Recap

$R–H + X_2 \rightarrow R–X + XH$
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

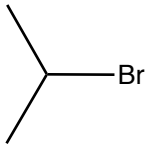
Naming of Alkyl Halides = Haloalkanes

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

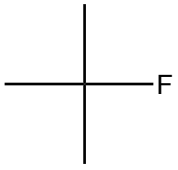
Structure and Nomenclature

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

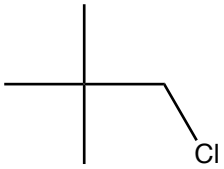
Examples:



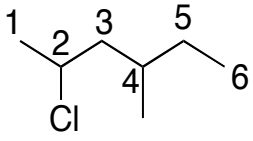
Isopropyl Bromide
2-Bromopropane



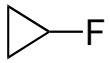
tert-Butyl fluoride
2-Fluoro-2-methylpropane



Neopentyl chloride
1-Chloro-2,2-dimethylpropane

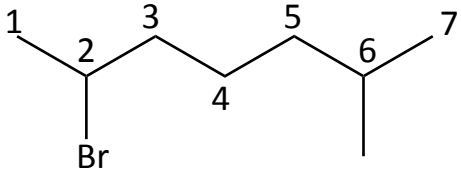


2 -chloro -4-methylhexane

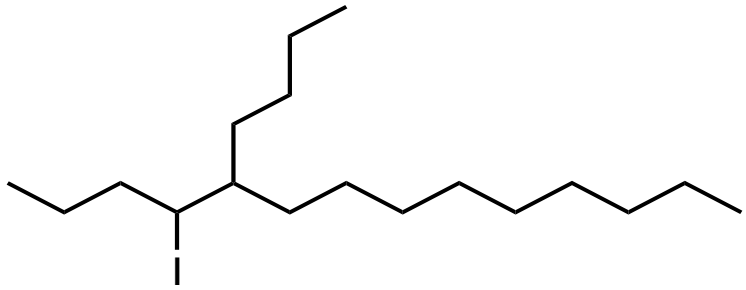


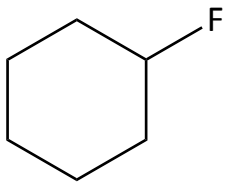
Fluorocyclopropane

Cyclopropyl fluoride



2-bromo-6-methylheptane



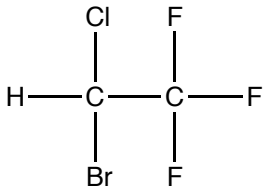


cyclohexyl fluoride
1-fluorocyclohexane

5-Butyl-4-iodotetradecane

Applications of Haloalkanes

1.) Halothane (anesthetic)



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

<u>Naming of Alkyl Halides = Haloalkanes</u>

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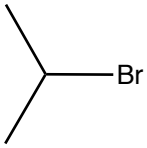
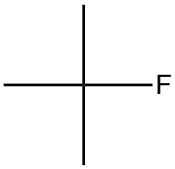


Isopropyl Bromide
2-Bromopropane



tert-Butyl fluoride
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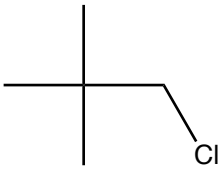
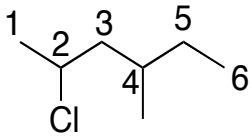
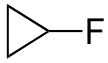


Neopentyl chloride
1-Chloro-2,2-dimethylpropane

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

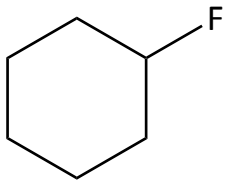


2 -chloro -4-methylhexane

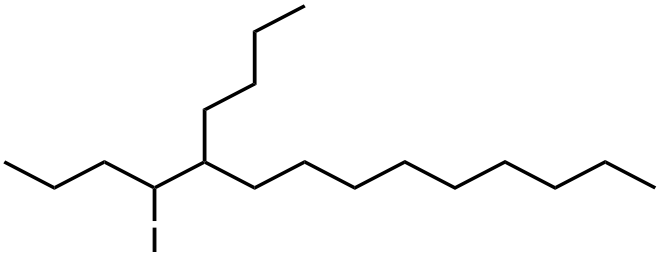


Fluorocyclopropane

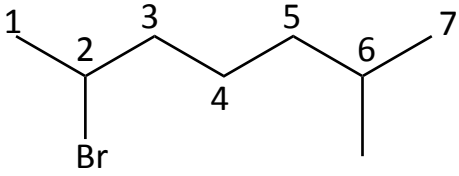
Cyclopropyl fluoride



cyclohexyl fluoride
1-fluorocyclohexane



4-iodo-5-butyldecane



2-bromo-6-methylheptane

Applications of Haloalkanes

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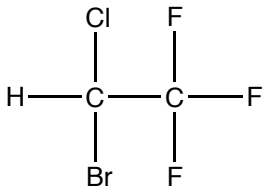
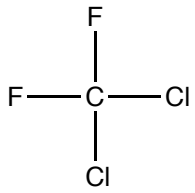
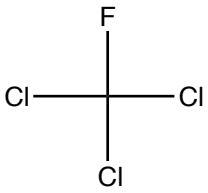


