

## What is Meant by Stereoisomers?

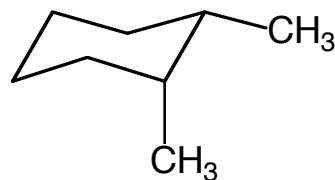
- they are any structure that have the same constitutional structure  
(have the same atoms bonded to the same atoms)  
but are arranged differently in three dimensions

Differ in the ORIENTATION of atoms in space

have already seen this with cis and trans ring structures



trans-dimethylcyclohexane



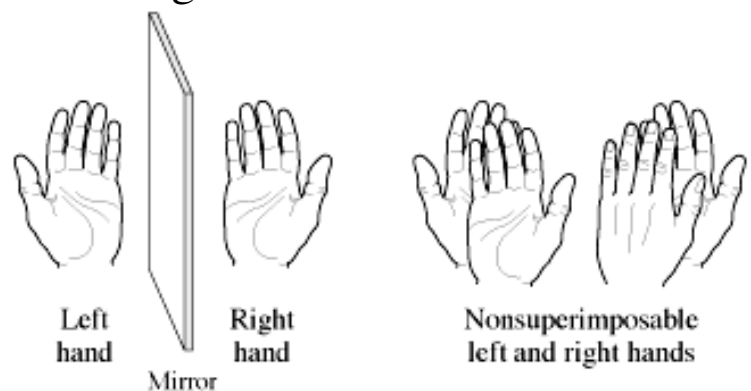
cis-dimethylcyclohexane

this difference in orientation can cause vastly different properties for the molecule

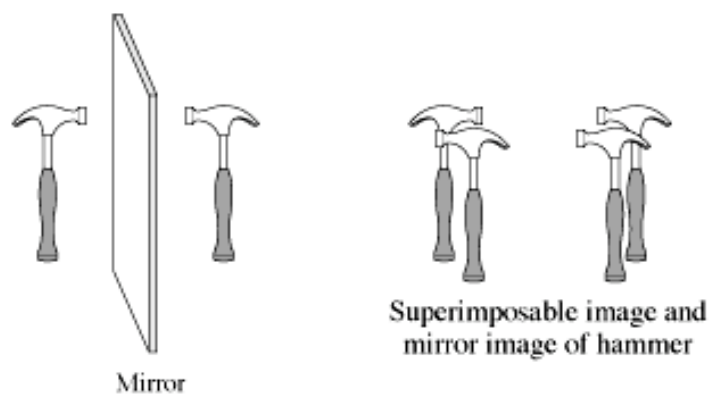
## How Do We Tell if Something is Chiral

chiral object has a mirror image that is different from the original object

mirror image is **NONSUPERIMPOSABLE**



**A**

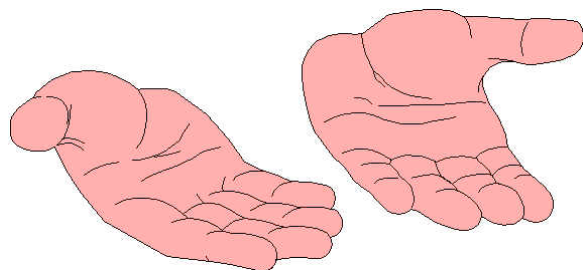


**B**

## Importance of Chirality

When two chiral objects interact a unique shape selectivity occurs  
(we will learn that with chiral organic molecules this leads to ENERGY differences)

Consider a hand and a glove:



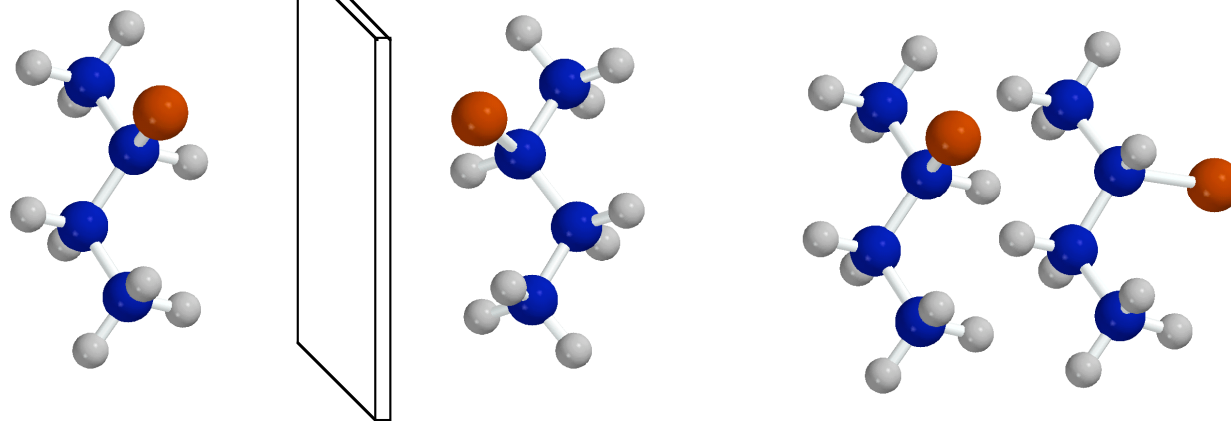
Both are chiral, therefore there is a different energetic fit if the left hand goes into a right-handed glove compared to a right hand

