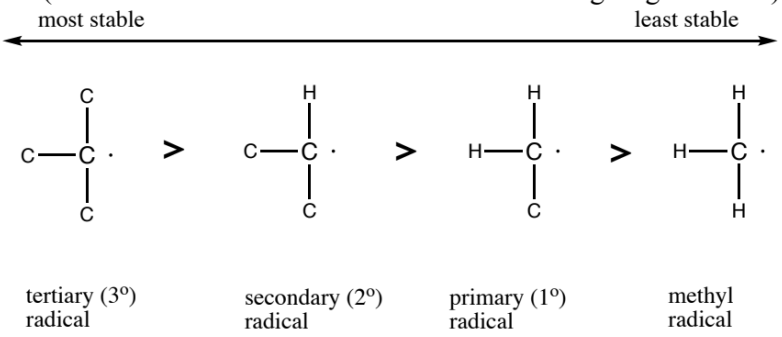
Recall:

Stability of radicals:

- Stability increases with alkyl substitution
- Alkyl groups are polarizable and donate electrons to electron deficient sites better than hydrogens (this is called **inductive effect** and occurs through sigma bonds)



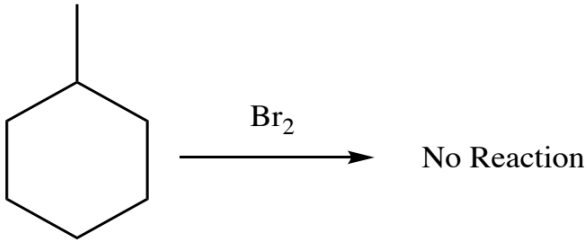
Or it can be summarized from least to most stable radicals:

$\cdot CH_3$	<	$\cdot CH_2R$	<	$\cdot CHR_2$	<	$\cdot CR_3$
methyl radical (least stable)		primary (1°) radical		secondary (2°) radical		tertiary (3°) radical (most stable)

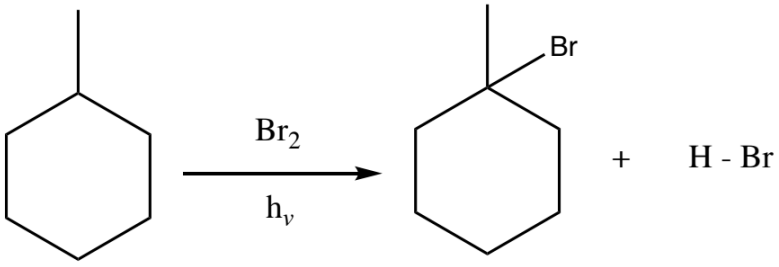
Halogenation of alkanes:

- requires light or heat to cause a reaction between the starting material and halogen.

Example:

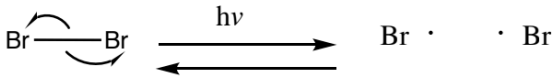


- requires light or heat to cause a reaction between the starting material and halogen.

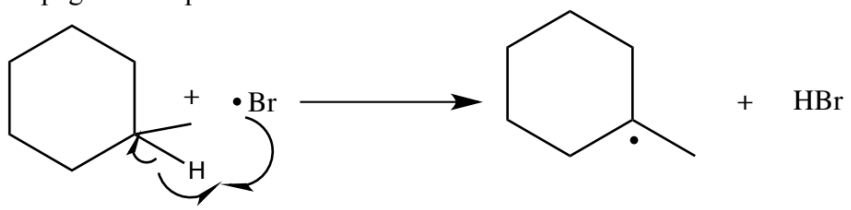


C_7H_{14}

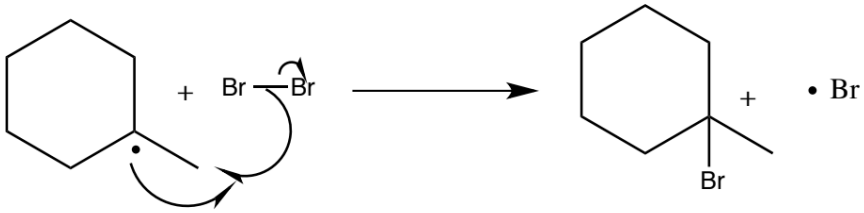
Initiation Step:



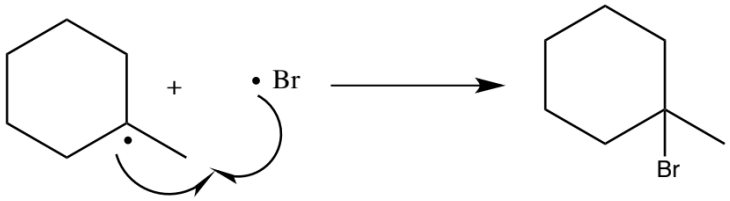
Propagation Step 1

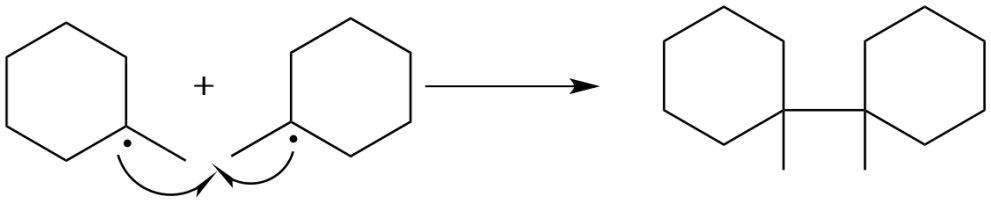


Propagation Step 2

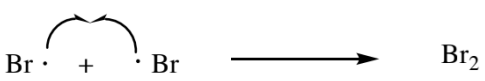


Termination Step: Radicals Recombine
-Very minor component of the reaction





Two alkyl radicals combining is highly unlikely because the chances of them finding one another is very low (they are low in concentration) – above also very crowded (steric effect)



Hammond Postulate

More reactive, less selective

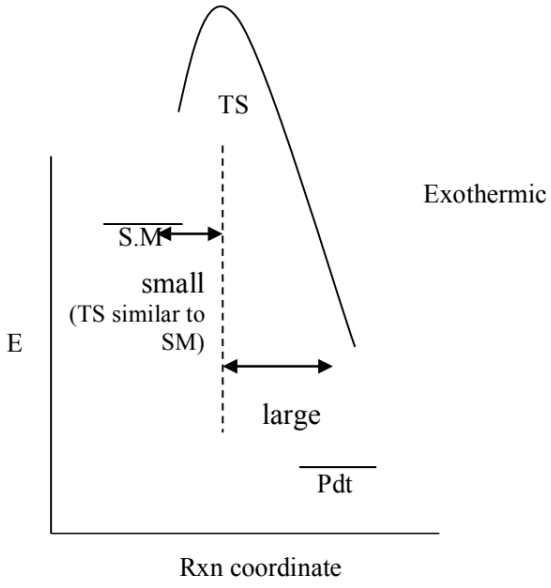
Less reactive, more selective

Exothermic T.S. (transition state) resembles S.M. (starting material)
Less selective reaction because of a small difference in Ea

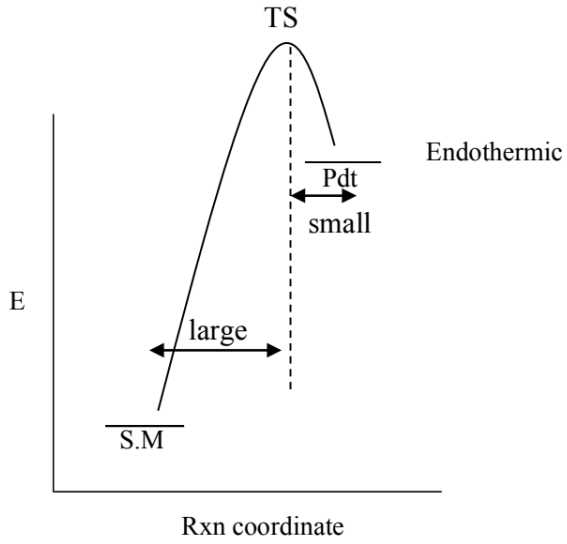
Endothermic T.S. resembles product
More selective because of a larger difference in Ea

Energy Diagrams for Halogenation Reactions

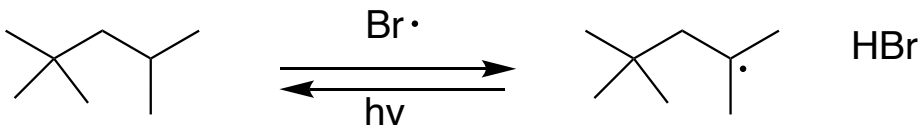
Fluorination ($\Delta H < 0$)



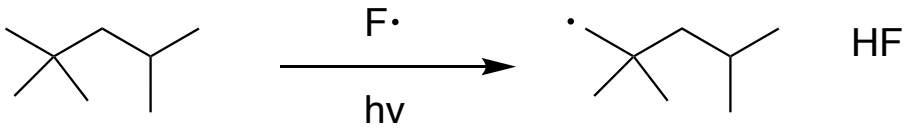
Bromination ($\Delta H > 0$)



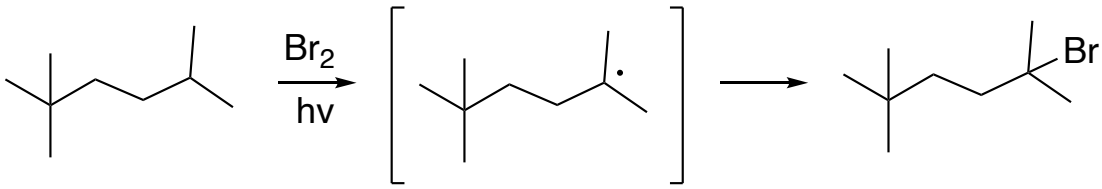
E = energy
TS = transition state
SM = starting material



Br_2 is less reactive, more selective, endothermic

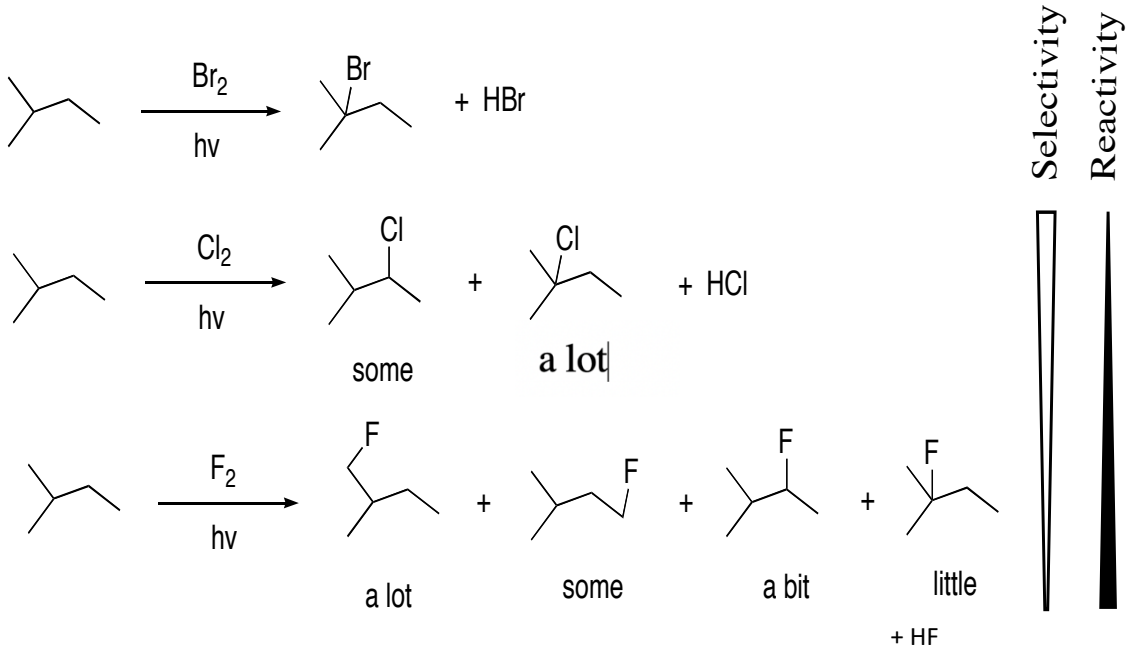


F_2 is more reactive, less selective, exothermic



Reactivity and Selectivity (Hammond Postulate)

e.g. Halogenation of 2-methylbutane



I_2 does not react as above

More exothermic, transition state resembles starting materials
More endothermic, transition state resembles the product

R–H + X_2 → R–X + XH
Reactivity: F_2 > Cl_2 > Br_2 >> I_2 (unreactive)
Selectivity: more reactive → less selective (mixture of products)
Less reactive → more selective (single products)
Hammond's postulate:
Chlorination → RDS is exothermic → early TS → small ΔEa
Bromination → RDS is endothermic → late TS → large ΔEa

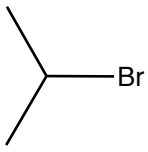
Naming of Alkyl Halides = Haloalkanes

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

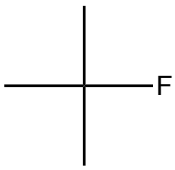
Structure and Nomenclature

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

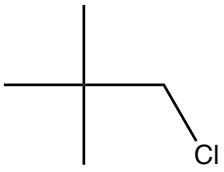
Examples:



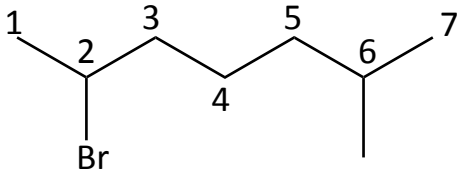
Isopropyl Bromide
2-Bromopropane



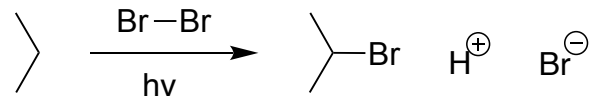
tert-Butyl fluoride
2-Fluoro-2-methylpropane



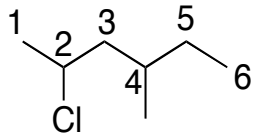
Neopentyl chloride
1-Chloro-2,2-dimethylpropane



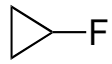
2-bromo-6-methylheptane



propane

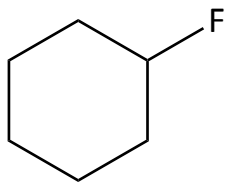


2 -chloro -4-methylhexane

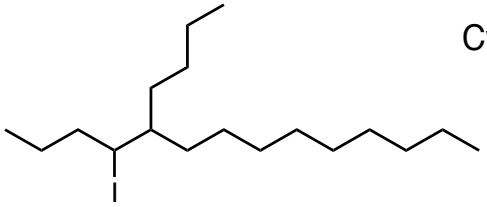


Fluorocyclopropane

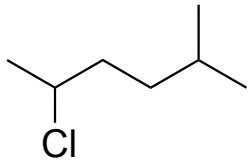
Cyclopropyl fluoride



cyclohexyl fluoride
1-fluorocyclohexane



5-Butyl-4-iodotetradecane

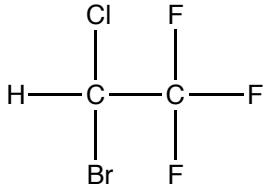


2-chloro-5-methylhexane

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

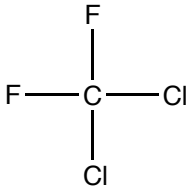
Applications of Haloalkanes

1.) Halothane (anesthetic)

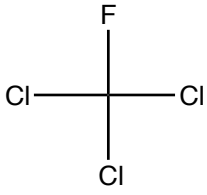


1,1,1-trifluoro-2-bromo-2-chloroethane

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

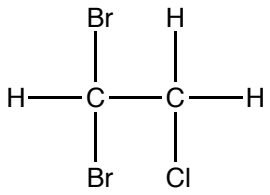


Freon 12



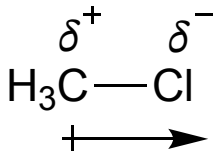
Freon 11

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



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

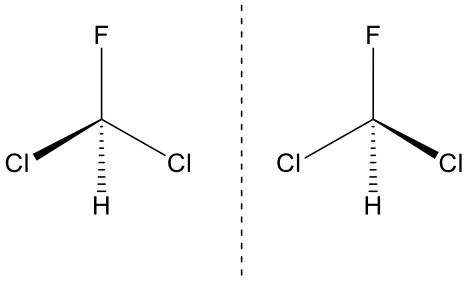
- Governed primarily by dipole-dipole interactions, more polar than hydrocarbons/alkanes.
- High MP and BP relative to hydrocarbons of similar molecular weight
- Good solvents for organic compounds e.g. methylene chloride (CH_2Cl_2) and chloroform ($CHCl_3$) are very common.
- If % composition ≥ 65% 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



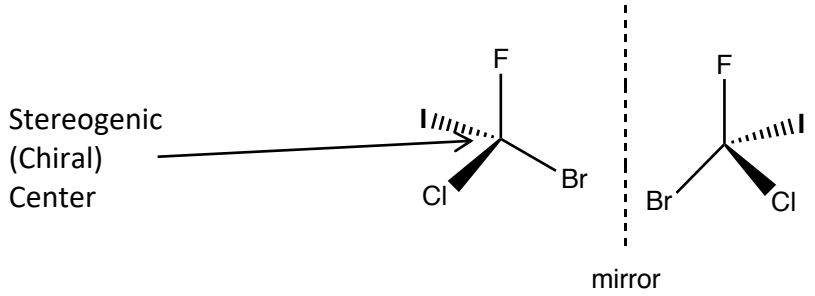
Introduction to Stereochemistry and Chirality (terminologies)

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)

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

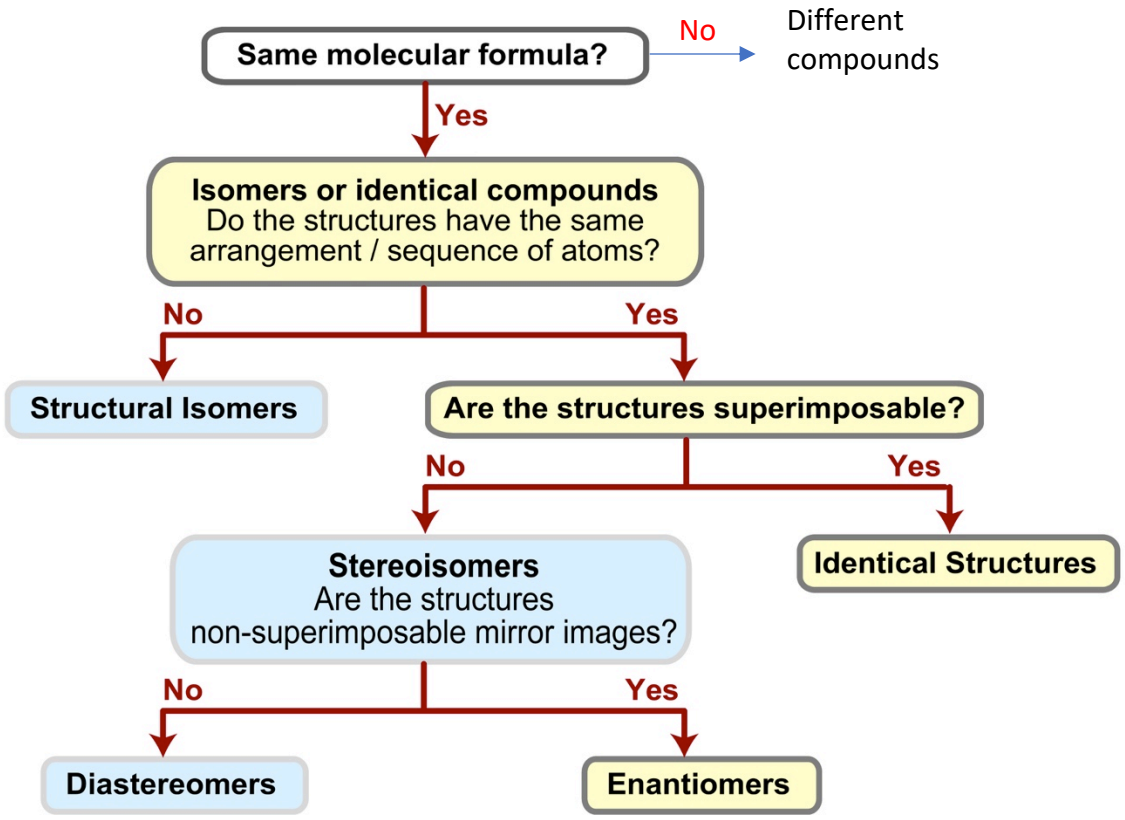
Resolution – separation of enantiomers

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.

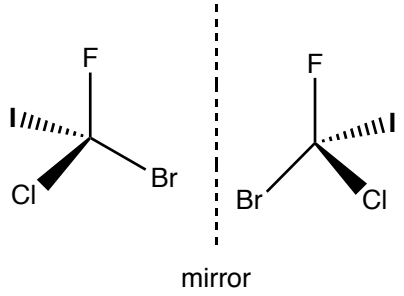
Diastereomers: all stereoisomers that are not enantiomers

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



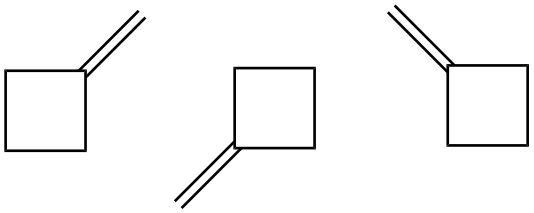
Example 1:



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

NON-SUPERIMPOSABLE → Enantiomers

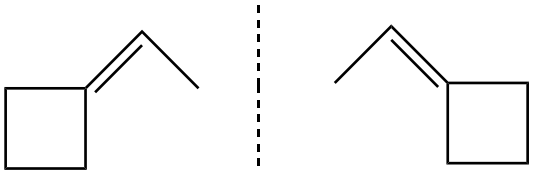
Example 2:



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

Identical structures, superimposable, achiral

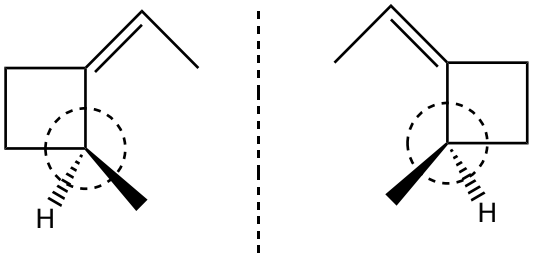
Example 3:



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

- achiral
- no stereogenic center

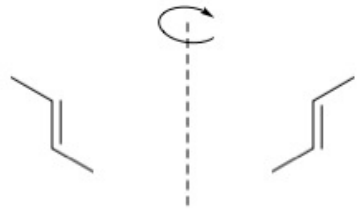
Same, identical compound



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

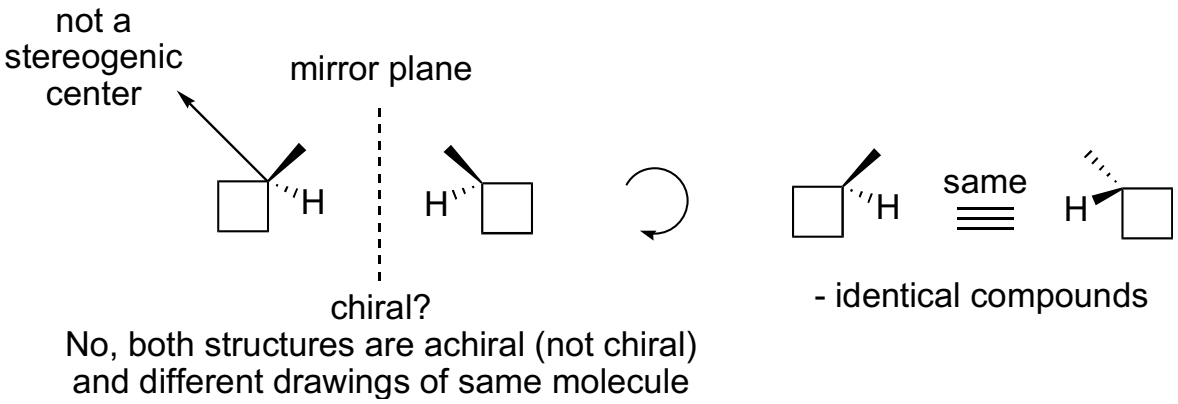
Example 4:



trans-2-butene is achiral

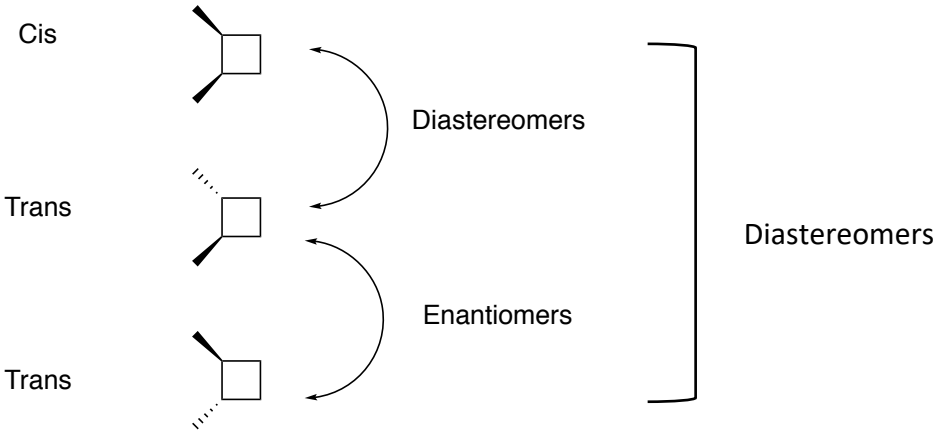
These two mirror images
are superimposable
as seen by a simple rotation

Examples of determining chirality within molecules



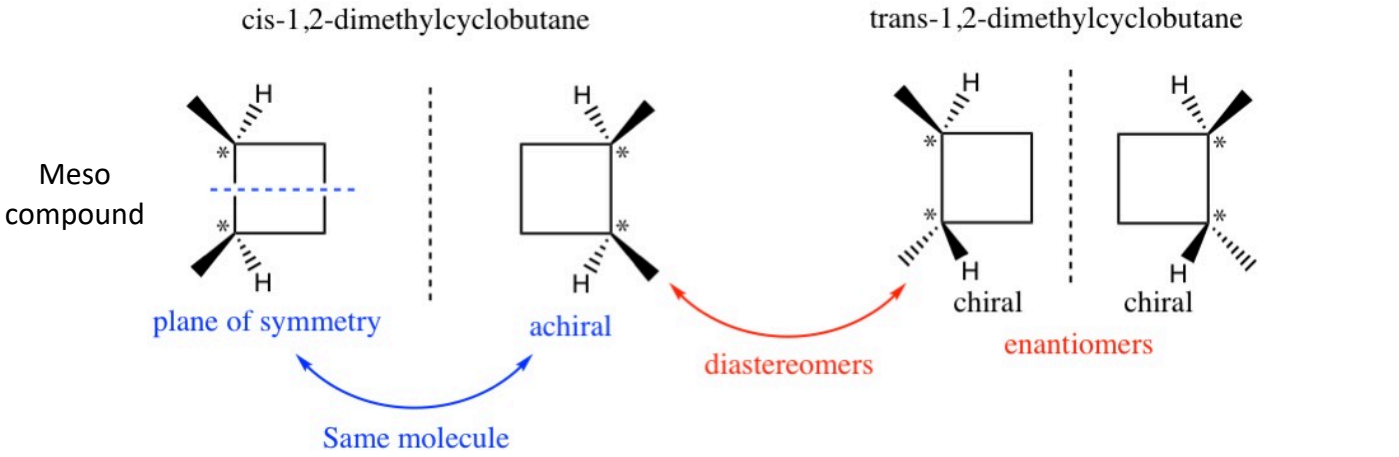
No, both structures are achiral (not chiral)
and different drawings of same molecule

Example:



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)

Meso compounds – molecules containing chiral (stereogenic) centers but has a plane of symmetry, therefore they are achiral

Labelling Stereocentres

R/S Nomenclature:

R and S designation of stereoisomers

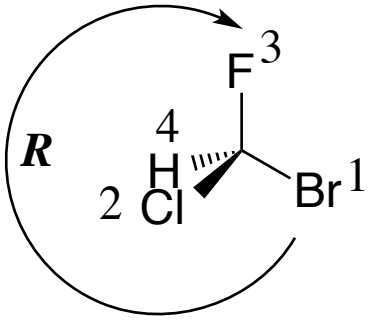
- R = Rectus (right, clockwise)
- S = Sinister (left, counterclockwise)

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:

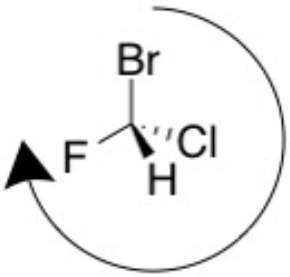


Place lowest priority to the back

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).

*What if we take **mirror image** of the molecule above making the lowest priority group now pointing forward?*



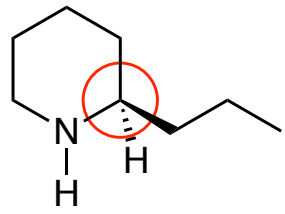
Counting 1, 2, 3 gives clockwise, BUT the smallest group is pointing forward, so the configuration is opposite of what you get if the smallest group is back

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

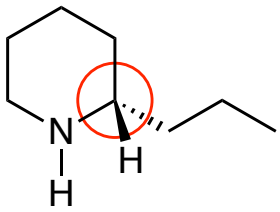
Enantiomers – non-superimposable mirror images of each other

Example

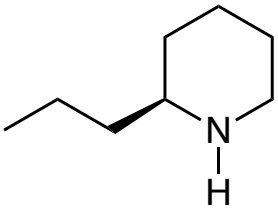
CONIINE, Poison hemlock, potent neurotoxin, killed Socrates



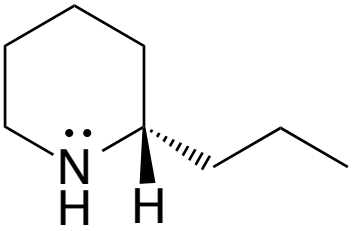
R - enantiomer of coniine
Non-toxic
invert EVERY stereocenter



