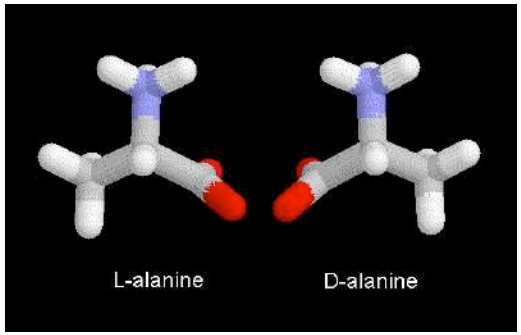
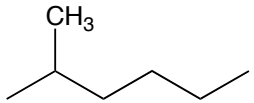
Chapter 4: Stereochemistry

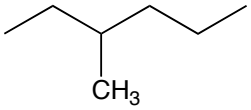


Introduction To Stereochemistry

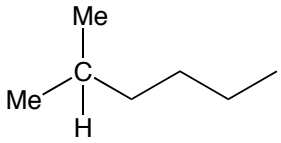
Consider two of the compounds we produced while finding all the isomers of C_7H_{16}:



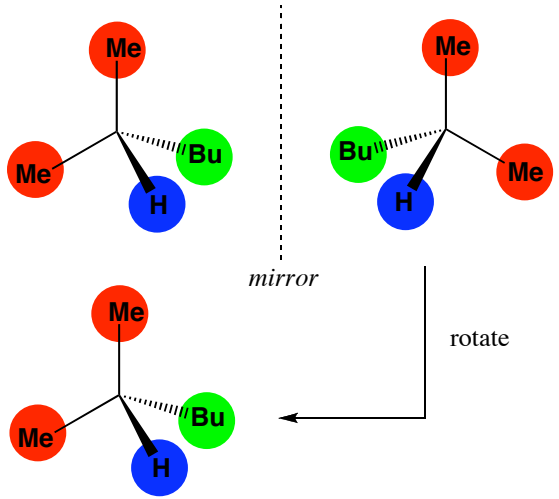
2-methylhexane



3-methylhexane



2-methylhexane



2-methylhexame is superimposable with its mirror image

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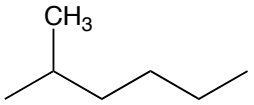

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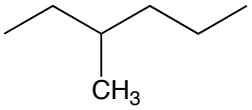

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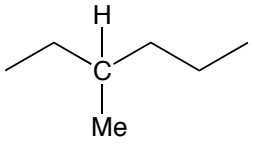
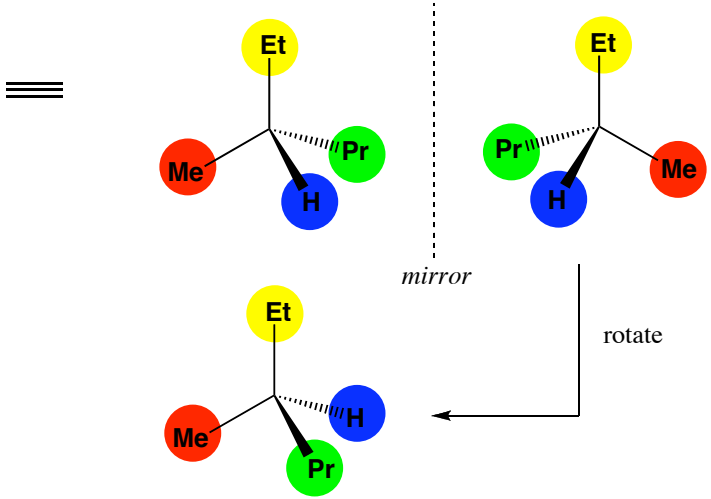


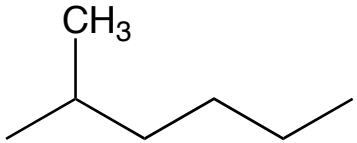
3-methylhexane



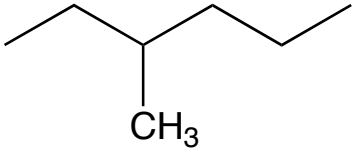
2-methylhexame is superimposable with its mirror image

Introduction To Stereochemistry

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



2-methylhexane



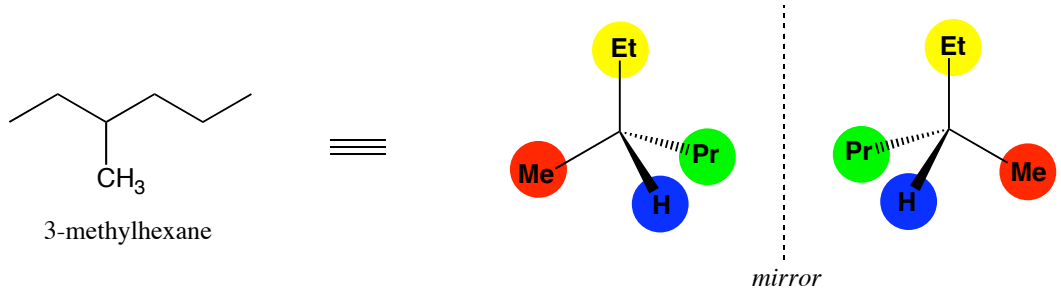
3-methylhexane

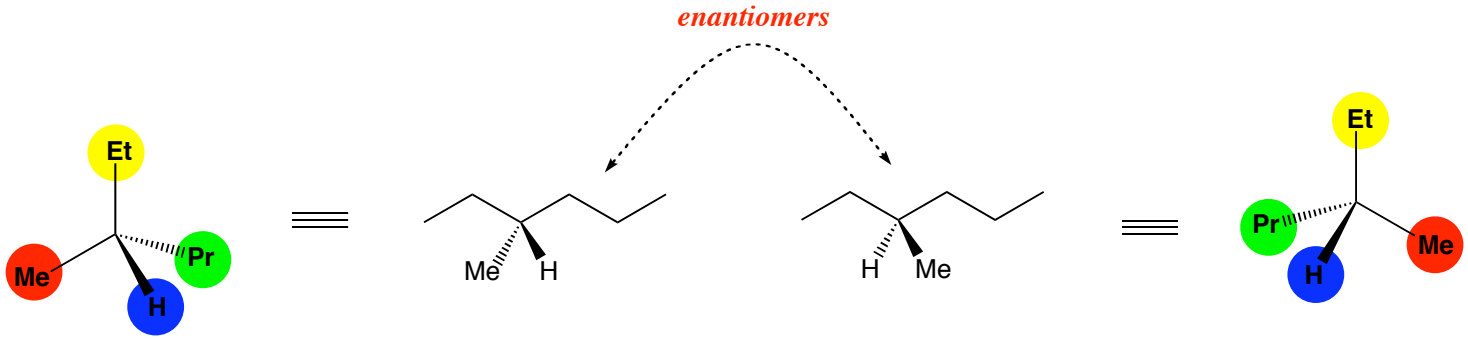
- Compounds that are not superimposable with their mirror image are called **chiral** (in Greek, chiral means "handed") 3-methylhexane is a chiral molecule.