this energetic difference is not present if one of the objects is achiral

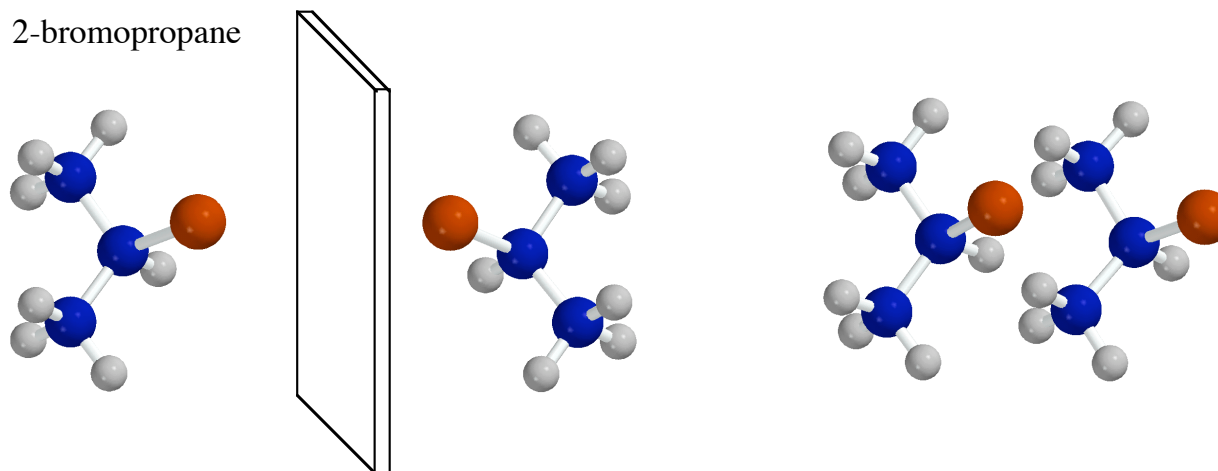
## Molecules can also be Chiral

whenever a molecule cannot be superimposed on its mirror image it is chiral

2-bromobutane



2-bromopropane

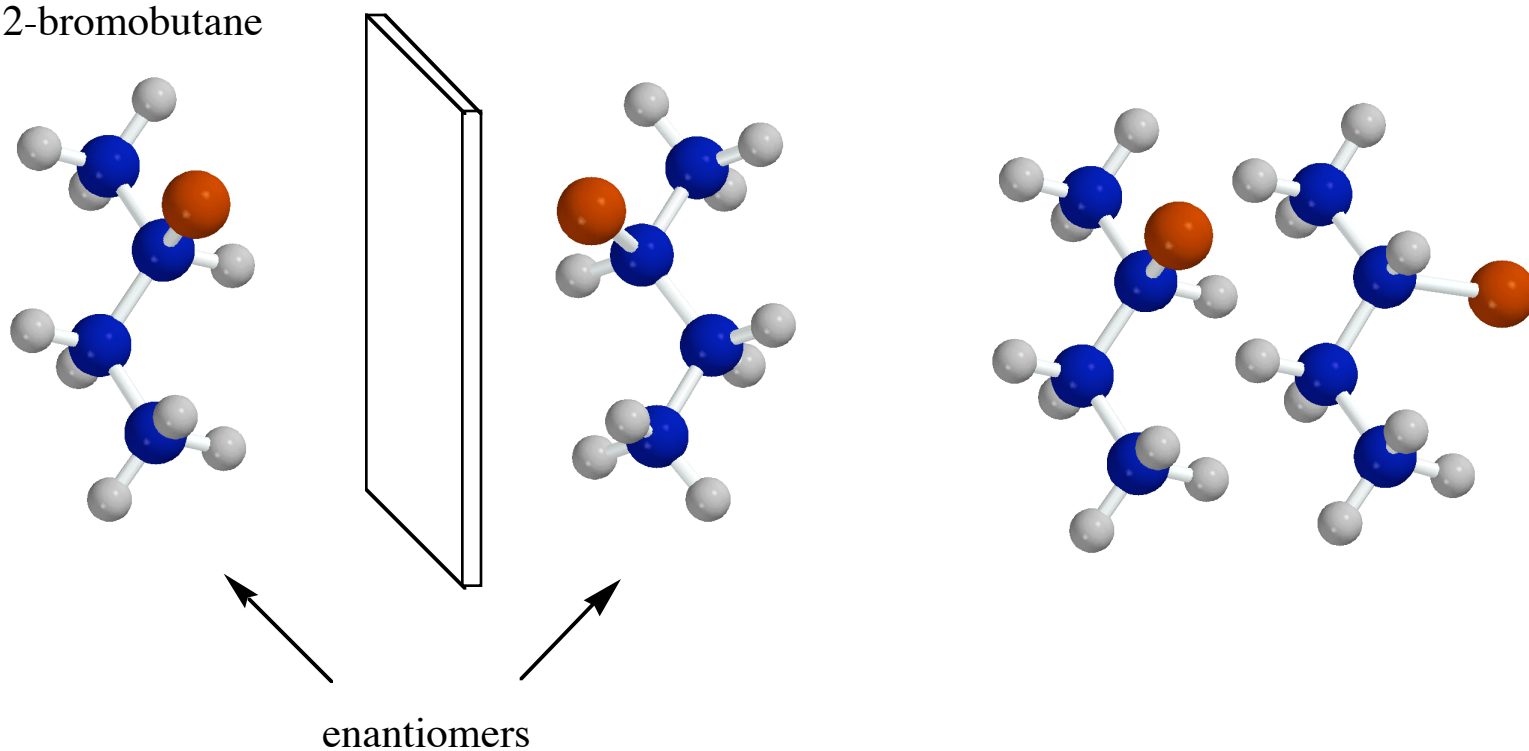


## Definition of Enantiomers

Enantiomers: any nonsuperimposable mirror image molecules

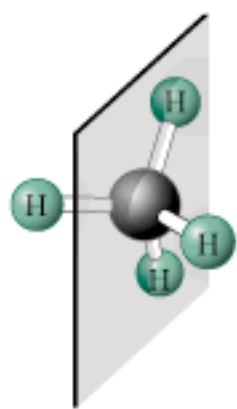
a chiral compound always has an enantiomer

2-bromobutane



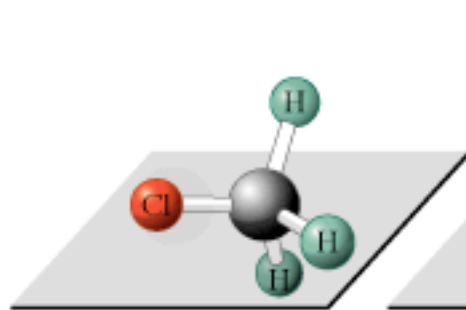
## Ultimately Symmetry Distinguishes Chiral Molecules

a chiral molecule can have no internal planes of symmetry



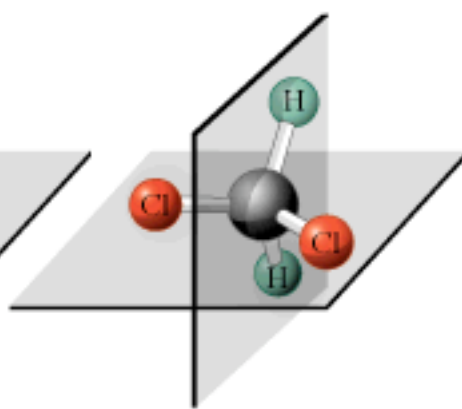
A

methane  
(1 of 4 planes)



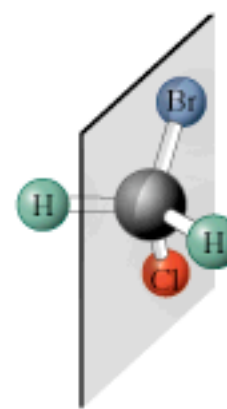
B

chloromethane  
(1 of 3 planes)



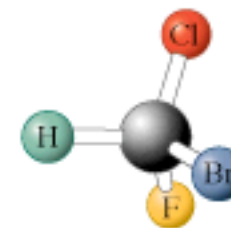
C

dichloromethane



D

bromochloro-  
methane



E

bromochloro-  
fluoromethane

A Chiral Carbon Atom must have FOUR different substituents

in order to have no internal planes of symmetry the four substituents  
on a carbon must be different

therefore a double bonded or triple bonded carbon atom is not chiral  
(2 or 3 substituents must be the same)

if a compound has only one chiral carbon atom, it is chiral

## Nomenclature for Chiral Carbon Atoms

the chiral center is defined as either R- or S-

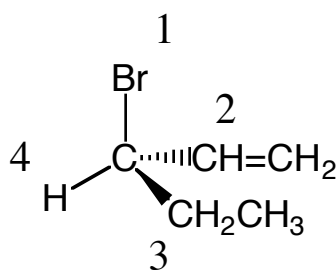
how to name:

1. prioritize atoms bonded to chiral carbon atom.  
the higher the molecular weight the higher the priority

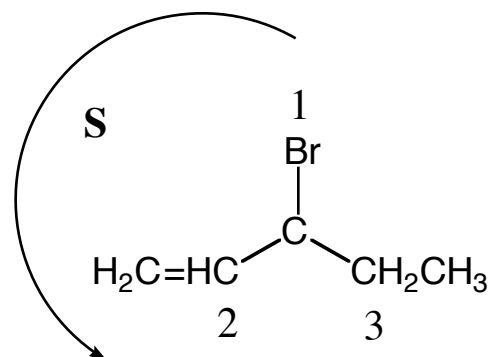
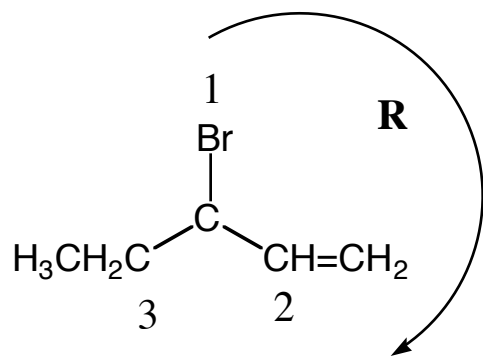
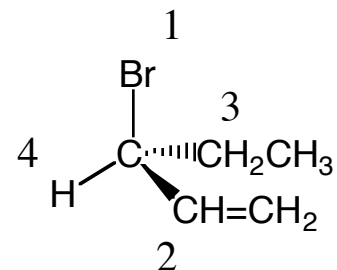
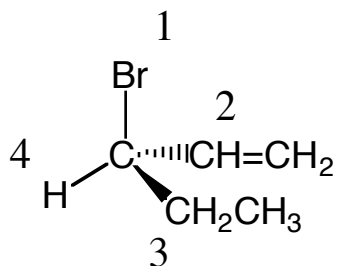
-if two substituents are the same at the initial substitution  
continue until point of difference

\*if both substituents are identical the carbon atom is not chiral!

-treat double and triple bonded species as multiple bond sites to carbon



2. place lowest priority substituent towards the back and draw an arrow from the highest priority towards the second priority



if this arrow is clockwise it is labeled R (Latin, *rectus*, “upright”)

if this arrow is counterclockwise it is labeled S (Latin, *sinister*, “left”)

## Enantiomers have Identical Energies

most typical physical properties are identical  
(melting point, boiling point, etc.)

How can we distinguish enantiomers?

usually to characterize different compounds we would record  
the melting point or boiling point of a pure sample,  
but this does not distinguish enantiomers

one important characteristic - their optical activity is different!

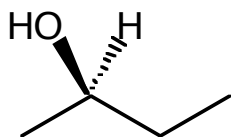
chiral compounds rotate plane polarized light

## Amount of Rotation Distinguishes Compounds

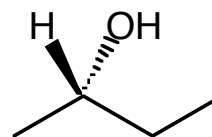
Enantiomeric compounds rotate the plane of polarized light by exactly the same amount,  
but in OPPOSITE directions

a compound will be labeled by its specific rotation

$$[\alpha] = \frac{\alpha(\text{observed})}{c \cdot l}$$

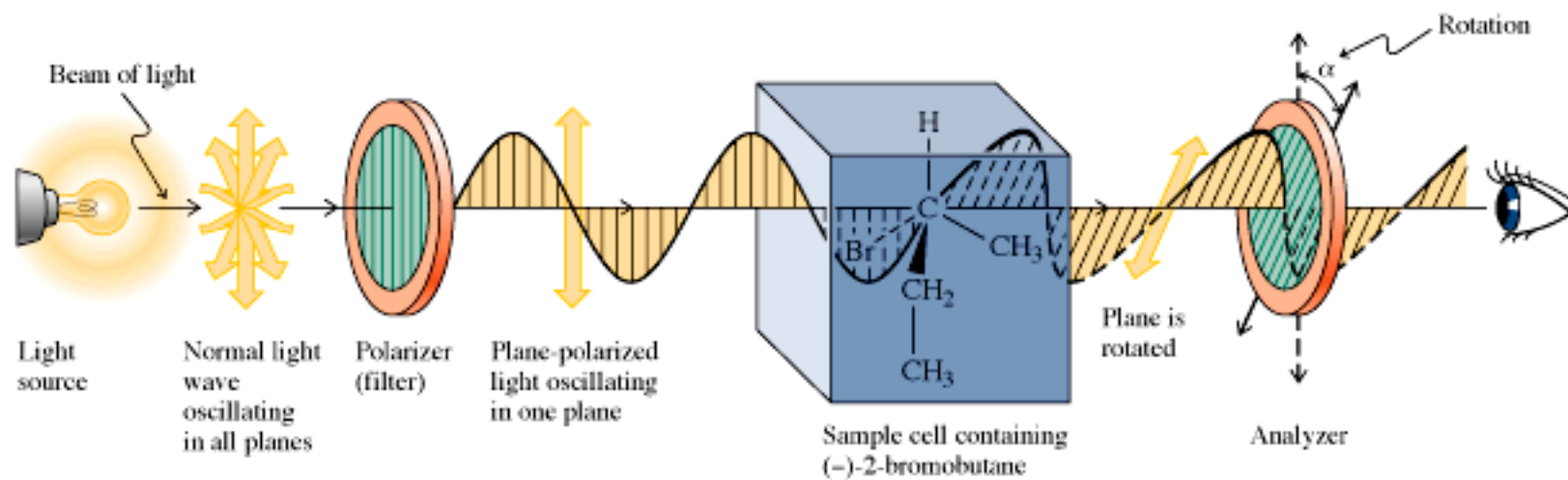


(R)-2-butanol  $-13.5^\circ$



(S)-2-butanol  $+13.5^\circ$

## Diagram for a Polarimeter



chiral compounds will rotate polarized light

## Few Chiral Compounds are Obtained in Only One Enantiomeric Form

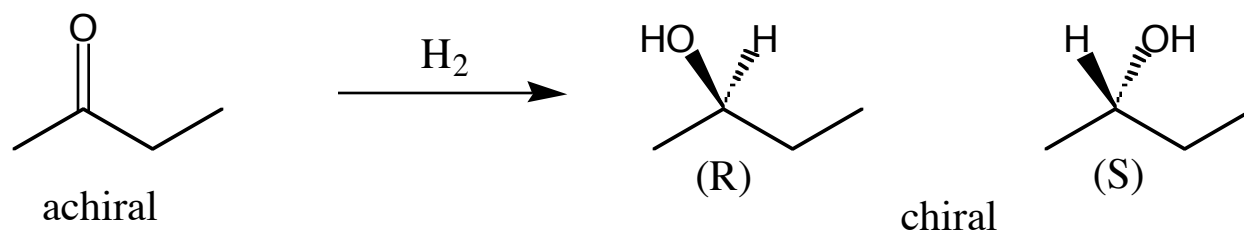
A solution of a chiral molecule might contain a majority of one enantiomer but a small fraction of the opposite enantiomer

if there are equal amounts of both enantiomers present  
it is called a RACEMIC mixture (or RACEMATE)

the optical rotation will be zero  
(since each enantiomer has opposite optical rotation)

