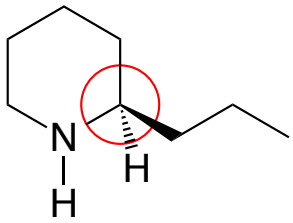
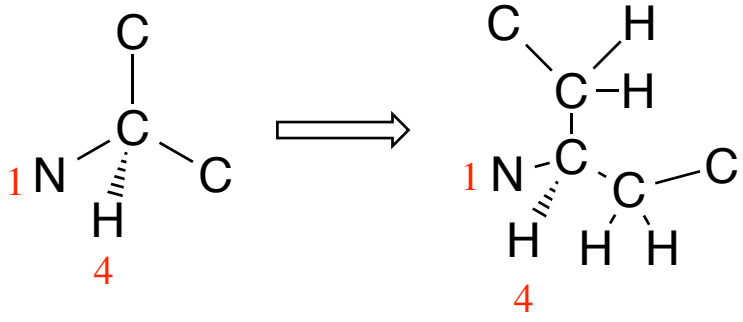
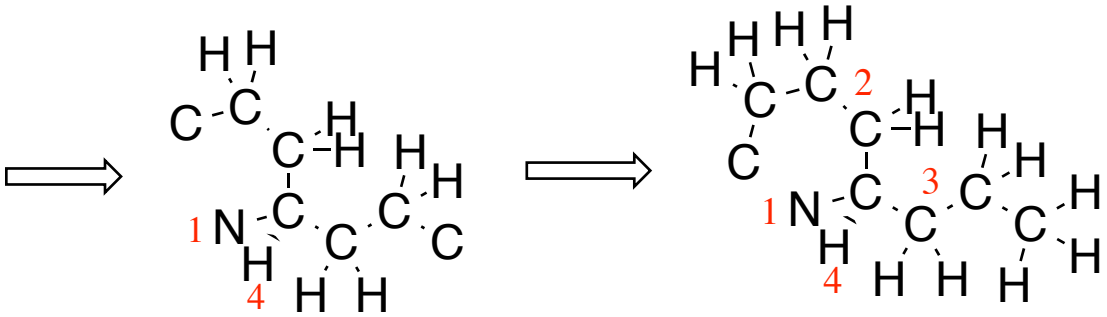
Previous lecture: Enantiomers of coniine (Review from last class)



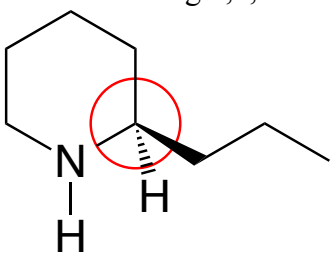
Determining R/S configuration of the stereocenter:



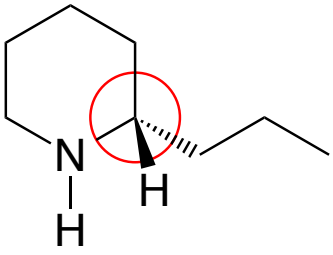
- We can assign highest priority to the N and lowest to the H, but cannot immediately tell which carbon attached to the stereocenter is of higher/lower priority. When this is the case, we look at the next substituents in the chain.



- We cannot tell at the second attached carbon, so we move on to the third.
- We still cannot tell at the third, so we move on to the fourth.
- At the fourth carbon we can see a difference. The carbon that is part of the propyl group ends in a CH_3 so it is bonded to three H, and the other carbon is bonded to two H and one C. The propyl group gets lower priority (3) and the other group gets higher priority (2).
- Counting 1,2,3 → clockwise is *R*. This is the *R* enantiomer.

