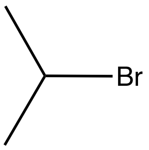
Naming of Alkyl Halides = Haloalkanes

CH_3Cl	CH_2Cl_2	$CHCl_3$	CCl_4
Methyl chloride Chloromethane	Methylene chloride Dichloromethane	Chloroform Trichloromethane	Carbon tetrachloride Tetrachloromethane

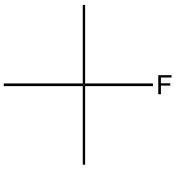
Structure and Nomenclature

1) Find longest chain with largest number of branches
2) Number from end so as to give 1st halogen the lowest number
3) Name prefix with "halo" (chloro, bromo, iodo, fluoro) OR name alkyl and add halide (chloride, bromide, iodide, fluoride) as the suffix

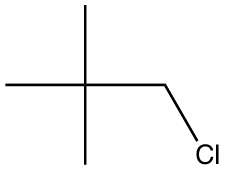
Examples:



Isopropyl Bromide
2-Bromopropane

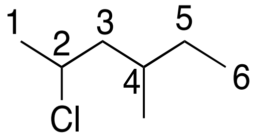


tert-Butyl fluoride
2-Fluoro-2-methylpropane



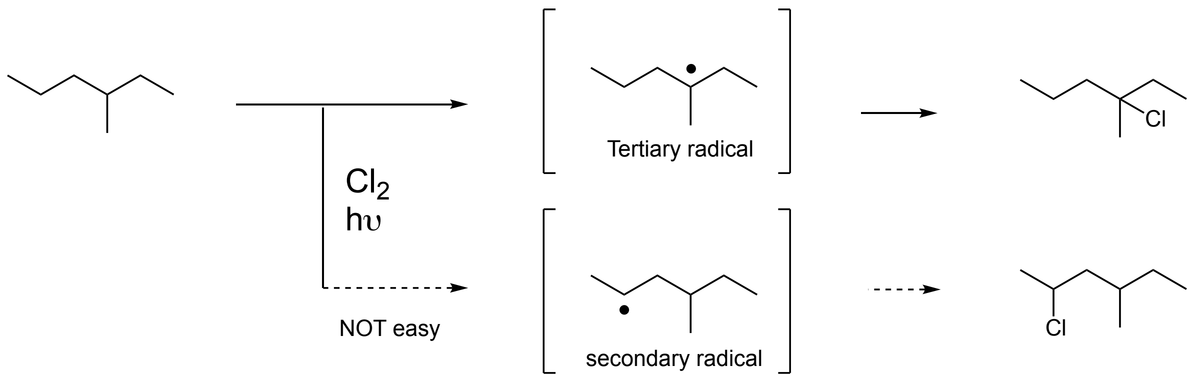
Neopentyl chloride
1-Chloro-2,2-dimethylpropane

Note: Tert-Butyl = t-Butyl = tertiary Butyl

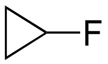


2 -chloro -4-methylhexane

RECALL:

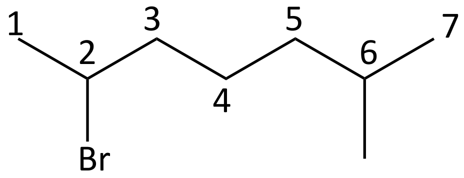


Tertiary radicals are more stable than secondary radicals

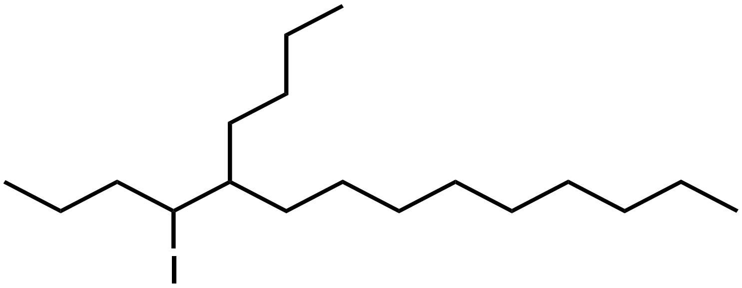


Fluorocyclopropane

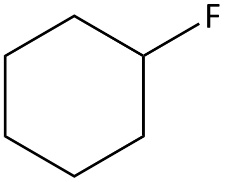
Cyclopropyl fluoride



2-bromo-6-methylheptane



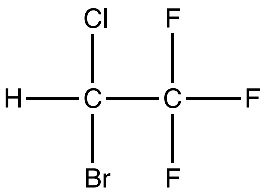
5-Butyl-4-iodotetradecane



cyclohexyl fluoride
1-fluorocyclohexane

Applications of Haloalkanes

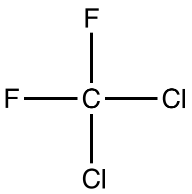
1.) Halothane (anesthetic)



