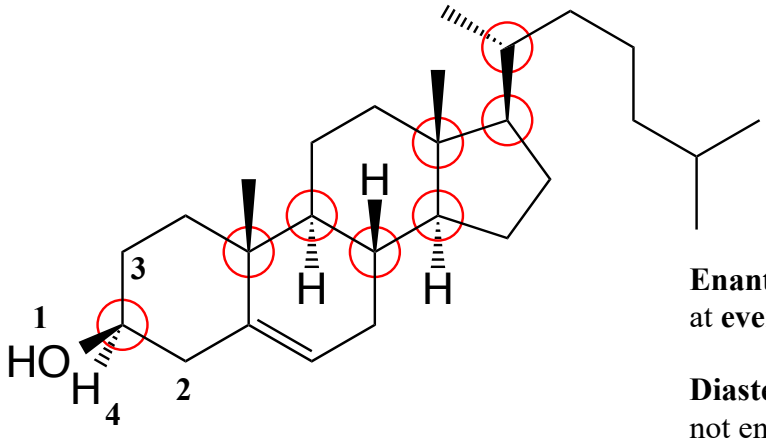
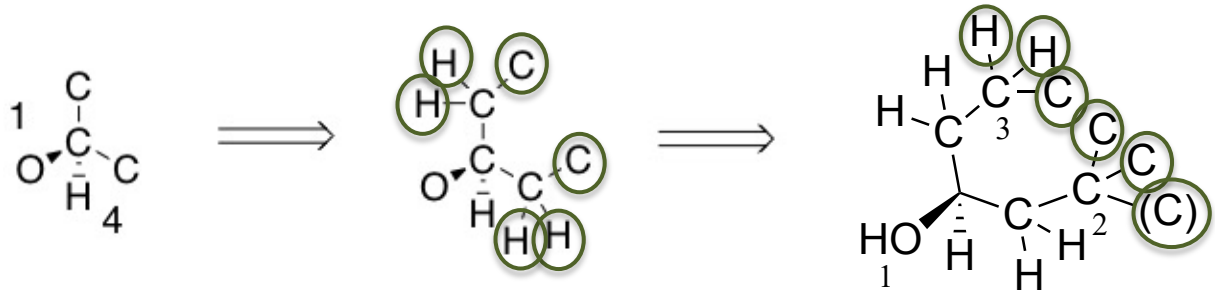
Cholesterol - A steroid with 8 stereogenic centers (red circles)



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

Diastereomers are all stereoisomers that are not enantiomers

Stereochemistry of carbon bearing the hydroxyl is **S**



Carbon in brackets represents the carbon-carbon double bond.

4

Stereoisomer calculation:
If only some (not all) stereogenic centers are inverted, then a diastereomer of cholesterol is produced.

8 stereocenters identified in cholesterol:

2^n = number of stereoisomers, where n = number of stereogenic centers

$2^n = 2^8 = 256$ stereoisomers, which are divided into three kinds below:

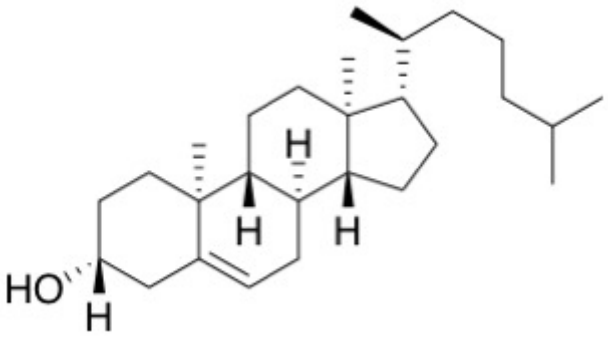
1 Cholesterol (the bioactive natural product)

