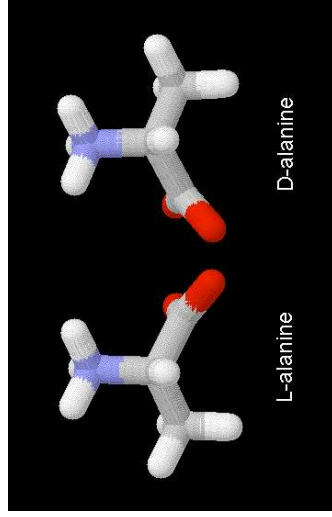


Chapter 4: Stereochemistry



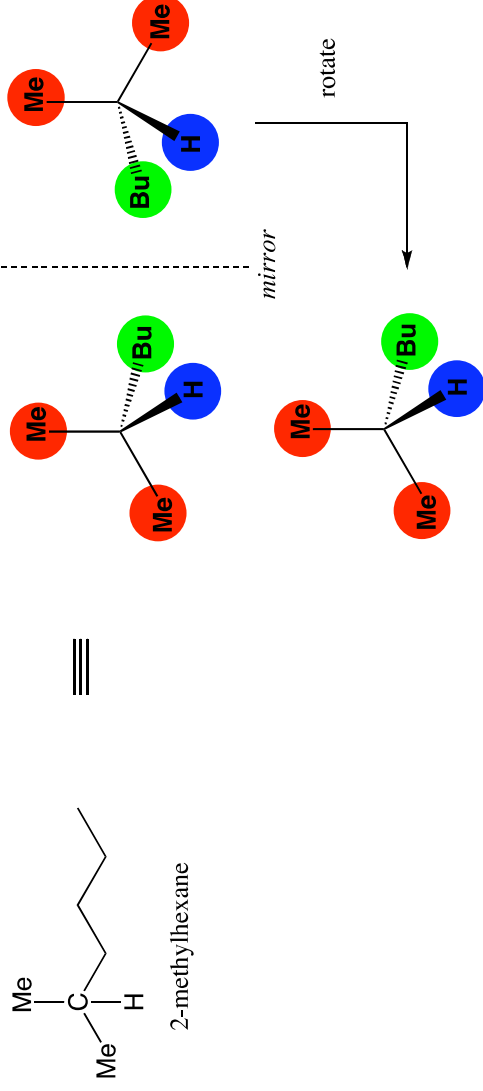
Introduction To Stereochemistry

Consider two of the compounds we produced while finding all the isomers of C_7H_{16} :



2-methylhexane

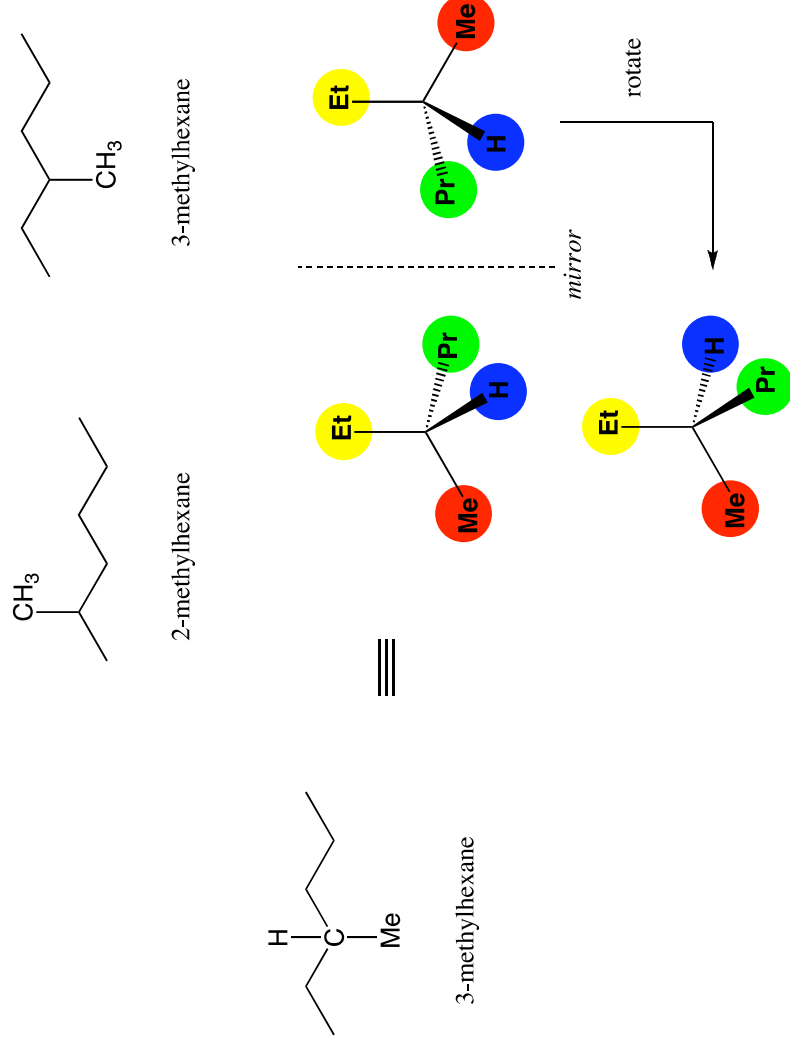
3-methylhexane



2-methylhexane is superimposable with its mirror image

Introduction To Stereochemistry

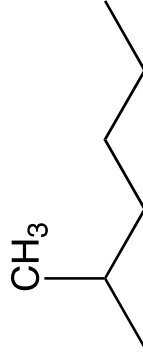
Consider two of the compounds we produced while finding all the isomers of C_7H_{16} :



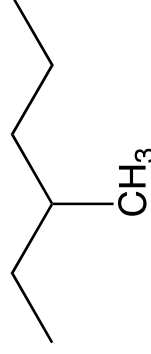
2-methylhexane is superimposable with its mirror image

Introduction To Stereochemistry

Consider two of the compounds we produced while finding all the isomers of C_7H_{16} :



