Activity

- Absolute rotation is 0 ° for achiral molecules
- Rotation of polarized light
  - Dextrorotatory (right) (+)
  - Levorotatory (left) (-)
- Pure enantiomers show equal but opposite rotation

Example: Carvone

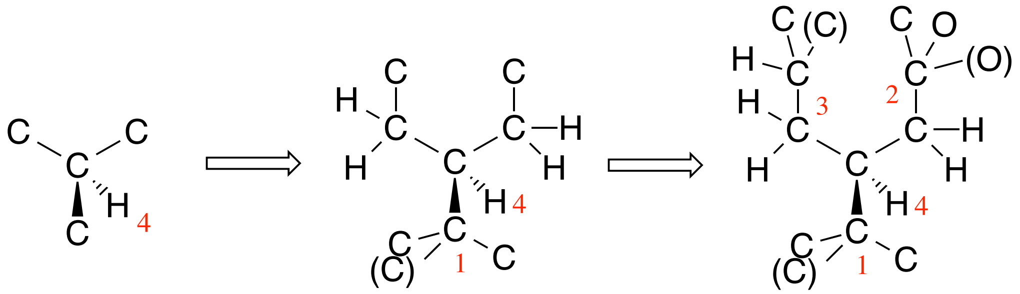
$[\alpha]_D = + 100^o$ $[\alpha]_D = - 100^o$



enantiomers

D-carvone (caraway) L-carvone (spearmint)
D = dextrorotatory (clockwise) L = levorotatory (counter clockwise)

Absolute configuration of D-carvone is S:



- R/S indicate nomenclature (naming convention) and
- D/L indicate optical activity (physical property)

They cannot be easily correlated theoretically (there is no reliable method to predict that a D or L compound would have certain R S stereogenic center designation).

Optical purity (experimental) = enantiomeric excess = e.e. (theoretical)

Optical purity is the excess of one enantiomer over the other

$[\alpha]_D$ = Absolute rotation of a compound

Calculating Optical Purity

For this example for D and S-carvone, assume the pure S enantiomer has +100^{o} rotation

R	**S**	**Rotation (^{o})**	**Optical Purity (%)**
100 %	0 %	-100 ^{o}	100 %
75 %	25 %	-50 ^{o}	50 %
50 %	50 %	0 ^{o}	0 %
25 %	75 %	+50 ^{o}	50 %
0 %	100 %	+ 100 ^{o}	100 %

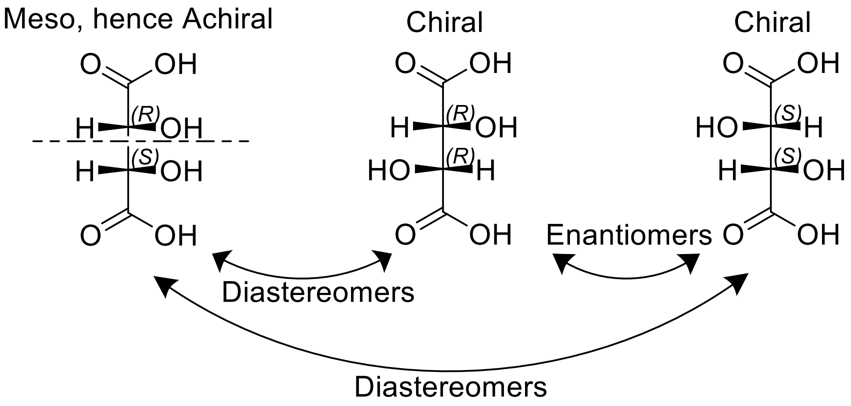
If a solution is an equivalent mix of 1:1 R + S enantiomers, α measured = 0 ^{o}

