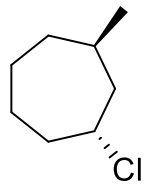
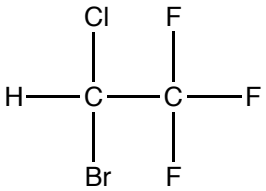
Applications of Haloalkanes

1.)



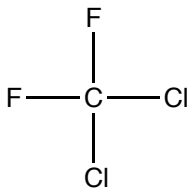
Trans-1-chloro-3-methylcyclohexane

2.) Halothane (anesthetic)

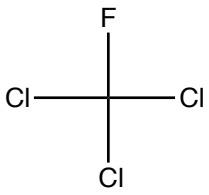


1,1,1-trifluoro-2-bromo-2-chloroethane

3.) Freon = refrigerants/coolants (react with ozone which protects us from strong UV)

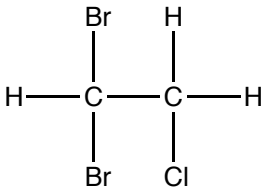


Freon 12



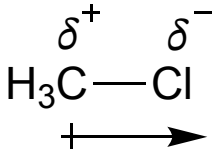
Freon 11

4.) 1,1-dibromo-2-chloroethane = male contraceptive (sperm count drops down to zero from 100 million/mL)

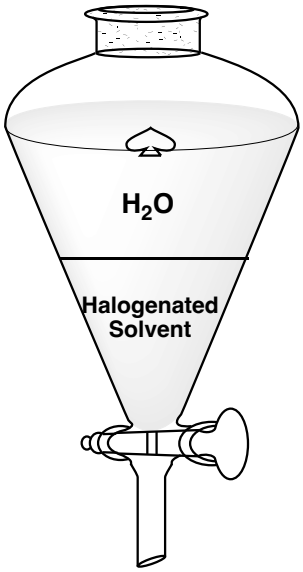


<u>Physical Properties of Alkyl Halides:</u>

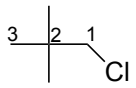
- Governed primarily by dipole-dipole interactions, more polar than hydrocarbons/alkanes.



- 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

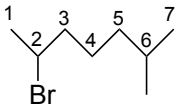


Structure and Nomenclature Practice



Neopentyl chloride, or
1-chloro-2,2,-dimethylpropane

Cyclopropyl Fluoride, or
1-Fluorocyclopropane

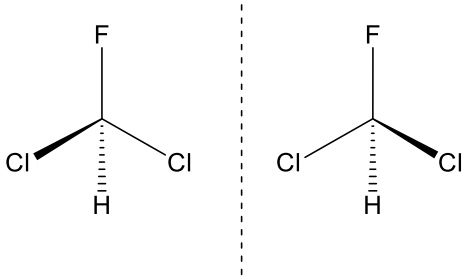


2-Bromo-6-methylheptane

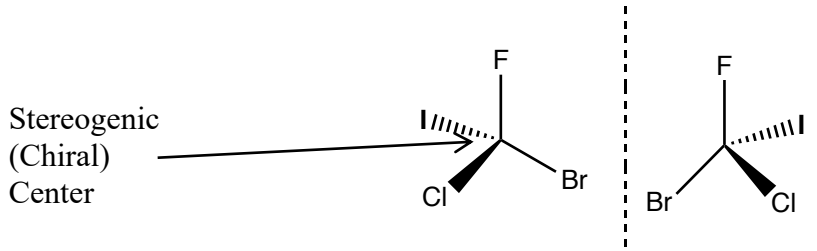
Introduction to Stereochemistry and Chirality (terminologies)

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

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



Achiral, identical – have a plane of symmetry



mirror

Non-superimposable

1850 - Louis Pasteur (1822-1895) separated the "right-handed" and "left-handed" forms of tartaric acid crystals (from wine). "Resolution" is the separation of mirror-image objects.