- 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

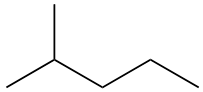




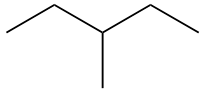
Two compounds that are non-superimposable mirror images (the two "hands") are called enantiomers.

Introduction To Stereochemistry

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

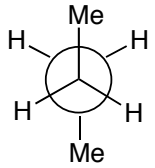


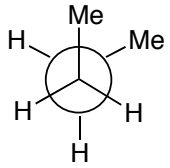
2-methylpentane



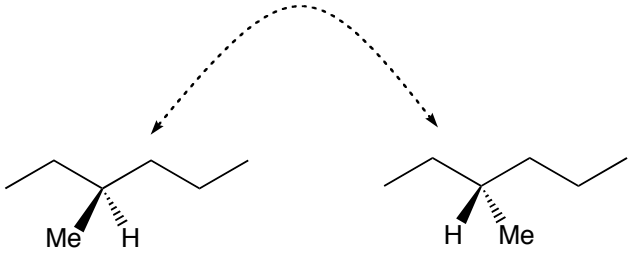
3-methylpentane

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)



3-methylhexane

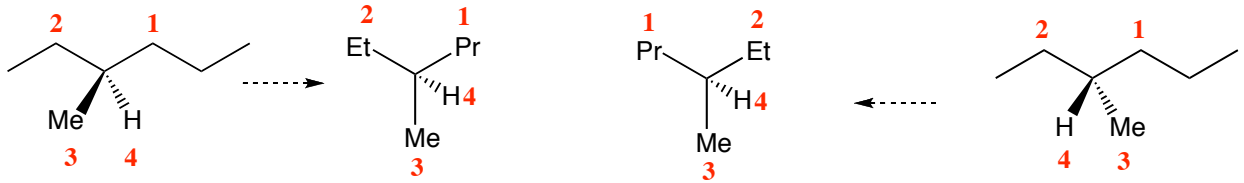
3-methylhexane

We need a a way to describe the stereochemistry!

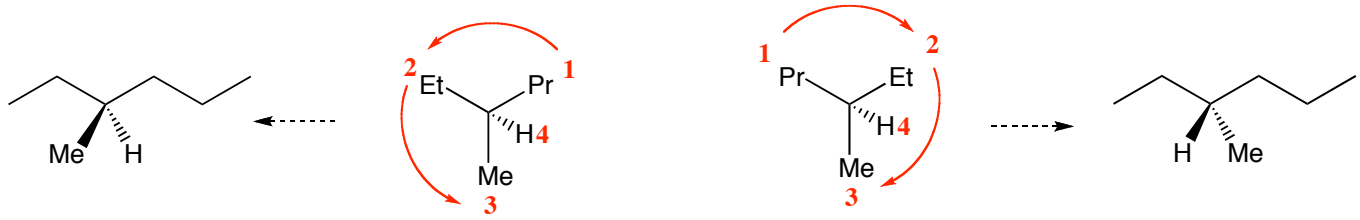
The CIP System Revisited

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

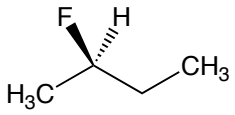


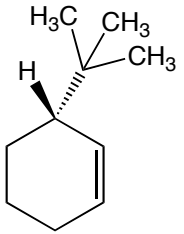
3. Draw a circular arrow from connecting substituents 1–3 from highest to lowest priority. If the arrow moves clockwise, the sterocenter is labeled (*R*) [this stands for *rectus*]. If the arrow moves counterclockwise, then the stereocenter is labeled (*S*) [this stands for *sinister*].

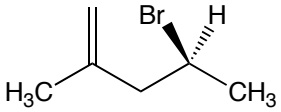


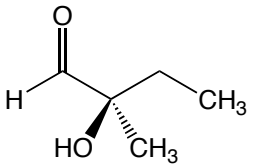
(*S*)-3-methylhexane *counterclockwise* *clockwise* (*R*)-3-methylhexane

The CIP System Revisited

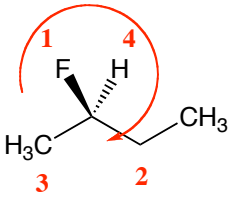


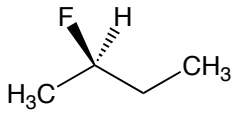




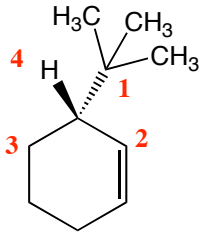


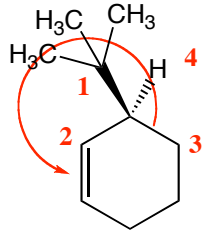
The CIP System Revisited



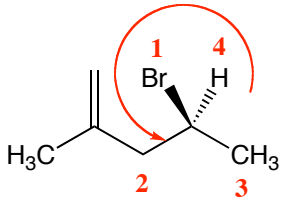


(R)-2-fluorobutane

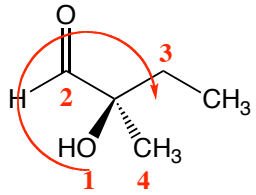




(S)-3-*tert*-butylcyclohexene



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



(R)-2-hydroxy-2-methyl-butanal

Properties of Chiral Molecules

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

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

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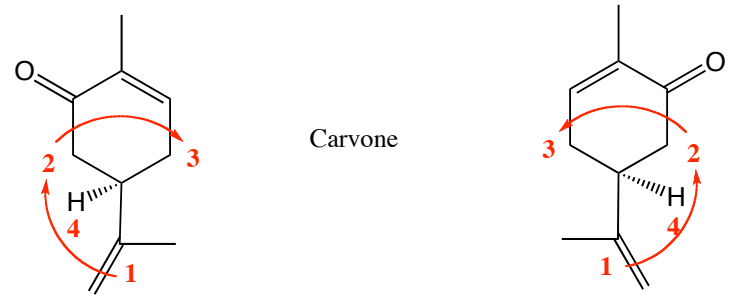
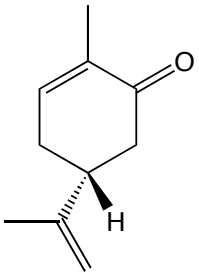