$$\mathrm{H-\overset{Cl}{\underset{Br}{C}}-\overset{F}{\underset{F}{C}}-F}$$

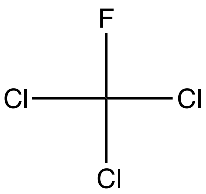
1,1,1-trifluoro-2-bromo-2-chloroethane

2.) Freon = refrigerants/coolants



$$\mathrm{F-\overset{F}{\underset{Cl}{C}}-Cl}$$

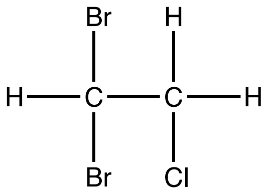
Freon 12



$$\mathrm{Cl-\overset{F}{\underset{Cl}{+}}-Cl}$$

Freon 11

3.) 1,1-dibromo-2-chloroethane = male contraceptive (sperm count drops down to zero from 100 million/mL)



Physical Properties of Alkyl Halides:

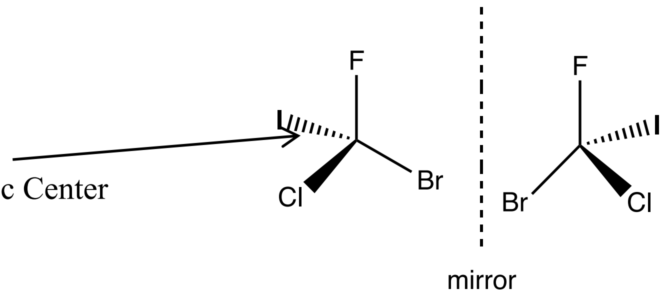
- Governed primarily by dipole-dipole interactions, more polar than hydrocarbons/alkanes.
- High MP and BP relative to hydrocarbons of similar molecular weight
- Good solvents for organic compounds e.g. methylene chloride (CH_2Cl_2) and chloroform ($CHCl_3$) are very common.
- If % composition ≥ 65% halogen by weight, then more dense than water ($\rho > 1.0$ g/cm^3)
- Immiscible (insoluble) in H_2O, which floats on top of the halide

NEXT SECTION: Lecture Outline 3: Stereochemistry and Chirality

Introduction to Stereochemistry and Chirality (terminologies)

Chiral object or molecule: has a non-superimposable mirror image
Achiral object: not chiral, has a superimposable mirror image

Tetrahedral carbon with 4 <u>different</u> groups are said to be **CHIRAL** and are said to contain a **STEREOGENIC (CHIRAL) CENTER**



Stereogenic Center

<u>1850</u> - Louis Pasteur separated the “right-handed” and “left-handed” forms of tartaric acid crystals (from wine)

1876 - J. van't Hoff and Le Bel proposed that differences are due to tetrahedral geometry of carbon
- Kolbe did not receive van't Hoff's idea very well
1901 - J. van't Hoff was the first recipient of the Nobel Prize in Chemistry