A 50:50 mixture of enantiomers is called a *racemic mixture*

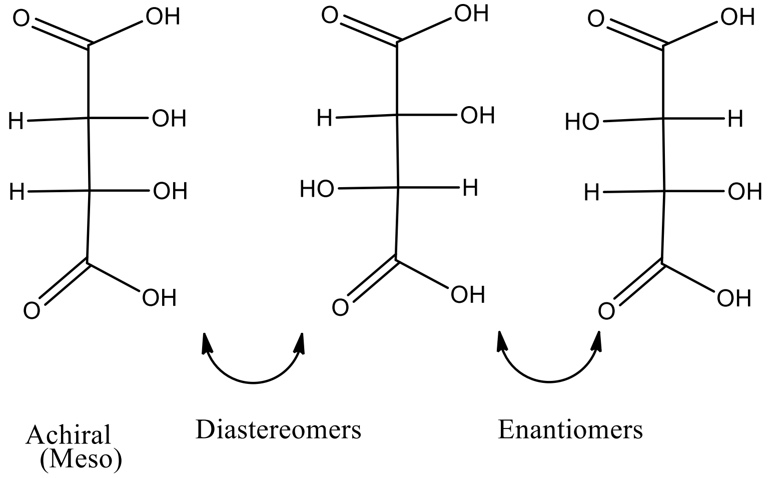
Fisher Projections

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

Example: tartaric acid



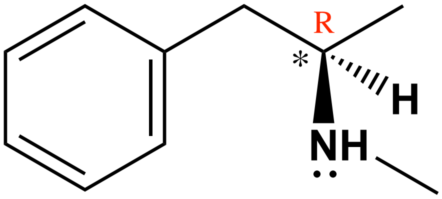
Fisher projections:



Resolution: Separation of enantiomers

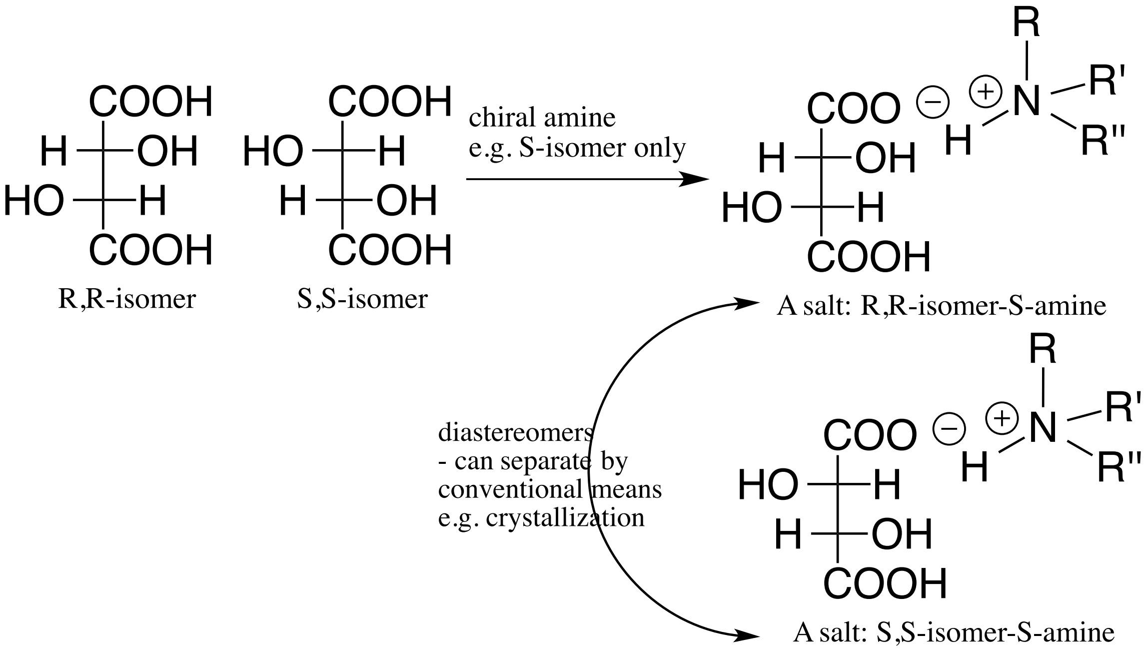
- Physical separation (crystallization of specific enantiomer)
- Conversion to diastereomers, which can be separated
    - e.g. Make salts by acid-base reaction
- A chiral agent is necessary to allow for this resolution