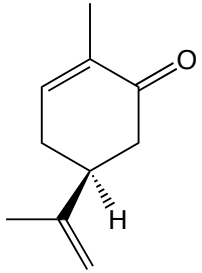
(*R*) (*S*)

Properties of Chiral Molecules

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



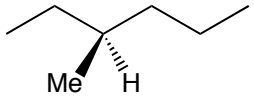
(*R*)-carvone [odor of spearmint]



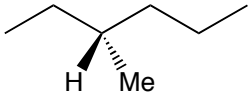
(*S*)-carvone [odor of caraway seed]

Multiple Stereocenters

1 stereocenter: 2 stereoisomers

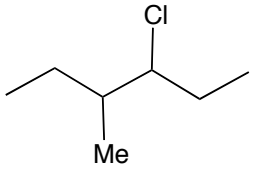


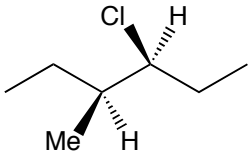
(*S*)-3-methylhexane



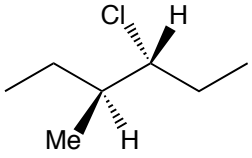
(*R*)-3-methylhexane

2 stereocenter: 4 stereoisomers

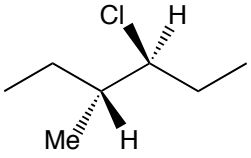




3(*S*), *4*(*S*)-3-chloro-4-methylhexane



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



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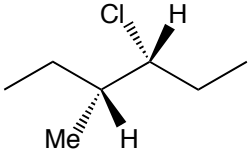
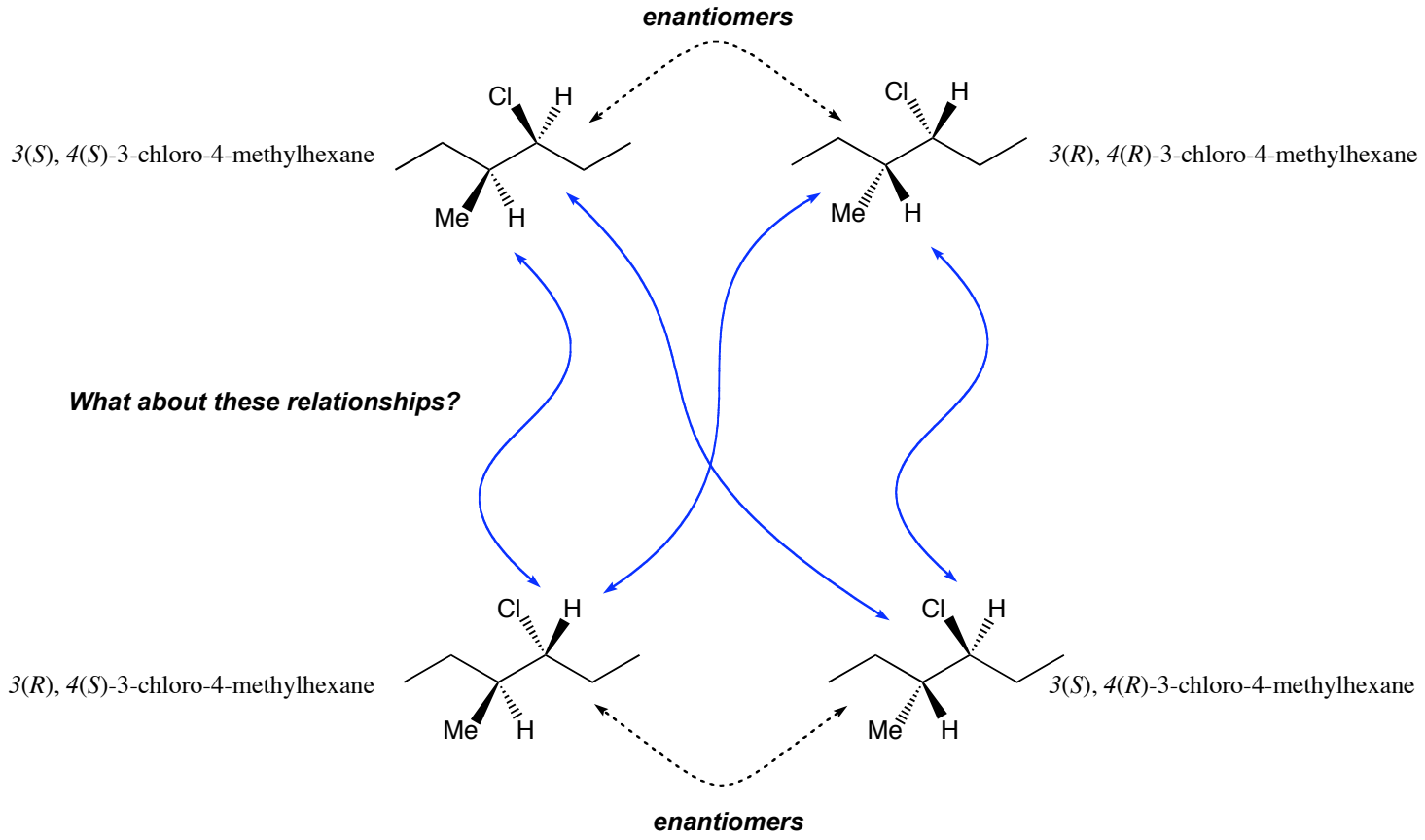


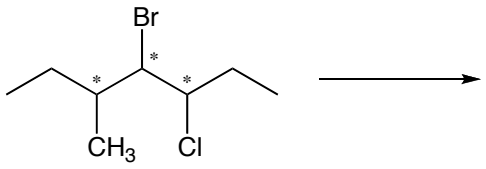
3(*R*), *4*(*R*)-3-chloro-4-methylhexane

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)

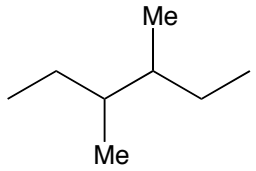
(R), (R), (S) (S), (S), (R)

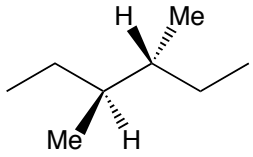
8 stereoisomers

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

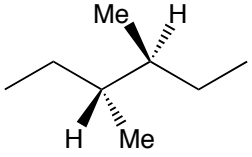
Multiple Stereocenters

How many stereoisomers for 3,4-dimethylhexane?

