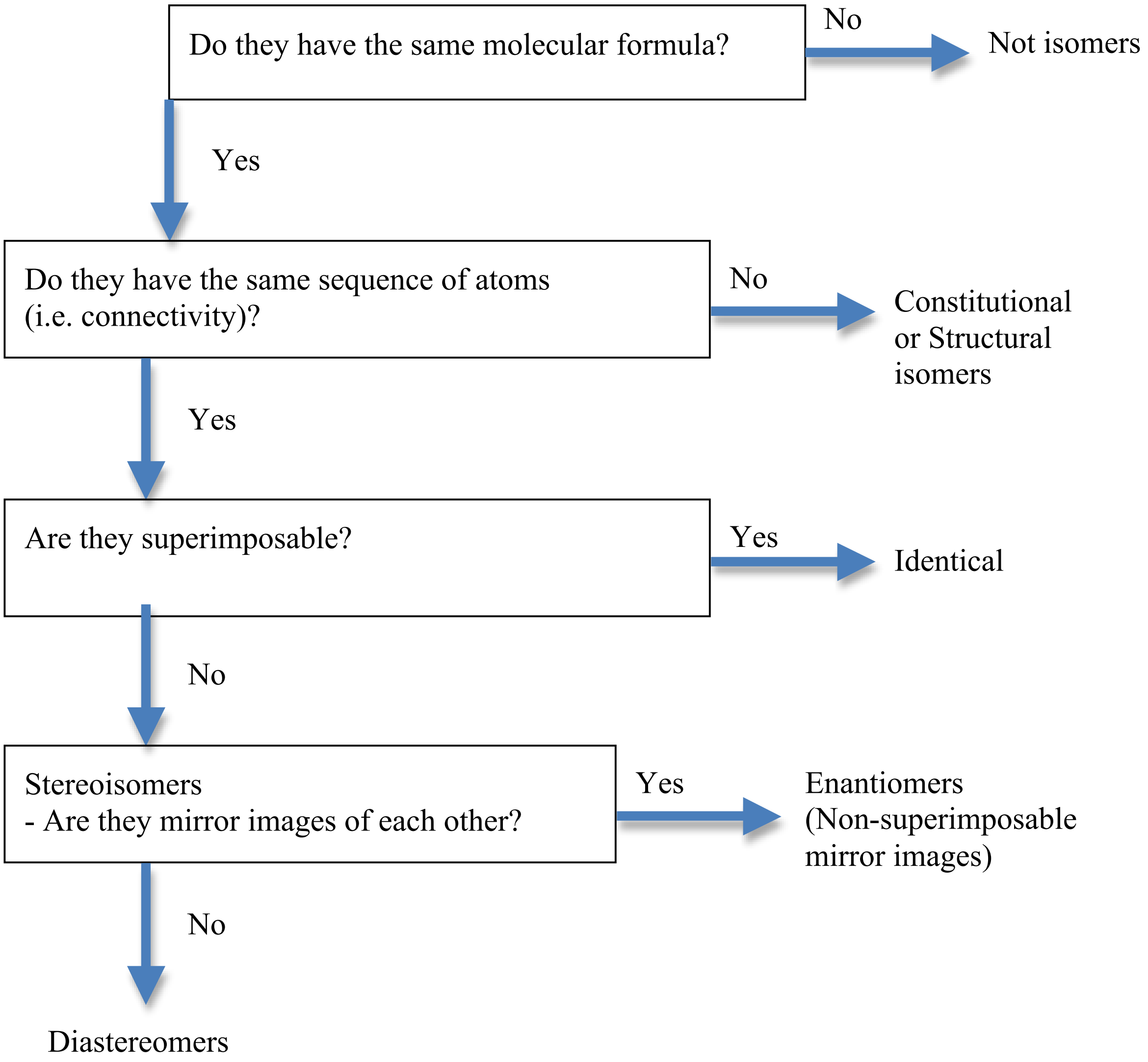
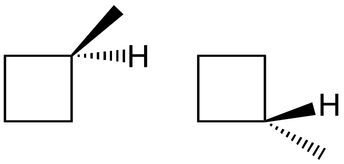
CHEM 263 **Oct 18, 2016**