1 enantiomer of cholesterol

254 are diastereomers of cholesterol

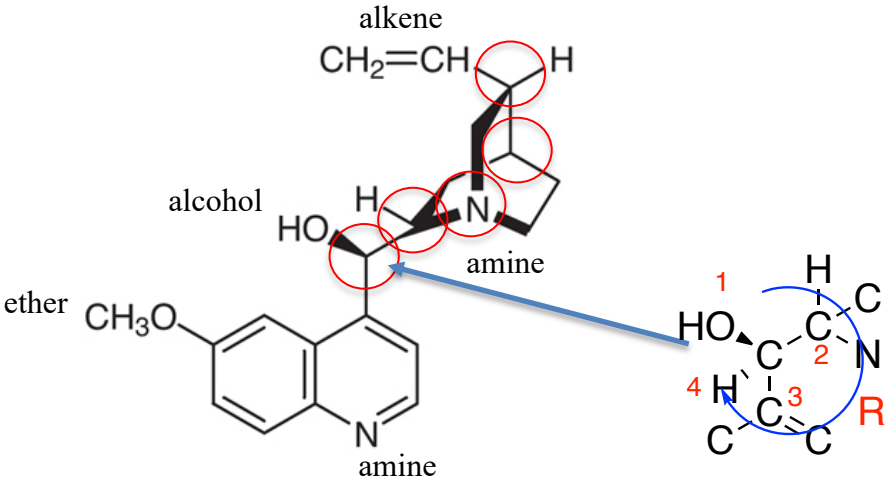
Enantiomer of cholesterol:

To make the enantiomer of cholesterol, invert every stereogenic center



Quinine:

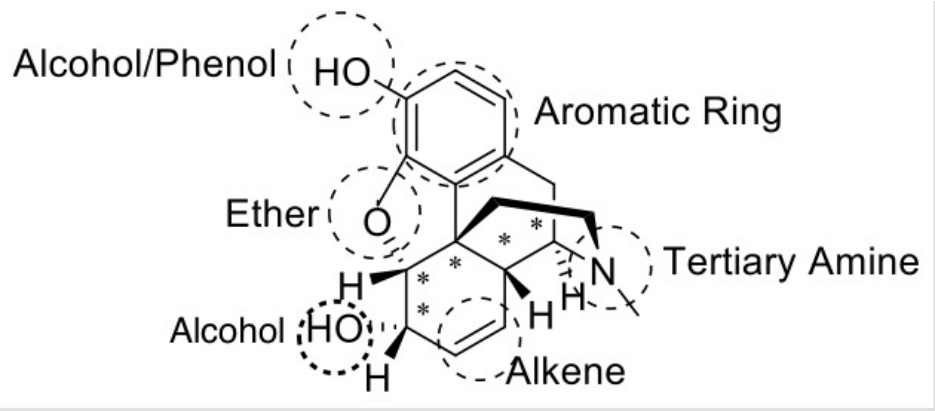
- An anti-malarial agent found in cinchona trees in South America
- Was brought to Spain by Jesuit missionaries in 1632 but was used by native populations long before
- Has 5 chiral centers (labeled in red)
- Here nitrogen is all tied back and **is** a stereogenic center, but typically it is not
- $2^5 = 32$ stereoisomers
    - 1 is quinine (itself)
    - 1 is the enantiomer
    - 30 are diastereomers



C attached to N will gain the 2nd priority because N has higher atomic number

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)



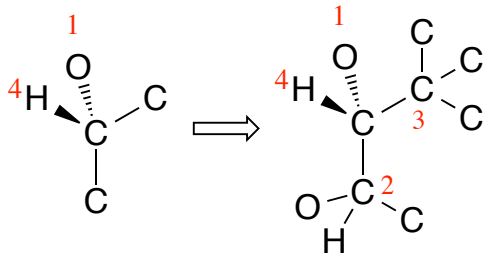
- 5 stereogenic centers in morphine (represented by *) – Nitrogen NOT a stereogenic centre because the methyl group can move up or down
    - $2^5 = 32$ stereoisomers possible, where:
    - 1 morphine (itself)
    - 1 enantiomer
    - 30 diastereoisomers

Mithridates VI (135-63 BC)

- Poisoned slaves and attempted to cure them using mixtures of different plants
- Favorite mixture was Theriac, which contained morphine

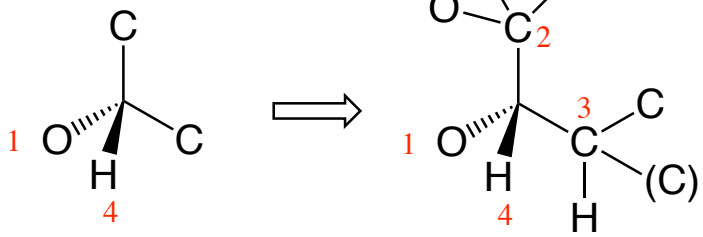
Examples of Configuration in Stereocenters of Morphine

Configuration at the **ether** stereocenter:

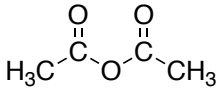


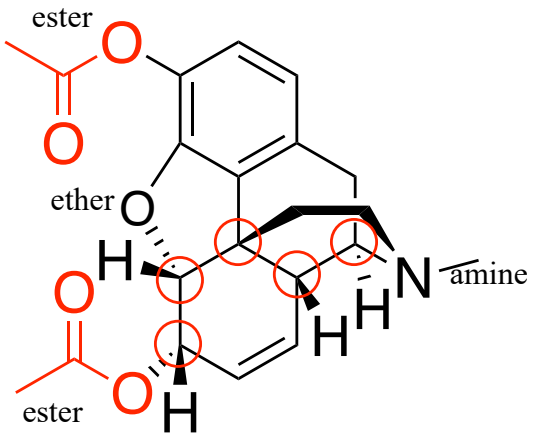
- Cannot assign 2, 3 at first try
- At the second atoms in the chain, there is a difference. The alcohol carbon is attached to one oxygen, one carbon, and one hydrogen. It has a higher priority than the other carbon which is attached to three carbons.
- Count 1, 2, 3: Counterclockwise
- This center is *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:



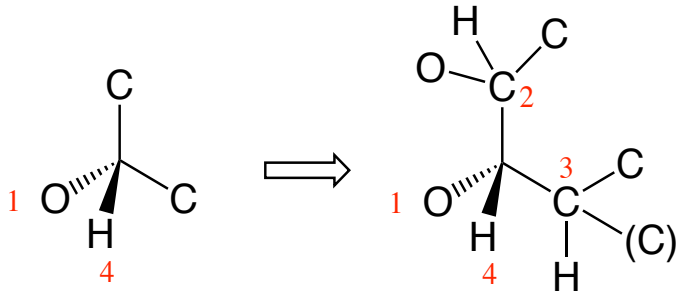
- Cannot assign 2, 3 at first try
- At the second atoms in the chain, the eth carbon is attached to one oxygen, one carl and one hydrogen. It has a higher priority the alkene carbon which is attached to tw carbons and one hydrogen
- Count 1, 2, 3: Clockwise
- This center is *S* and not *R* because the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

If you substitute CH_3COO for the two alcohol residues in morphine by reacting with acetic anhydride (), you then create **HEROIN.**



1000x stronger as analgesic and more addictive than morphine

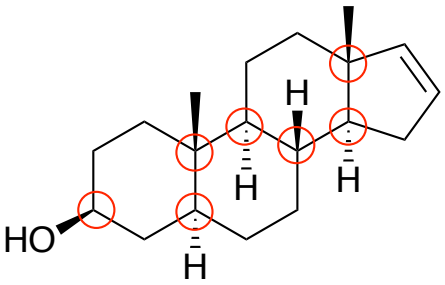
Configuration at the **C** attached to ester stereocenter:



- 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

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

Male Pheromone:

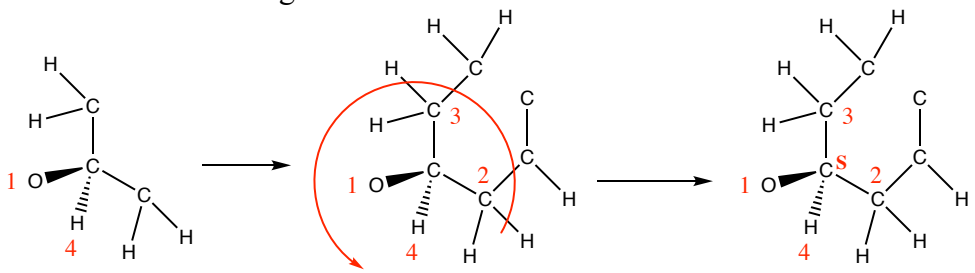


Only about 50 % of the population can smell this compound, which is genetically determined. About half find the smell disgusting while the other half find it tolerable or pleasant.

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

Contain 7 stereogenic centers, circled in red above; ~ 128 stereoisomers

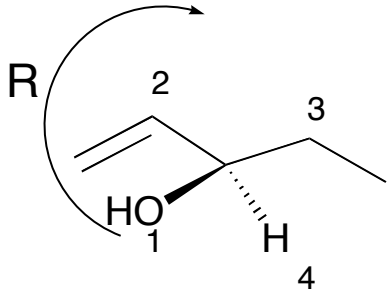
What is the R/S configuration of the carbon attached to OH?