Stereochemistry and Chirality

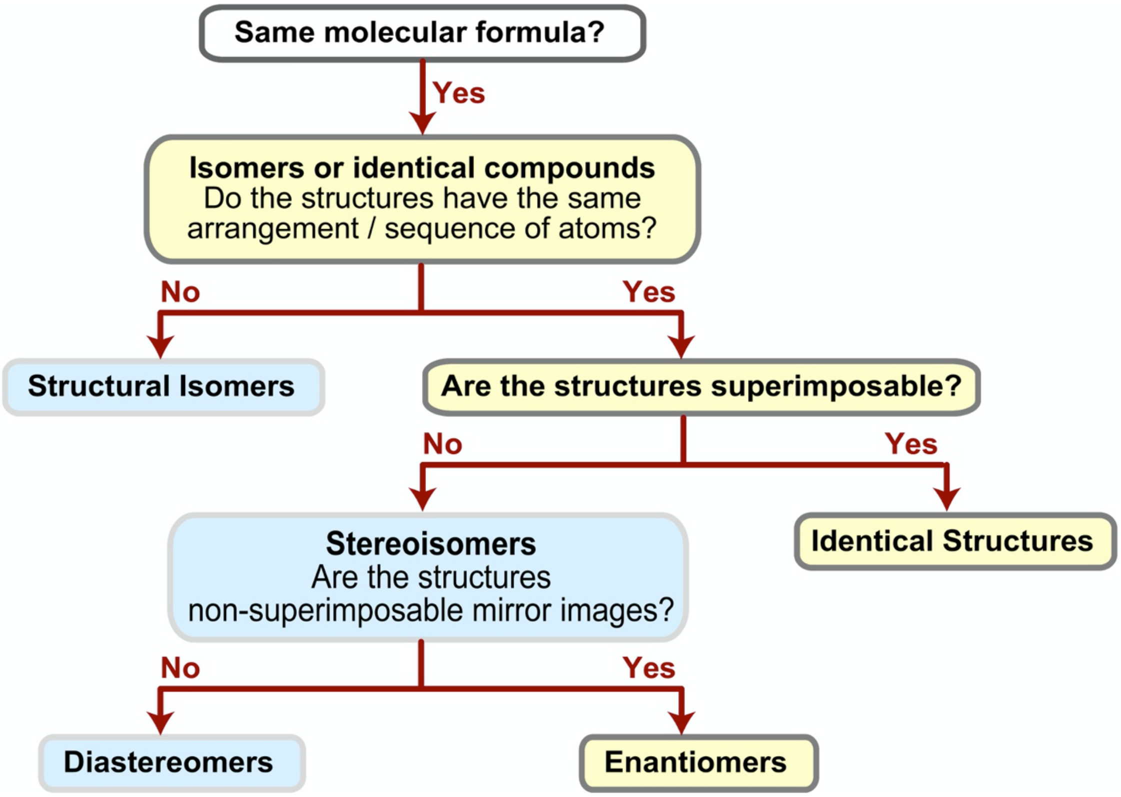
Chiral object or molecule: has a non-superimposable mirror image
Achiral object: not chiral, has a superimposable mirror image

Resolution - Separation of right and left-handed forms (enantiomers)

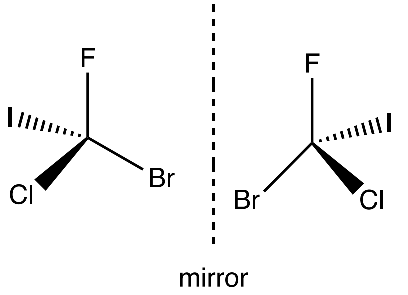
Enantiomers: molecules that are stereoisomers and are non-superimposable mirror images of each other. Physical properties of enantiomers are the same, as far as they are measured in an achiral environment. A chiral agent of molecule is necessary to distinguish them.

Diastereomers: stereoisomers that are not enantiomers.

How to Determine Relationships Among Structures

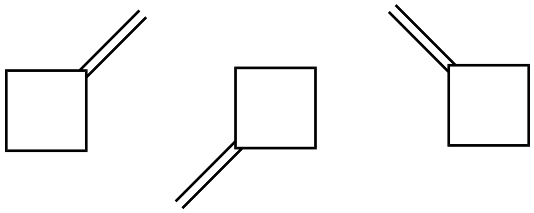


Example 1:



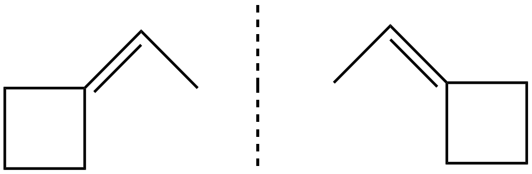
NON-SUPERIMPOSABLE → Enantiomers

Example 2:

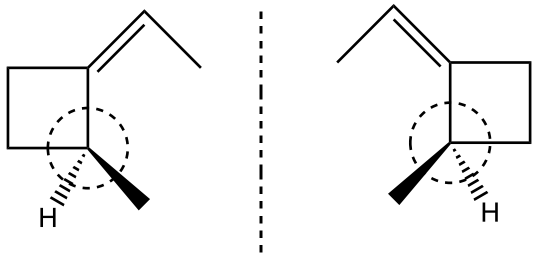


Identical structures, superimposable

Example 3:

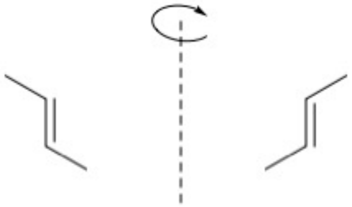


- achiral
- no stereogenic center



- enantiomers
- dashed circle is stereogenic center carbon atom

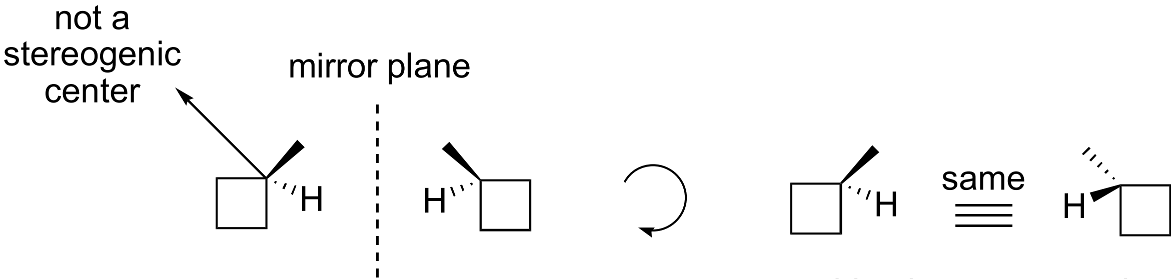
Example 4:



trans-2-butene is achiral

These two mirror images
are superimposable
as seen by a simple rotation

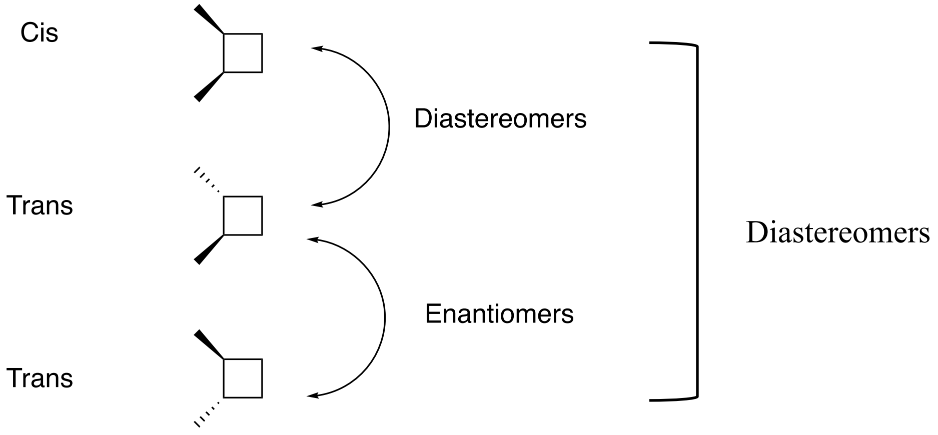
Examples of determining chirality within molecules



chiral?
No, both structures are achiral (not chiral)
and different drawings of same molecule