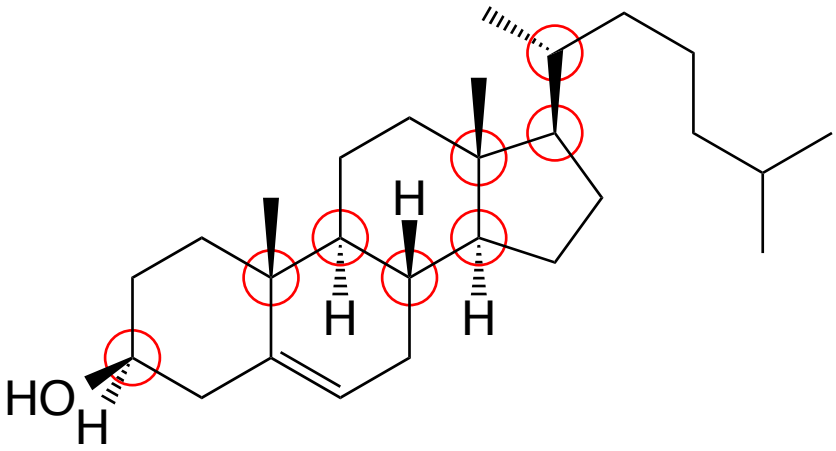


R - enantiomer of coniine



S - enantiomer of coniine - invert EVERY stereocenter

CHOLESTEROL



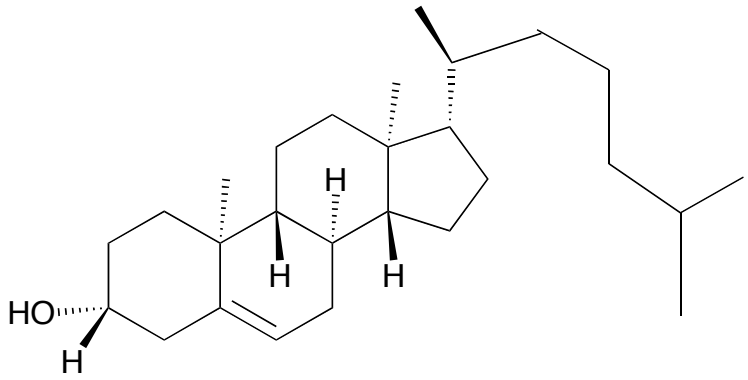
8 Stereocenters identified
2^8 = 256 Stereoisomers, which is divided into three kinds below:

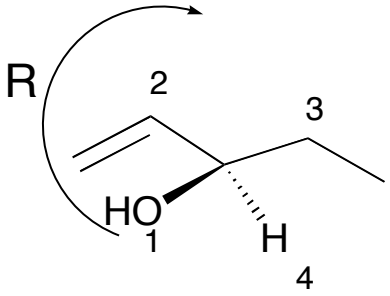
1 Cholesterol (itself)
1 Enantiomer
254 are Diastereomers

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

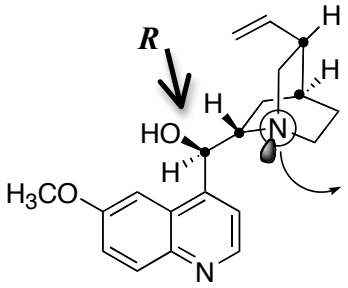
DRAWING ENANTIOMER OF COMPOUND

- Change every stereo center (e.g. compare and contrast the cholesterol above and below images)





Chiral Centers:

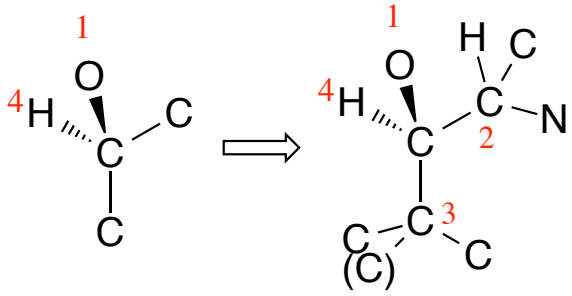


quinine - anti-malarial drug
from the bark of the tree
Cinchona officinalis

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

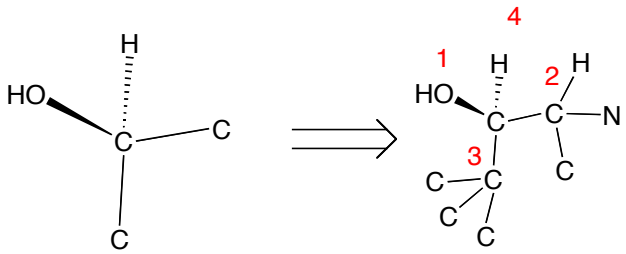
- Carbon stereocenters are shown with dots in this example.
- Nitrogen is a stereocenter here because it can't invert freely. The ring structure restricts its geometry.