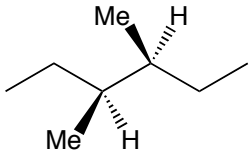




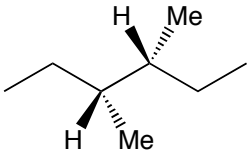
??-3,4-dimethylhexane



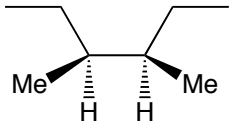
??-3,4-dimethylhexane

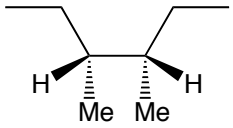


(3*S*,4*S*)-3,4-dimethylhexane



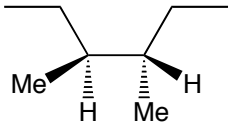
(3*R*,4*R*)-3,4-dimethylhexane

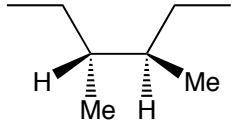




The same compound!

(superimposable)

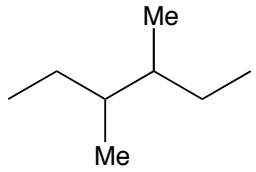


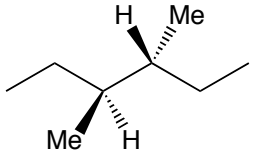


enantiomers

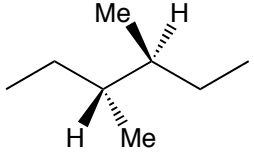
Meso Compounds

3,4-dimethylhexane has 3 stereoisomers!

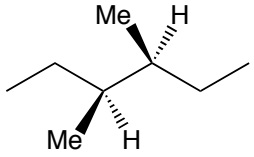




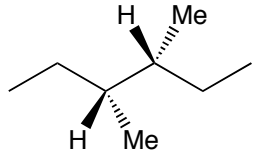
meso-3,4-dimethylhexane



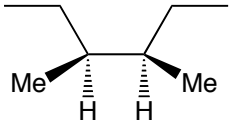
meso-3,4-dimethylhexane

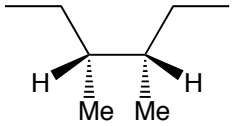


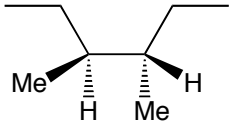
(3*S*,4*S*)-3,4-dimethylhexane

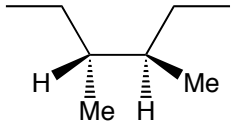


(3*R*,4*R*)-3,4-dimethylhexane







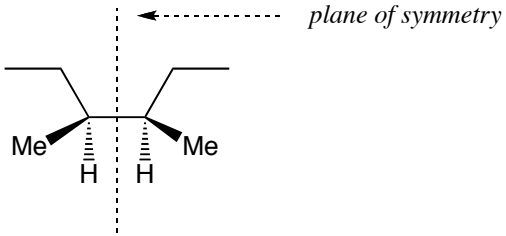


A Meso Compound (achiral)

Enantiomers (chiral)

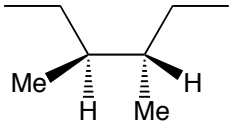
Meso Compounds

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:

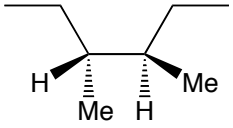


meso-3,4-dimethylhexane

Compounds containing a plane of symmetry are achiral!