S - enantiomer of coniine - highly toxic - natural

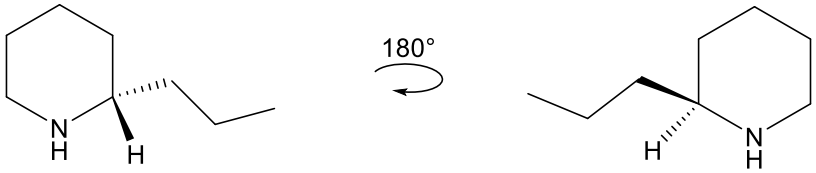


Stereogenic center (chiral centers or asymmetric centers) is circled in red

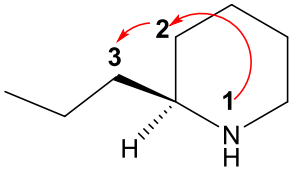


Assigning Configuration:

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

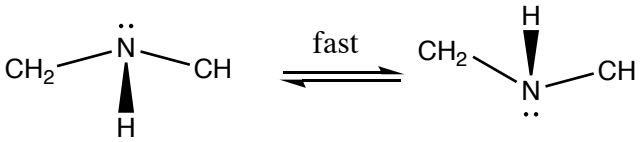


2) Assign priority to the remaining substituents. Then count 1,2,3.



Counterclockwise S enantiomer

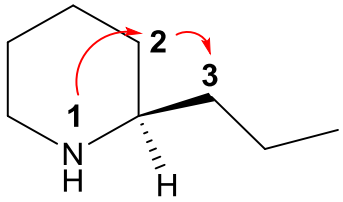
The nitrogen is nominally a stereogenic center since it has 4 different substituents, however it inverts rapidly, and so is not considered stereogenic. (unless all 3 groups are linked/held back by a ring)



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

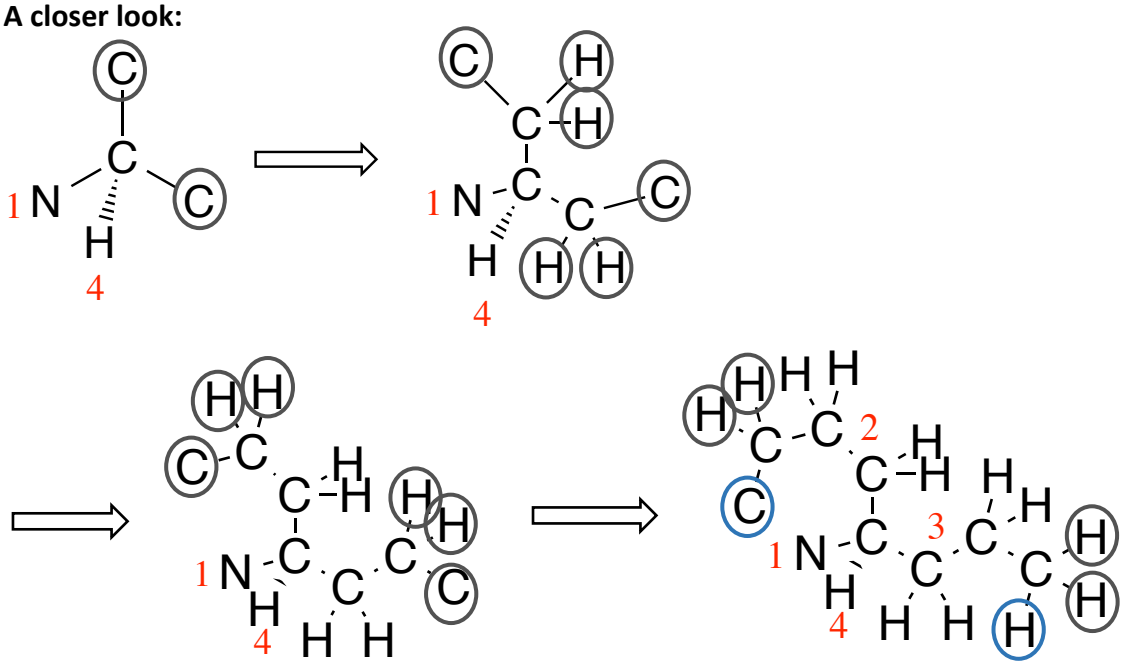
Example of determining priority of groups in enantiomer on natural coniine

- 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 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.