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

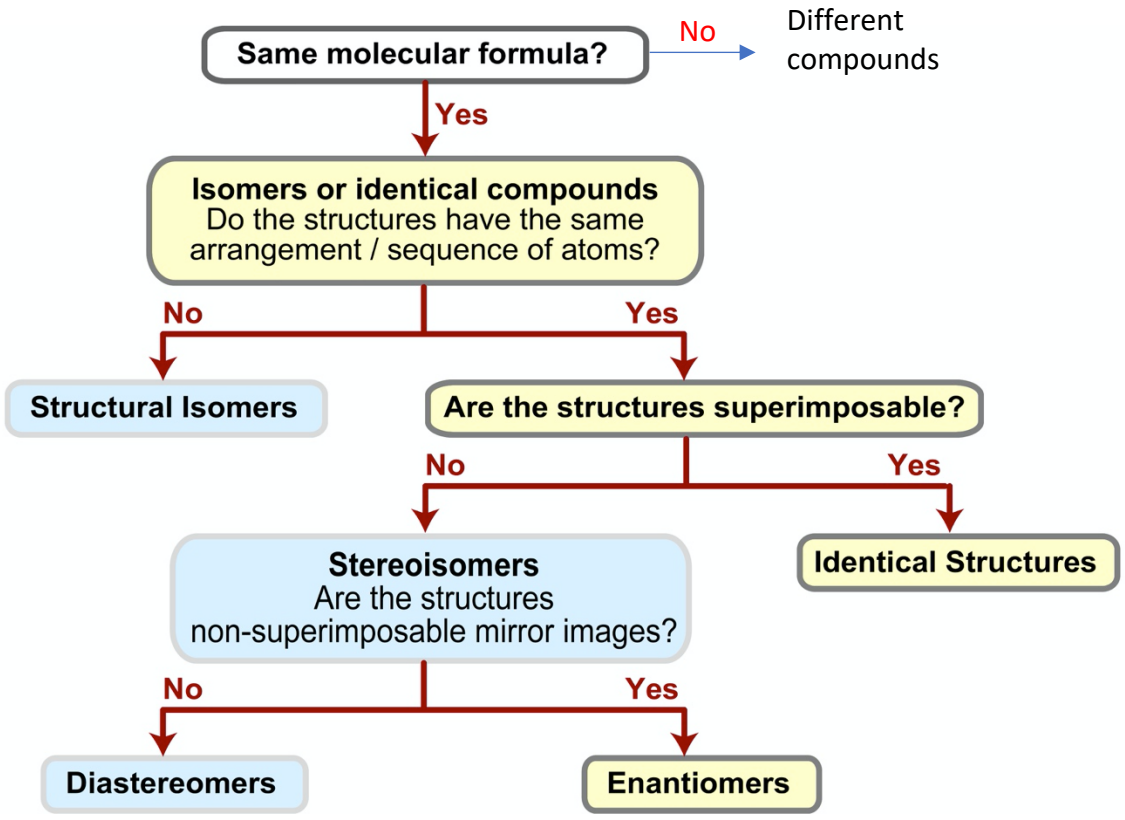
Resolution – separation of enantiomers

Enantiomers: molecules that are stereoisomers and are non-superimposable mirror images of each other. Opposite stereochemistry at every chiral center. 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.

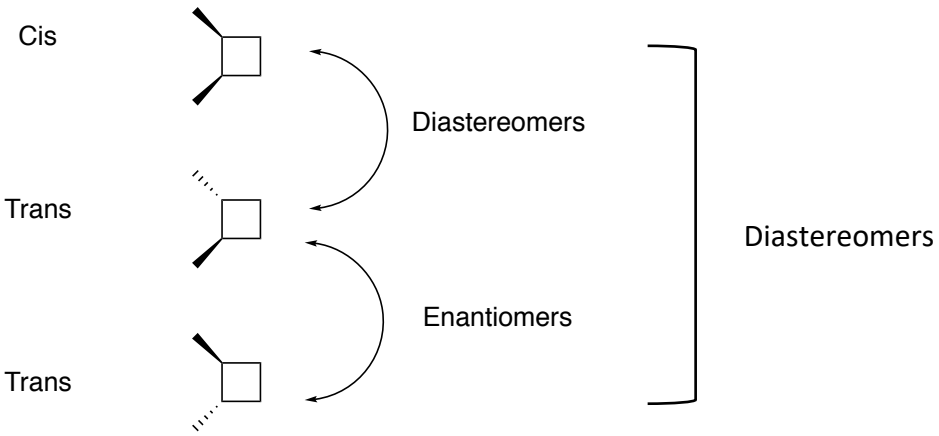
Diastereomers: all stereoisomers that are not enantiomers

Enantiomers	**Diastereomers**
Same physical properties (i.e., m.p, b.p, etc.)	Different chemical properties
Bend polarized light differently	
Hard to separate	Easier to separate
Mirror images	Not mirror images
Non-superimposable	Non-superimposable

How to Determine Relationships Among Structures

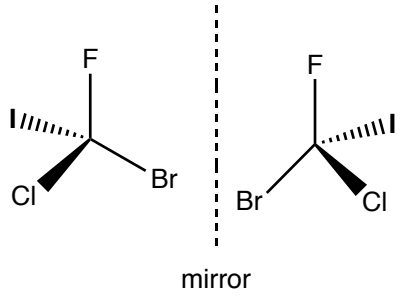


Example 1:



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

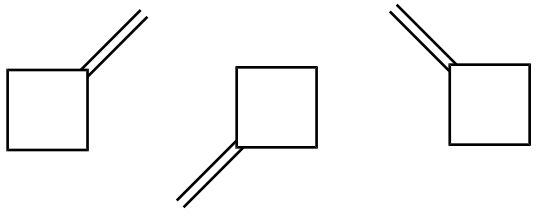
Diastereomers are all stereoisomers that are not enantiomers



1) Same molecular formula? Yes
2) Same arrangement of atoms? Yes
3) Superimposable? No
4) Non-superimposable mirror images? Yes

NON-SUPERIMPOSABLE → Enantiomers

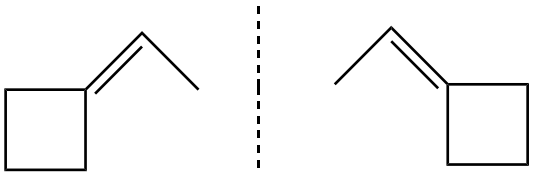
Example 2:



1. Same molecular formula? Yes
2. Same arrangement of atoms? Yes
3. Superimposable? Yes

Identical structures, superimposable, achiral

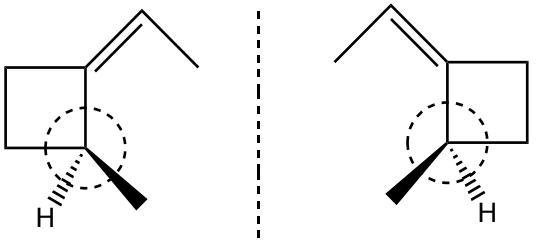
Example 3:



1. Same molecular formula? Yes
2. Same arrangement of atoms? Yes
3. Superimposable? Yes

- achiral
- no stereogenic center

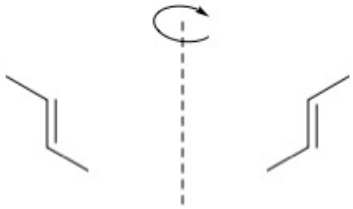
Same, identical compound



1. Same molecular formula? Yes
2. Same arrangement of atoms? Yes
3. Superimposable? No
4. Non-superimposable mirror images? Yes

- enantiomers
- dashed circle is stereogenic center carbon atom

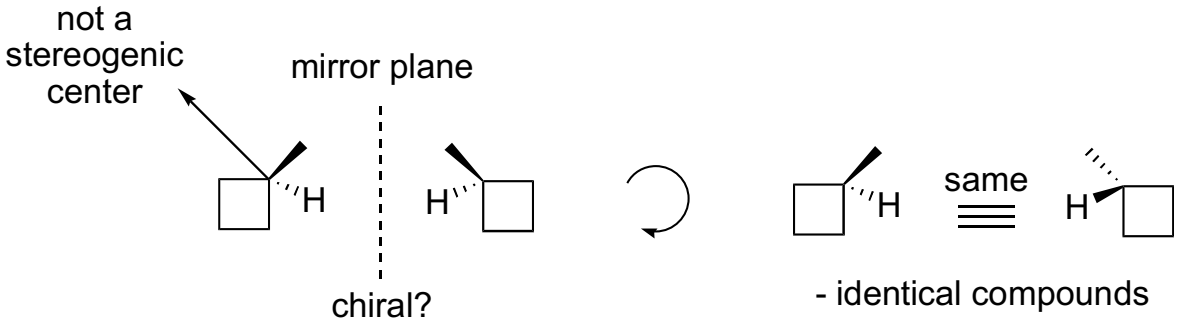
Example 4:



trans-2-butene is achiral

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

Examples of determining chirality within molecules



Labelling Stereocentres

R/S Nomenclature:

R and S designation of stereoisomers

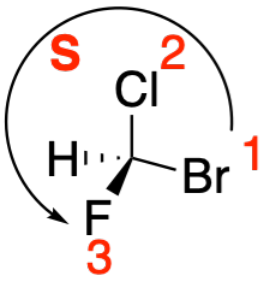
- R = Rectus (right-handed, clockwise)
- S = Sinister (left-handed, counterclockwise)

Labelling 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:

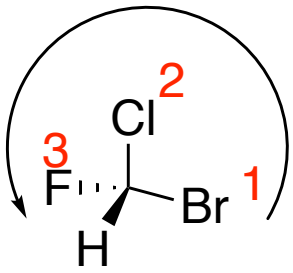


Place lowest priority to the back

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).

What if the lowest priority group is pointing forward?



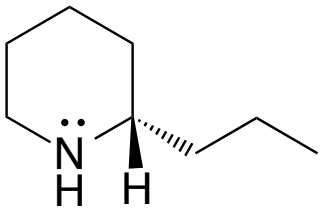
Counting 1, 2, 3 gives clockwise, BUT the smallest group is pointing forward, so the configuration is opposite of what you get if the smallest group is back

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

Example

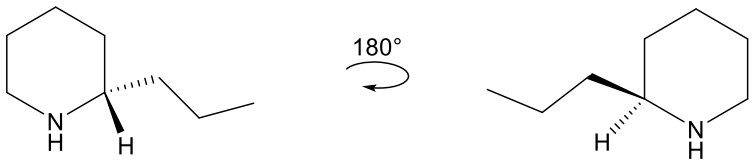
CONIINE, Poison hemlock, potent neurotoxin, killed Socrates

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

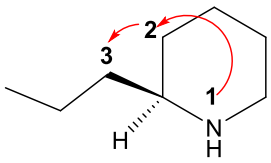


Assigning Configuration:

1) Move the lowest priority atom to the back (i.e., H)

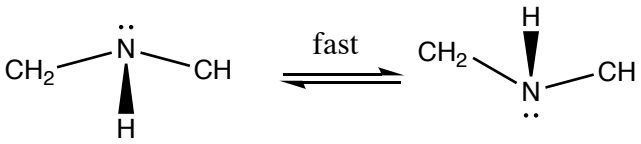


2) Assign priority to the remaining substituents. Then count 1,2,3.



Counterclockwise **S enantiomer**

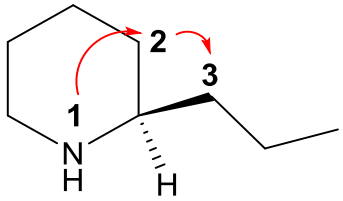
The nitrogen is nominally a stereogenic center since it has 4 different substituents, however it inverts rapidly, and so is not considered stereogenic. (unless all 3 groups are linked/held back by a ring)



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

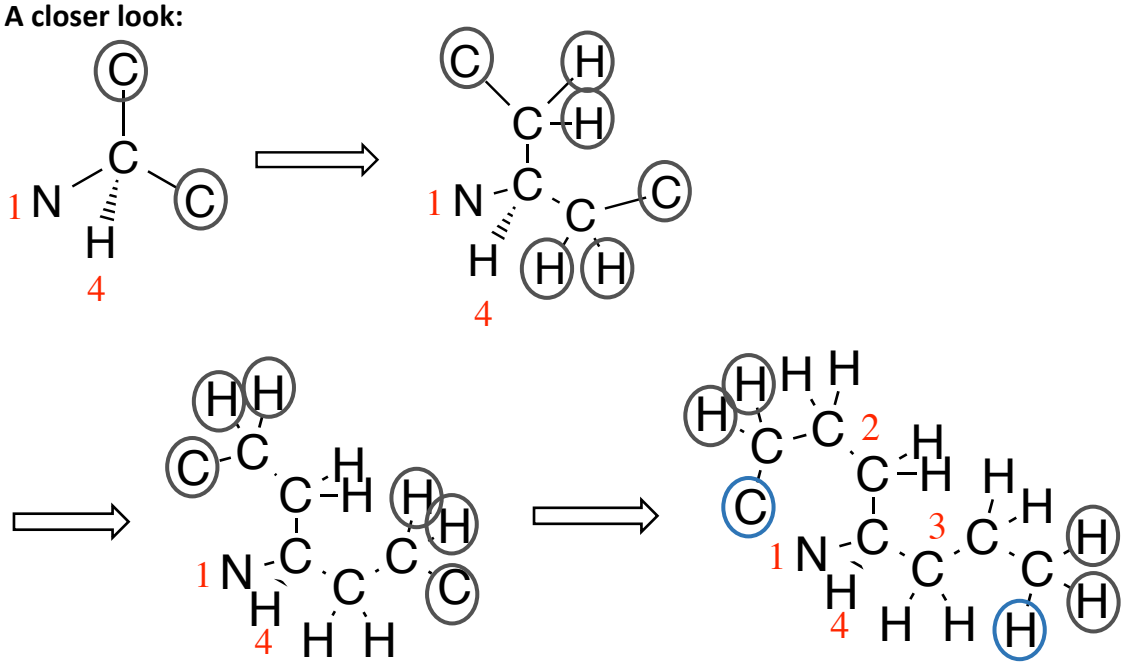
Example of determining priority of groups in enantiomer on natural coniine