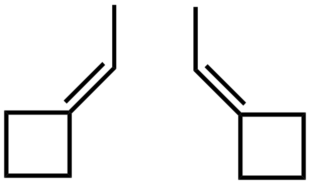
To compare the relationship of 2 structures:



Examples:



Identical
Achiral (not chiral)
No stereogenic centres
Plane of symmetry



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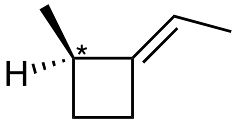
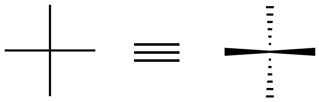
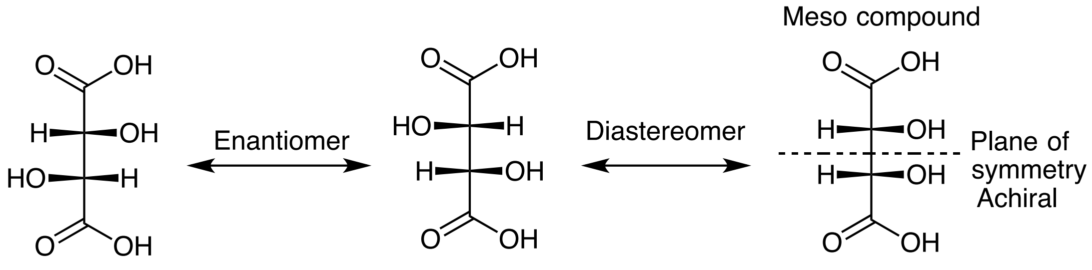


Chiral
Stereogenic centre

Fischer Projection:

- Groups on horizontal are coming toward you
- Groups on vertical are pointed away from you





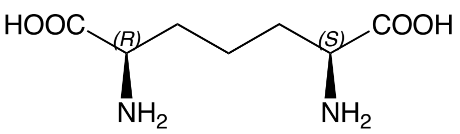
R,R-Tartaric acid S,S Tartaric acid R,S Tartaric acid

Reminder:

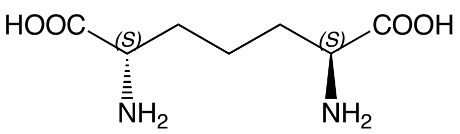
- Enantiomers have identical physical properties
- Diastereomers have different physical properties

Another example:

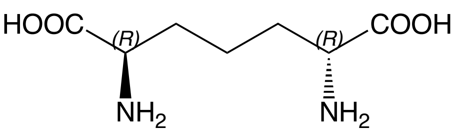
A



B



C



Meso compound – Has stereogenic centres but is achiral due to a plane of symmetry

A is achiral - there is a plane of symmetry going down the middle of the molecule. It does have stereogenic centres, but overall is achiral and it is a **meso** compound.

A and B are diastereomers, as are A and C. (A does not have an enantiomer because its own mirror images are superimposable = identical).

B and C are chiral and are enantiomers of each other.

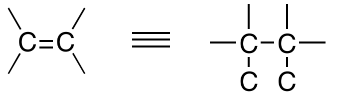
R/S Nomenclature of Stereogenic Centres - Review

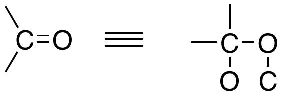
To assign the configuration of a stereogenic center, the Cahn-Ingold-Prelog rules were created. The configuration at a stereocenter is described as being R, from latin *rectus* (or right-handed), or S, from the latin *sinister* (or left-handed), depending on the order in which the different substituents are arranged around the stereocenter. The rules that are applied are as follows:

1) Each group attached to the stereocenter is assigned a priority, where the higher the atomic number, the higher the priority. For example, Cl > O > N > C > H.
   For isotopes of the same atom, the one with the higher atomic weight takes priority. Tritium, an isotope of hydrogen, has an atomic weight of 3 and has a higher priority than deuterium, which has an atomic weight of 2. Hydrogen with an atomic weight of 1 has the lowest priority. T > D > H

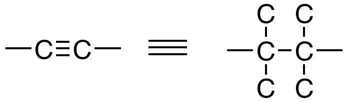
2) If two identical atoms are attached to the stereocenter, the next atom in both chains are examined until a difference is found moving away from the stereocenter. A priority assignment is made at the first point at which the atoms of different priorities are found.