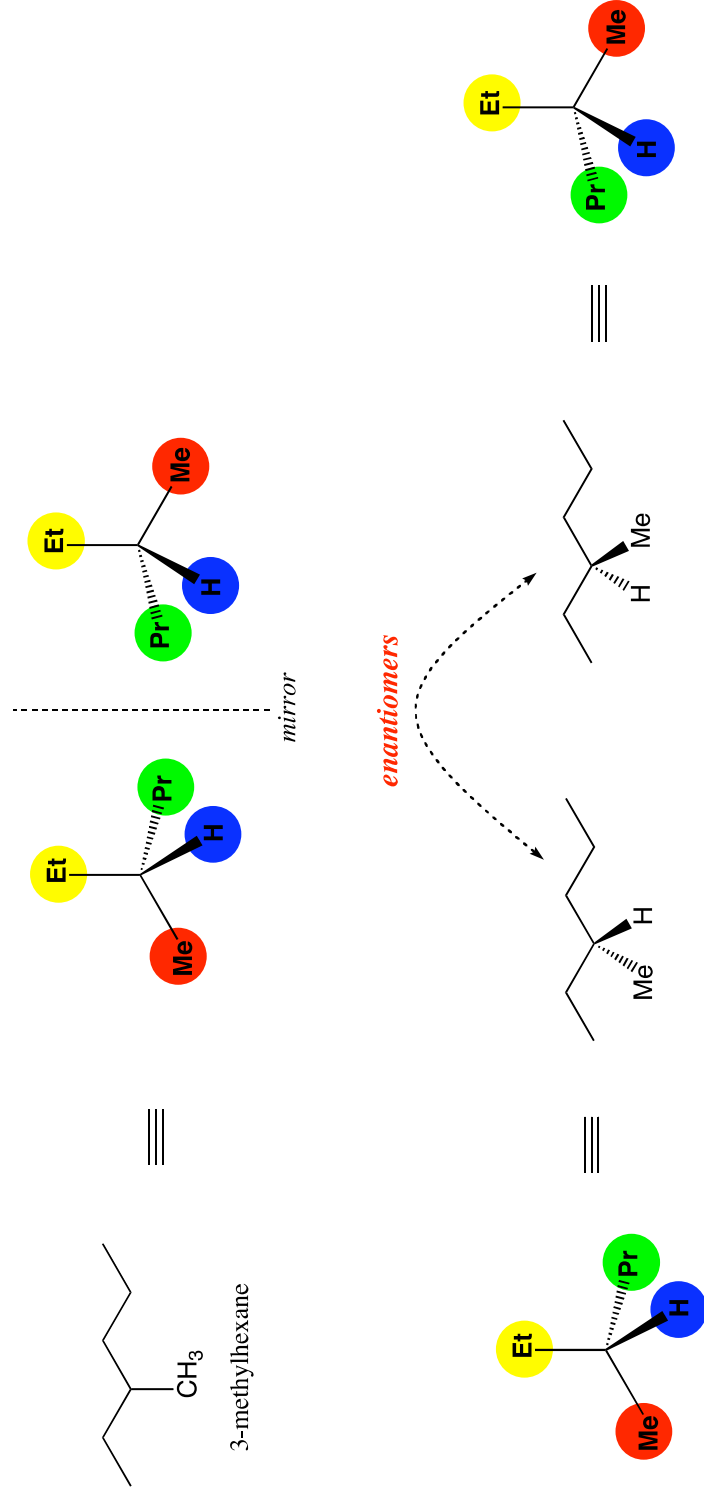
2-methylhexane



3-methylhexane

- Compounds that are not superimposable with their mirror image are called **chiral** (in Greek, chiral means "handed") 3-methylhexane is a chiral molecule.
- Compounds that are superimposable with their mirror image are called **achiral**. 2-methylhexane is an achiral molecule.
- An atom (usually carbon) with 4 different substituents is called a **stereogenic center** or **stereocenter**.

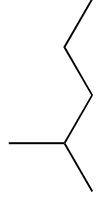
Enantiomers



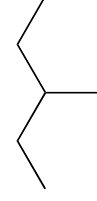
Two compounds that are non-superimposable mirror images (the two "hands") are called enantiomers.

Introduction To Stereochemistry

Structural (constitutional) Isomers - Compounds of the same molecular formula with different connectivity (structure, constitution)

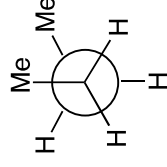
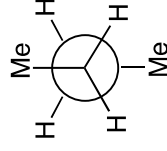


2-methylpentane

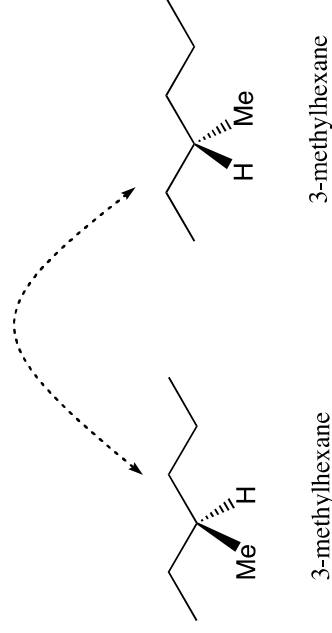


3-methylpentane

Conformational Isomers - Compounds of the same structure that differ in rotation around one or more single bonds



Configurational Isomers or **Stereoisomers** - Compounds of the same structure that differ in one or more aspects of stereochemistry (how groups are oriented in space - enantiomers or diastereomers)



We need a way to describe the stereochemistry!

3-methylhexane

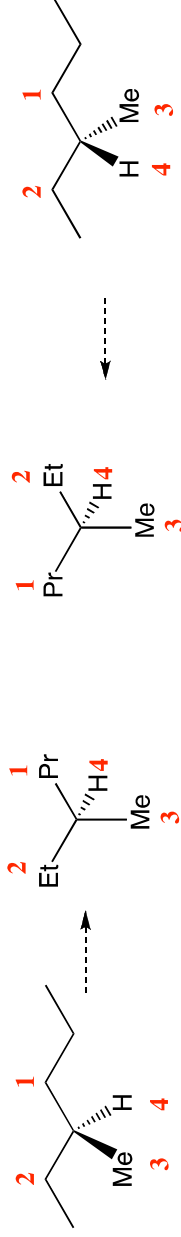
3-methylhexane

The CIP System Revisited

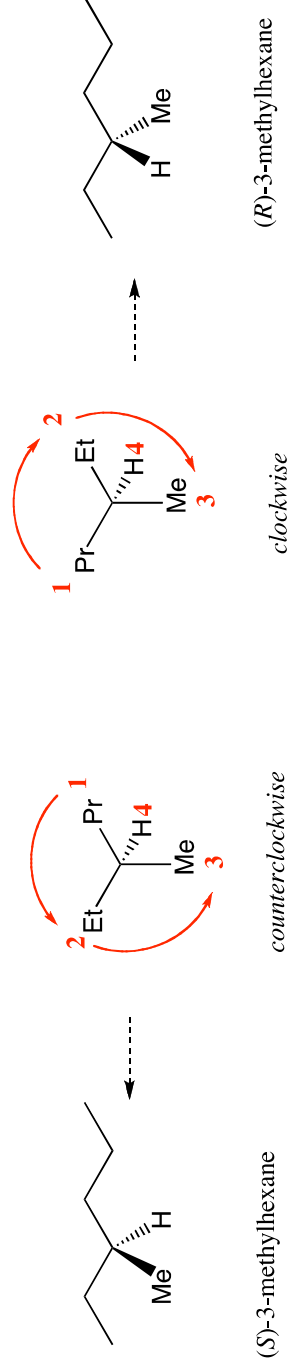
1. Rank each substituent attached to the stereocenter according to the CIP priority system (1 = highest, 4 = lowest)



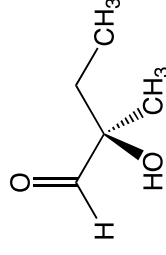
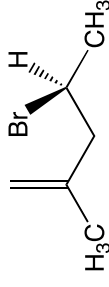
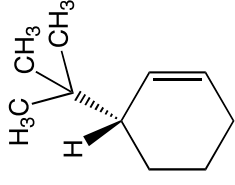
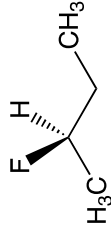
2. "View" the compound with the lowest priority substituent pointing away from you



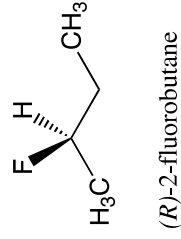
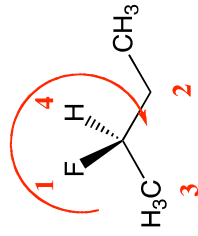
3. Draw a circular arrow from connecting substituents 1–3 from highest to lowest priority. If the arrow moves clockwise, the stereocenter is labeled (*R*) [this stands for *rectus*]. If the arrow moves counterclockwise, then the stereocenter is labeled (*S*) [this stands for *sinister*].