S configuration of stereogenic center

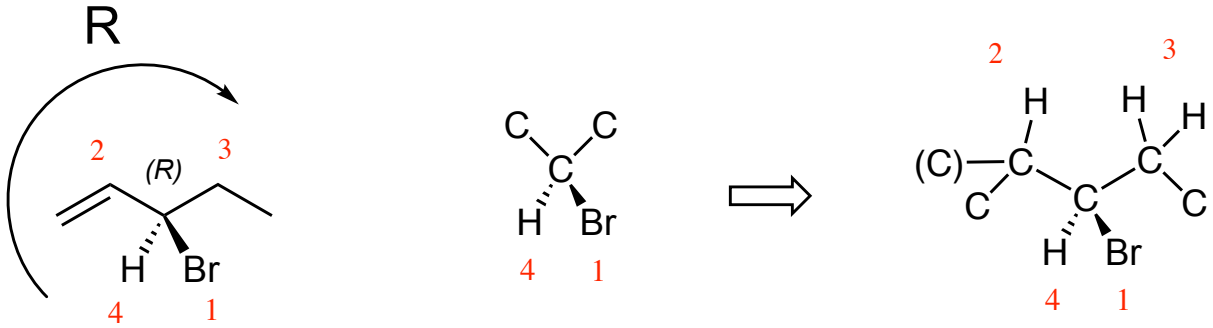
Chiral (Sterogenic) Centers also called Stereocentres:

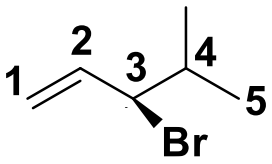
Example: 3-hydroxy-pent-1-ene



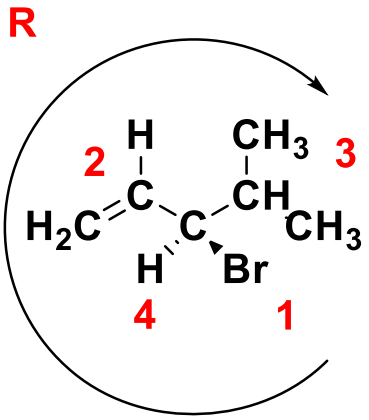
Carbon double bounded to another carbon is equivalent to a carbon bound to two carbons when considering priority

Example:





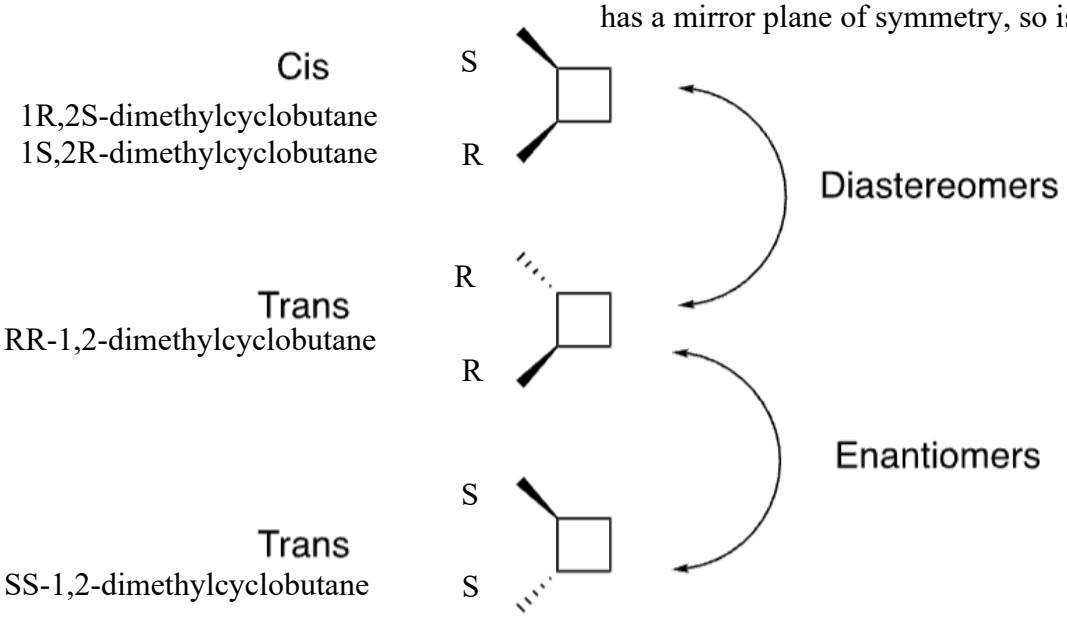
(*R*)-3-bromo-4-methyl-1-pentene



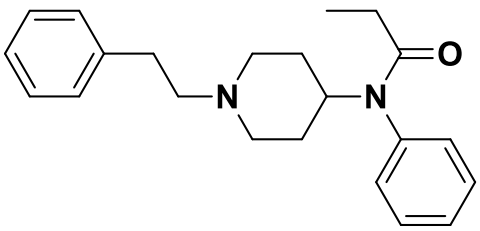
Example:

Achiral

meso compound - has stereogenic centers, but has a mirror plane of symmetry, so is achiral

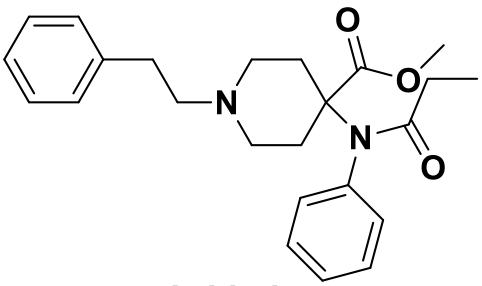


Fentanyl



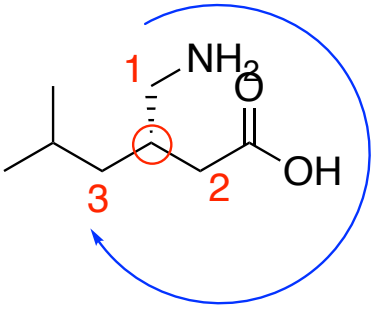
Achiral

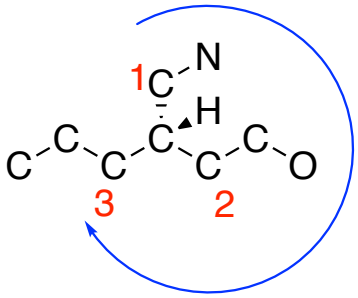
Carfentanyl



Achiral

Lyrica Pregabalin- An analgesic developed by Richard Silverman

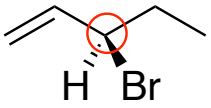


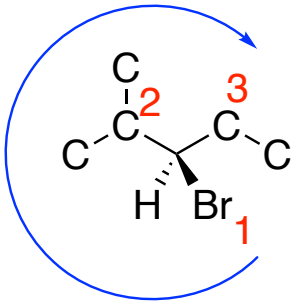


Note: The priority numbers are rotating clockwise however the lowest priority (H) is pointing towards you, hence it is S.