Configuration at the alcohol center (arrow on quinine):

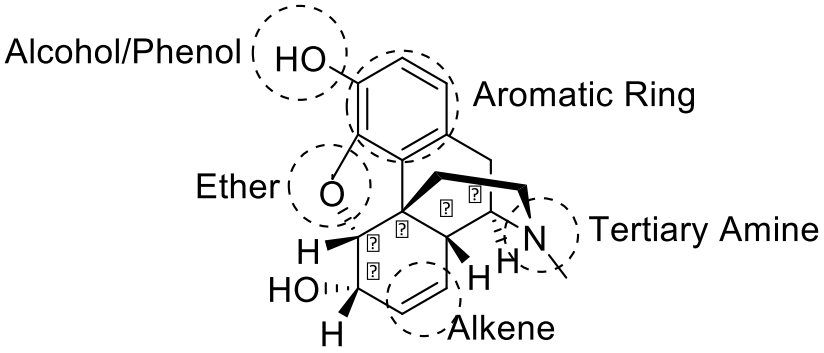


- Cannot assign 2, 3 at first try
- At the second atoms in the chain, there is a difference. The carbon attached to one nitrogen, one carbon, and one hydrogen has a higher priority than the carbon attached to three carbons.
- One nitrogen trumps three carbons.
- Count 1, 2, 3: Clockwise is *R*.

Stereochemistry of Carbon bearing the hydroxyl group is **R**



MORPHINE

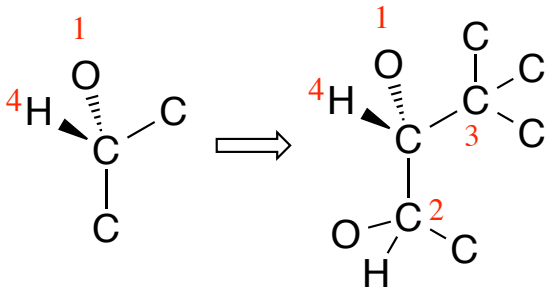


- Morphine (from Morpheus, Greek god of sleep)
- Opium: Sap from the seed pod of opium poppy (*Papaver somniferum*)
- ~10% of opium is morphine
- Morphine is used as an analgesic
- Heroin (diacetylmorphine) is even more potent (and more addictive)

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

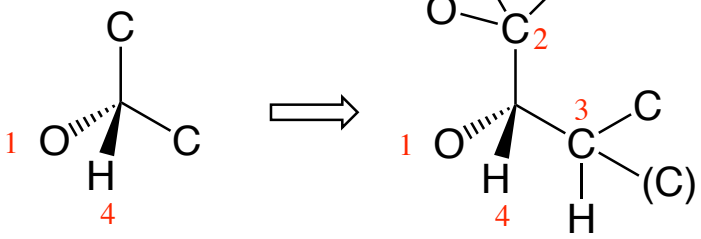
Other Examples of Configuration in Stereocenters of Morphine

Configuration at the **ether** stereocenter:



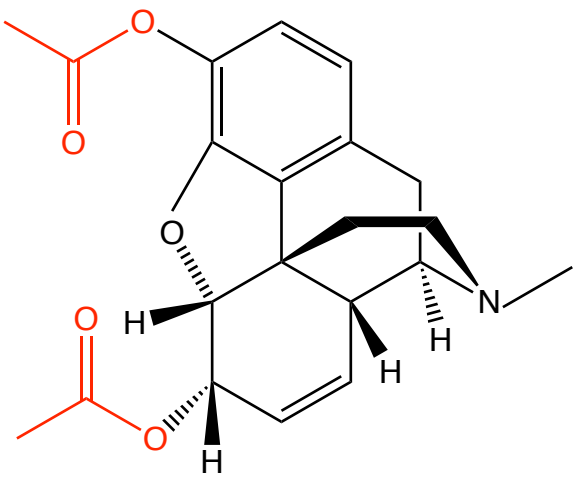
- Cannot assign 2, 3 at first try
- At the second atoms in the chain, there is a difference. The alcohol carbon is attached to one oxygen, one carbon, and one hydrogen. It has a higher priority than the other carbon which is attached to three carbons.
- Count 1, 2, 3: Counterclockwise
- This center is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



Or if CH_3 in amine group is substituted with CH2–CH=CH2, you then create nalorphine an antagonist of morphine at the opioid receptor and an anti-fentanyl compound