A racemate can be formed in two ways:

1. add equal amounts of each pure enantiomer (hard)
2. react an achiral molecule to generate a chiral center using only achiral reagents



## Enantiomeric Excess (or optical purity)

for other cases where there is an abundance of one enantiomer relative to the other the compound is quantified by its enantiomeric excess (e.e.)

the enantiomeric purity is defined by this e.e.

$$\frac{R - S}{R + S} \times 100\% = \text{e.e.}$$

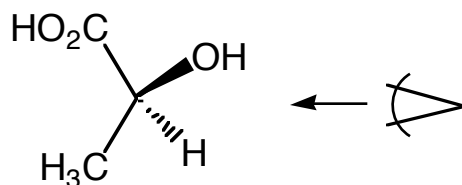
therefore if a given solution has 70% of one enantiomer (say R) and 30% of the other enantiomer (S) then the enantiomer excess (e.e.) is 40%

$$[(70-30) / (70+30)](100\%) = 40\%$$

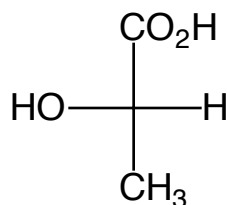
Another convenient way to represent stereochemistry is with a Fischer projection

to draw:

1. Draw molecule with extended carbon chain in continuous trans conformation
2. Orient the molecule so the substituents are directed toward the viewer

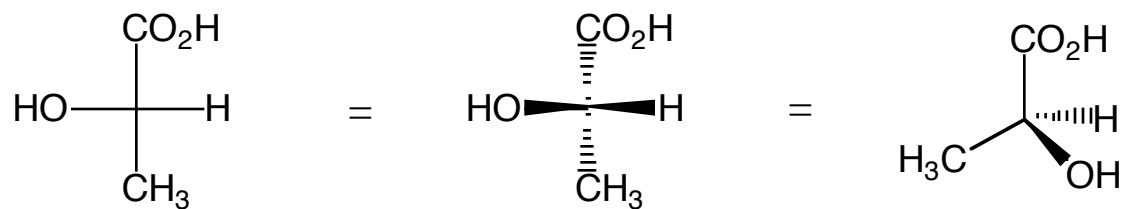


3. Draw molecule as flat with substituents as crosses off the main chain



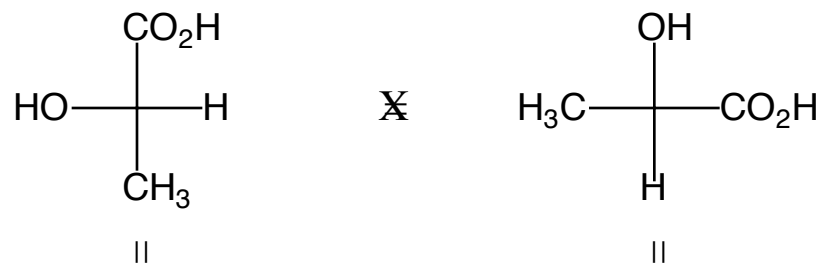
## Important Points:

- crosses are always pointing out of the paper
- extended chain is directed away from the paper

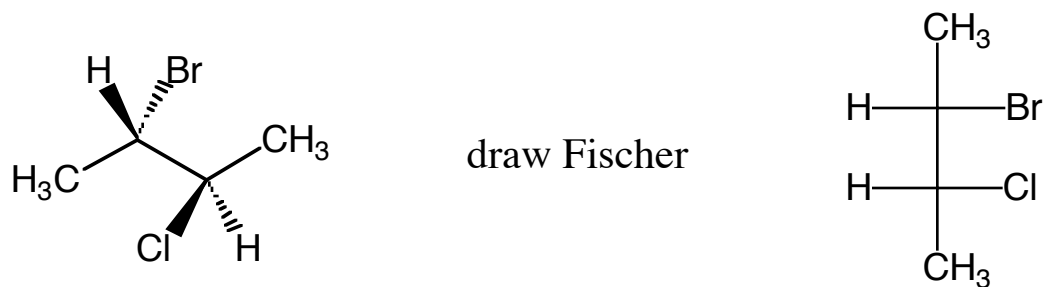


## Rotation of Fischer Projections

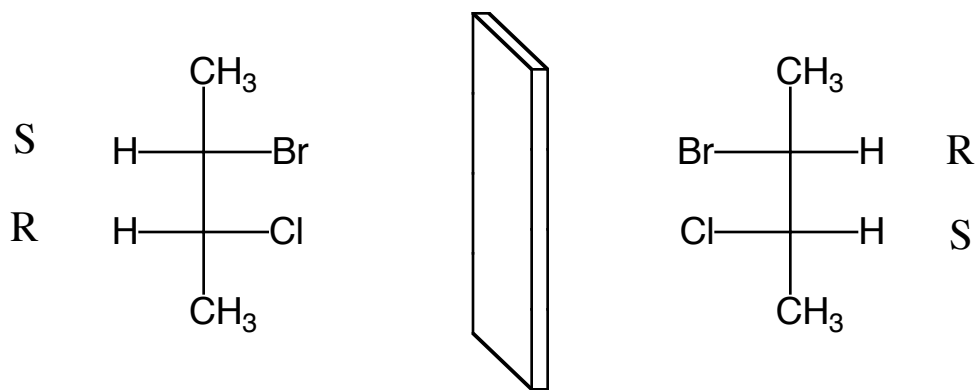
a Fischer projection can be rotated 180°, but NOT 90°



What occurs with more than 1 stereocenter

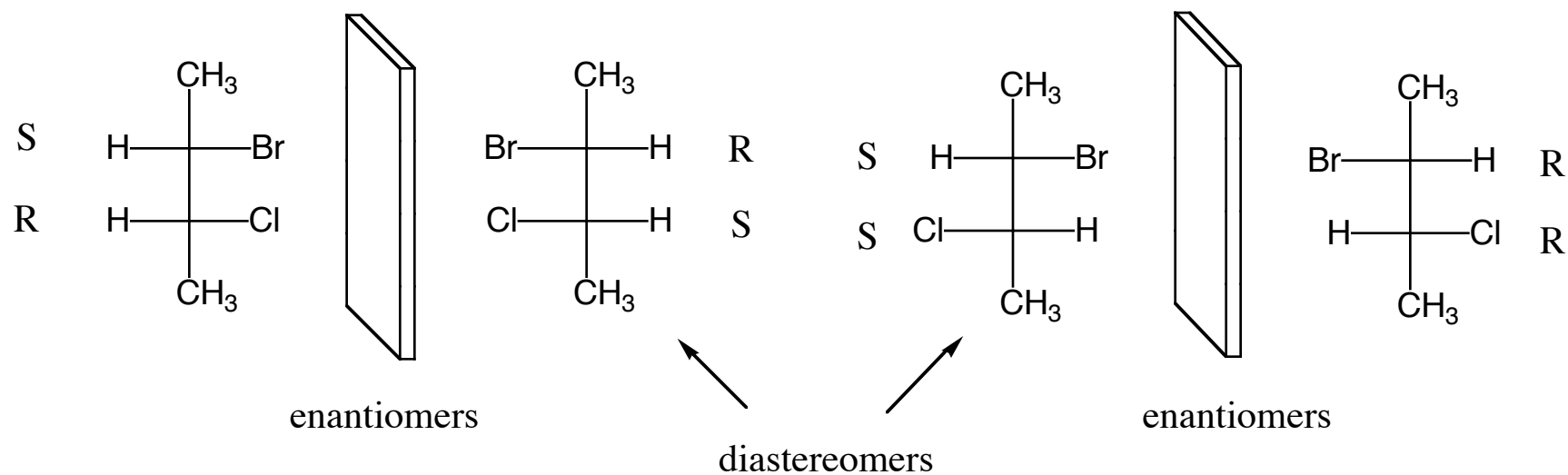


an enantiomer is easily seen with a Fischer projection



With n Stereocenters there are a possible  $2^n$  Stereoisomers

therefore with two stereocenters there are a possible four stereoisomers



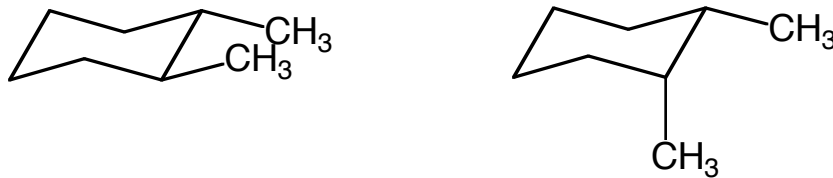
## Diastereomers

- any stereoisomer that is not an enantiomer

therefore the two stereoisomers are not mirror images

enantiomers: mirror image structures that are not superimposable

already saw diastereomers with chair stereoisomers



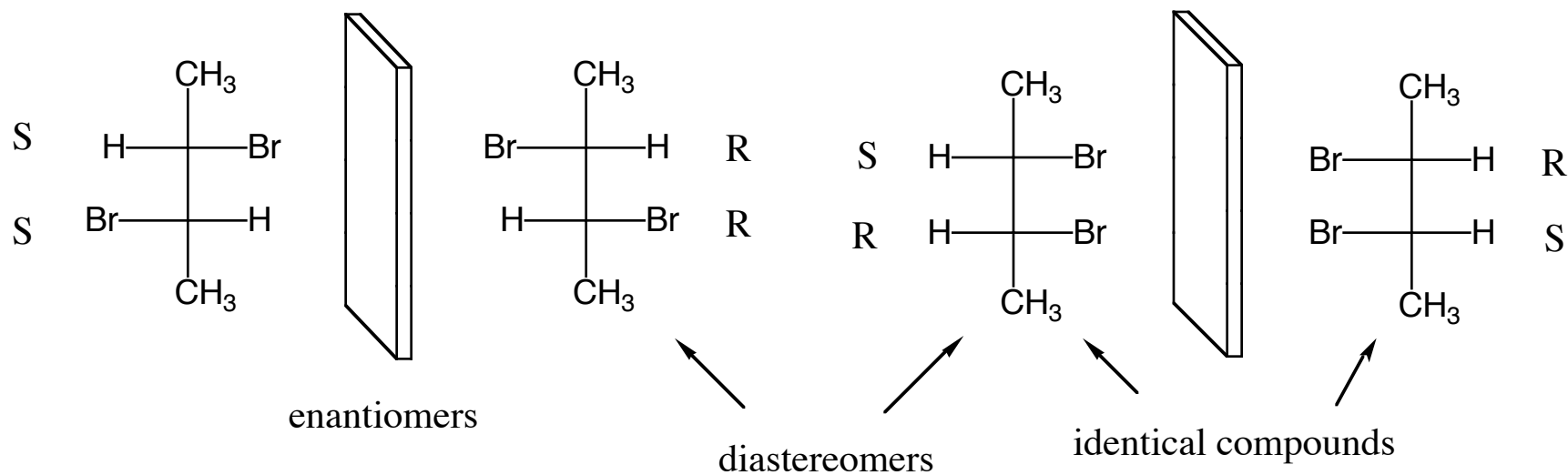
stereoisomers, but not mirror images

therefore diastereomers

# Meso Compounds

sometimes there are compounds that are achiral but have chiral carbon atoms  
(called MESO compounds)

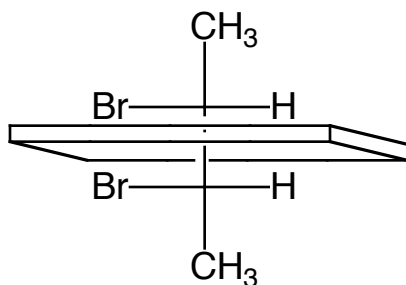
maximum possible  $2^n$  stereoisomers



the meso compounds are identical (therefore not stereoisomers)

this structure has three stereoisomers

meso compounds are generally a result of an internal plane of symmetry between two  
(or more symmetrically disposed) chiral centers