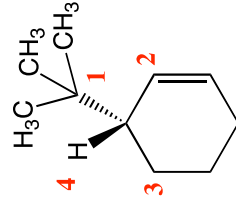
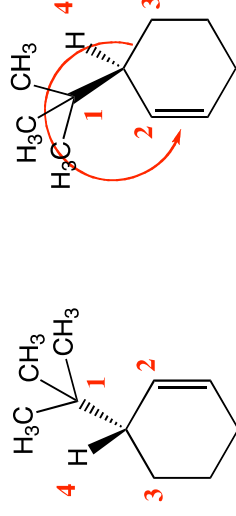
The CIP System Revisited



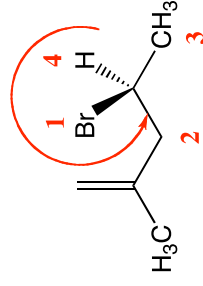
The CIP System Revisited



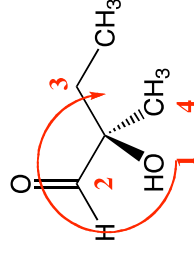
(*R*)-2-fluorobutane



(*S*)-3-*tert*-butylcyclohexene



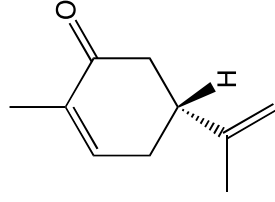
(*S*)-4-bromo-2-methyl-1-pentene



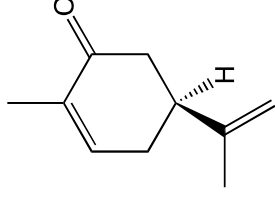
(*R*)-2-hydroxy-2-methylbutanal

Properties of Chiral Molecules

Chiral objects can only be "recognized" as chiral by another chiral object



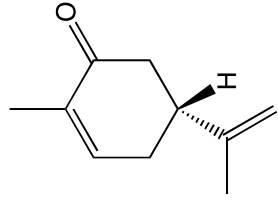
Carvone



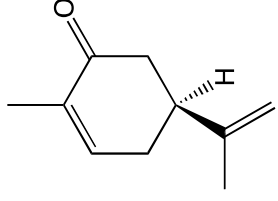
Which is (S) and which is (R)? [Your nose can tell!]

Properties of Chiral Molecules

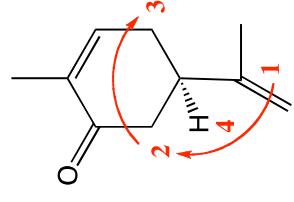
Chiral objects can only be "recognized" as chiral by another chiral object



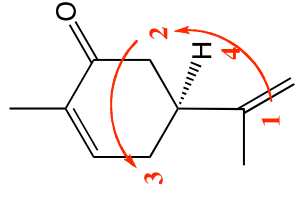
Carvone



Which is (S) and which is (R)? [Your nose can tell!]



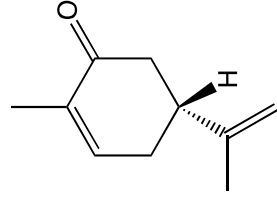
(R)



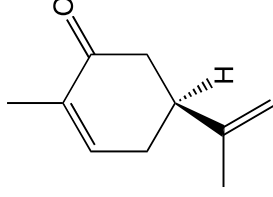
(S)

Properties of Chiral Molecules

Chiral objects can only be "recognized" as chiral by another chiral object



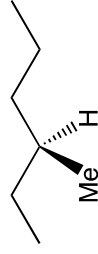
(*R*)-carvone [odor of spearmint]



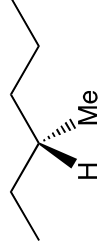
(*S*)-carvone [odor of caraway seed]

Multiple Stereocenters

1 stereocenter: 2 stereoisomers

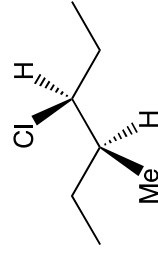
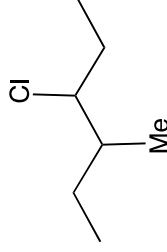


