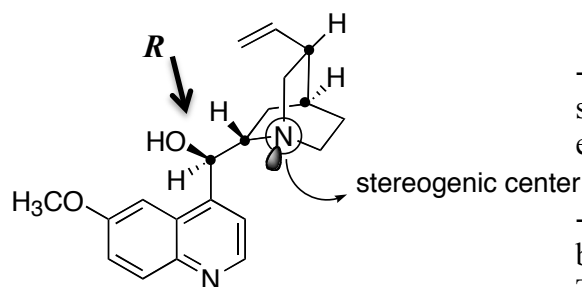
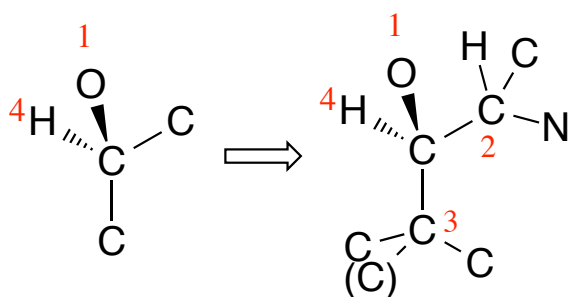


Chiral Centers:

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

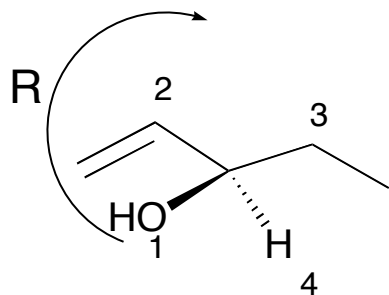
malaria is caused by *Plasmodium* species
transmitted by *Anopheles* mosquito

- 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.

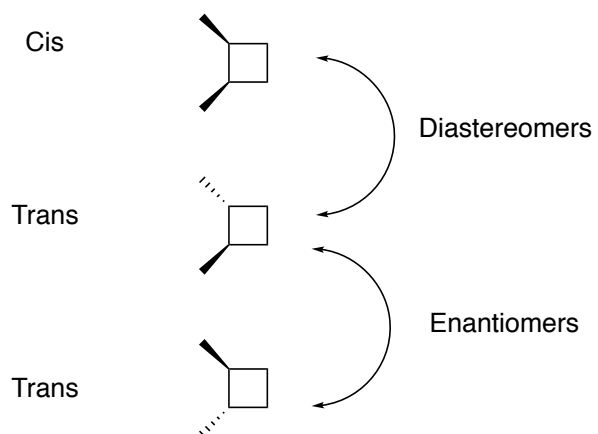
Configuration at the alcohol center (arrow on quinine):

- 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*.

Example: 3-hydroxy-pent-1-ene



RECALL:



Enantiomers have opposite stereochemistry at **every** stereocenter (chiral center)

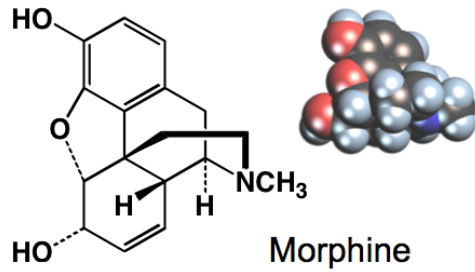
Diastereomers are all stereoisomers that are not enantiomers



*Papaver
somniferum*



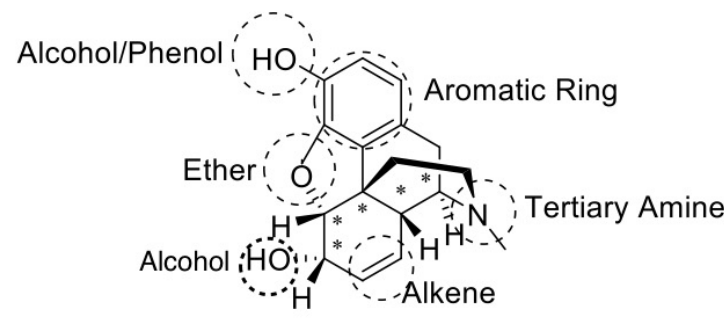
Friedrich Sertürner 1804



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*)
 - o (poppy sleep-carrying)
- ~10% of opium is morphine
- Morphine is used as an analgesic