1,1,1-trifluoro-2-bromo-2-chloroethane

2.) Freon = refrigerants/coolants

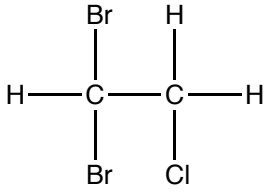


Freon 12



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>

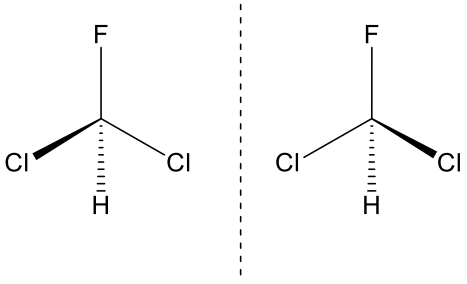
- Governed primarily by dipole-dipole interactions, more polar than hydrocarbons/alkanes.
- High MP and BP relative to hydrocarbons of similar molecular weight
- Good solvents for organic compounds e.g. methylene chloride (CH_2Cl_2) and chloroform ($CHCl_3$) are very common.
- If % composition ≥ 65%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

NEXT SECTION: Lecture Outline 3: Stereochemistry and Chirality

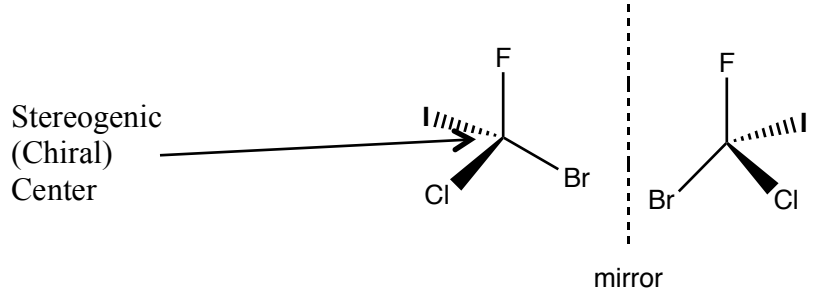
Introduction to Stereochemistry and Chirality (terminologies)

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

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



Achiral, identical



mirror

Non-superimposable

1850 - 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

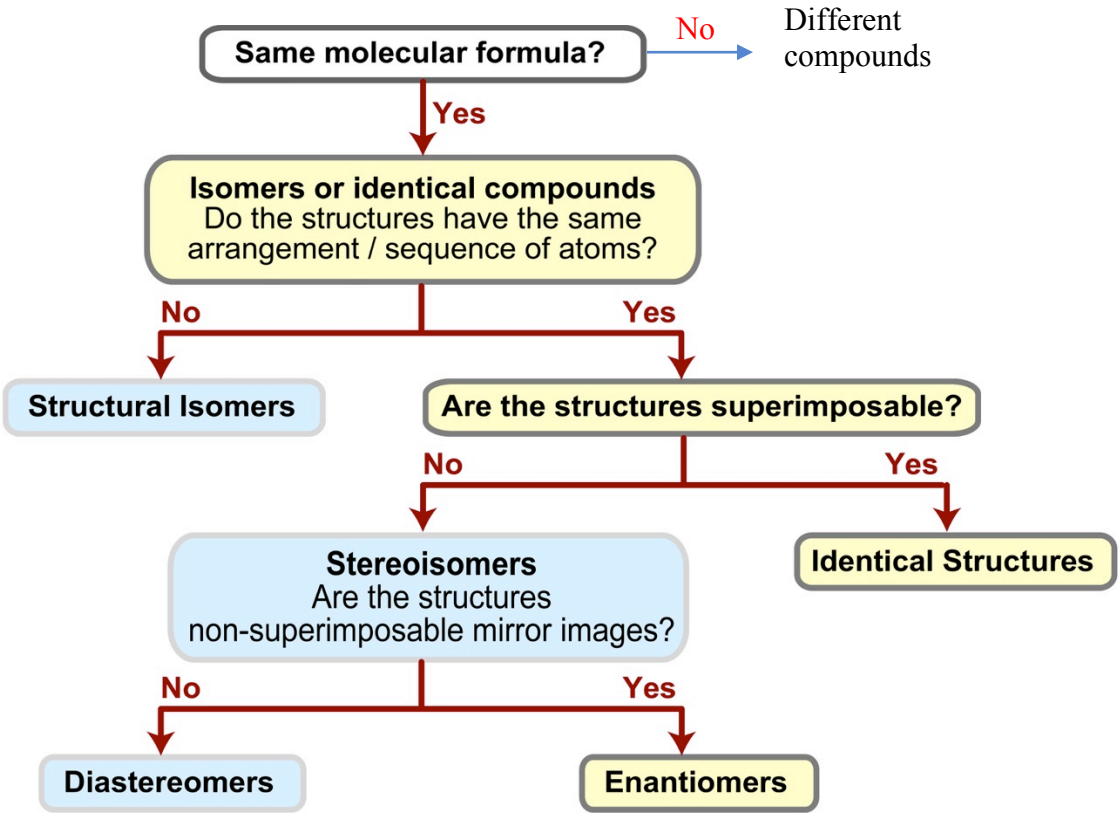
Resolution - Separation of right and left-handed forms (enantiomers)

Enantiomers: molecules that are stereoisomers and are non-superimposable mirror images of each other. 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.

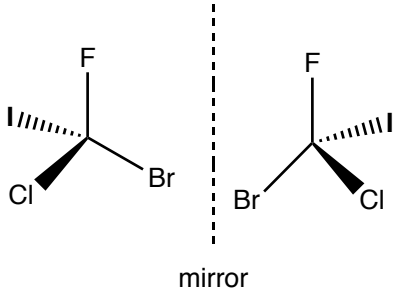
Diastereomers: all stereoisomers that are not enantiomers.

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



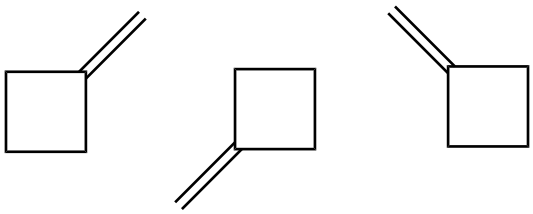
Example 1:



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

NON-SUPERIMPOSABLE → Enantiomers

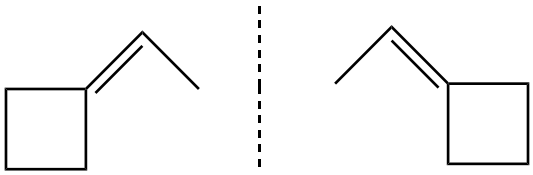
Example 2:



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

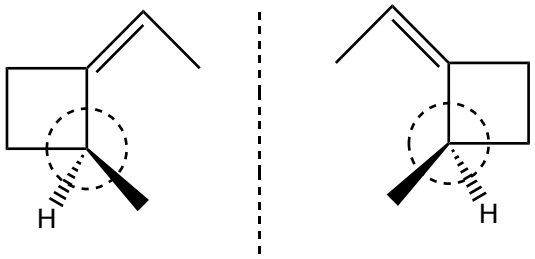
Identical structures, superimposable

Example 3:



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

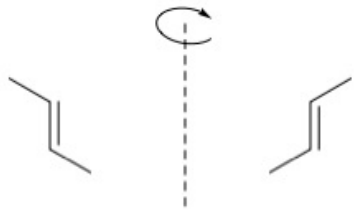
- achiral
- no stereogenic center



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

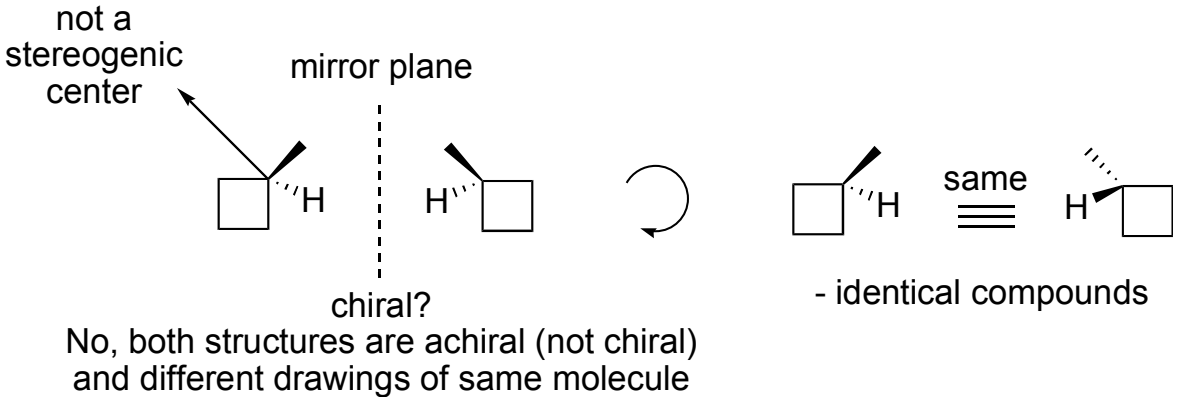
Example 4:



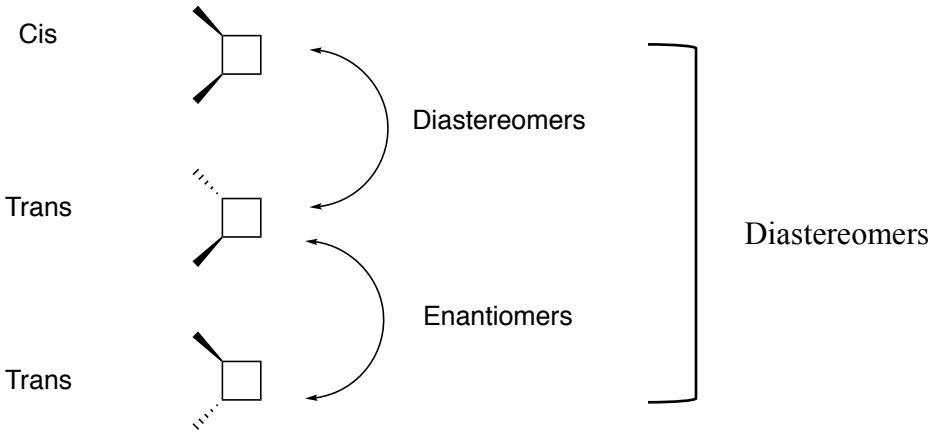
trans-2-butene is achiral

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

Examples of determining chirality within molecules

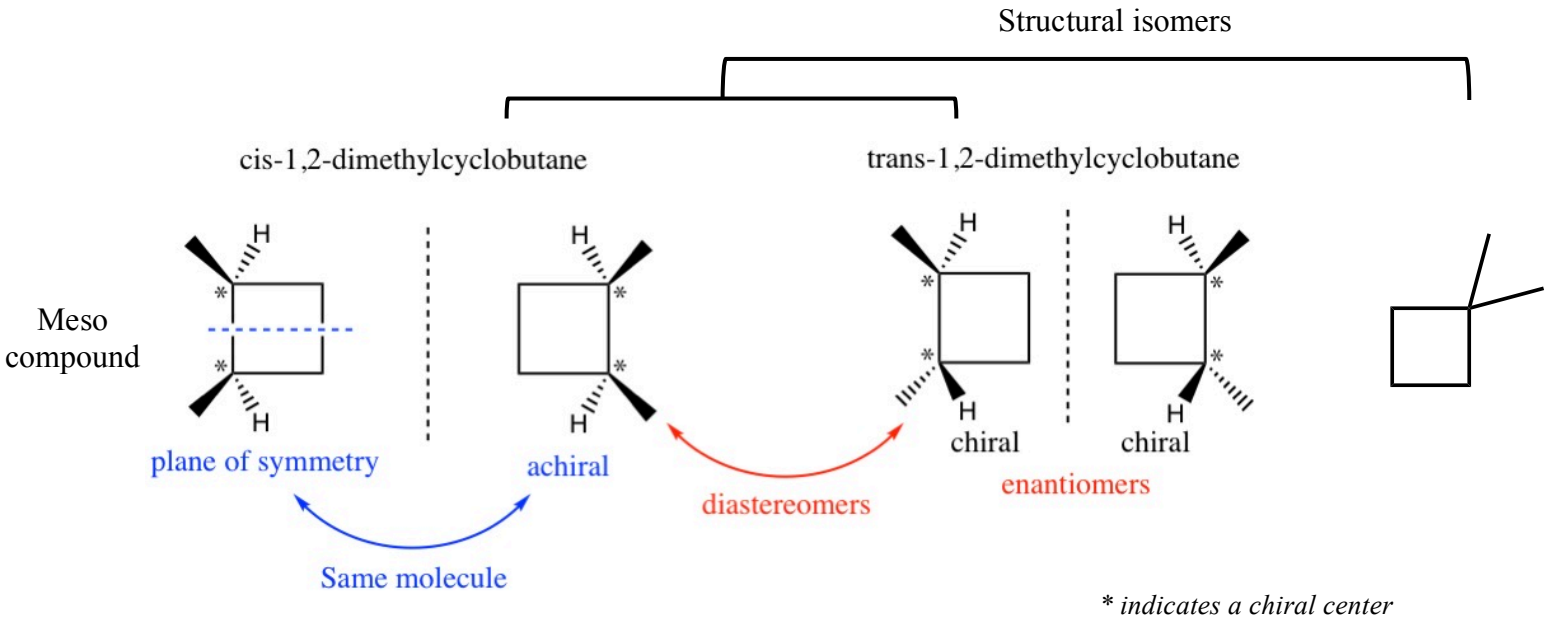


No, both structures are achiral (not chiral)
and different drawings of same molecule



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

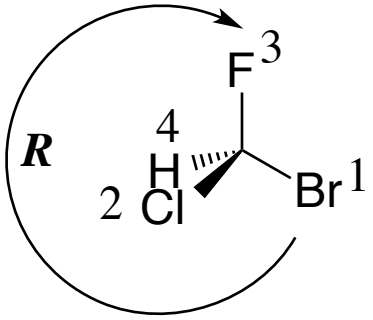
- R = Rectus (right, clockwise)
- S = Sinister (left, counterclockwise)

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:

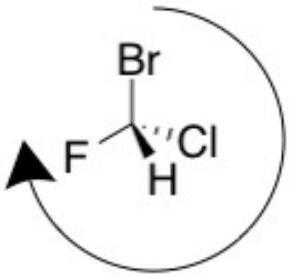


Place lowest priority to the back

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 the lowest priority group is pointing forward?



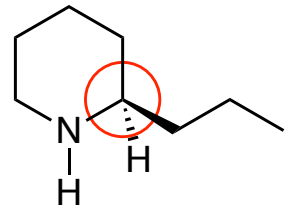
Counting 1, 2, 3 gives clockwise, BUT the smallest group is pointing forward, so the configuration is opposite of what you get if the smallest group is back

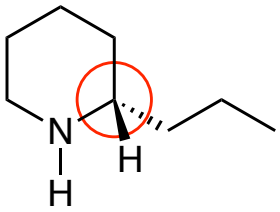
In this case, the configuration of the stereogenic center is "***S***"

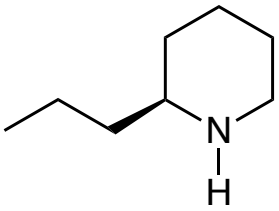
Example

CONIINE, Poison hemlock, potent neurotoxin, killed Socrates

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

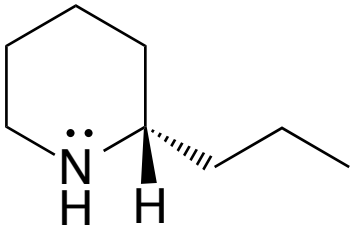






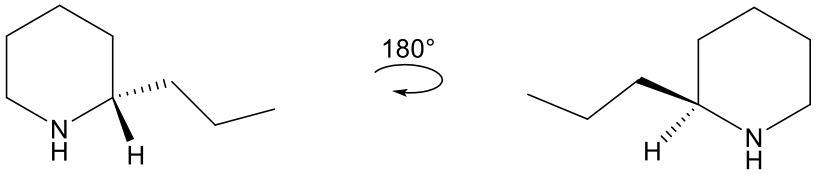
R - enantiomer of coniine
Non-toxic
invert EVERY stereocenter

S - enantiomer of coniine - highly toxic - natural

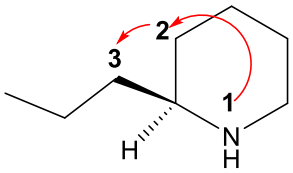


Assigning Configuration:

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

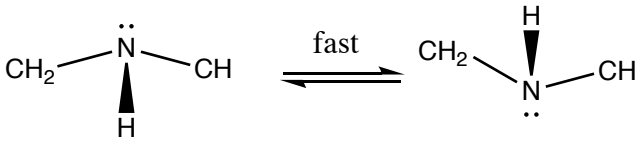


2) Assign priority to the remaining substituents. Then count 1,2,3.



Counterclockwise ® S enantiomer

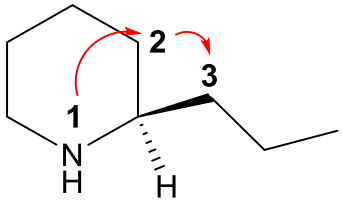
The nitrogen is nominally a stereogenic center since it has 4 different substituents, however it inverts rapidly, and so is not considered stereogenic.



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

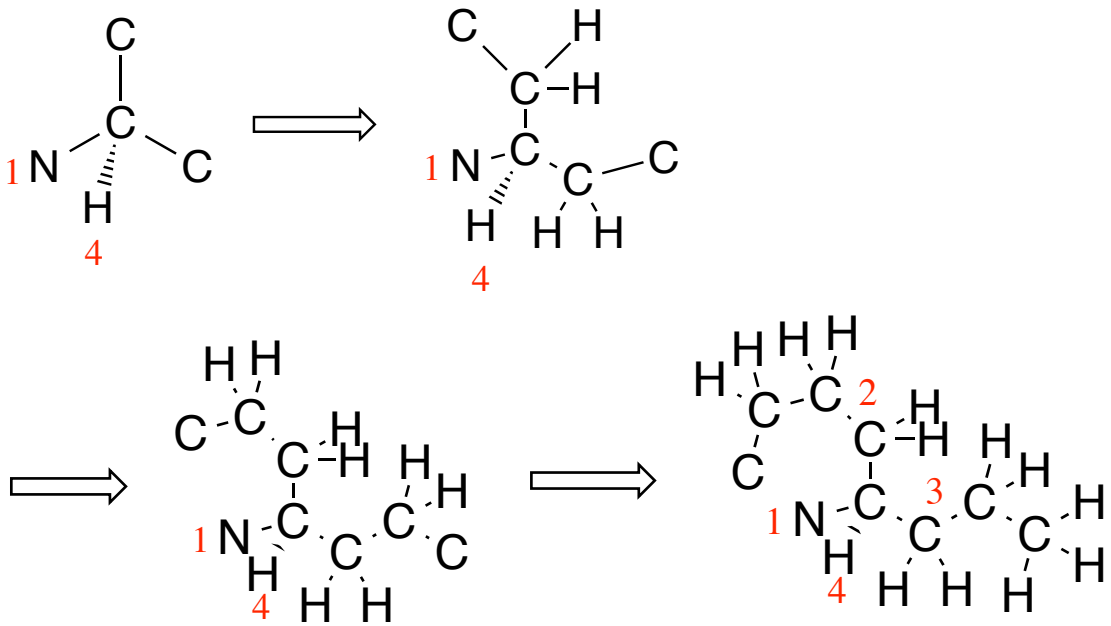
Example of determining priority of groups in enantiomer on natural coniine

- 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.

RECAP

$$R-H + X_2 \longrightarrow R-X + HX$$

$$F_2 > Cl_2 > Br_2 >> I_2$$

Selectivity

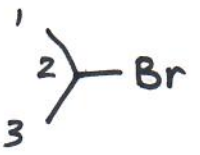
More reactive => less selective => mixture of products

Less reactive => more selective => single product.

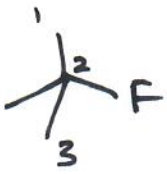
Hammond's postulate:

Chlorination => Exothermic RDS => Early TS => Small ΔE_a

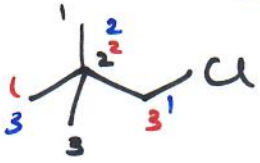
Bromination => Endothermic RDS => Late TS => Large ΔE_a.



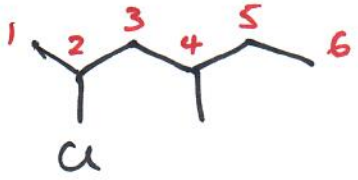
2-bromopropane



2-fluoro-2-methyl propane

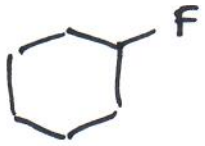


1-chloro-2,2-dimethyl propane

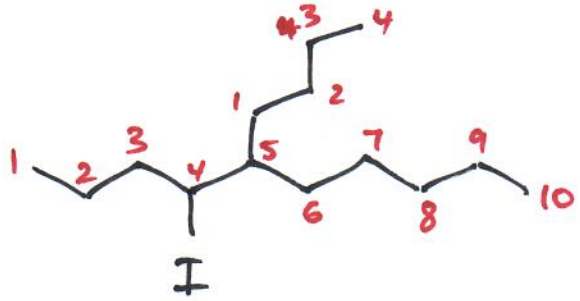


2-chloro-4-methyl hexane

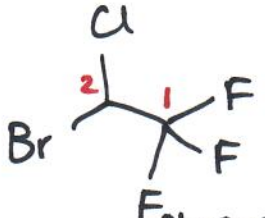
cyclopropyl fluoride
OR
fluorocyclopropane



cyclohexyl fluoride
fluorocyclohexane



4-iodo-5-butyldecane



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

Physical properties of haloalkanes

- more polar than alkanes
- dipole-dipole interactions
- higher m.p. and b.p. than alkanes
- good solvents
- $\geq$ 65% halogen => more dense than H_2O
- immiscible with H_2O

STEREOCHEMISTRY + CHIRALITY.

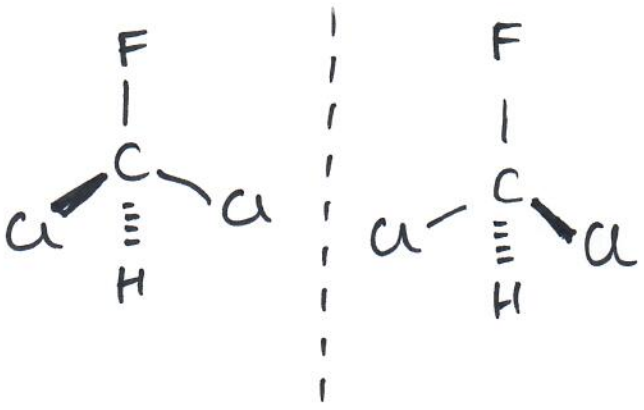
CHIRAL - NOT superimposable on its mirror image

↑ Greek word for hand.

CHIRAL ATOM / STEREOGENIC CENTRE

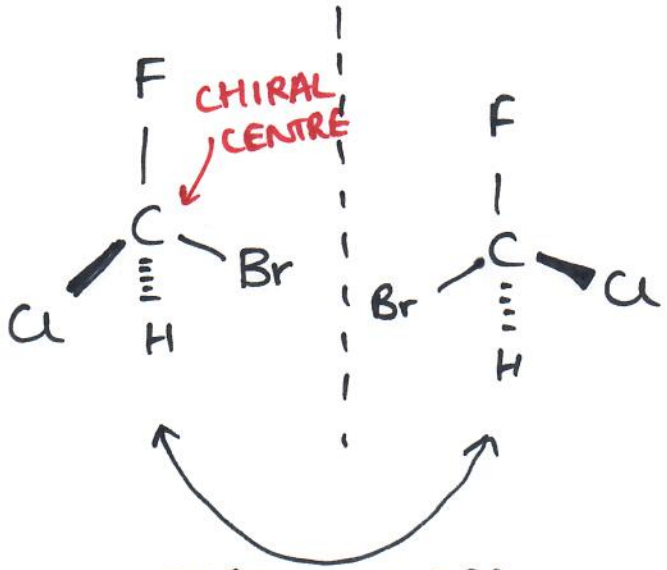
↳ 4 different groups

NON-CHIRAL / ACHIRAL:



superimposable.

CHIRAL:



ENANTIOMERS
NON-superimposable

DEFINITIONS:

CHIRAL - HAS a non-superimposable mirror image

ACHIRAL - HAS a superimposable mirror image

ENANTIOMERS - Opposite stereochemistry at every chiral centre

DIASTEREOMERS - All stereoisomers that are not enantiomers

RESOLUTION - separation of enantiomers

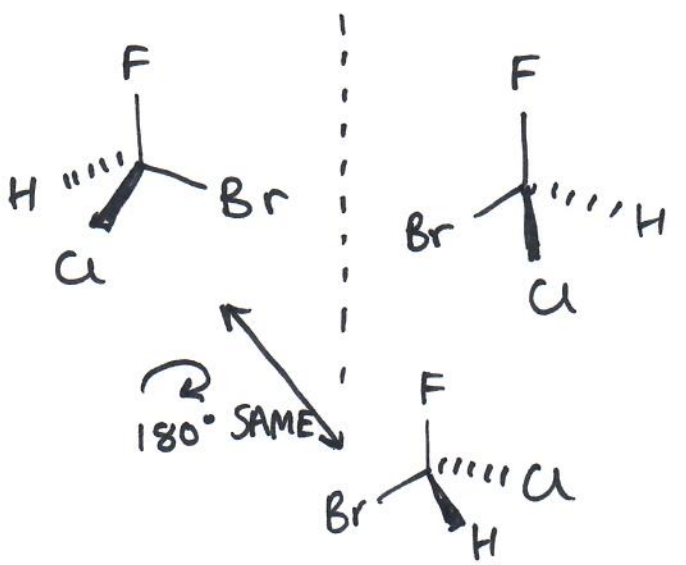
ENATIOMERS	DIASTEREOMERS
Same physical properties (b.p., m.p., etc)	Different chemical properties
Bend polarised light differently	
Hard to separate	Easier to separate
Mirror images	Not mirror images
Non-superimposable	Non-superimposable.

1) Same molecular formula?
- NO → Different compounds!
- YES ↓

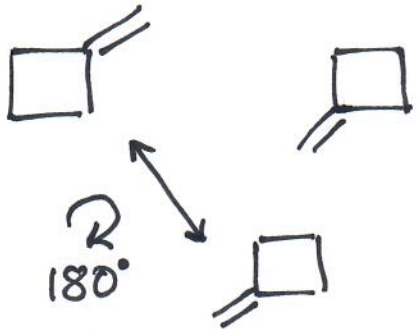
2) Same arrangement/sequence of atoms?
- NO → Structural isomers
- YES ↓

3) Superimposable?
- NO → Stereoisomers
- YES → Identical compounds

4) Non-superimposable mirror image?
- NO → DIASTEREOMERS
- YES → ENANTIOMERS

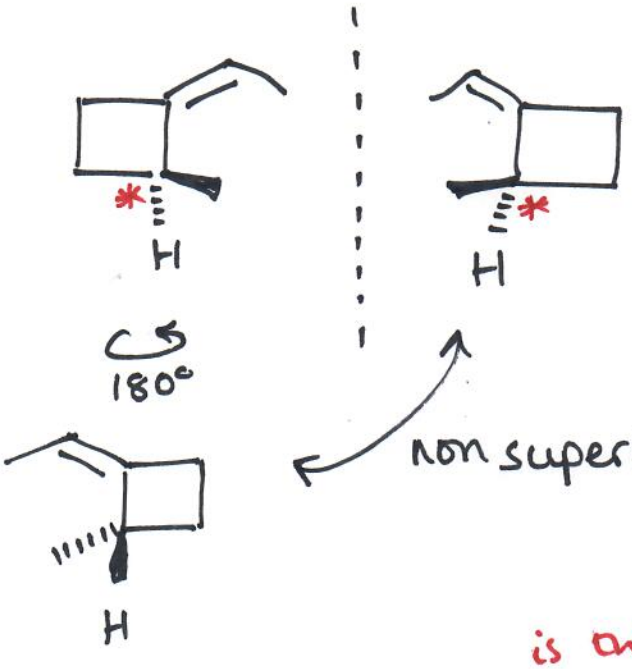
① 

1) YES
2) YES
3) NO - stereoisomers
4) YES - enantiomers

② 

1) YES
2) YES
3) YES - identical

(3)

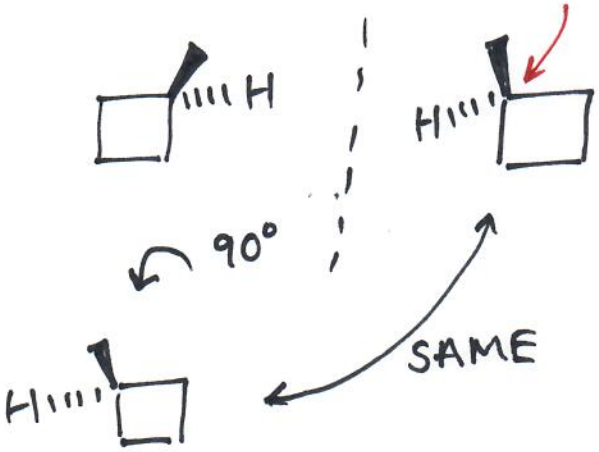


(5)