(*S*)-3-methylhexane

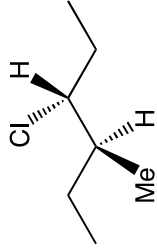


(*R*)-3-methylhexane

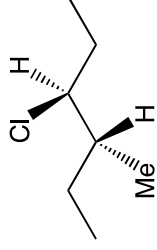
2 stereocenter: 4 stereoisomers



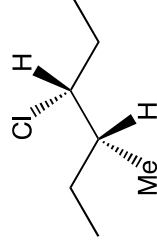
3(*S*), 4(*S*)-3-chloro-4-methylhexane



3(*R*), 4(*R*)-3-chloro-4-methylhexane

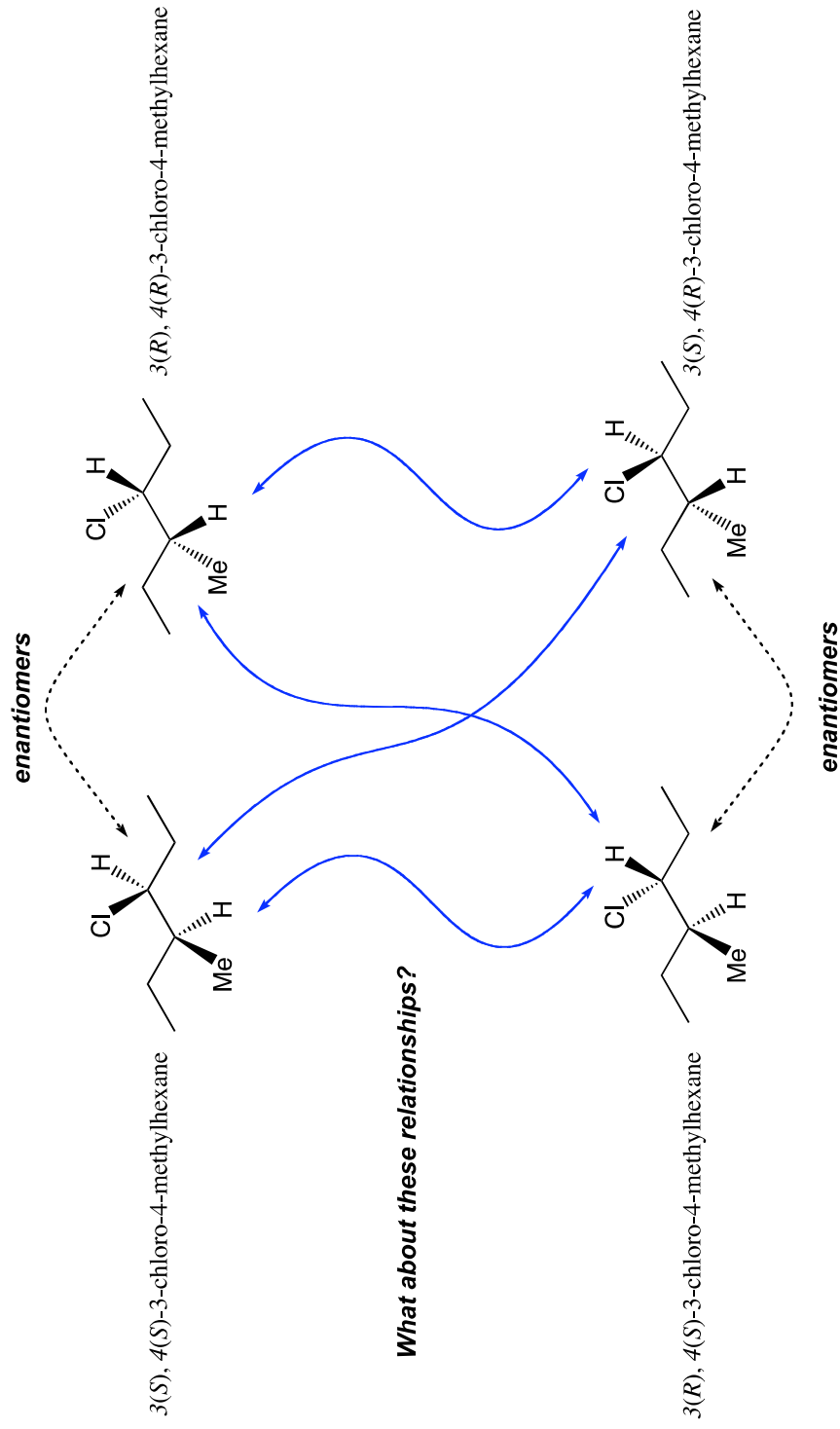


3(*S*), 4(*R*)-3-chloro-4-methylhexane



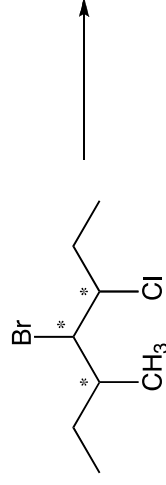
3(*R*), 4(*R*)-3-chloro-4-methylhexane

Multiple Stereocenters



Stereoisomers that are not enantiomers (non-superimposable mirror images) are called **diastereomers**

Multiple Stereocenters



3 stereocenters

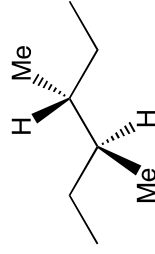
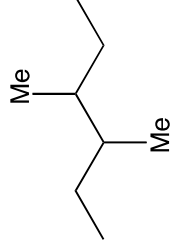
(R), (R), (R) (S), (S), (S)
(S), (R), (R) (R), (S), (S)
(R), (S), (R) (S), (R), (S)
(R), (R), (S) (S), (S), (R)

8 stereoisomers

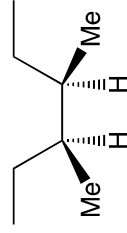
For any compound, the **maximum** number of stereoisomers is 2^n where n is the number of stereocenters.

Multiple Stereocenters

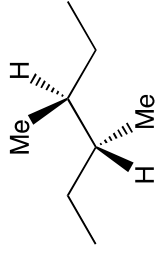
How many stereoisomers for 3,4-dimethylhexane?



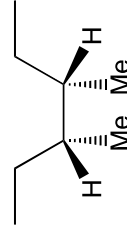
??-3,4-dimethylhexane



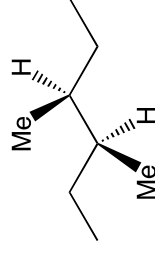
The same compound!
(superimposable)



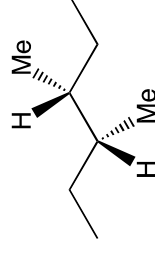
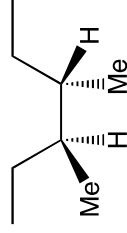
??-3,4-dimethylhexane



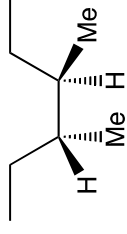
enantiomers



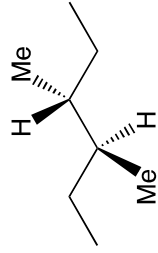
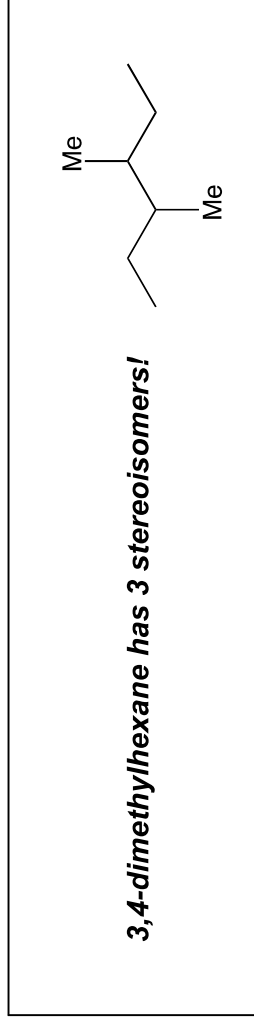
(3*S*,4*S*)-3,4-dimethylhexane



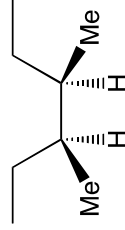
(3*R*,4*R*)-3,4-dimethylhexane



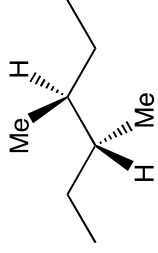
Meso Compounds



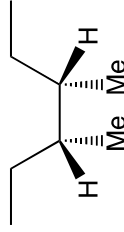
meso-3,4-dimethylhexane



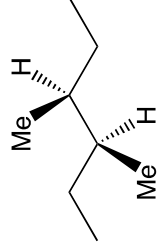
A Meso Compound (achiral)



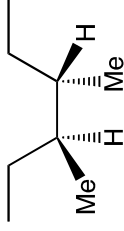
meso-3,4-dimethylhexane



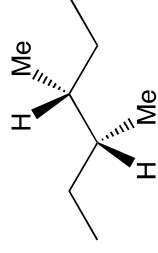
A Meso Compound (achiral)



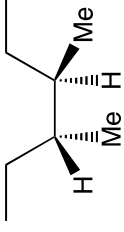
(3*S*,4*S*)-3,4-dimethylhexane



Enantiomers (chiral)



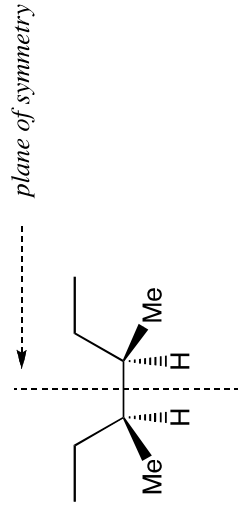
(3*R*,4*R*)-3,4-dimethylhexane



Enantiomers (chiral)

Meso Compounds

The best way to identify a meso compound is to prove that it is superimposable with its mirror image. However, a quick test is to see if it contains a plane of symmetry:



meso-3,4-dimethylhexane



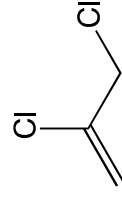
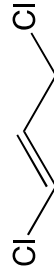
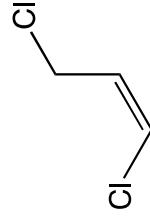
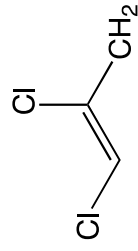
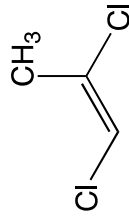
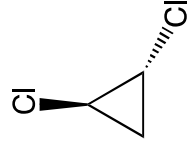
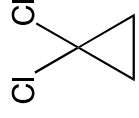
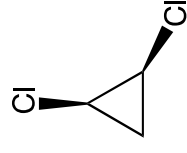
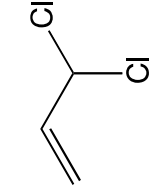
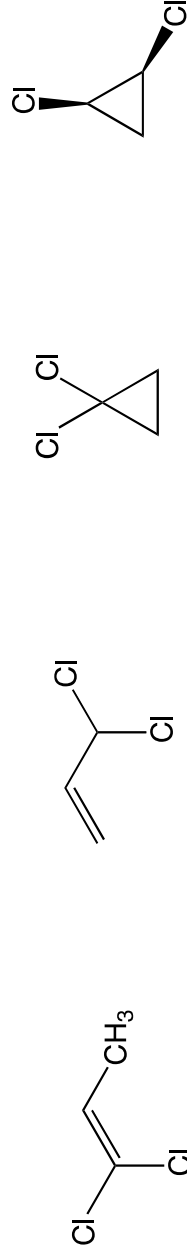
(3*S*,4*S*)-3,4-dimethylhexane