S-pregabalin

More examples

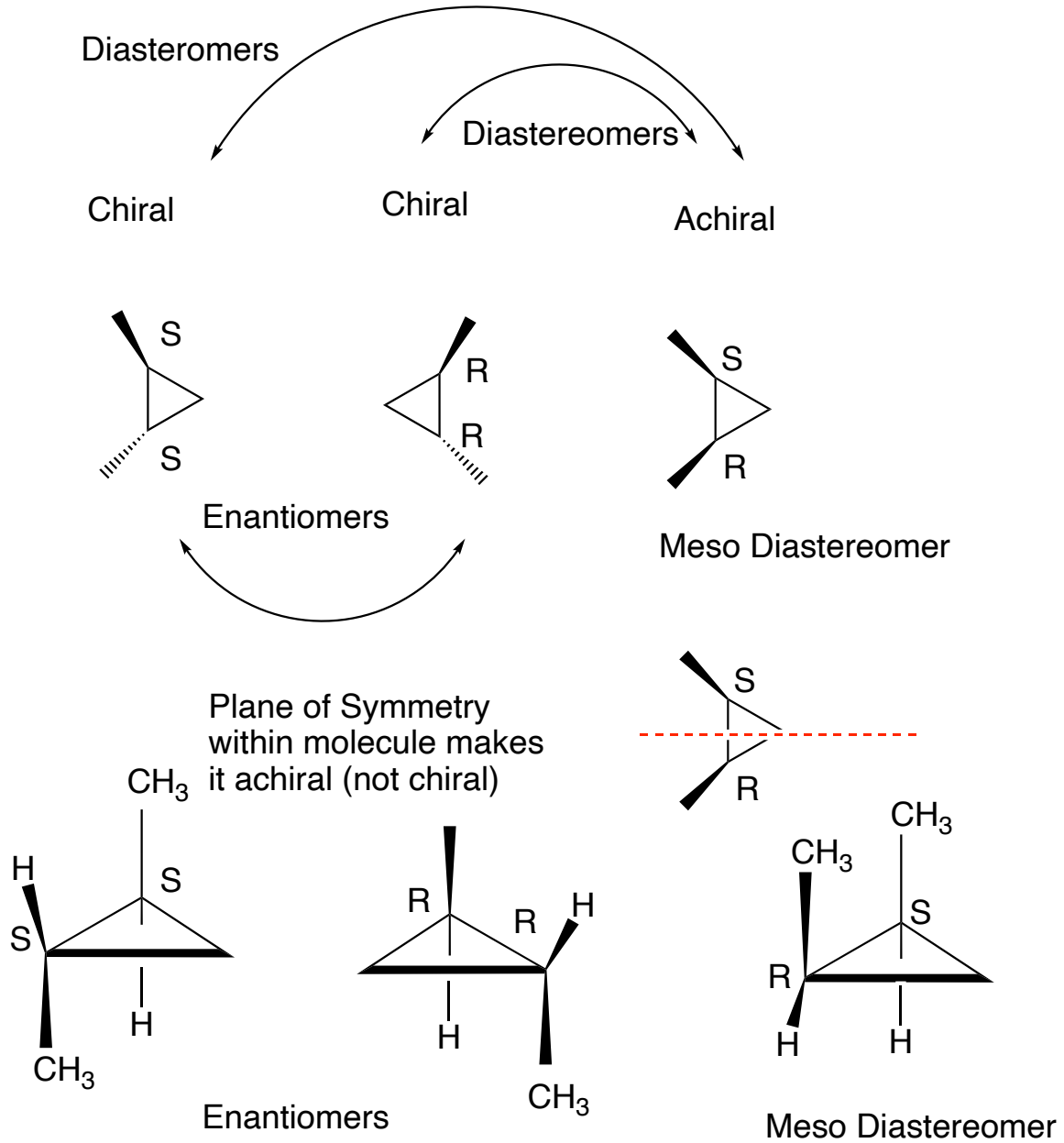




Priorities are rotating clockwise, hence this is **R**

Consider trans and cis 1,2-dimethylcyclopropanes

3 stereoisomers possible

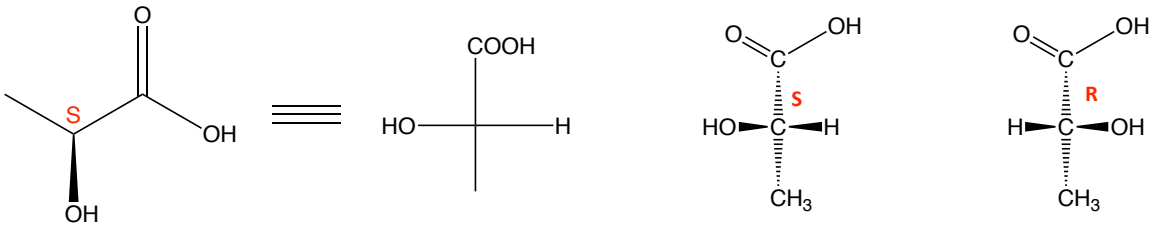


Trans Isomers **Cis Isomer**

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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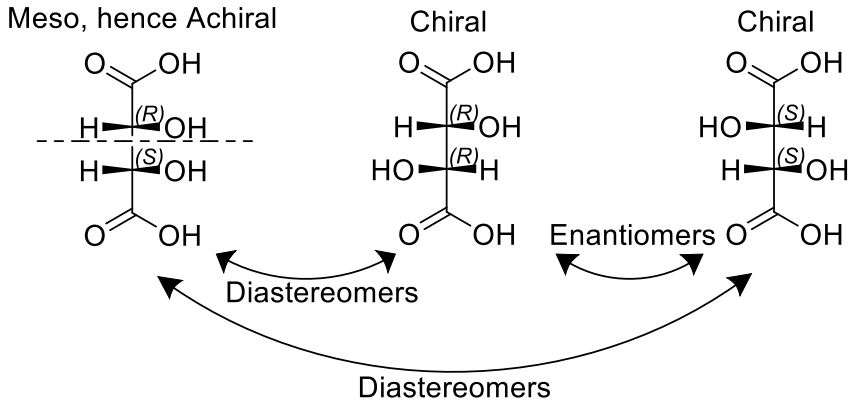
Example #2: Tartaric acid



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