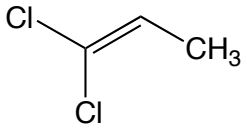
(3*S*,4*S*)-3,4-dimethylhexane

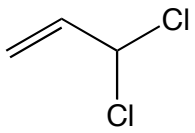


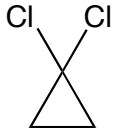
(3*R*,4*R*)-3,4-dimethylhexane

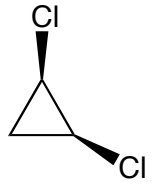
No plane of symmetry

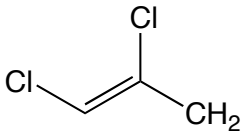
The Isomers of $C_3H_4Cl_2$, Revisited

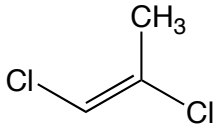


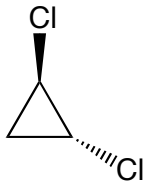


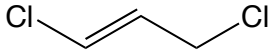


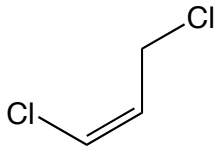


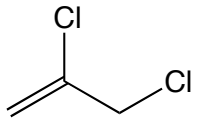




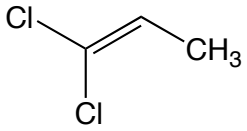


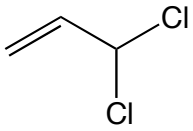


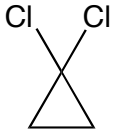


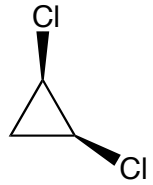


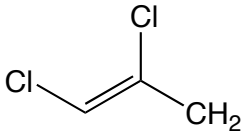
The Isomers of $C_3H_4Cl_2$, Revisited

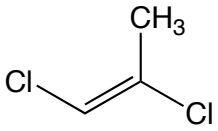


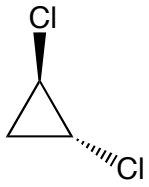


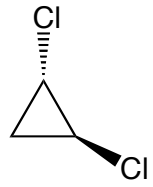


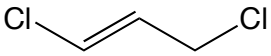


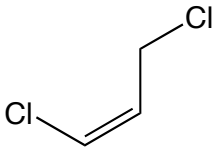


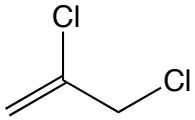




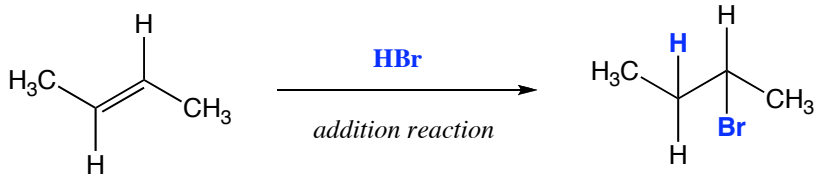








Racemic Mixtures



(*E*)-2-butene

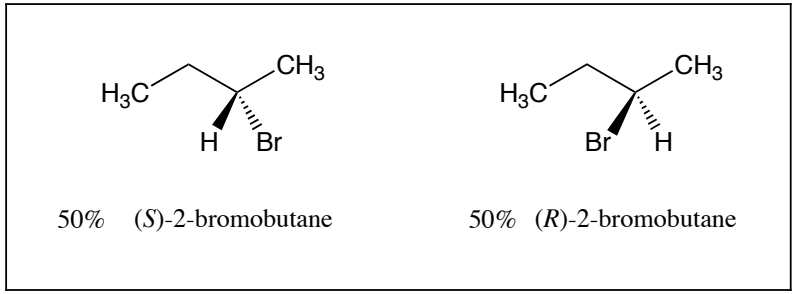
achiral

2-bromobutane

chiral

But do we get (R) or (S)?

We get both!

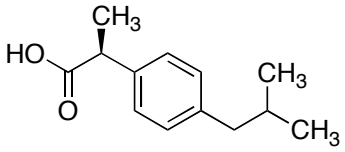


50% (*S*)-2-bromobutane

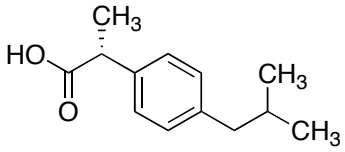
50% (*R*)-2-bromobutane

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

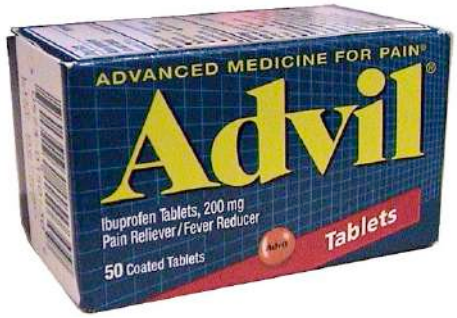
Racemic Mixtures In Medicine

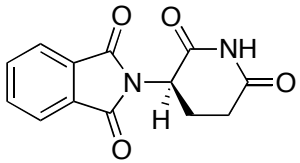


(S)-ibuprofen
(active)

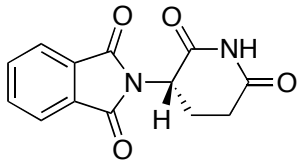


(R)-ibuprofen
(inactive)





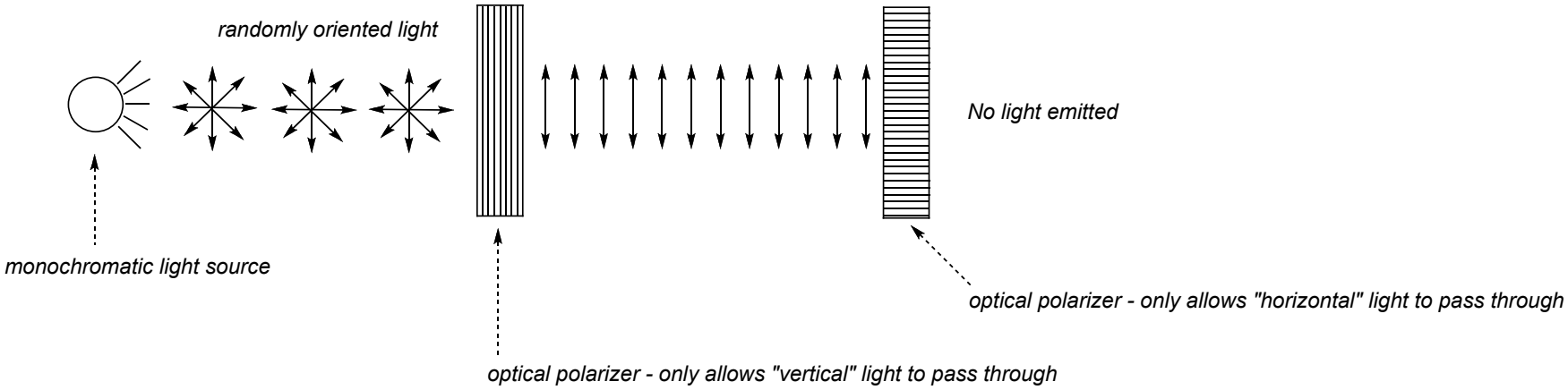
(R)-Thalidomide
(analgesic)



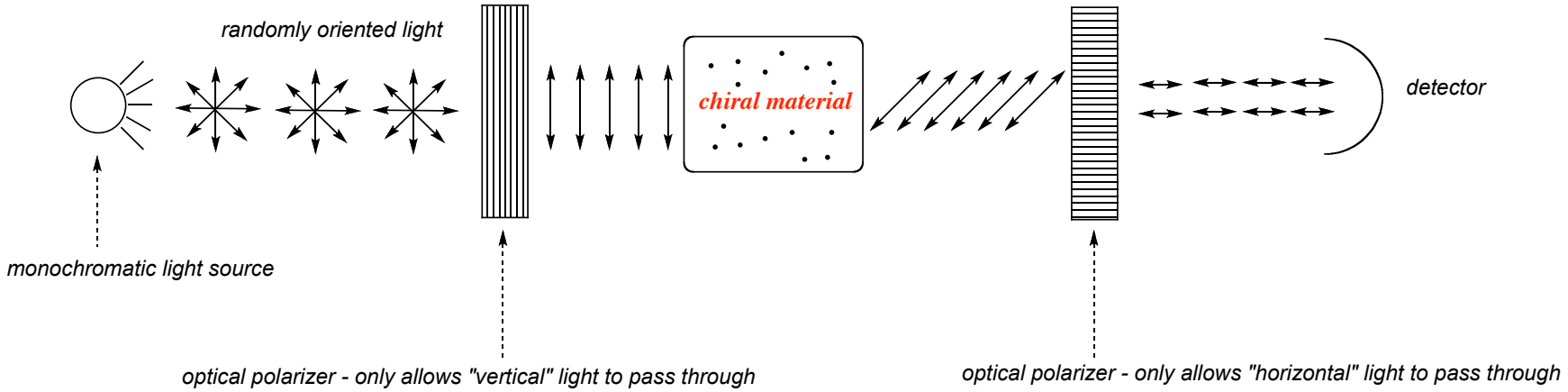
(S)-Thalidomide
(teratogenic)