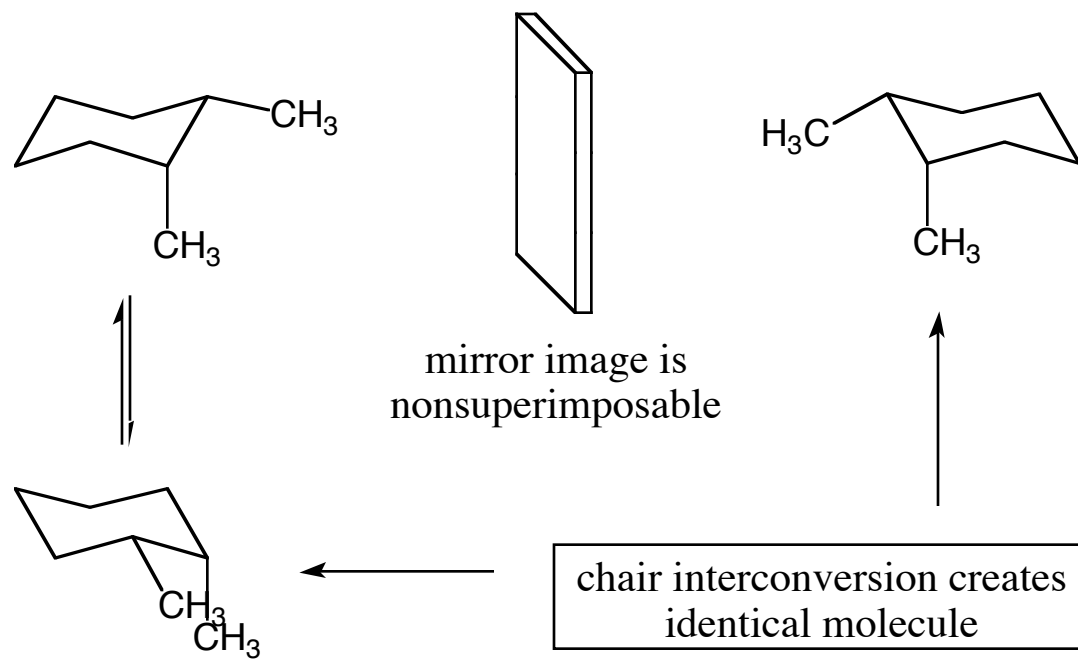


2,3-(2R, 3S)dibromobutane has an  
internal plane of symmetry as shown

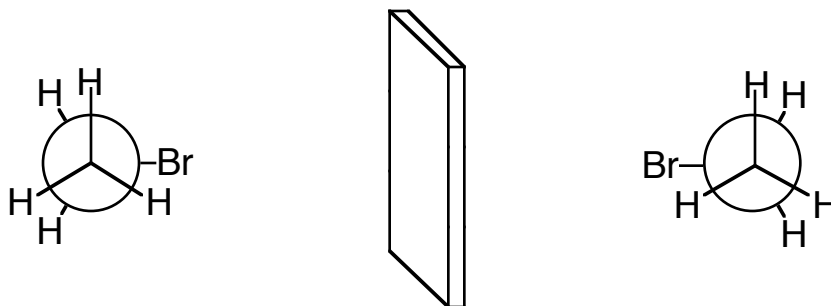
## Chirality of Conformationally Flexible Molecules

a molecule **CANNOT** be optically active if its chiral conformations  
are in equilibrium with their mirror images

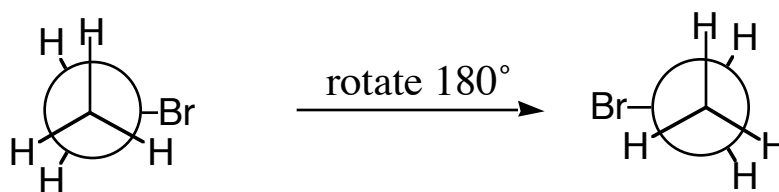
remember the chair-chair interconversion



therefore: if a mirror image is conformationally accessible then the molecule is not chiral



there two frozen snapshots are not superimposable

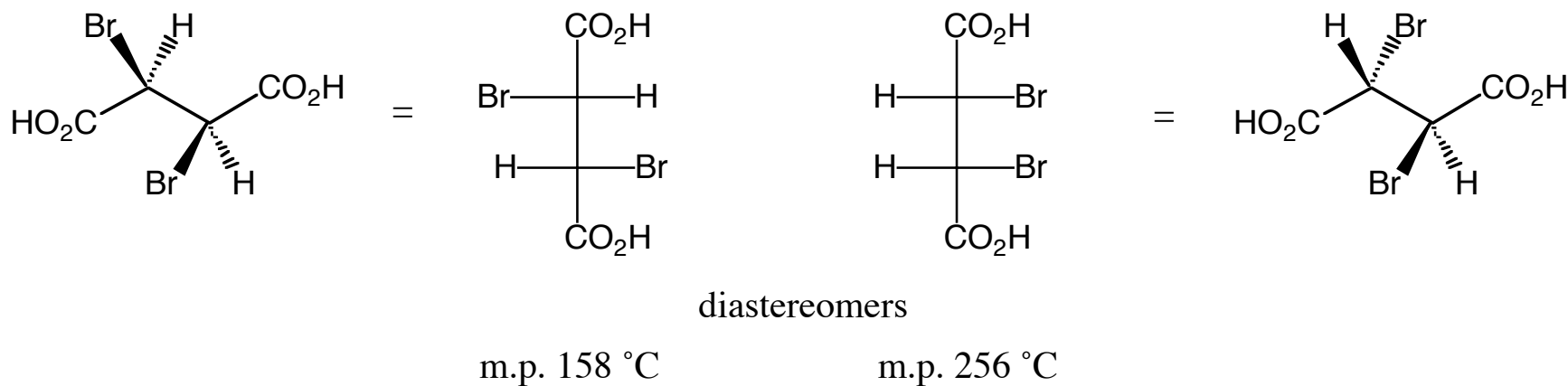


we can rotate one however so it is identical to the mirror image

## Energy Differences

remember enantiomers have the same energy value

diastereomers can have vastly different energies



therefore separation of diastereomers is easier

## How can Enantiomers be Separated?

optical rotation can distinguish between two enantiomers

- it does not separate enantiomers

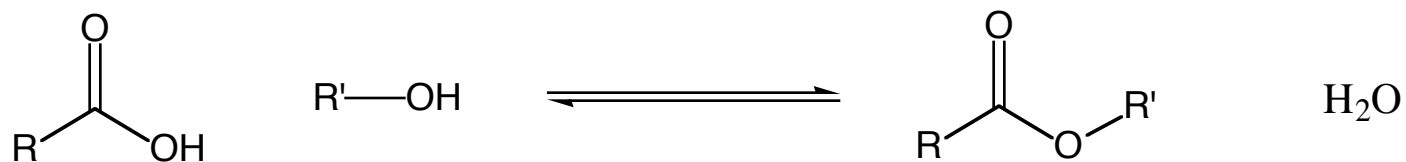
need a way to change the relative energies of the enantiomers

(if the energy of the two remain the same separation becomes nearly impossible)

## Resolution of Enantiomers

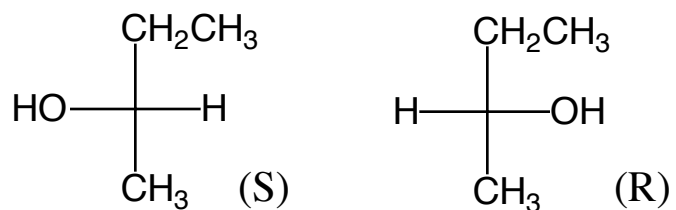
to “resolve” (separate) the enantiomers can be reacted to form diastereomers  
(which have different energies!)

can reversibly create an ester from an alcohol and an acid



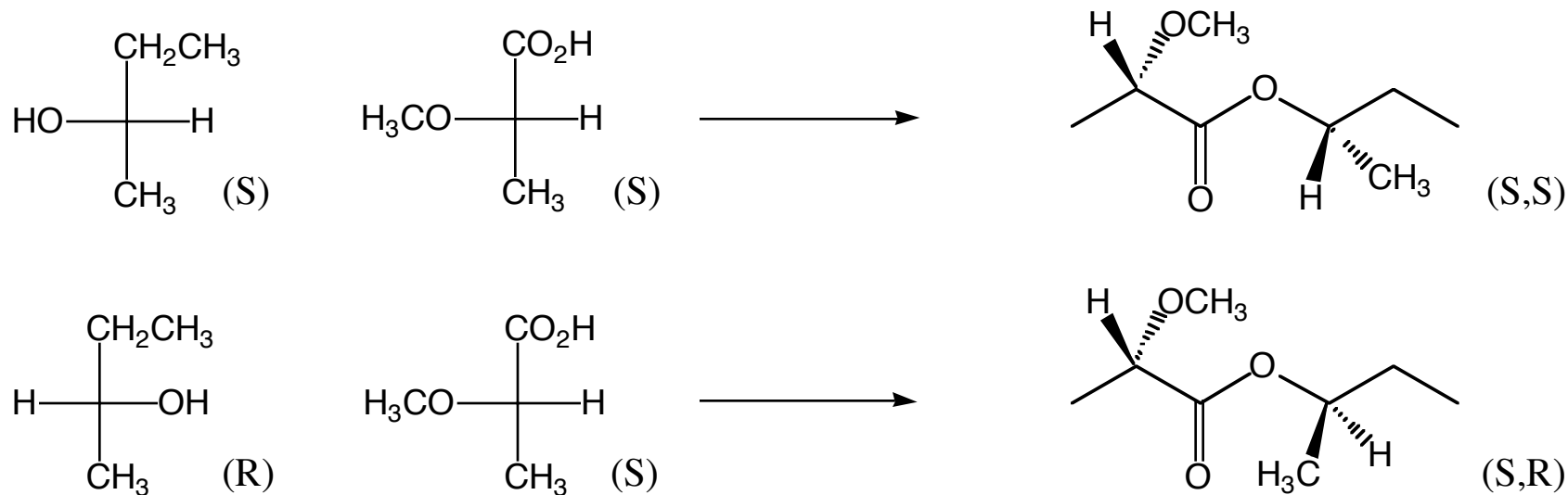
using this fact we can create diastereomers in order to separate