(3*R*,4*R*)-3,4-dimethylhexane

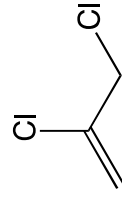
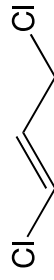
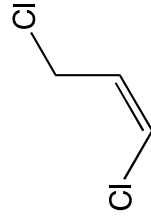
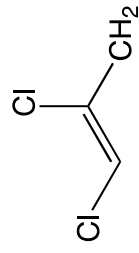
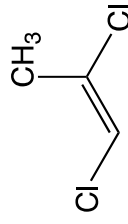
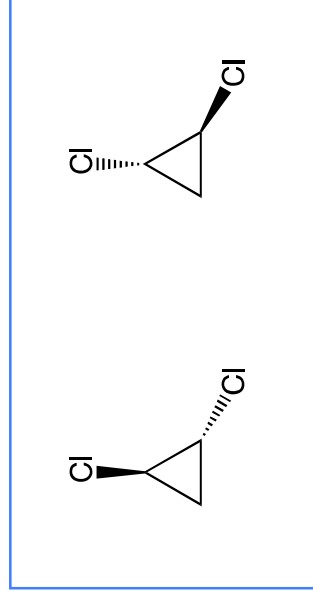
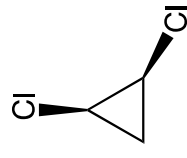
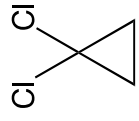
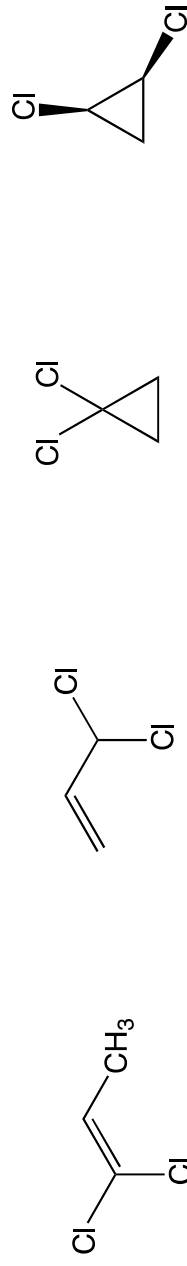
Compounds containing a plane of symmetry are achiral!

No plane of symmetry

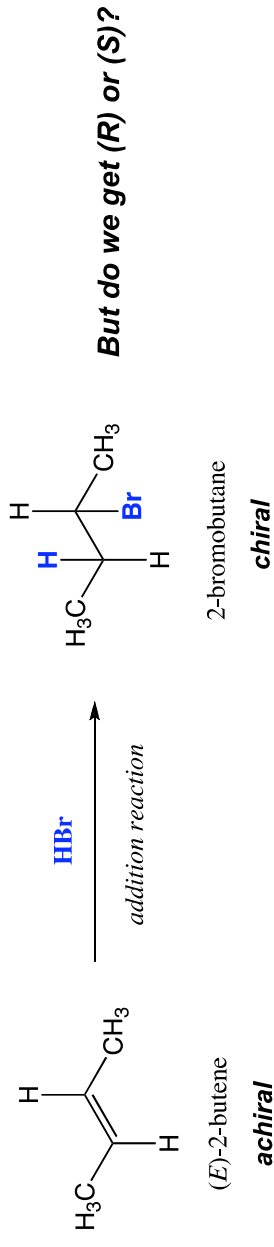
The Isomers of $C_3H_4Cl_2$, Revisited



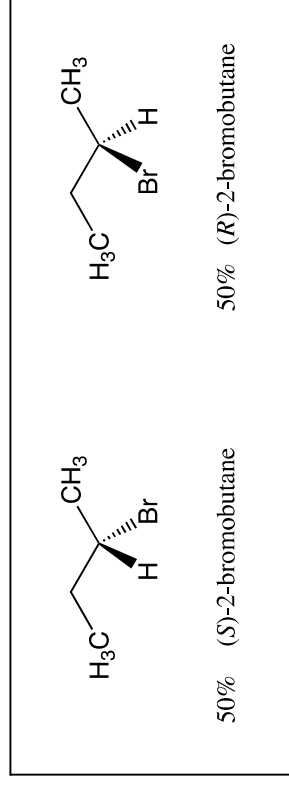
The Isomers of $C_3H_4Cl_2$, Revisited



Racemic Mixtures

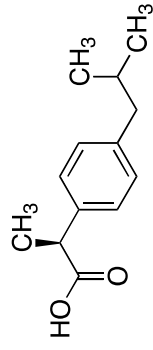


We get both!

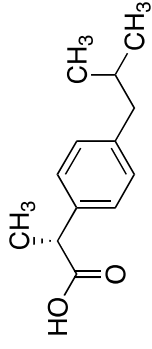


A 50:50 mixture of 2 enantiomers is called a **racemic mixture** or a **racemate**.

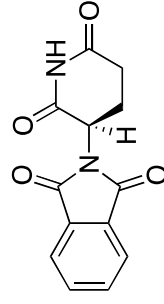
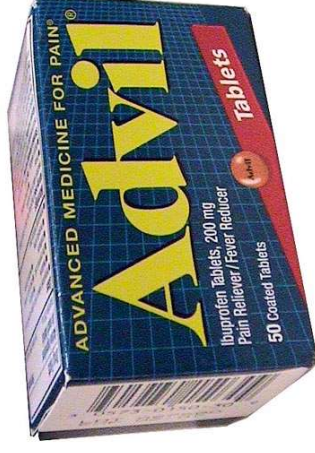
Racemic Mixtures In Medicine



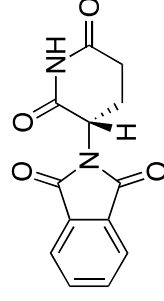
(S)-ibuprofen
(active)



(R)-ibuprofen
(inactive)



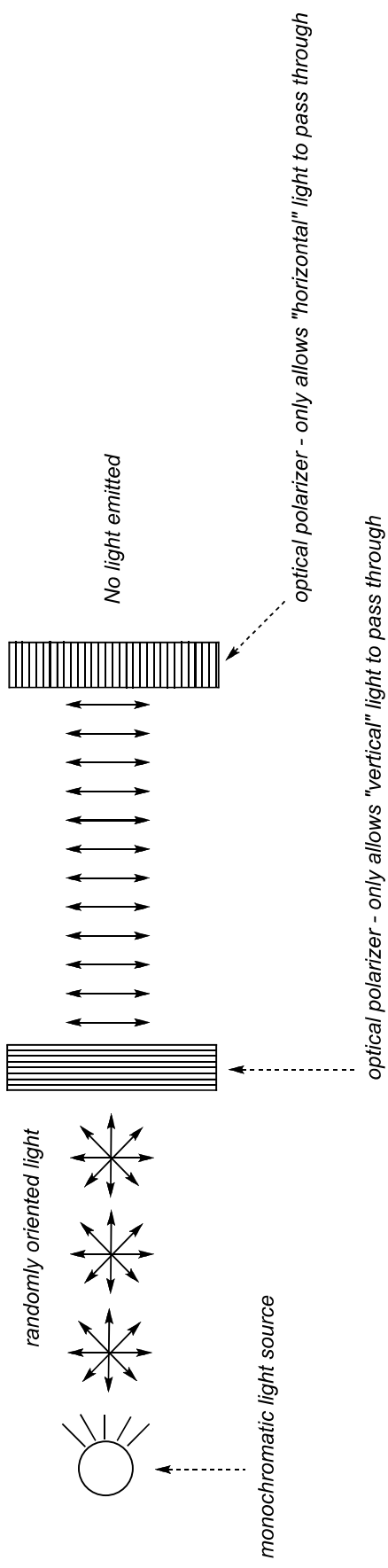
(R)-Thalidomide
(analgesic)