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

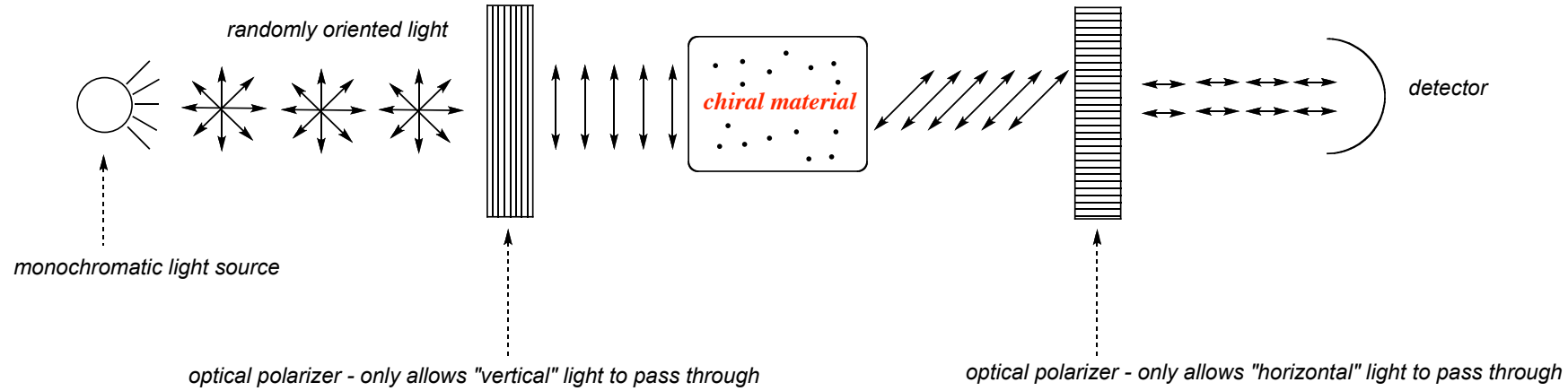
Optical Rotation and Polarimetry



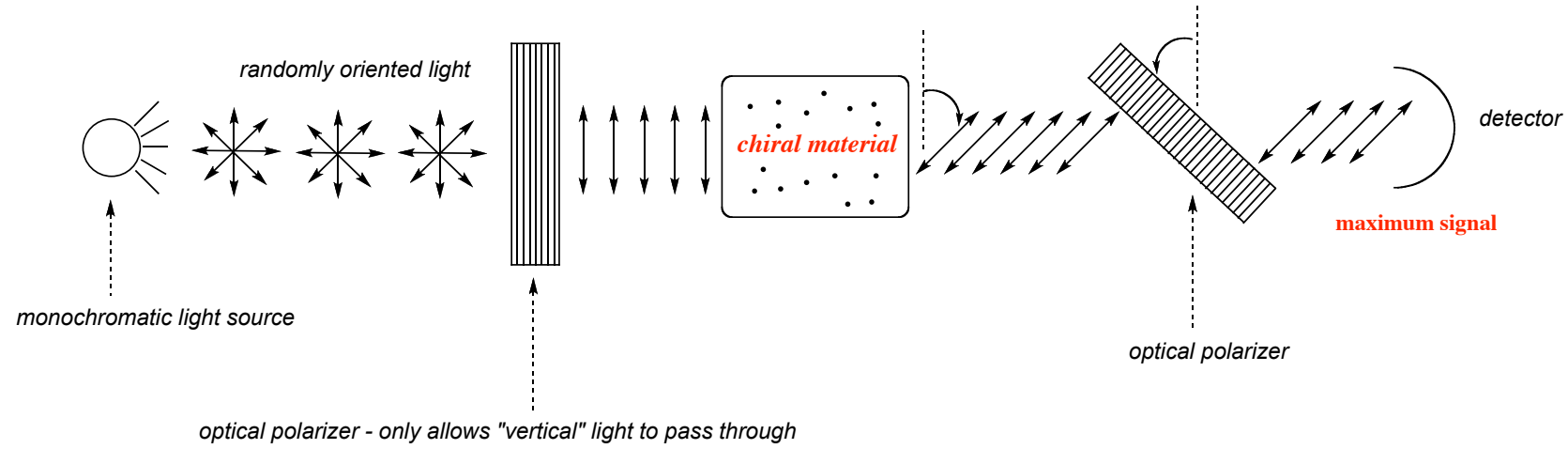
Chiral molecules will rotate polarized light:



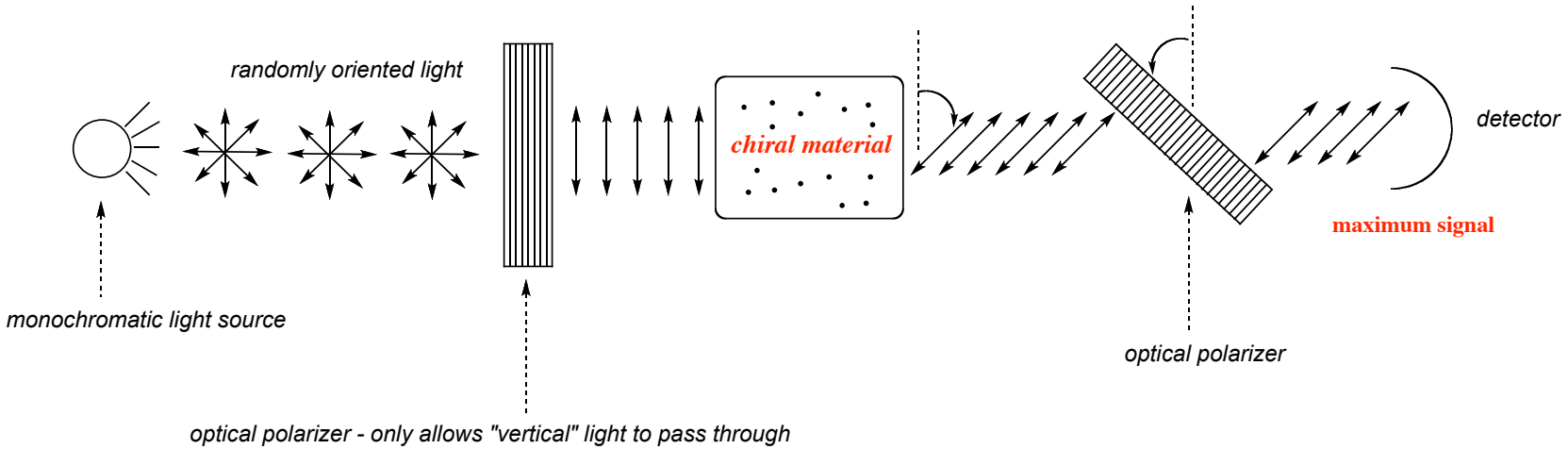
Optical Rotation and Polarimetry



The maximum signal will be optained 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 entantiomer of that compound. Optical purity is usually reported in percent **entantiomeric 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

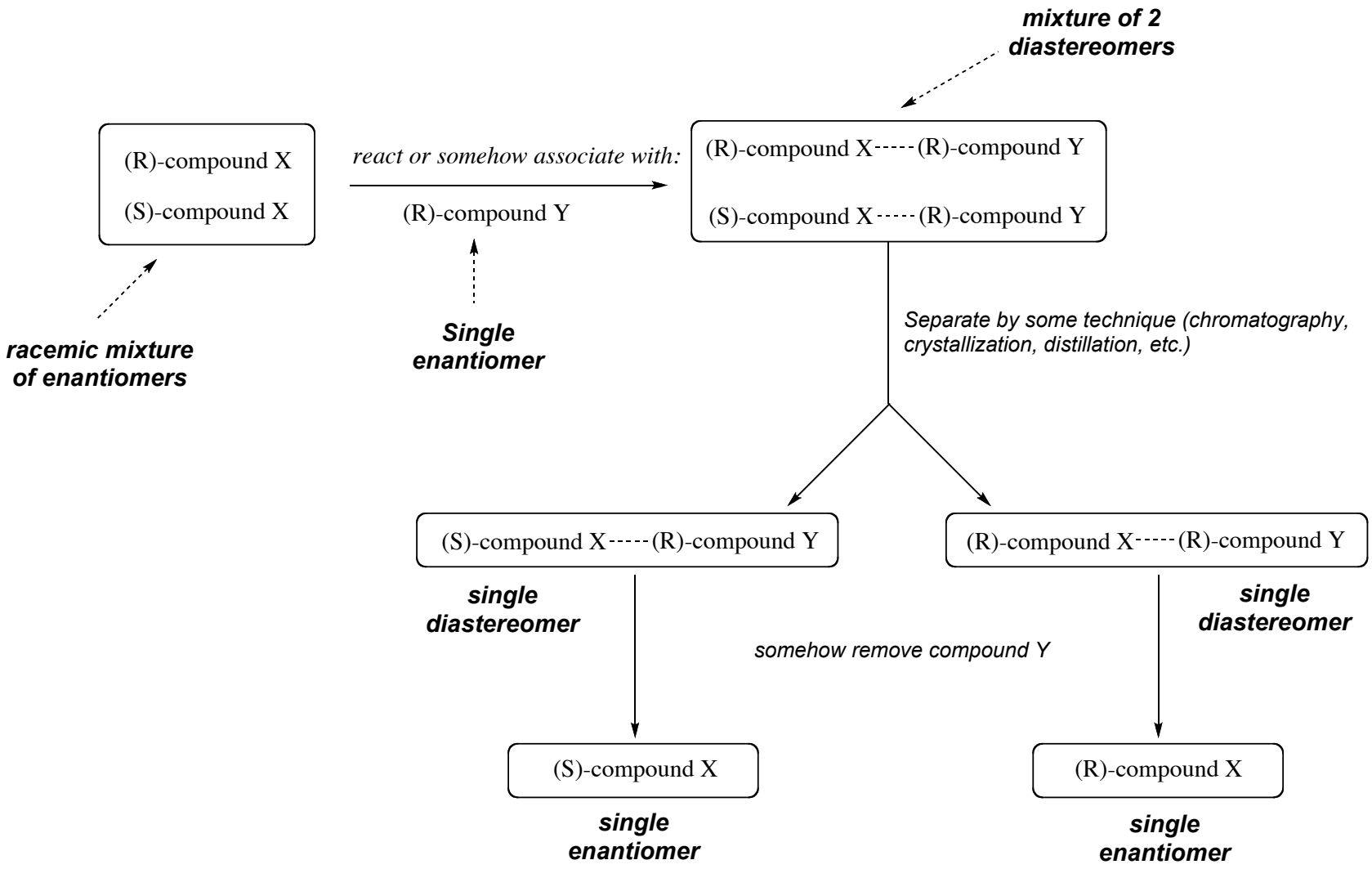
•**(R) or (S):** identifies the configuration of a stereocenter using the CIP priority system

•***d*- or (+):** indicates that a (chiral) compound rotates light in a clockwise direction (this has no correlation with S or R)

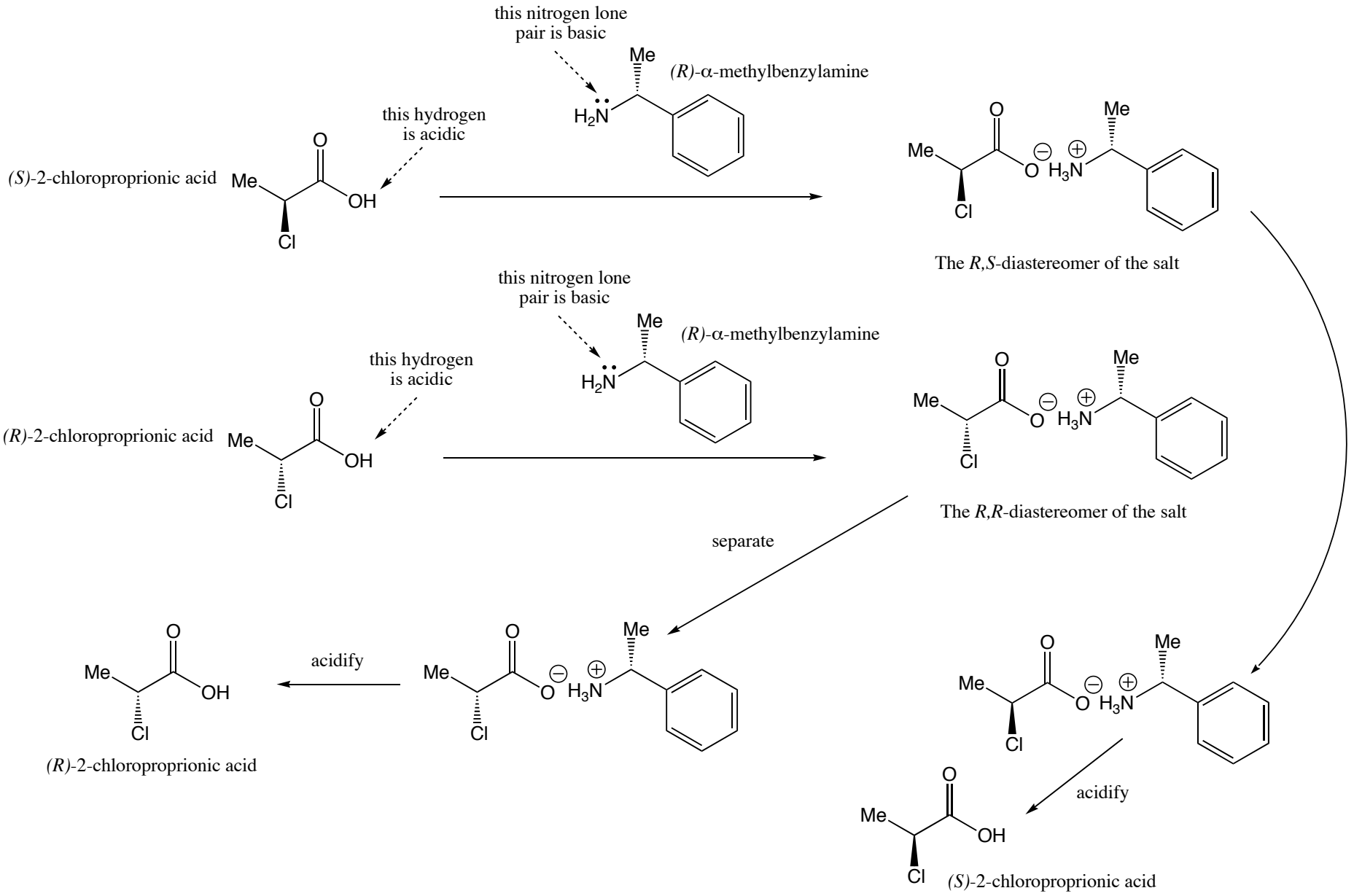
•***l* or (-):** indicates that a (chiral) compound rotates light in a counterclockwise direction (this has no correlation with S or R)

•***dl* or (+/-) or *rac*-:** indicates a racemate

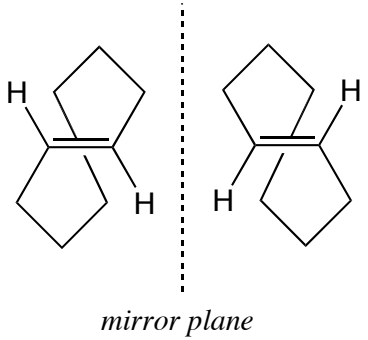
Resolution of Enantiomers

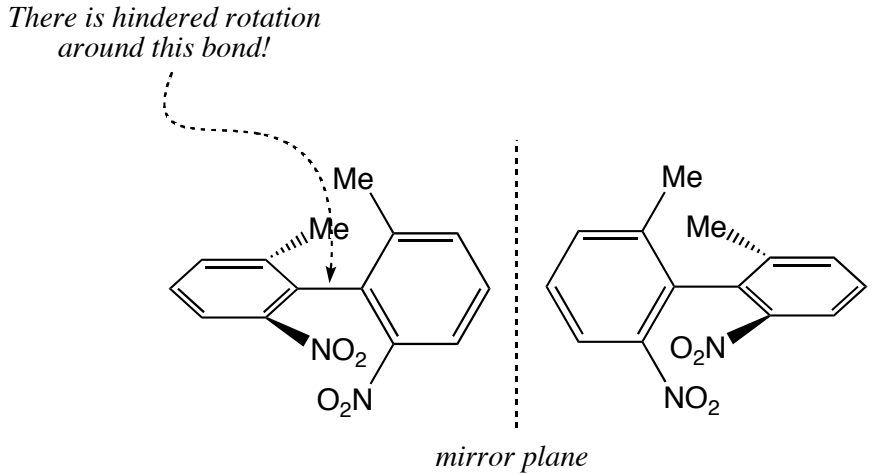


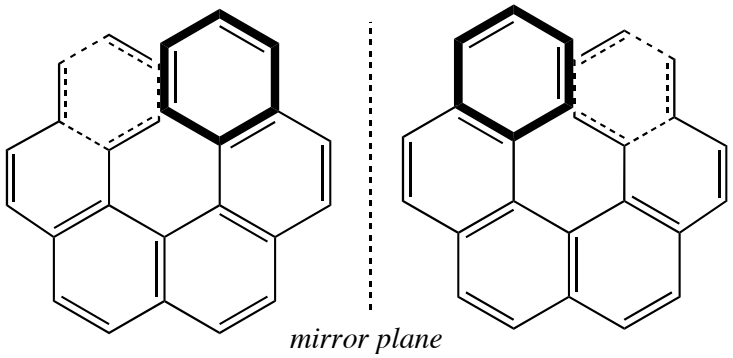
Resolution of Enantiomers



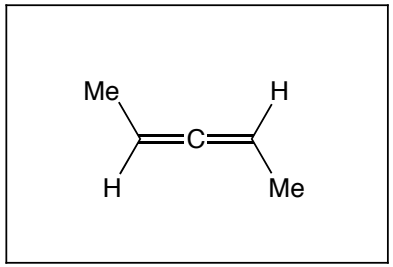
Chirality Without Stereocenters







Chirality Without Stereocenters



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