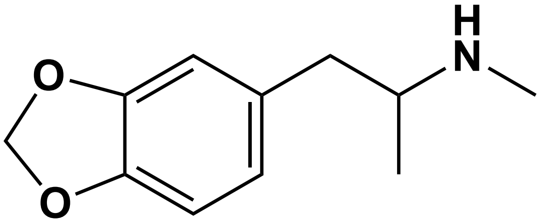
For example, the enantiomers of tartaric acid can be separated by forming diastereomeric salts with a chiral amine, such as methedrine:



Methedrine's full structure

Salt formation with methedrine:

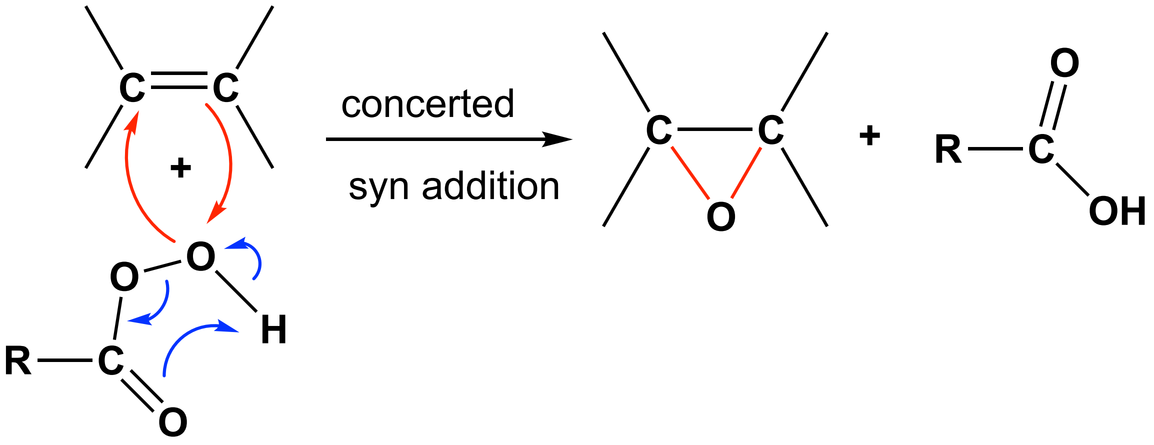




3,4-Methylenedioxymethamphetamine (aka mdma or ecstasy)

Stereospecific Reactions: A process wherein the starting material determines the stereochemistry of the product(s)

Example: formation of epoxides

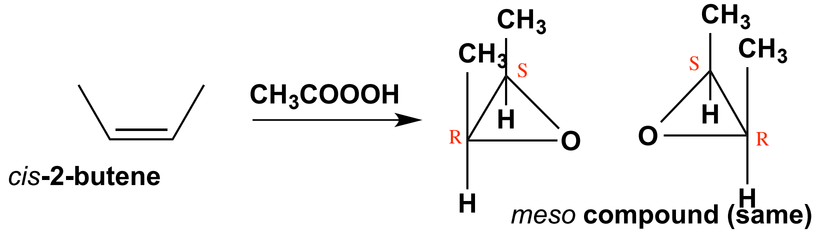


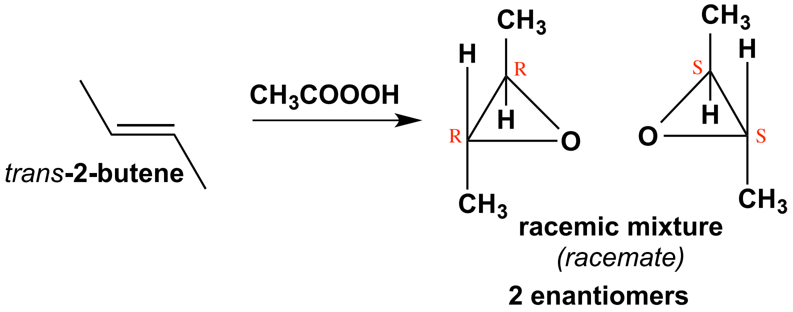
2-butene and peracid react in a concerted syn addition to produce an oxirane or epoxide (which is a 3-membered ring ether)

Concerted: all the bonds are broken and formed at the same time

Syn addition: both additions occur on the same face of the molecule

Comparing cis vs trans:





achiral starting material leads to achiral outcome (meso or racemate) – but cis-2-butene gives meso whereas trans-2-butene gives a 1:1 mix of enantiomers