- 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.

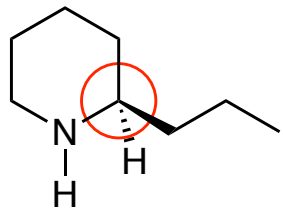


Clockwise R enantiomer

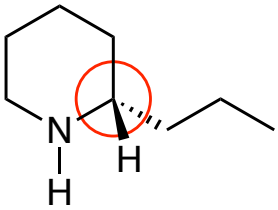
A closer look:



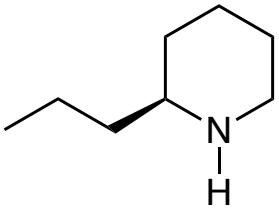
- We cannot tell at the second attached carbon, so we move on to the third.
- We still cannot tell at the third, so we move on to the fourth.
- At the fourth carbon we can see a difference. The carbon that is part of the propyl group ends in a CH_3 so it is bonded to three H, and the other carbon is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



R - enantiomer of coniine
Non-toxic
invert EVERY stereocenter



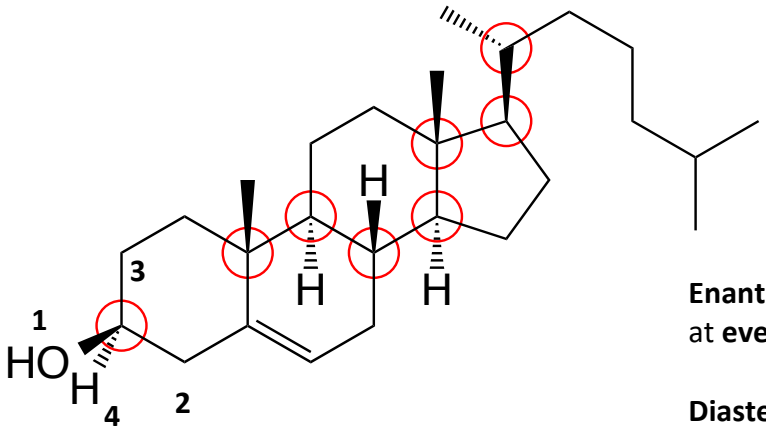
S - enantiomer of coniine - highly toxic - natural



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.

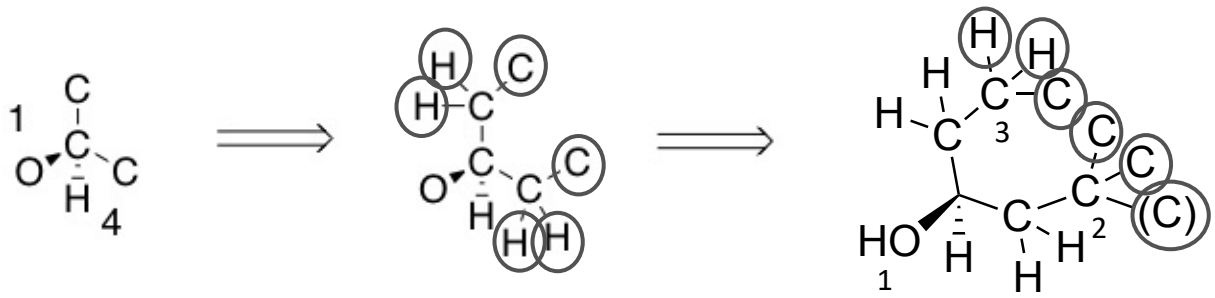
Cholesterol - A steroid with 8 stereogenic centers (red circles)



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