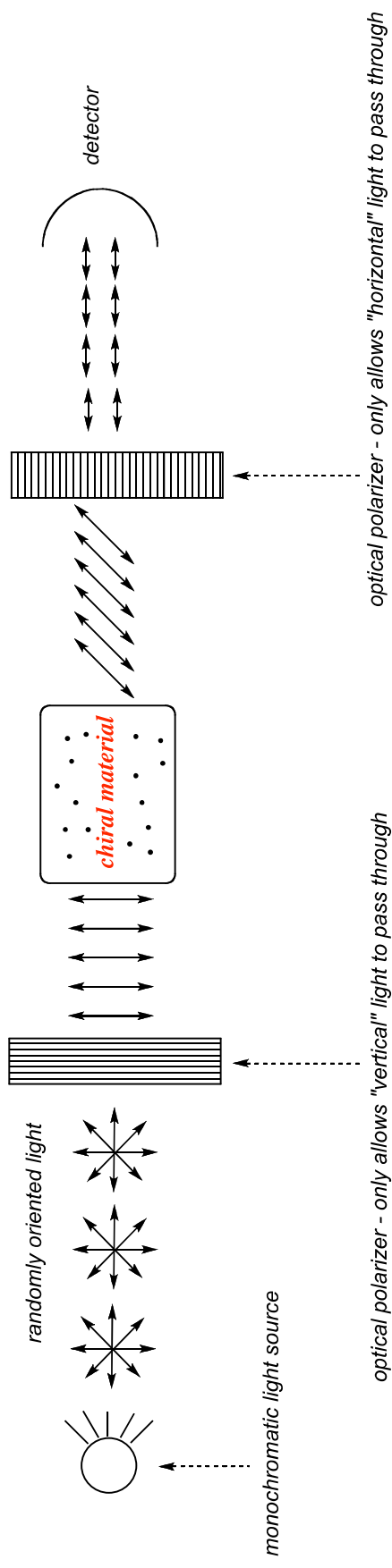
(S)-Thalidomide
(teratogenic)

Prescribed worldwide from 1957-1961 for morning sickness and as a sleep aid

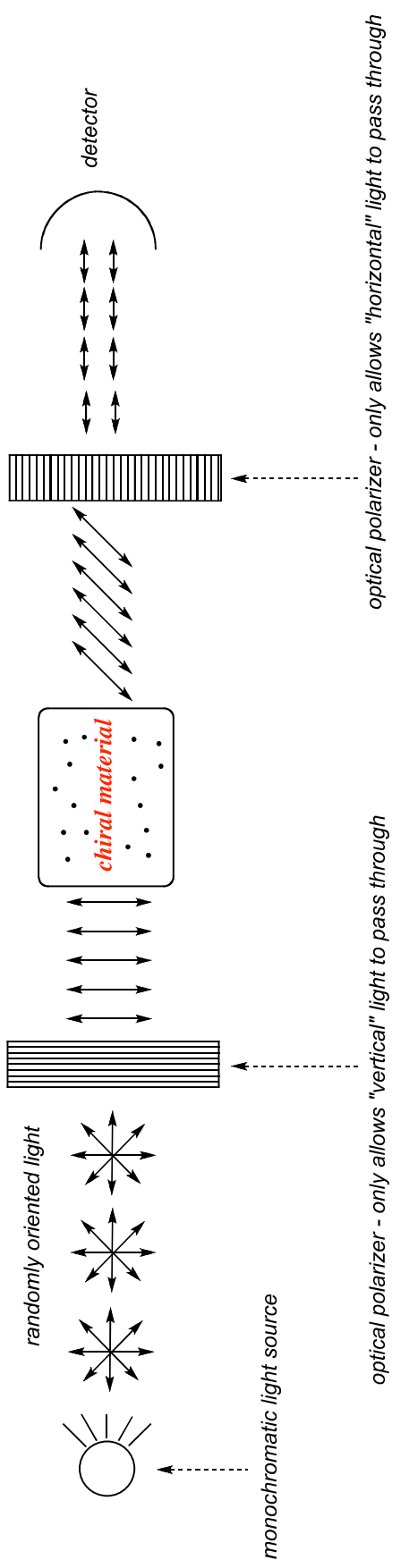
Optical Rotation and Polarimetry



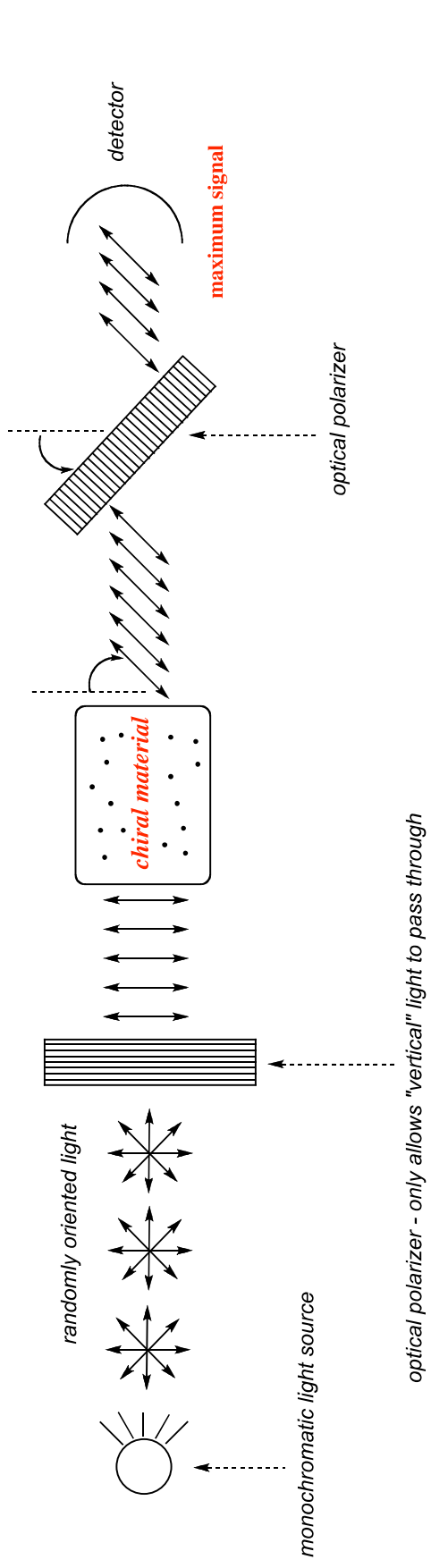
Chiral molecules will rotate polarized light:



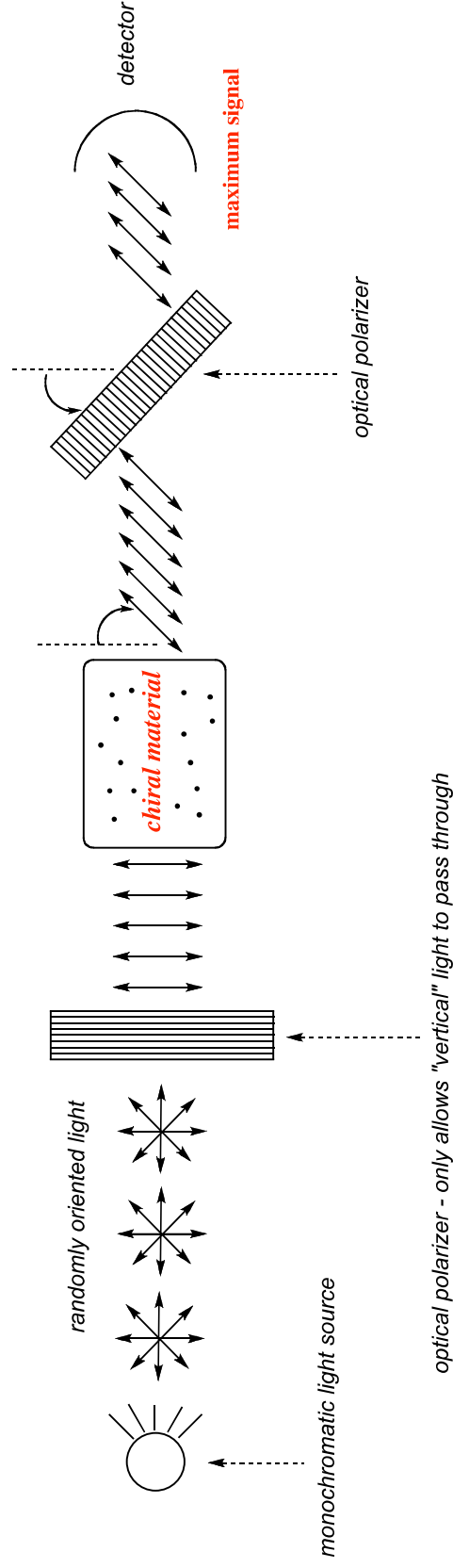
Optical Rotation and Polarimetry



The maximum signal will be obtained if the second polarizer is rotated to match the light rotation:



Optical Rotation and Polarimetry



The amount (in degrees) that a chiral material will rotate light is called the **optical rotation**. Different chiral molecules will have optical rotations that vary in direction and size of the optical rotation. Enantiomers will always have equal optical rotations but in opposite directions.

The **optical purity** of a substance can be measured by comparing the optical rotation of the sample to the known optical rotation of a single enantiomer of that compound. Optical purity is usually reported in percent **enantiomeric excess (%ee)**.

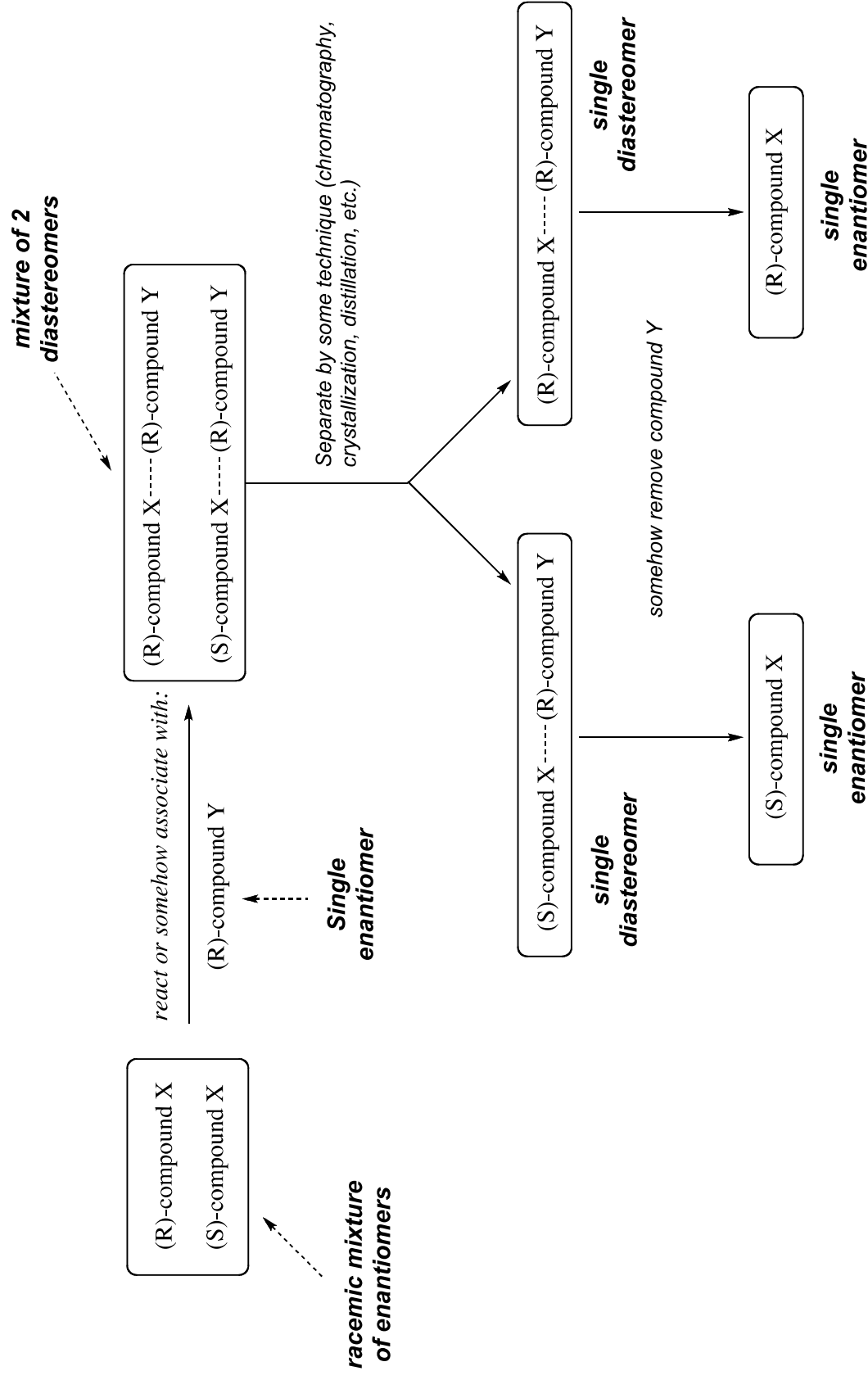
$$\%ee = \frac{\text{sample rotation}}{\text{single enantiomer rotation}} \times 100$$

Enantiomeric excess is the % of the sample that is non-racemic. For example, 80% ee means that there is 90% of one enantiomer and 10% of the other.