consider 2-butanol



enantiomers have  
same energy

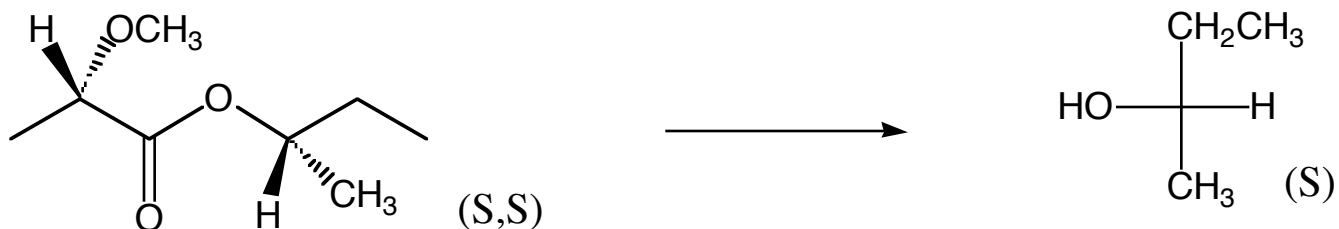
the two enantiomers can be reacted with a chiral acid



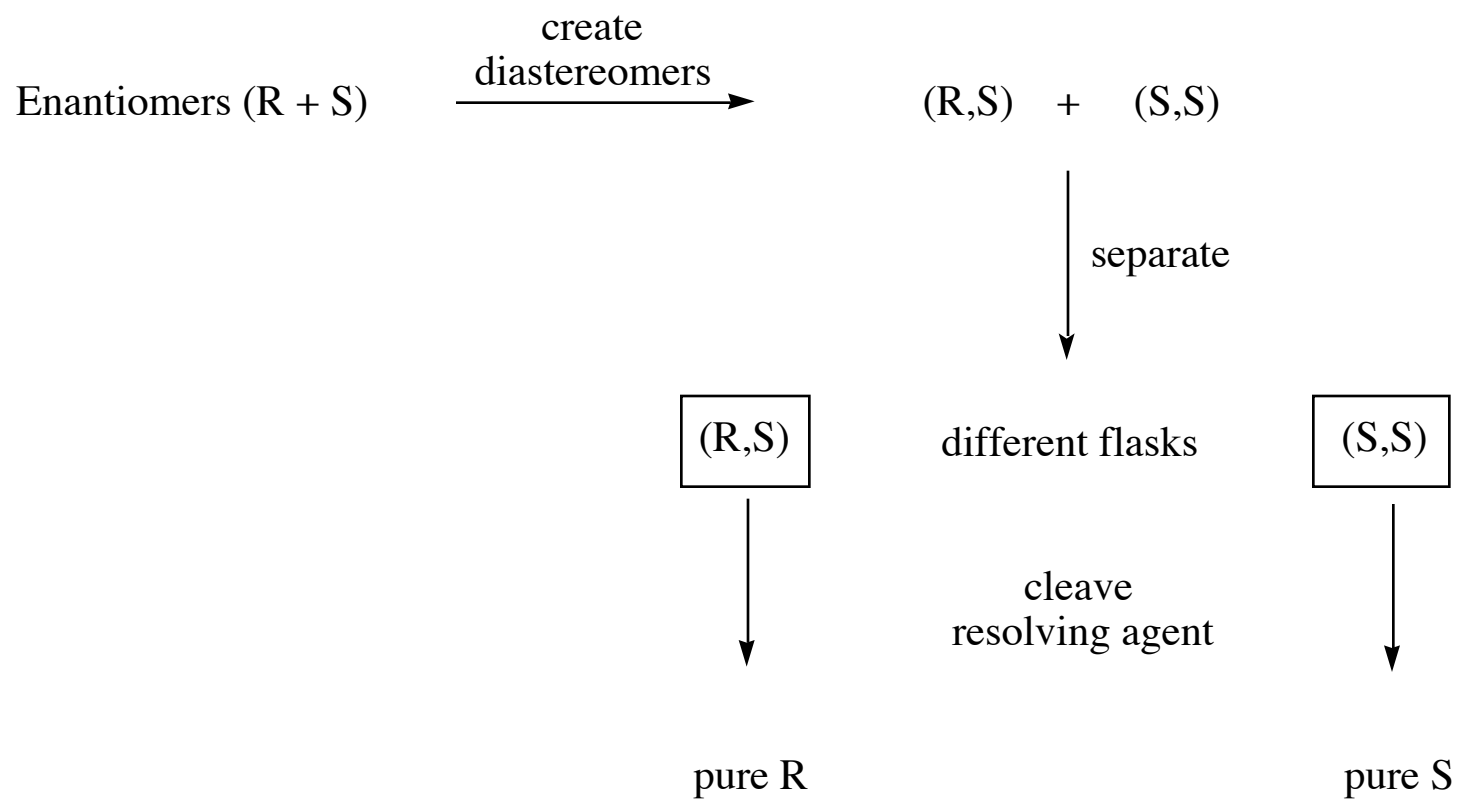
this generates **DIASTEREOMERIC** esters

-the two diastereomers can now be separated due to their energy differences

once separated the alcohol can be obtained in pure form



## Overall Scheme for Resolving Enantiomers



## Importance of Chirality

Remember that two enantiomers have the same physical properties, but when two enantiomers interact with another chiral object distinct energetic interactions occur (a diastereomeric interaction occurs)

-same consideration as when a left or right hand is inserted into a baseball glove, the hands and the glove are chiral - hence an energy difference occurs

In biological interactions often an organic molecule will interact with a receptor. The receptors are often proteins which are chiral (are made from chiral building blocks,  $\alpha$ -amino acids, and form a chiral three dimensional shape)

If the organic molecule interacting with the protein is also chiral, then there will be an energy difference depending upon which enantiomer is interacting with the protein