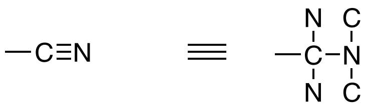
3) A double bond is counted as two single bonds for both atoms involved.





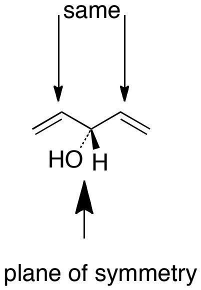
   The same principle is extended to triple bonds.

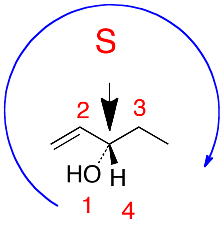




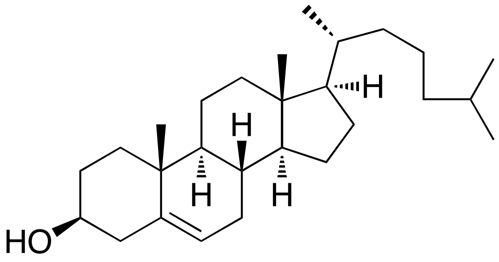
4) After priorities have been assigned, the molecule is viewed with the lowest priority away from the viewer. If you can trace a clockwise path from the group of highest priority to the one of second priority and then to the one of third priority, the stereocenter is assigned the R configuration. If the arrangement is in a counterclockwise path, the stereocenter is assigned the S configuration.

Examples:





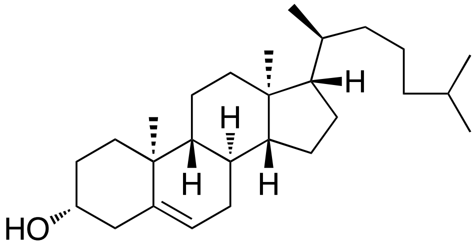
The priority decreases clockwise **but**
the smallest group is pointing towards you.
Therefore, the centre is the opposite (i.e.,
it is S instead of R)



Cholesterol is a steroid

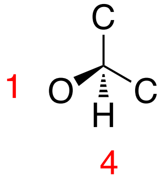
carbon centre bearing alcohol is S

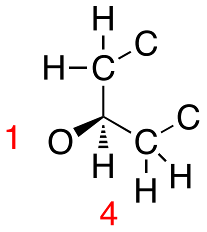
Steroid skeleton

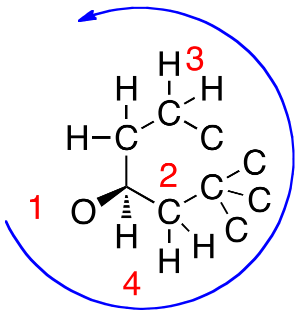


the enantiomer of cholesterol

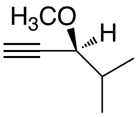
Cholesterol has 8 stereogenic centres, which means that it has $2^8 = 256$ stereoisomers. 1 is cholesterol, 1 is the enantiomer, and the other 254 are diastereomers.