1) YES
2) YES
3) NO - stereoisomers
4) YES - enantiomers

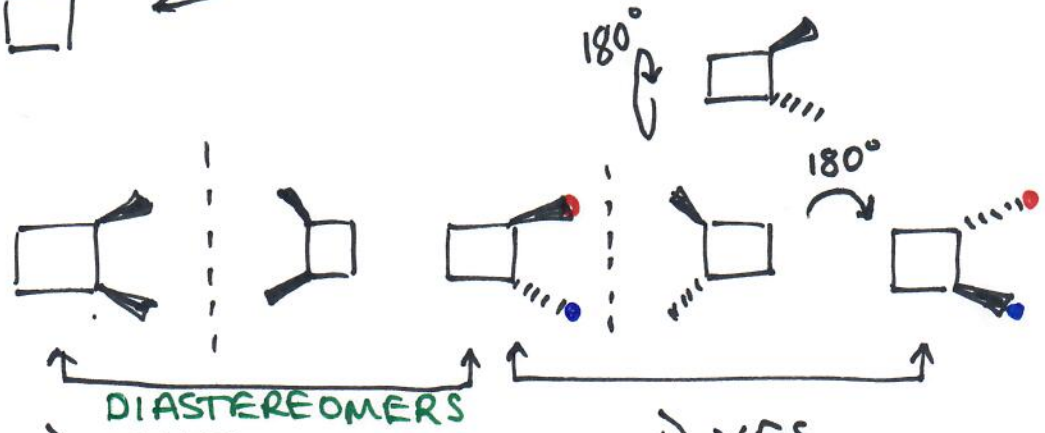
(4)

is this chiral? NO.



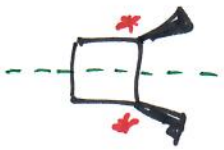
1) YES
2) YES
3) YES - identical

(5)

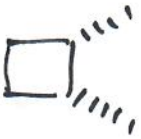


1) YES
2) YES
3) NO - stereoisomers
4) NO - diastereomers

1) YES
2) YES
3) NO - stereoisomers
4) YES - enantiomers



180°



1) YES
2) YES
3) YES - identical

6

Stereogenic centres - yes
Chiral - not

MESO compounds

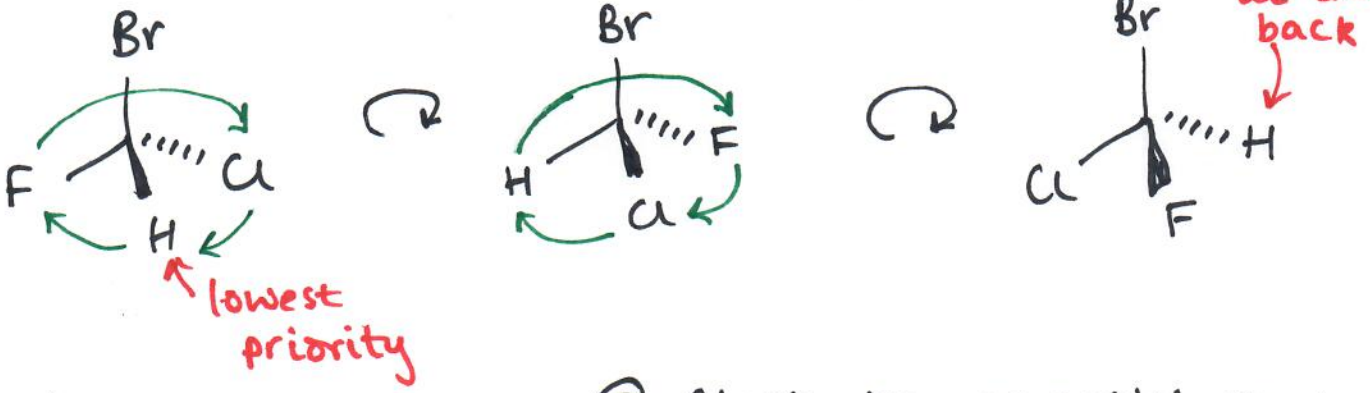
Labelling Stereocentres

R => clockwise

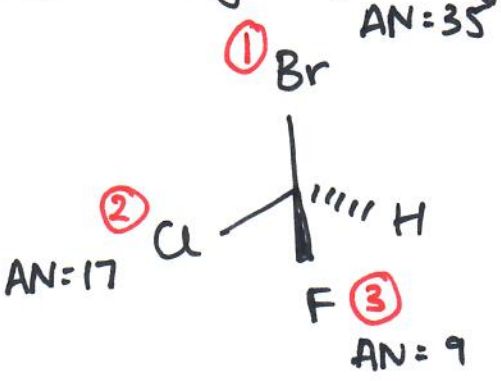
S => anticlockwise

Example

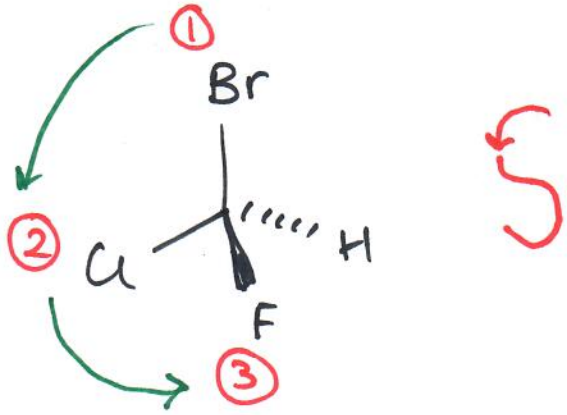
① Put the lowest priority group (lowest atomic number) at the back.



② Assign priority



③ Clockwise or anticlockwise



① Lowest priority at back

② Assign priority