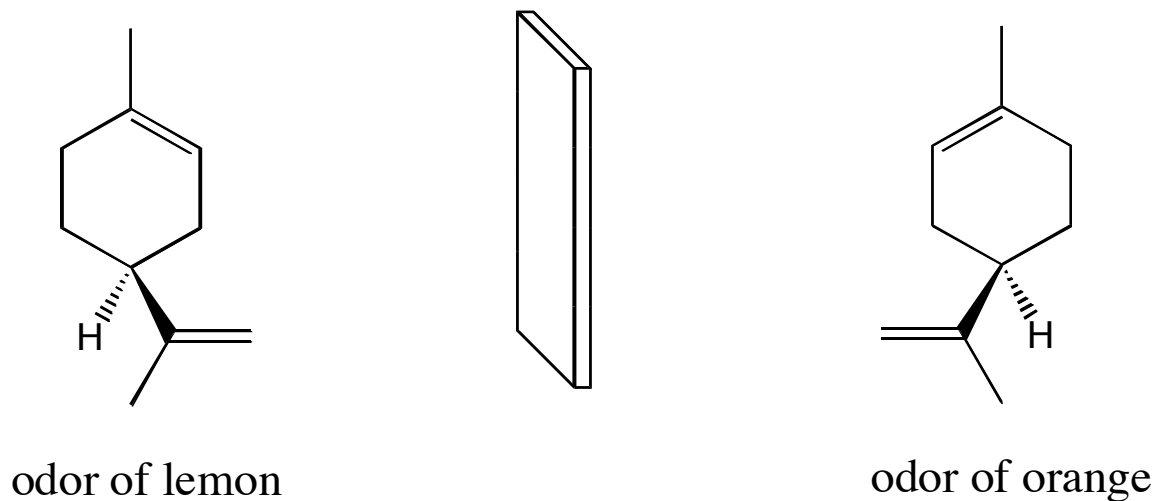
## Consequence of Diastereomeric Interactions

These stereochemical interactions lead to potentially vastly different properties

Some Examples: Smell

Our brain interprets a smell if the object in question binds with a receptor

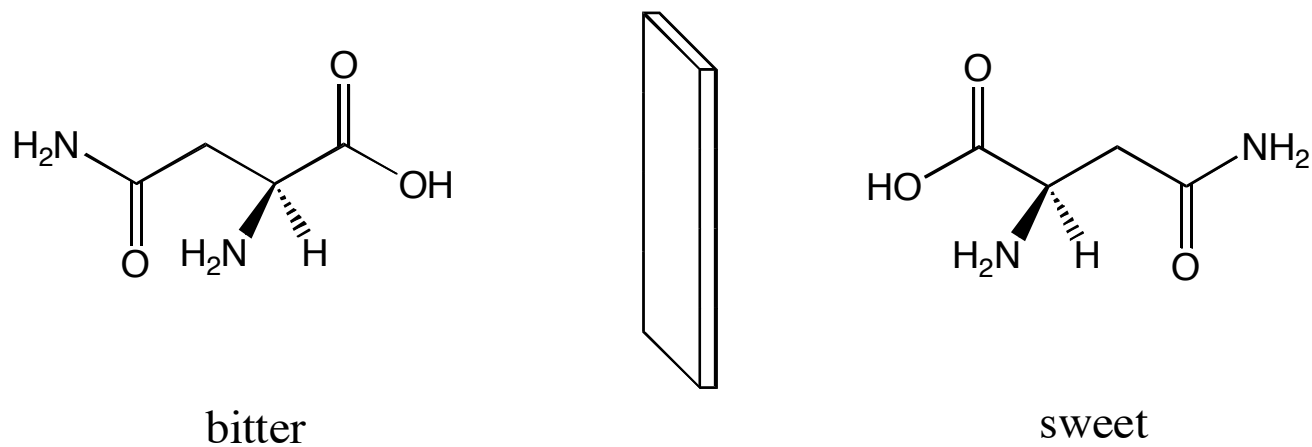
Two enantiomers of Limonene



# Taste

Taste is also interpreted when an molecule interacts with a receptor

Consider two enantiomers of Asparagine

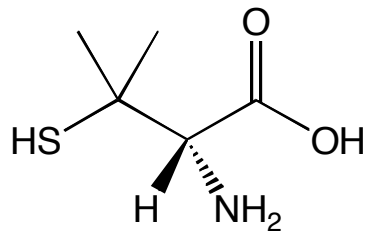


## Drug Interactions

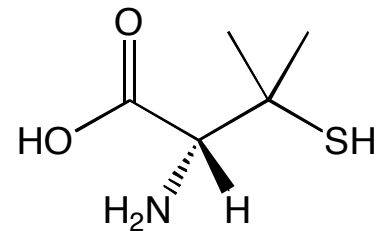
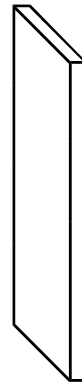
A potentially more serious consequence of chirality is the interaction of drugs  
Drugs are often chiral and they interact with a chiral protein receptor in the body

Enantiomers, therefore, have different physiological responses

Penicillamine



antiarthritic

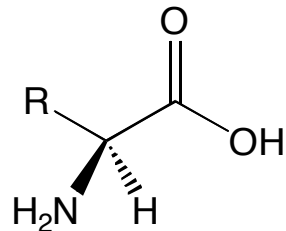


toxic

## Chirality of Proteins

Proteins are biopolymers of  $\alpha$ -amino acids

There are 20 natural  $\alpha$ -amino acids which are used to make proteins  
-of these amino acids, 19 are chiral



glycine has R=H

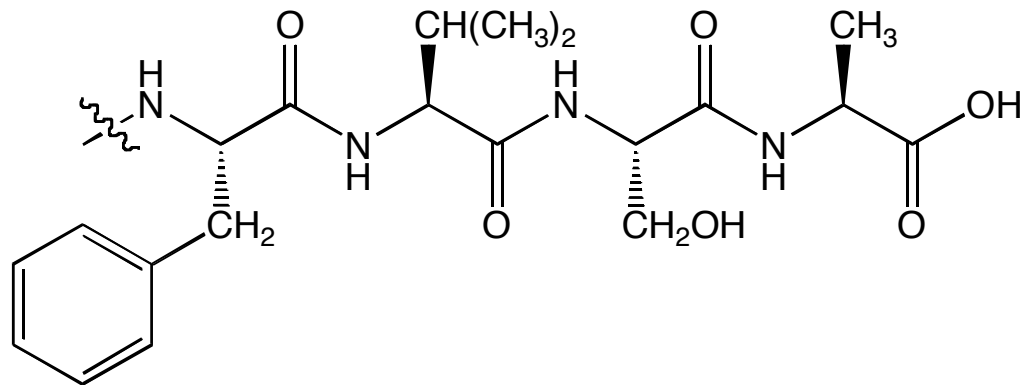
$\alpha$ -amino acids

natural chiral amino acids have an (S) designation

\*except for cysteine - due to sulfur atom

compare 3-dimensional structures

Proteins are polymers of these amino acid building parts



short peptide section

the chiral building blocks make a chiral environment

when chiral molecules interact with the peptide,  
one enantiomer can have a different energetic interaction

What would happen if the protein was made with a different chirality of amino acids?