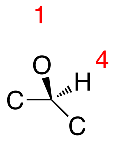


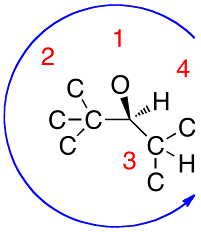




S-3-methoxy-4-methyl-1-pentyne



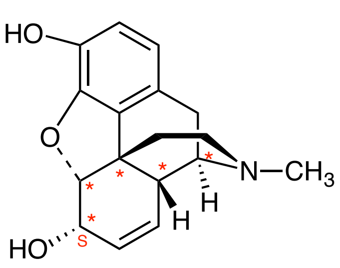




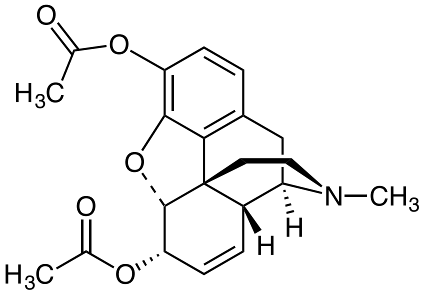
Alkaloids

- Alkaloids are N-containing compounds from plants

Morphine is an analgesic that acts on opioid receptors in the body
Diacetylmorphine (heroin) is 1000x more potent



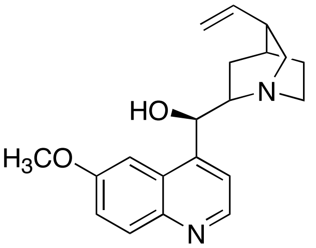
Morphine



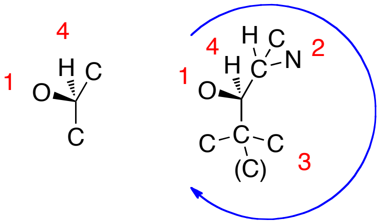
Heroin

Quinine is an anti-malarial compound from the *Cinchona officinalis*. It has five stereogenic centres and a wide range of different functional groups including an ether, alcohol, amines (2), aromatic rings (2), alkene.

Quinine

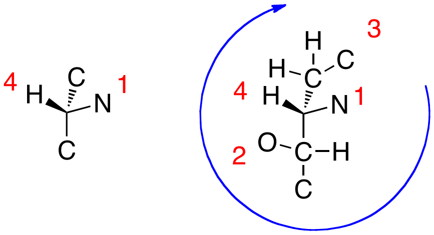


carbon centre bearing alcohol is R



carbon centre bearing single bonded N is S

The priority decreases clockwise **but**
the smallest group is pointing towards you.
Therefore, the centre is the opposite (i.e.,
it is S instead of R)



The R/S configuration of the alcohol is shown to be R. The highest priority is given to the oxygen and the lowest given to the hydrogen. The carbon "next door" to the stereogenic center that is bonded to the nitrogen takes higher priority than the carbon in the aromatic ring since nitrogen has a higher atomic number than carbon. When the hydrogen is pointing away, a clockwise path is found and is assigned the R configuration.

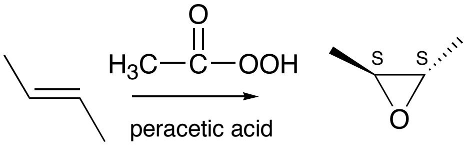
Since there are 5 stereogenic centres, there are $2^5 = 32$ stereoisomers, 1 is quinine, 1 is the enantiomer, and the other 30 are diastereomers

Preparation of ethers from alkenes – Epoxidation

Stereospecific reaction – Stereochemistry of starting material determines the stereochemistry of the product

Epoxide = oxirane – a 3-membered ether

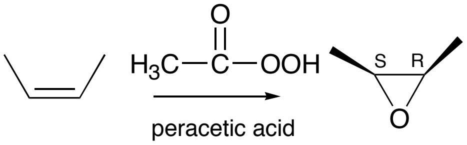
Epoxide formation is a concerted and stereospecific reaction



formed as racemate

(**racemic mixture =**

1:1 mix of enantiomers)



formed as single compound

(**meso compound =**

achiral but has stereocentres)

Note that achiral starting material (2-butene) and peracetic acid (achiral) give net achiral product(s). That is, the products are either racemic (SS and RR isomers in equal amounts – only SS isomer shown above) from the trans 2-butene, or a meso compound from the cis-2-butene.