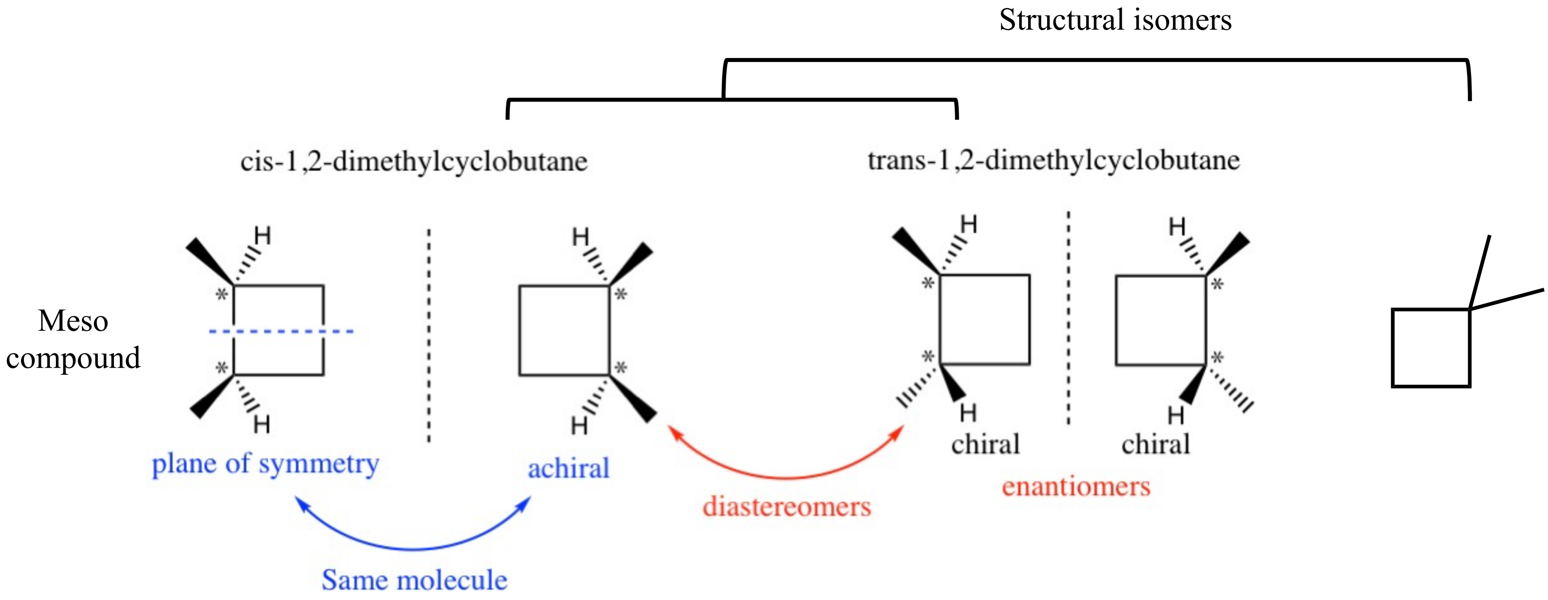
- identical compounds

<u>RECALL:</u>



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

Diastereomers are all stereoisomers that are not enantiomers



** indicates a chiral center*

Diastereomers have different physical properties (e.g. mp, bp, etc), and can be separated. Stereogenic centers can exist in a molecule but if there is a plane of symmetry, it renders the whole molecule achiral.

Note: a chiral center (or stereogenic center) exists if *4 different groups* are attached to the carbon in question
If there is plane of symmetry within a molecule, then the molecule is **achiral** (not chiral)

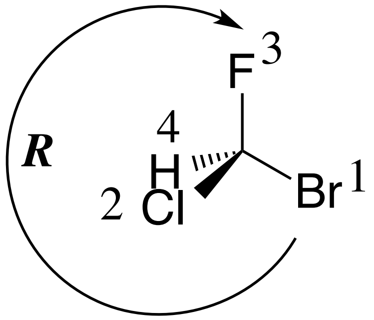
R/S Nomenclature:

R and S designation of stereoisomers
- R = Rectus (right, clockwise)
- S = Sinister (left, counterclockwise)

Labeling a stereogenic center as R or S:
- Identify all stereogenic centers (i.e. 4 different substituents)
- Look at atomic number of atoms attached to the stereogenic center
- Assign priority based on atomic number. If you cannot decide, go to the next set of atoms.
- Number from highest to lowest priority, then with the lowest priority group pointing back, count 1, 2, 3:
    - Clockwise → R configuration
    - Counterclockwise → S configuration

Each stereogenic center in a molecule is analyzed separately

Example:

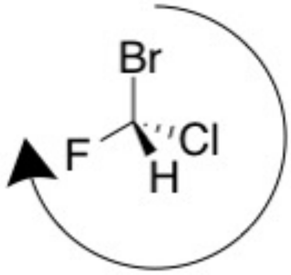


Place lowest priority to the back

1,2,3 --> clockwise = "R"
1,2,3 --> counterclockwise = "S"

Bromine has the highest atomic number (35), followed by chlorine (17), then fluorine (9), and lastly hydrogen (1).