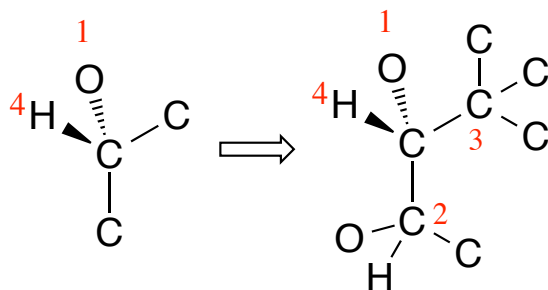
- Heroin (diacetylmorphine) is even more potent (and more addictive)



- 5 stereogenic centers in morphine (represented by *)
 - $2^5 = 32$ stereoisomers possible, where:
 - 1 morphine (itself)
 - 1 enantiomer
 - 30 diastereoisomers

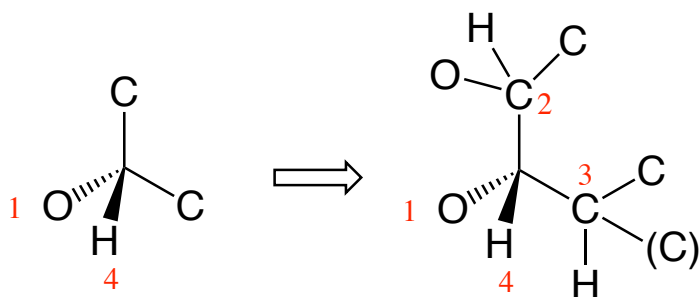
Examples of Configuration in Stereocenters of Morphine

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.

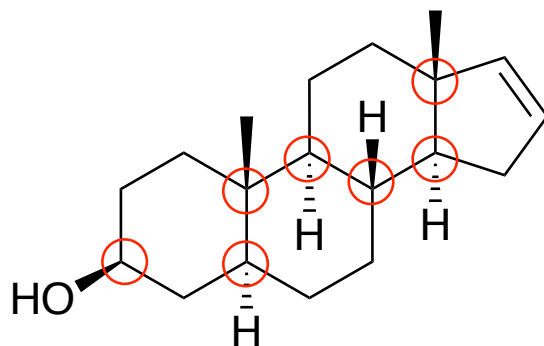
Configuration at the **alcohol** stereocenter:



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

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

Male Pheromone:

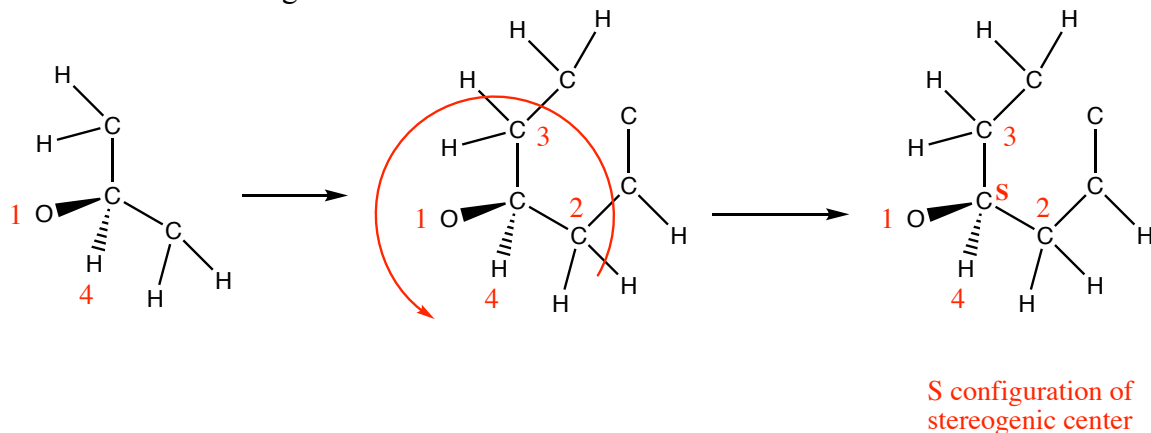


Only about 50 % of the population can smell this compound, which is genetically determined. About half find the smell disgusting while the other half find it tolerable or pleasant.

Can be detected by insects at concentrations of 10^{-17} molar.

Contain 7 stereogenic centers, circled in red above.

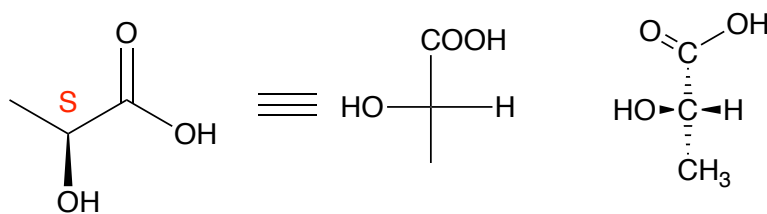
What is the R/S configuration of the carbon attached to OH?



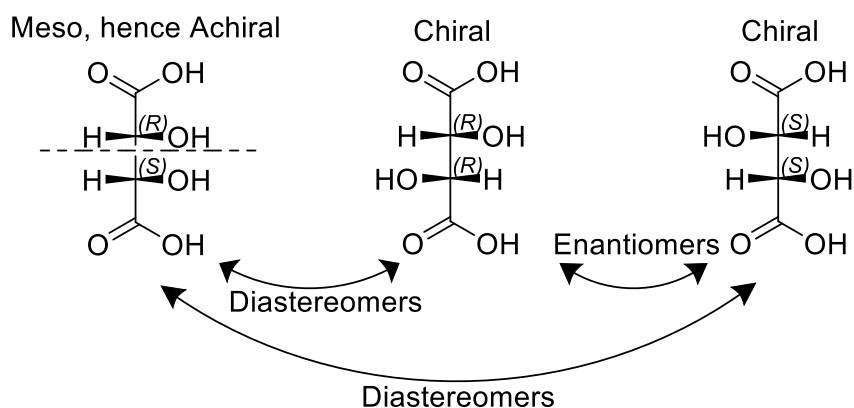
Fischer Projections

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



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

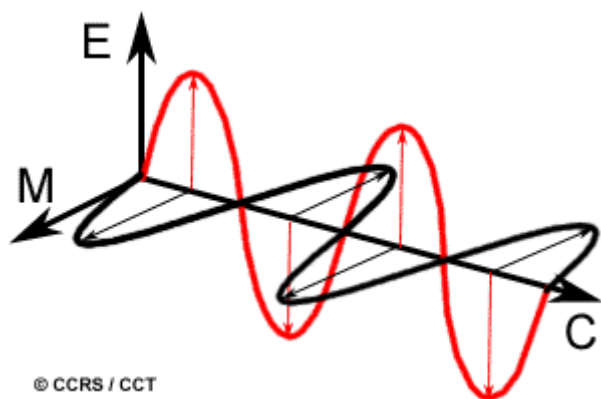
Physical Properties of Enantiomers

- Same physical properties with achiral agents or procedures
 - o 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)

Optical Activity

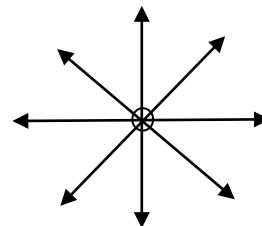
- Rotation of plane of polarized light
- α = measured rotation ($^{\circ}$)
- $[\alpha]_D$ = Absolute rotation
 - o (+) (clockwise)
 - o (-) (counter-clockwise)
- Absolute rotation is 0° for achiral molecules

Pure enantiomers show equal but opposite rotation

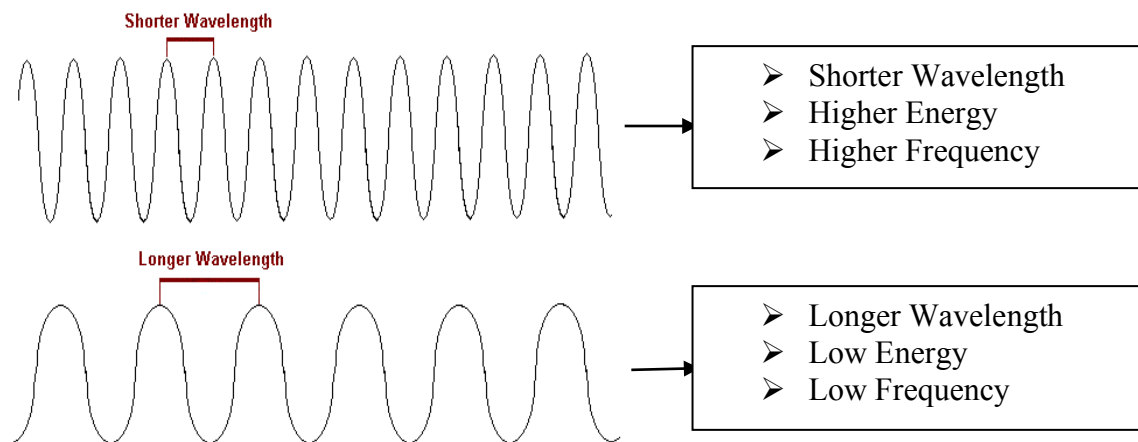


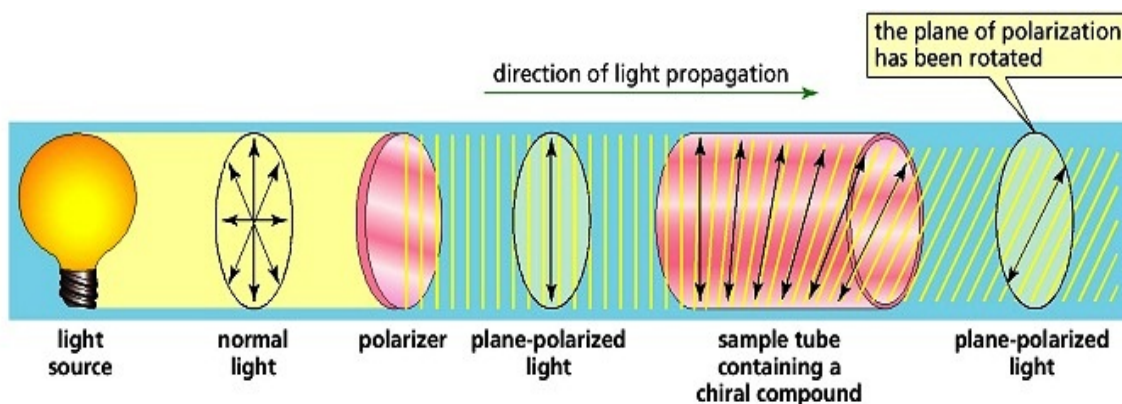
© CCRS / CCT

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.





Optical Rotation

Factors affecting optical rotation:

- Concentration of compound (c)
- Path length that light travels through the solution (l)

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

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

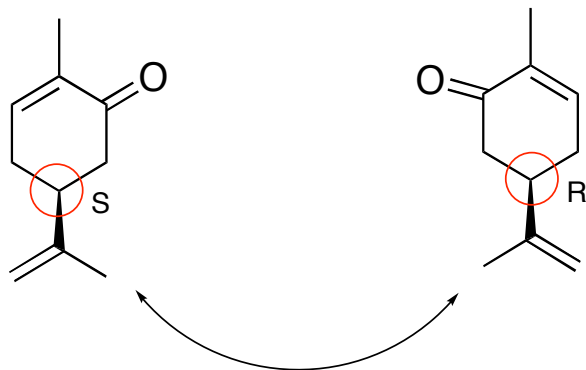
α = measured rotation ($^\circ$) c = concentration (g/cm^3) l = path length (cm)
 D = D-line of sodium light $[\alpha]$ = absolute rotation

Degrees ($^\circ$) = + : Clockwise
 - : Anticlockwise

Example: Carvone

$[\alpha]_D = -100^\circ$

$[\alpha]_D = +100^\circ$



Enantiomers

S-carvone (caraway)

R-carvone (spearmint)

Calculating Optical Purity

For this example for S-carvone, assume the pure S enantiomer has $+100^\circ$ rotation

| <u>R</u> | <u>S</u> | <u>Rotation (°)</u> | <u>Optical Purity (%)</u> |
|-----------------|-----------------|----------------------------|----------------------------------|
| 100 % | 0 % | -100 ° | 100 % |
| 75 % | 25 % | -50 ° | 50 % |
| 50 % | 50 % | 0 ° | 0 % |
| 25 % | 75 % | +50 ° | 50 % |
| 0 % | 100 % | + 100 ° | 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)