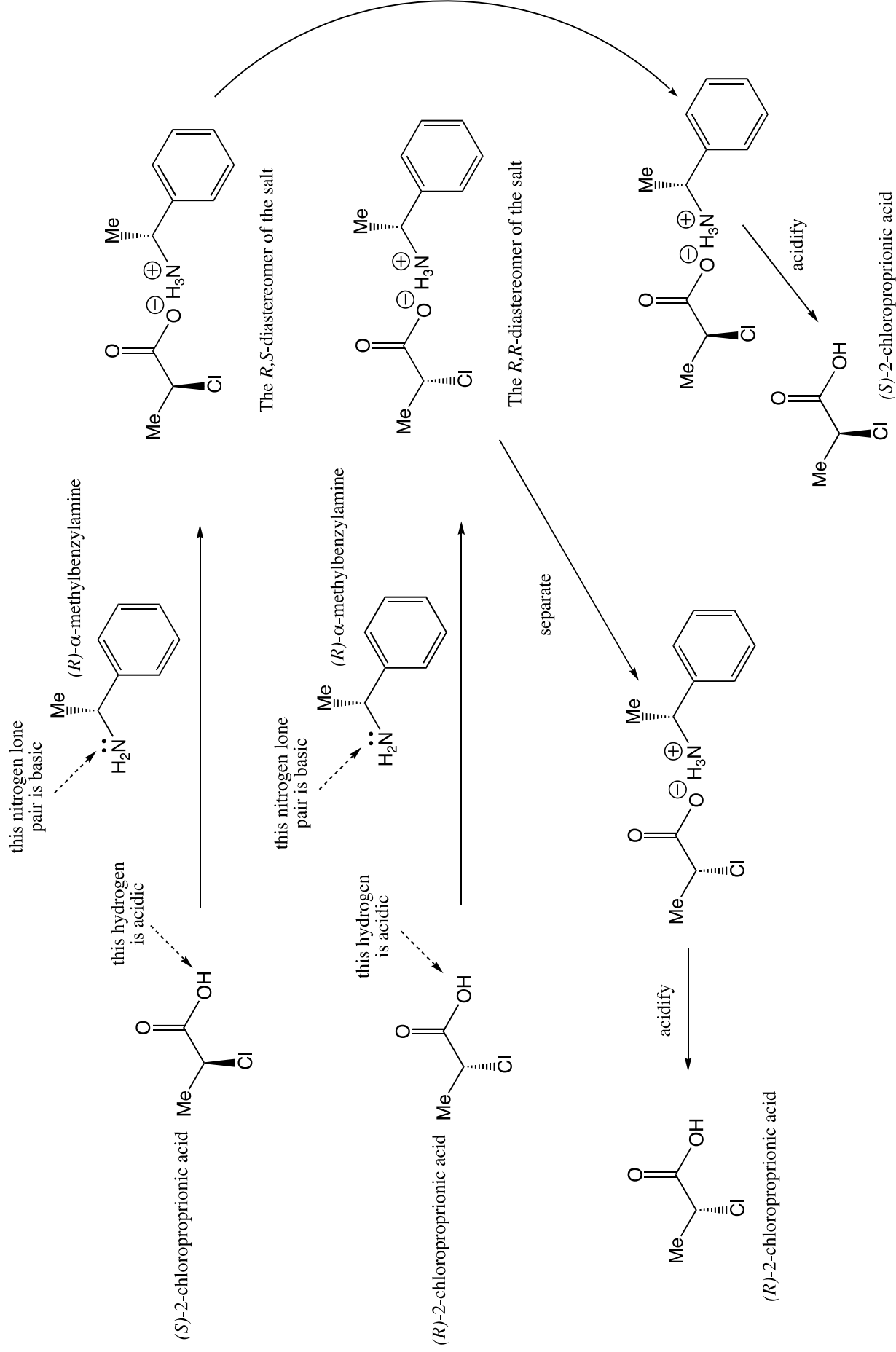
Vocabulary

- **(R) or (S)**: identifies the configuration of a stereocenter using the CIP priority system
- **d- or (+)**: indicates that a (chiral) compound rotates light in a clockwise direction (this has no correlation with S or R)
- **l or (-)**: indicates that a (chiral) compound rotates light in a counterclockwise direction (this has no correlation with S or R)
- **d/ or (+/-) or rac-**: indicates a racemate

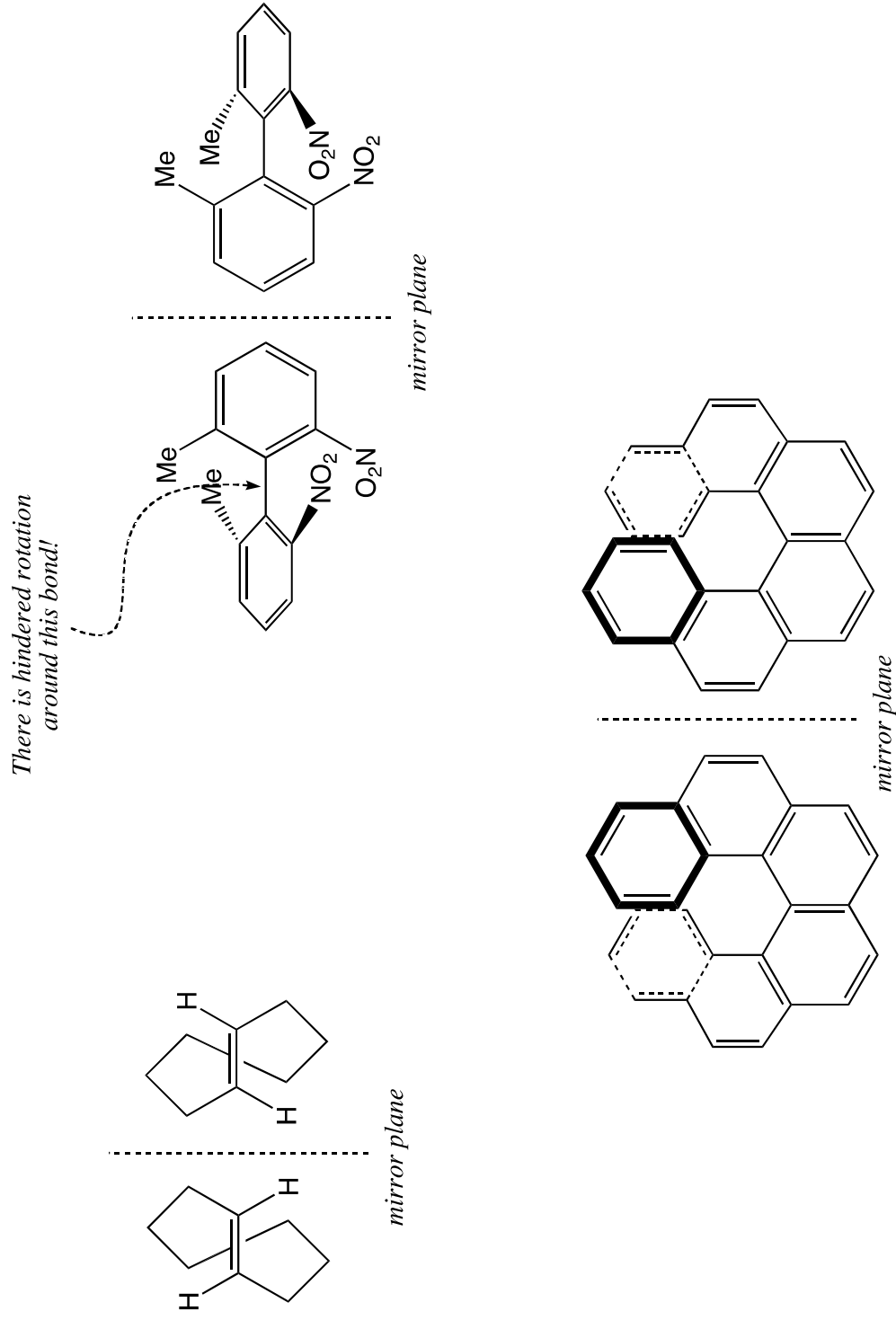
Resolution of Enantiomers



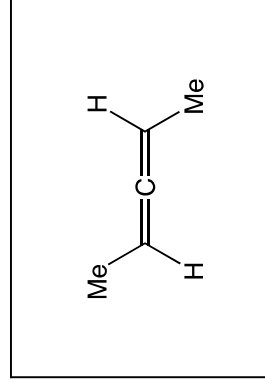
Resolution of Enantiomers



Chirality Without Stereocenters



Chirality Without Stereocenters



Why is 1,3-dimethylallene (1,3-dimethyl-2,3-pentadiene) chiral?