<u>What if the lowest priority group is pointing forward?</u>



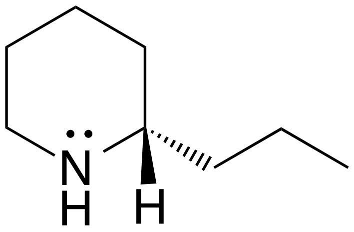
Counting 1, 2, 3 gives clockwise, BUT the smallest group is pointing forward, so the configuration is opposite of what you get if the smallest group is back

In this case, the configuration of the stereogenic center is "***S***"

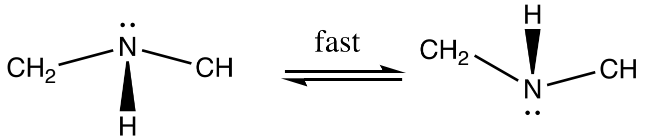
Example

CONIINE, Poison hemlock, potent neurotoxin, killed Socrates

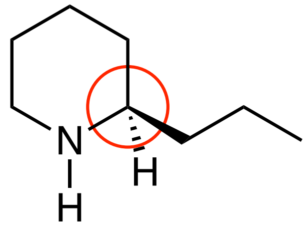
Stereogenic center (chiral centers or asymmetric centers) is circled in red



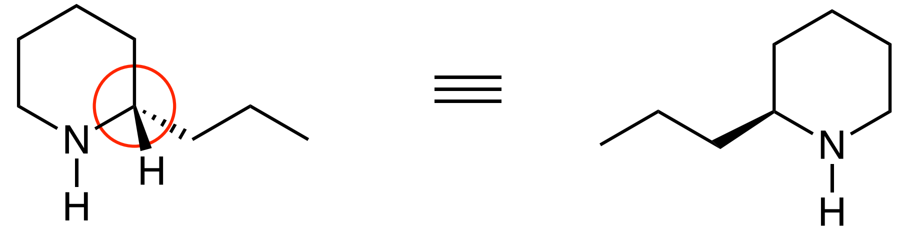
The nitrogen is nominally a stereogenic center since it has 4 different substituents, however it inverts rapidly, and so is not considered stereogenic.



To draw the enantiomer of coniine, invert the geometry at the stereocenter



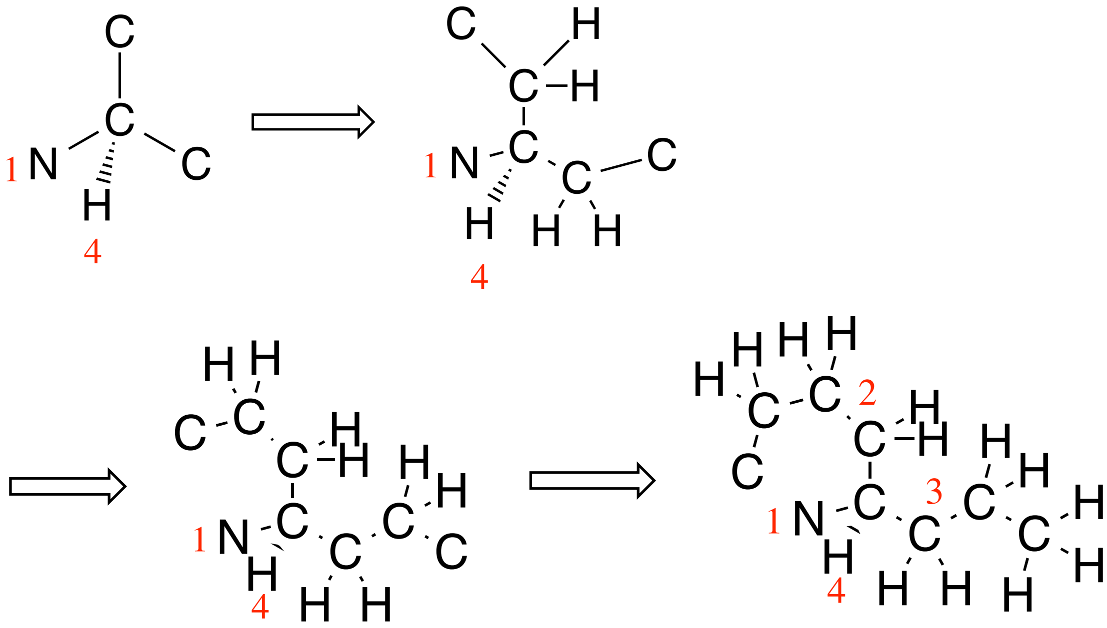
R - enantiomer of coniine
Non-toxic
invert EVERY stereocenter



S - enantiomer of coniine - highly toxic - natural

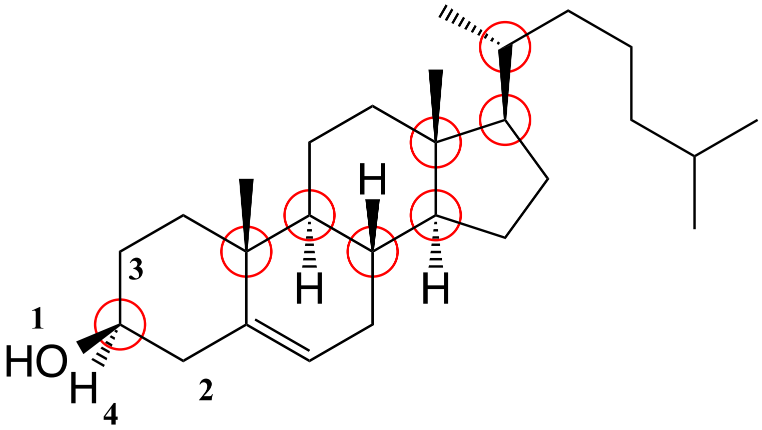
Example of determining priority of groups in enantiomer on natural coniine

- 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.

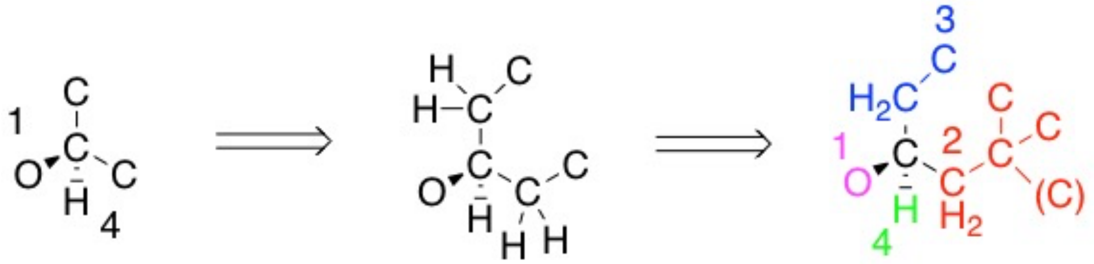


- We cannot tell at the second attached carbon, so we move on to the third.
- We still cannot tell at the third, so we move on to the fourth.
- At the fourth carbon we can see a difference. The carbon that is part of the propyl group ends in a CH_3 so it is bonded to three H, and the other carbon is 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.

Cholesterol - A steroid with stereogenic centers (red circles)



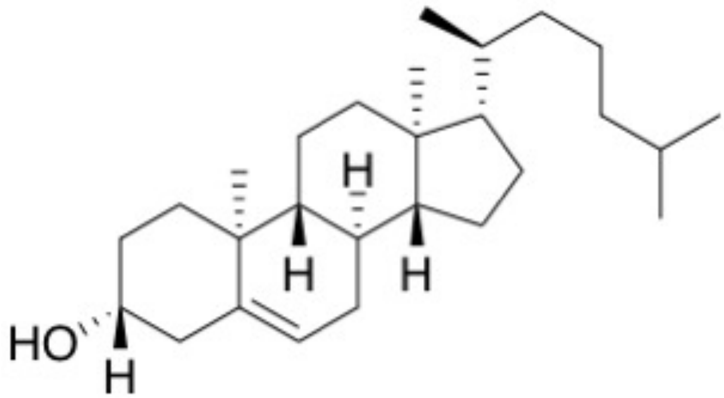
NB: Stereochemistry of carbon bearing the hydroxyl is **S**



Carbon in brackets represents the carbon-carbon double bond.

Enantiomer of cholesterol:

To make the enantiomer of cholesterol, invert every stereogenic center



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

8 stereocenters identified in cholesterol:

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

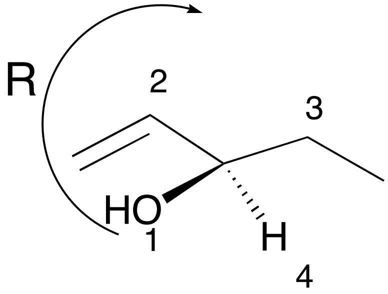
1 Cholesterol (the bioactive natural product)

1 enantiomer of cholesterol

254 are diastereomers of cholesterol

<u>Chiral Centers:</u>

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: