

# CH103: Introductory Chemistry

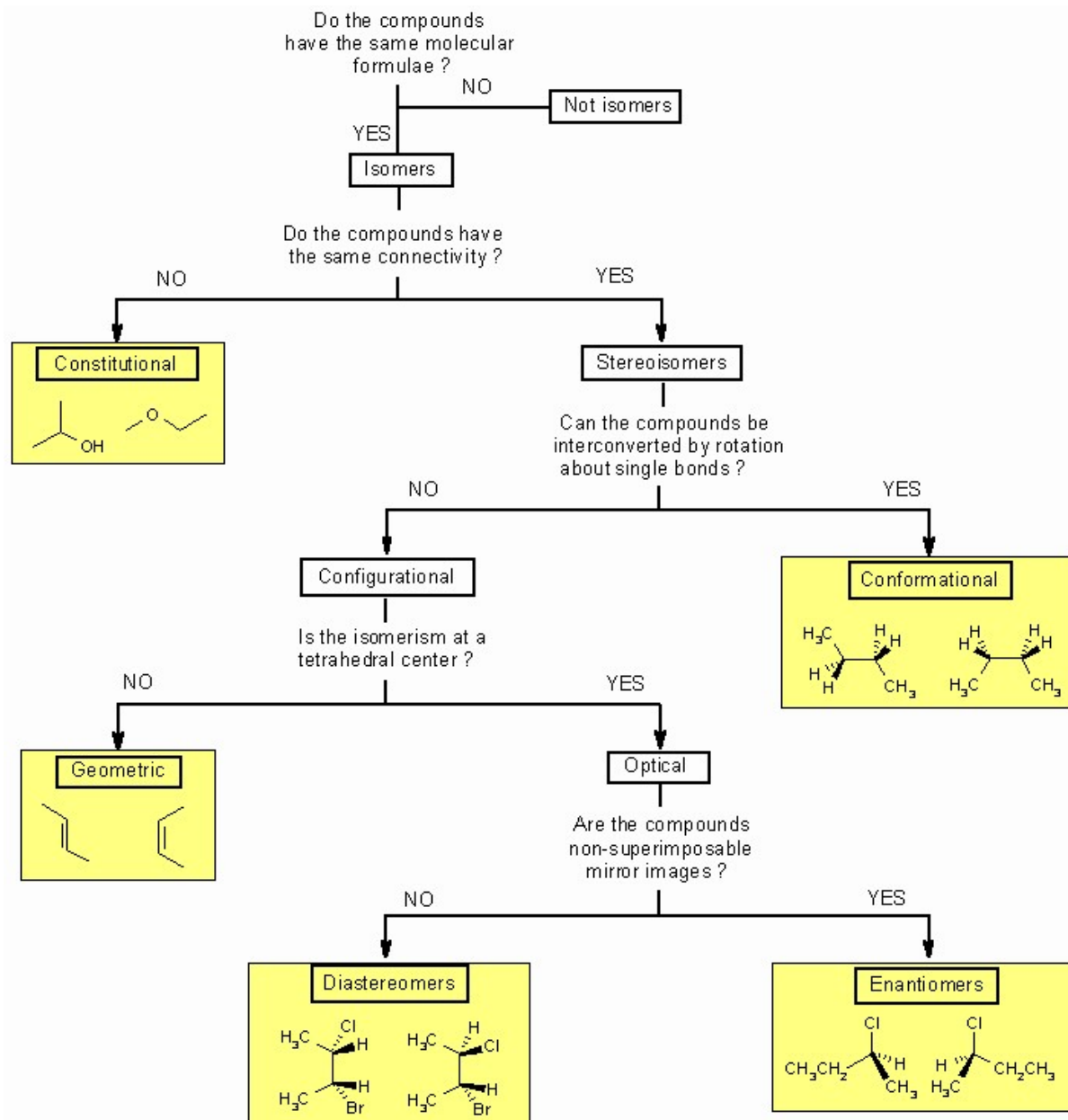


## Stereochemistry

# Stereochemistry

- Stereochemistry refers to the 3-dimensional properties and reactions of molecules. It has its own language and terms that need to be learned in order to fully communicate and understand the concepts.

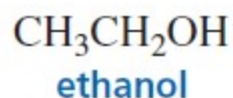
# Stereochemistry



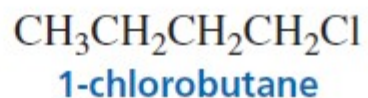
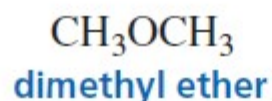
# Constitutional isomers

- Same Molecular formula
- Differ in the way their atoms are connected

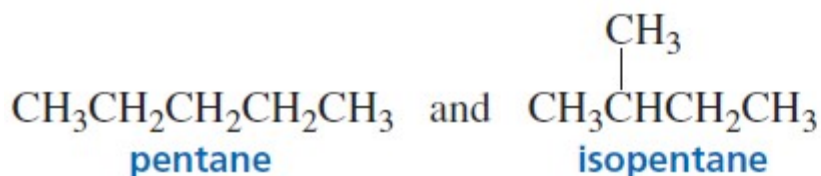
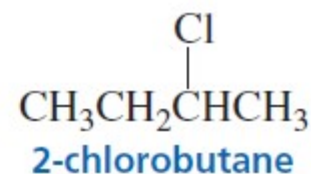
constitutional isomers



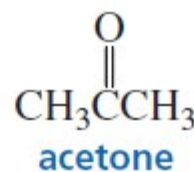
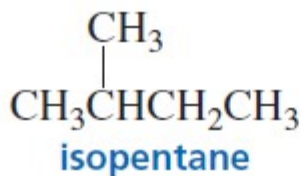
and



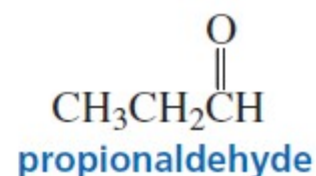
and



and

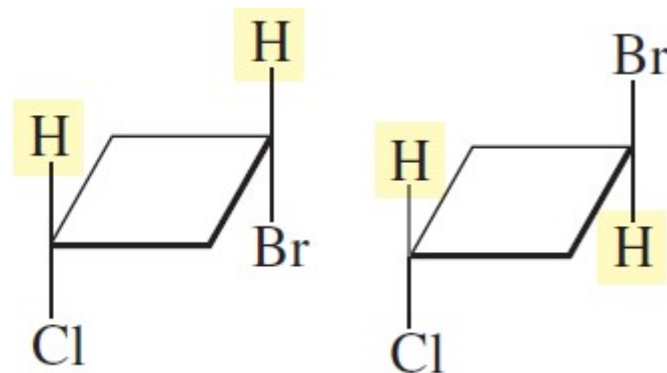
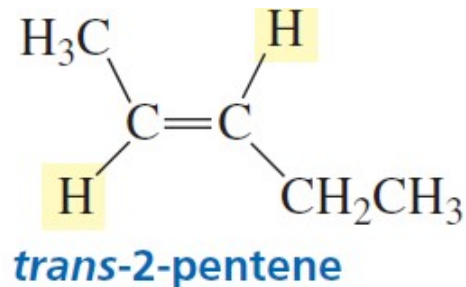
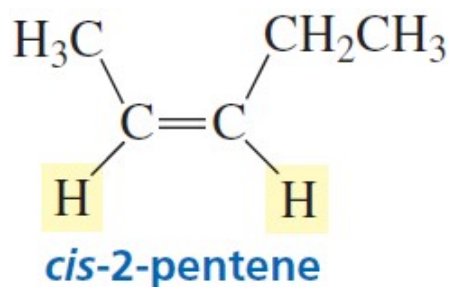


and



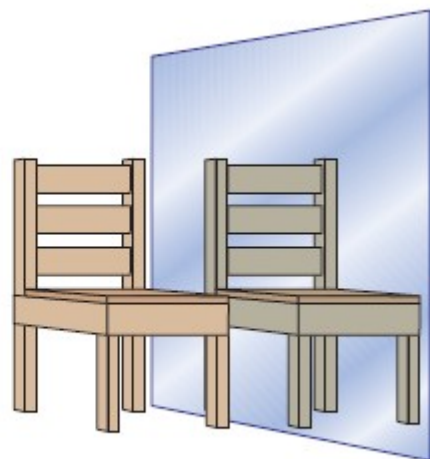
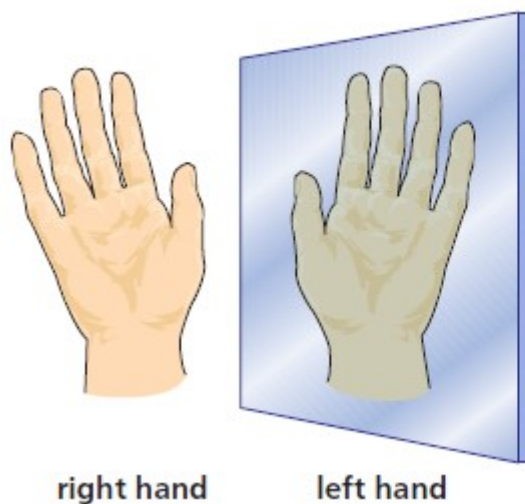
# Stereoisomers

- The atoms in stereoisomers are connected in the same way
  - Configurational Isomers
    - **Cis–Trans Isomers:** result from restricted rotation
      - restricted rotation about a carbon–carbon double bond
      - Cyclic compounds



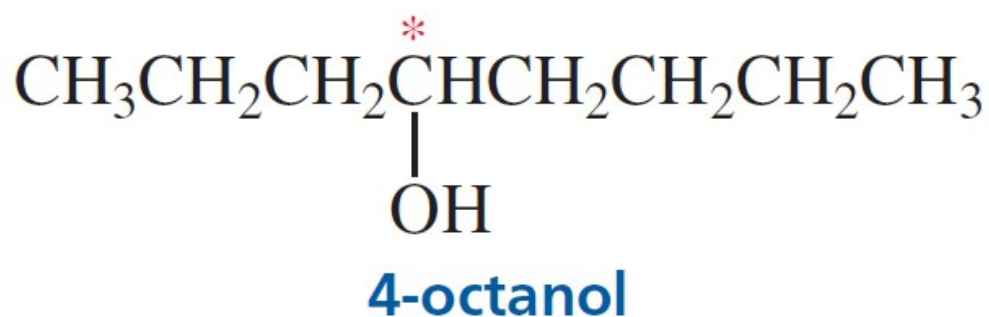
# Optical isomers

- **Chirality:**
- A **chiral** object has a nonsuperimposable mirror image
- An **achiral** object has a superimposable mirror image



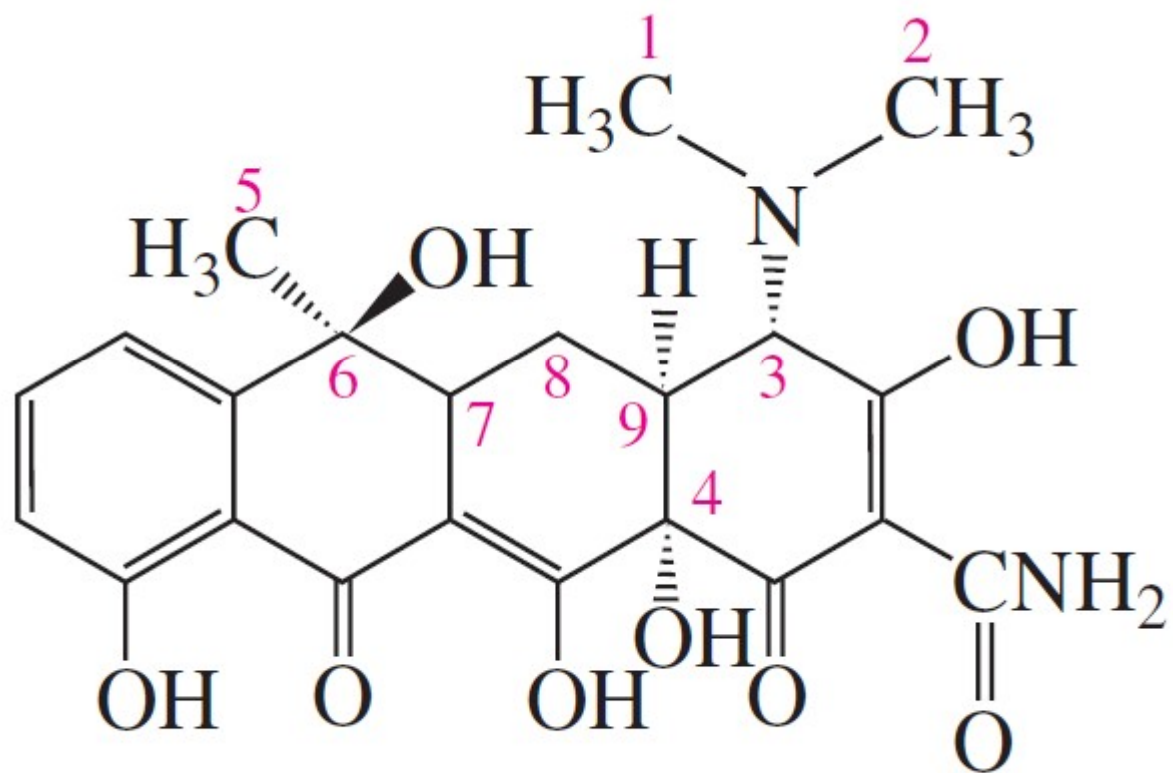
# Optical isomers

- **Chirality in molecules:**
- An **asymmetric carbon**: carbon atom that is bonded to four different groups



- $sp^2$  and  $sp$  hybridized carbons cannot be asymmetric carbons

# Optical isomers

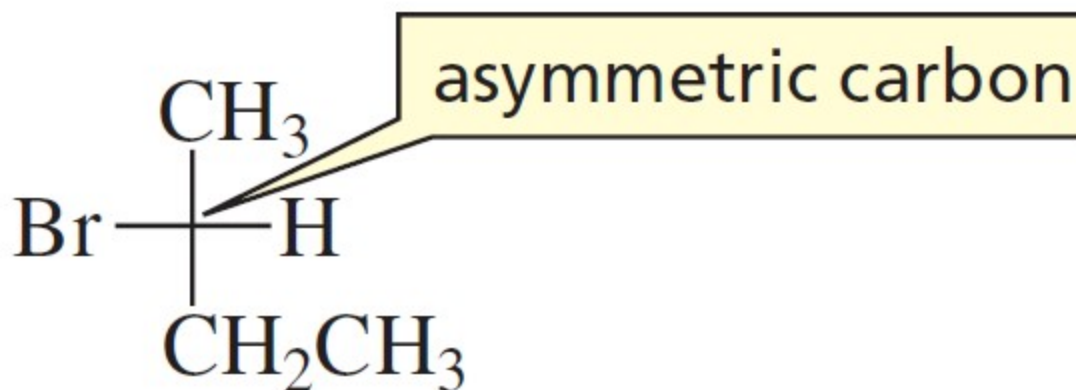
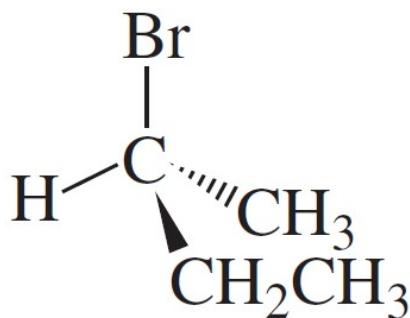


tetracycline



# Enantiomers

- **Enantiomers** – stereoisomers that are non-superimposable mirror image molecules; only properties that differ are direction (+ or -) of optical rotation
- **Drawing Enantiomers:**
  - **Perspective formulas** and **Fischer projections**



# Definitions

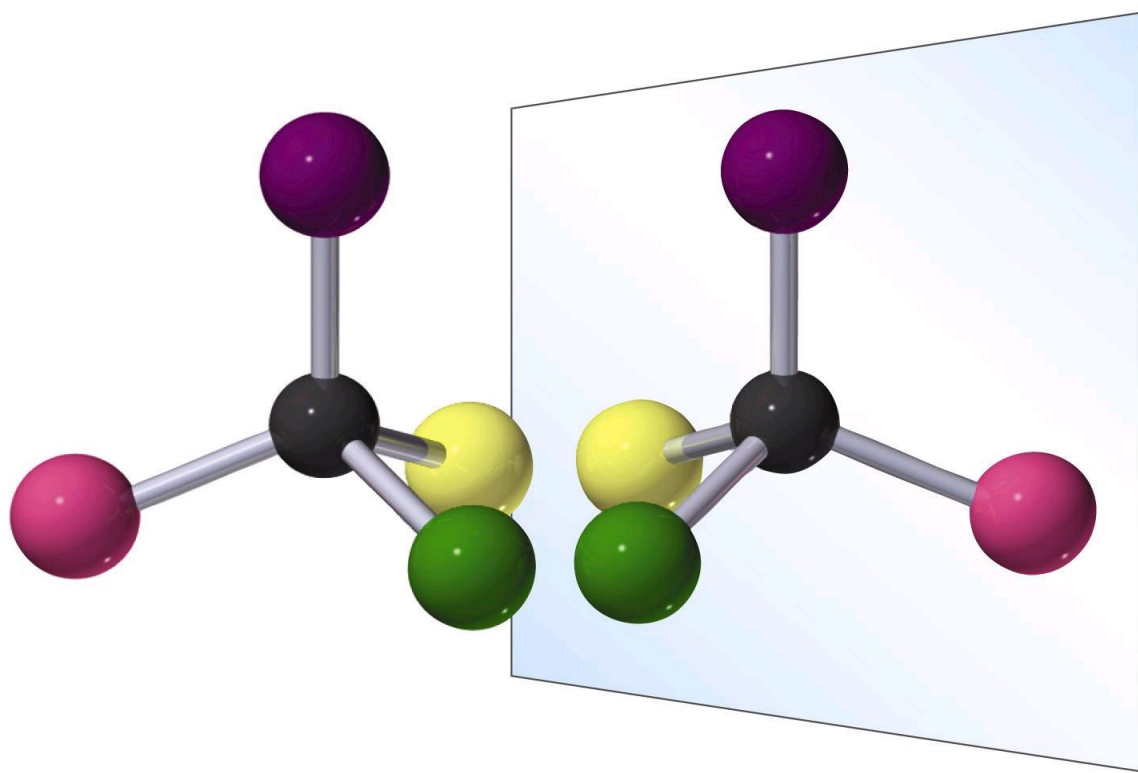
- **Stereoisomers** – compounds with the same connectivity, different arrangement in space
- **Enantiomers** – stereoisomers that are non-superimposable mirror images; only properties that differ are direction (+ or -) of optical rotation
- **Diastereomers** – stereoisomers that are not mirror images; different compounds with different physical properties

## More Definitions

- **Asymmetric center** –  $sp^3$  carbon with 4 different groups attached
- **Optical activity** – the ability to rotate the plane of plane –polarized light
- **Chiral compound** – a compound that is optically active (**achiral compound** will not rotate light)
- **Polarimeter** – device that measures the optical rotation of the chiral compound

# Chirality Center

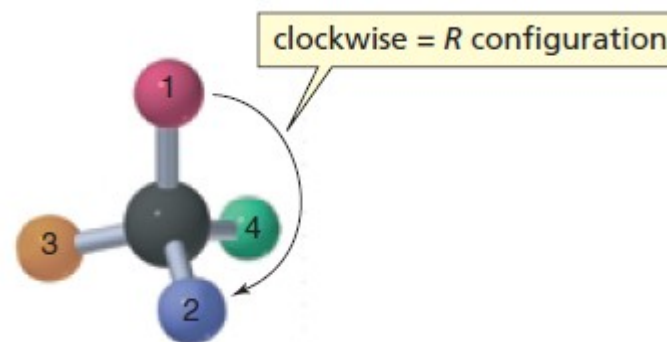
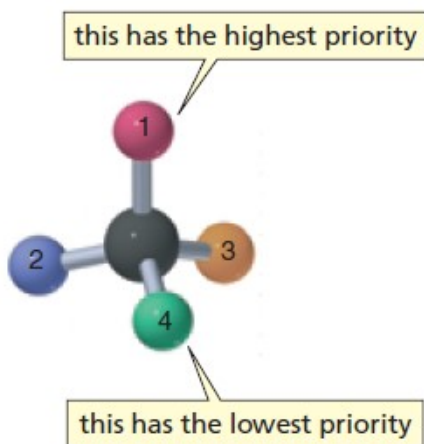
Carbon has four different groups attached



nonsuperimposable  
mirror images

# Naming Enantiomers

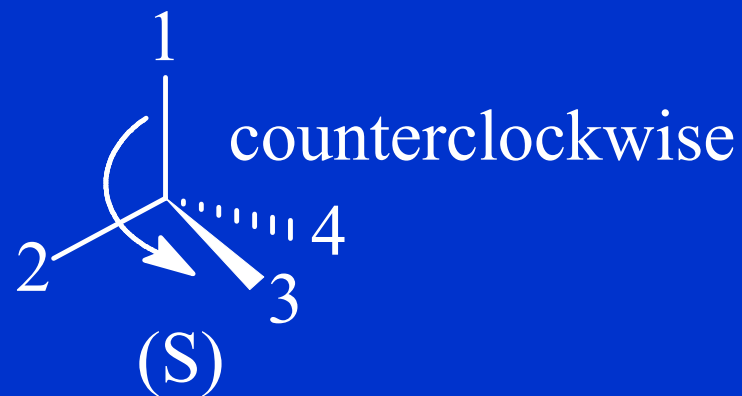
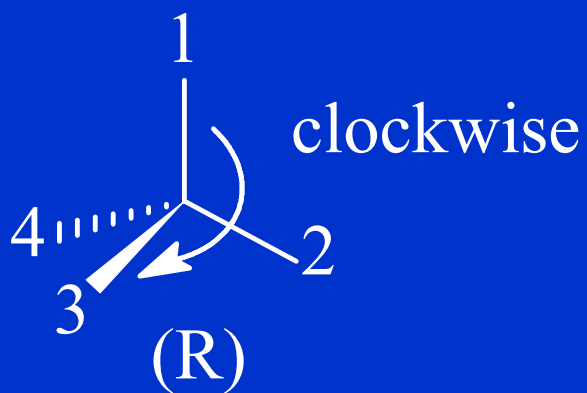
- **R,S** System of Nomenclature:
  1. Rank the groups (or atoms) bonded to the asymmetric carbon in order of priority
  2. Orient the molecule so that the group (or atom) with the **lowest priority (4) is directed away from you**. Then draw an imaginary arrow from the group (or atom) with the highest priority (1) to the group (or atom) with the next highest priority (2).



# Absolute Configuration

Use Cahn, Ingold, Prelog priorities

Place the lowest priority group back  
(focus down C - 4 bond)  
draw arrow from 1-2-3



# CIP Priority Rules

- Higher atomic number precedes lower
  - S>F>O>N>C>H
- Higher atomic mass precedes lower
  - T>D>H
- Cis precedes Trans and R precedes S

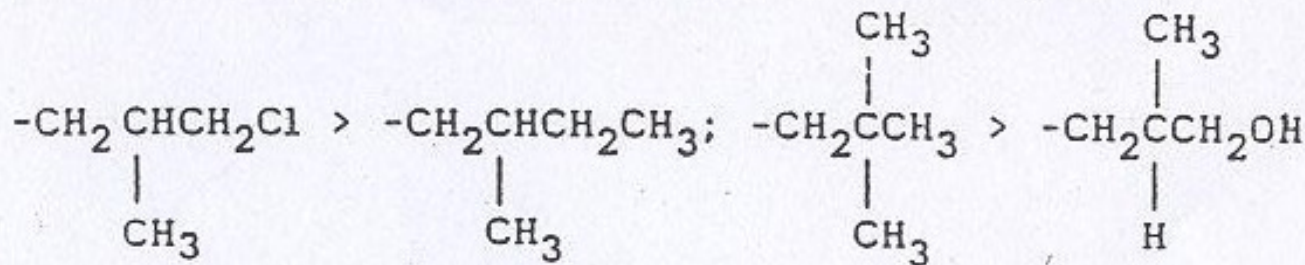
# CIP Priority Rules

- Atoms directly attached to the central chiral atom must be sequenced first



(Decision is reached at the italicised atoms)

- In case a ligand bifurcates, one must proceed along the branch providing the highest precedence until a difference is



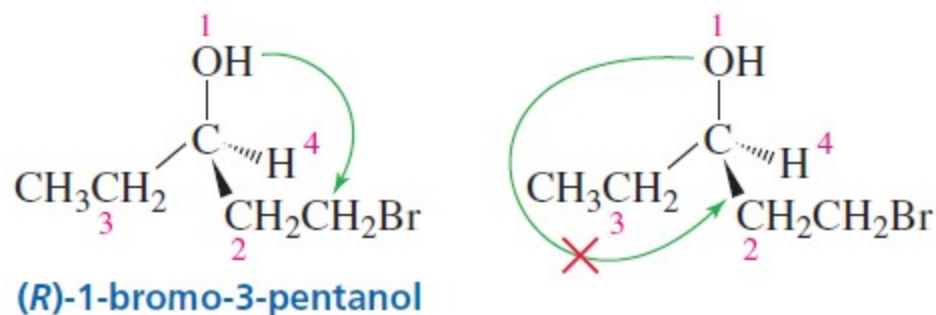
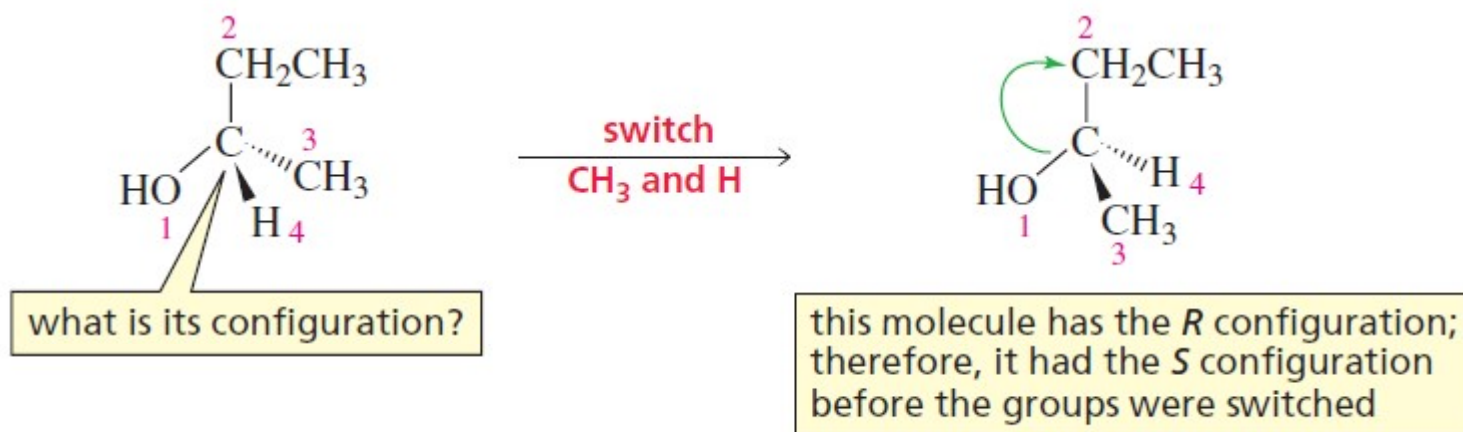


# CIP Priority Rules

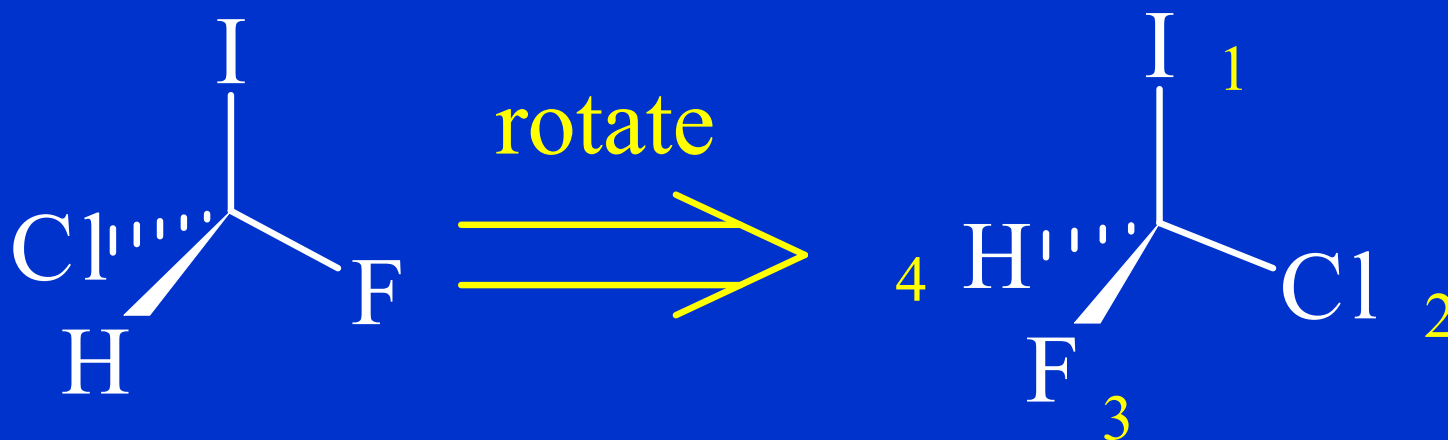
Table 4.1 Atoms and groups with increasing priority

1. H	10. CH = CH <sub>2</sub>	19. CO <sub>2</sub> R	28. OCOR
2. D	11. C(CH <sub>3</sub> ) <sub>3</sub>	20. NH <sub>2</sub>	29. F
3. CH <sub>3</sub>	12. C ≡ CH	21. NHCH <sub>3</sub>	30. SH
4. CH <sub>2</sub> CH <sub>3</sub>	13. C <sub>6</sub> H <sub>5</sub>	22. N(CH <sub>3</sub> ) <sub>2</sub>	31. SR
5. CH <sub>2</sub> (CH <sub>2</sub> ) <sub>n</sub> CH <sub>3</sub>	14. CH <sub>2</sub> OH	23. NO	32. SOR
6. CH <sub>2</sub> - CH = CH <sub>2</sub>	15. CH = O	24. NO <sub>2</sub>	33. SO <sub>2</sub> R
7. CH <sub>2</sub> - C ≡ CH	16. COR	25. OH	34. Cl
8. CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	17. CONH <sub>2</sub>	26. OCH <sub>3</sub>	35. Br
9. CH(CH <sub>3</sub> ) <sub>2</sub>	18. CO <sub>2</sub> H	27. OC <sub>6</sub> H <sub>5</sub>	36. I

# Naming Enantiomers

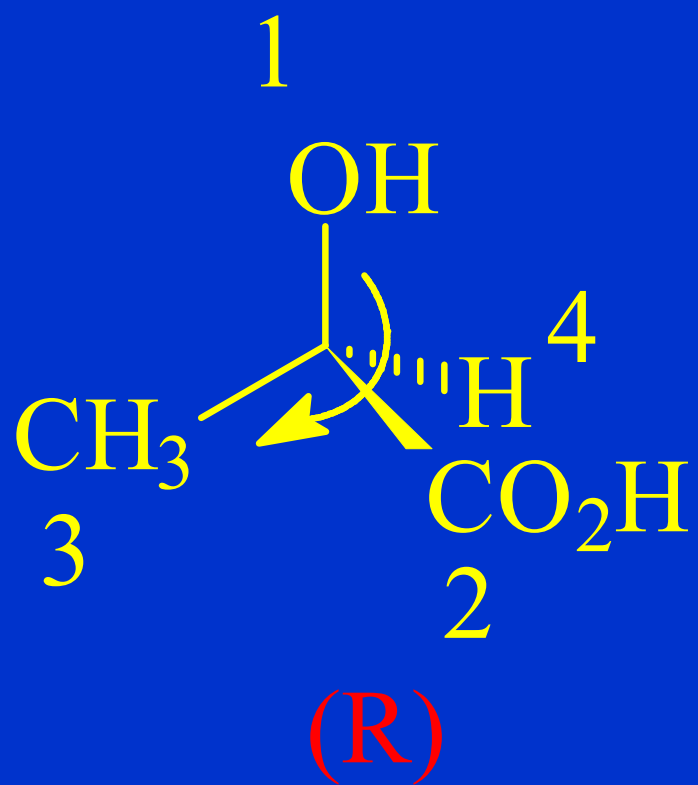
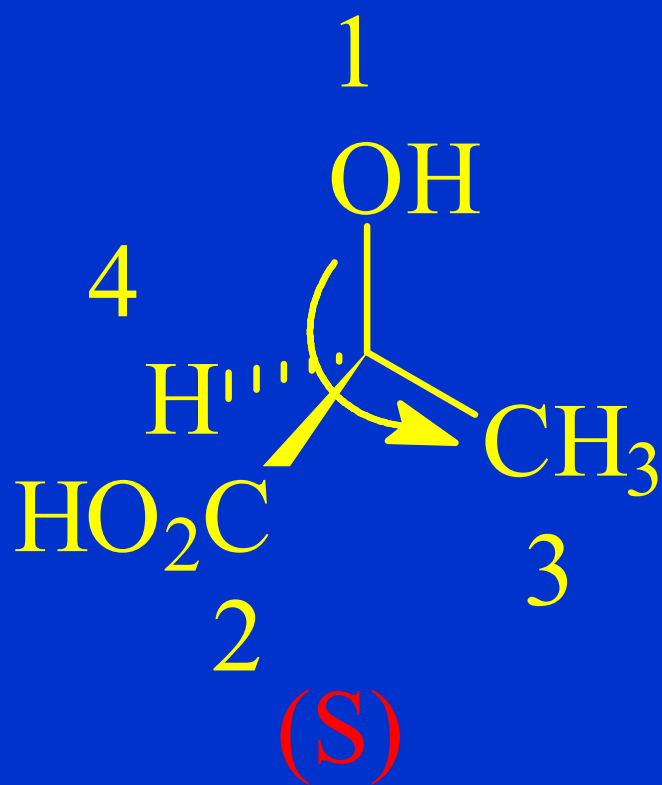


# Assign Priority to each Group on Asymmetric Center

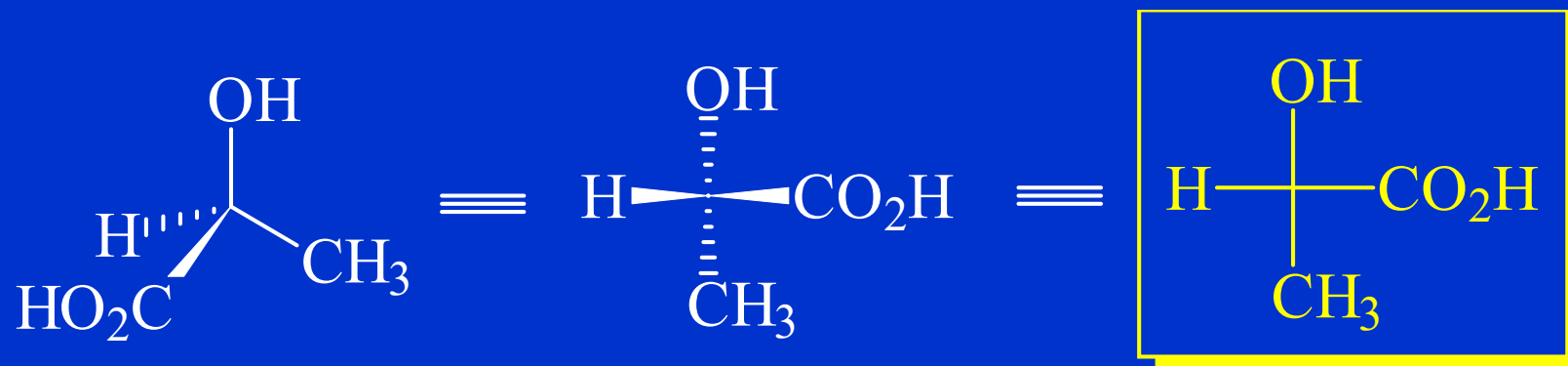


focus down C-4 bond

# Lactic Acid



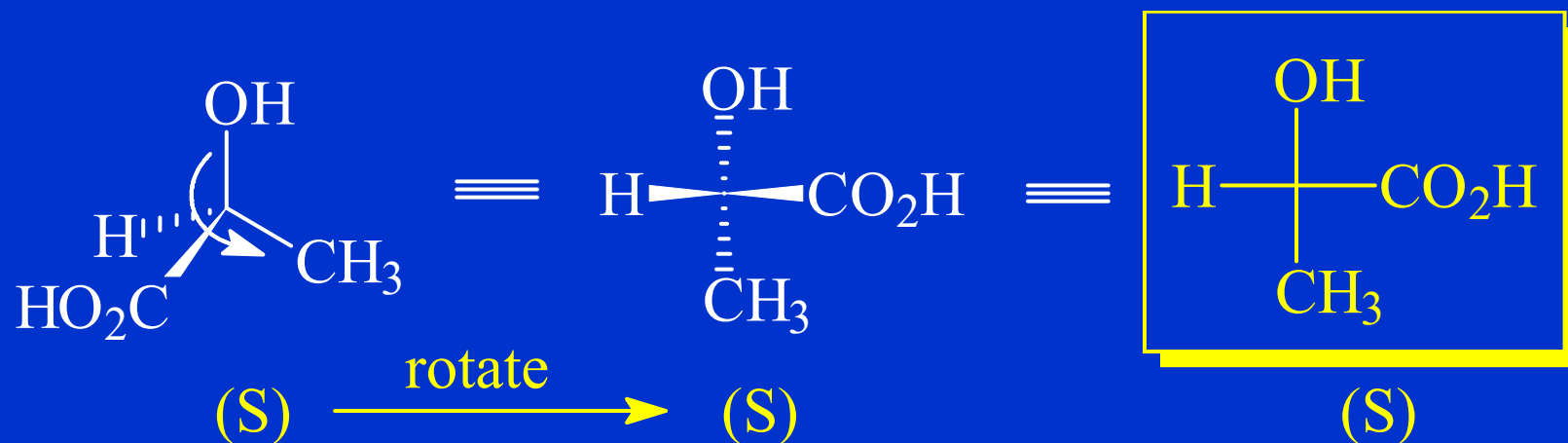
# Fischer Projections



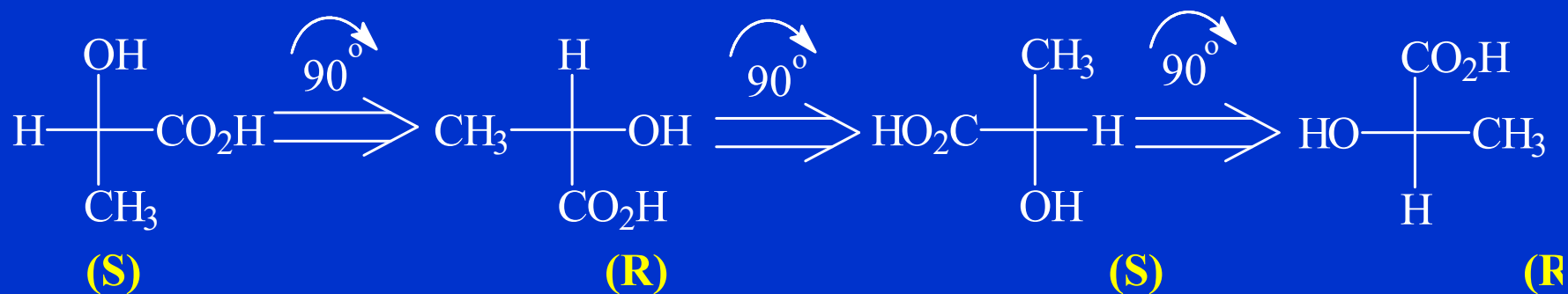
**Horizontal bonds approach you (wedge bonds)**

**Vertical bonds move away (dashed bonds)**

# Assigning Absolute Configuration to Fischer Projections

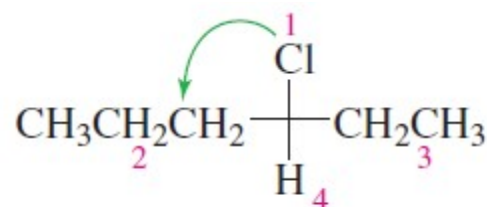
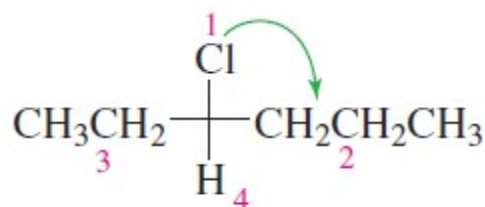


# Rotation of the Projection 90° Reverses Absolute Configuration

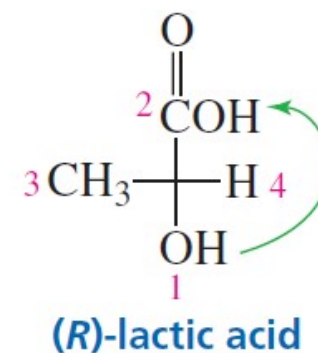
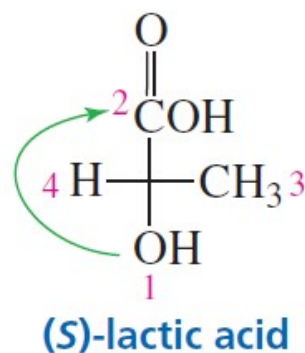
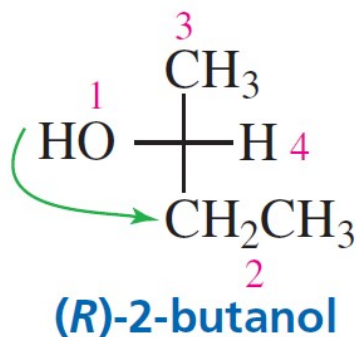
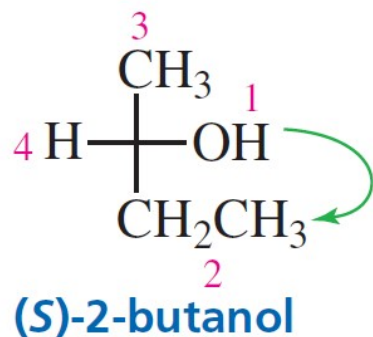


# Fischer Projection

- The lowest priority is on a **horizontal bond**

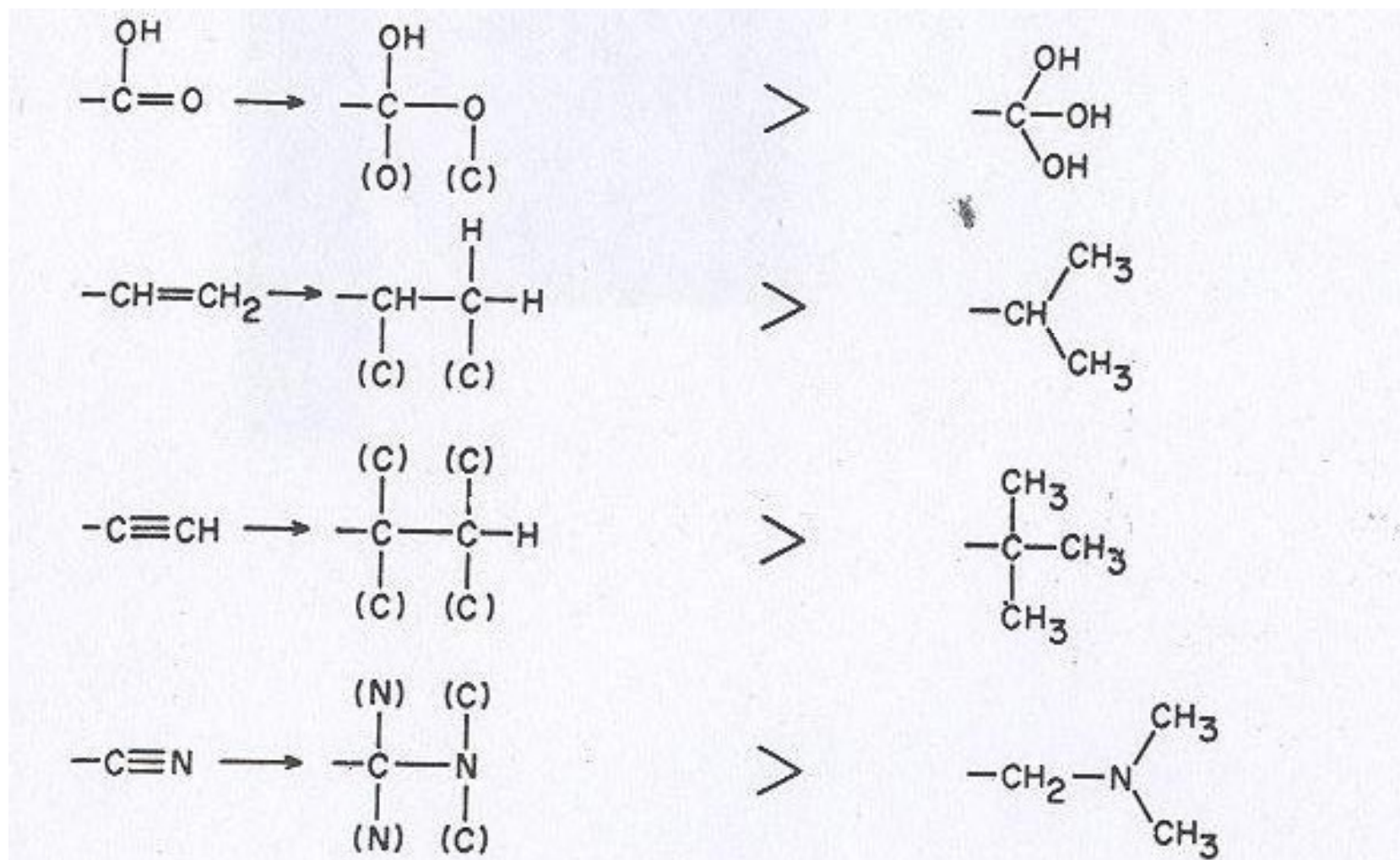


- The lowest priority is on a **vertical bond**



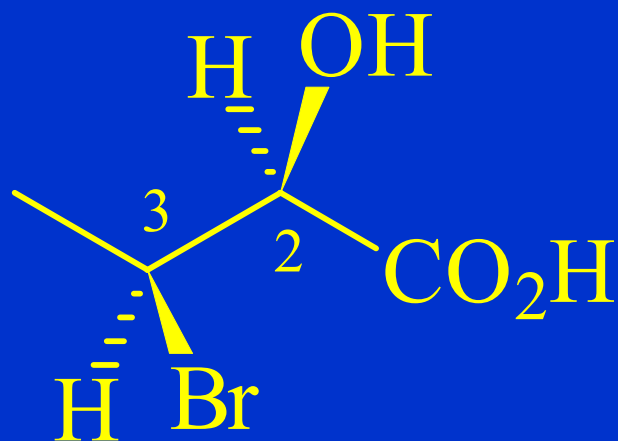


# Phantom Atoms in CIP Priority

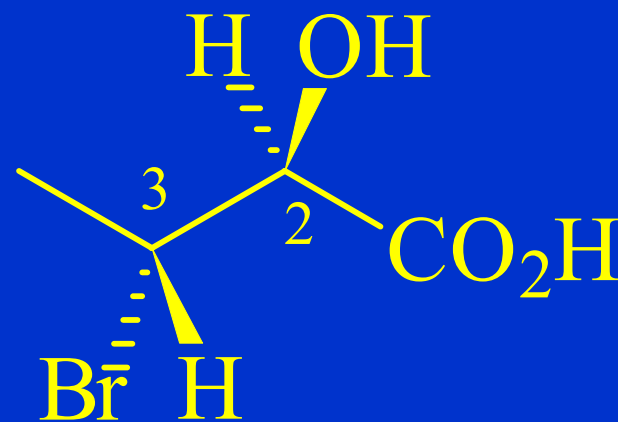


# Diastereomers

## Stereoisomers That Are Not Mirror Images



(2S,3S)

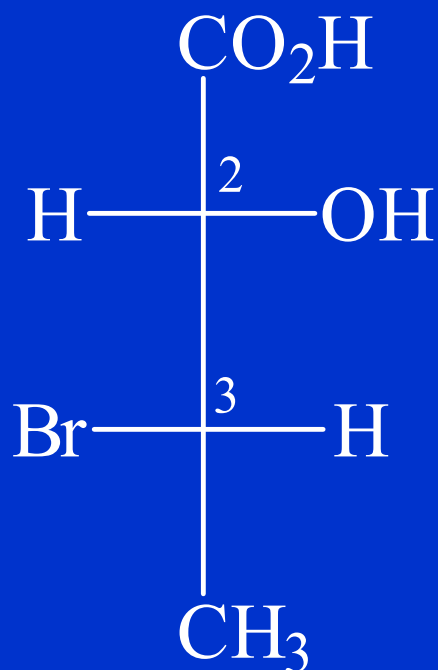


(2S,3R)

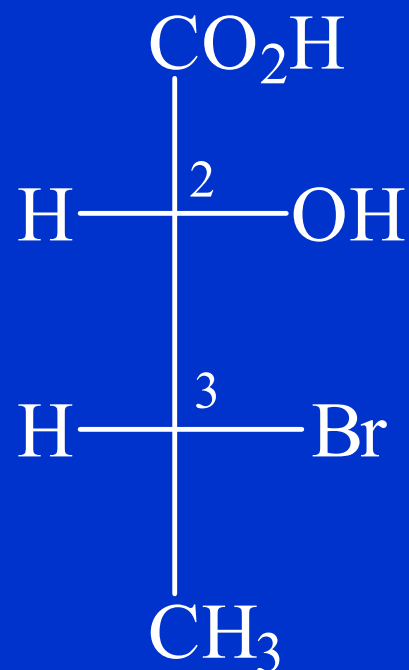
same stereochemistry at C<sub>2</sub> (S)

opposite stereochemistry at C<sub>3</sub>

# Fischer Projections with 2 Chiral Centers

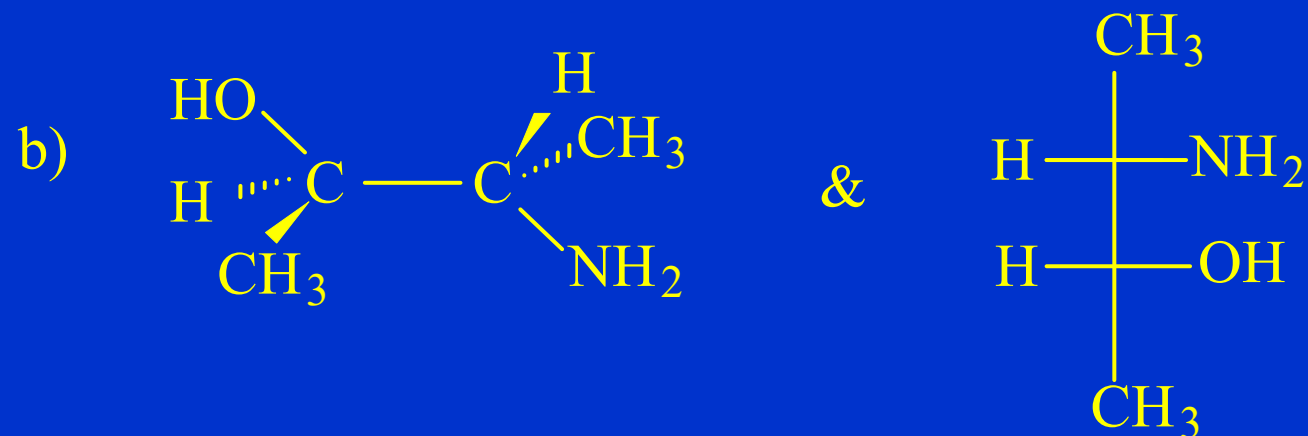
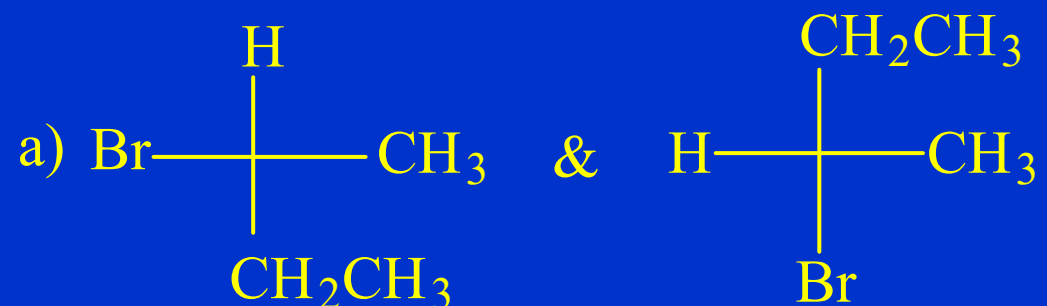


**(2S,3S)**



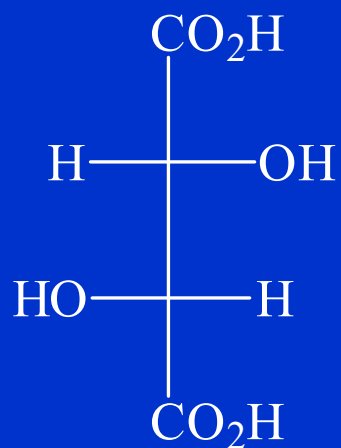
**(2S,3R)**

# Identical, Enantiomers or Diastereomers?

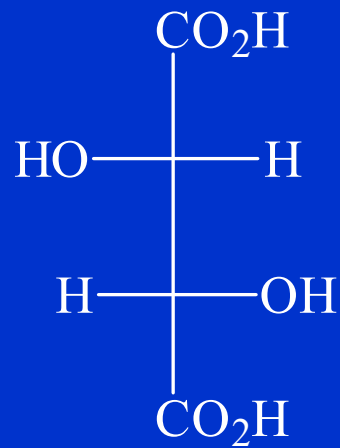


# Tartaric Acids

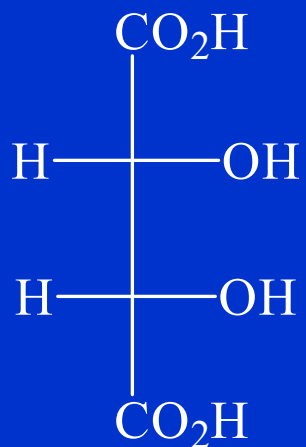
**R,R**



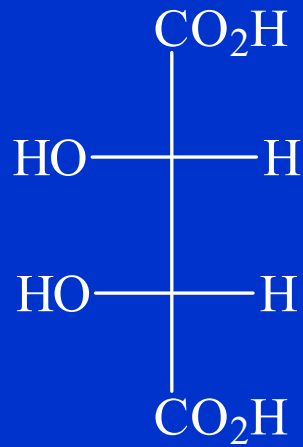
**S,S**



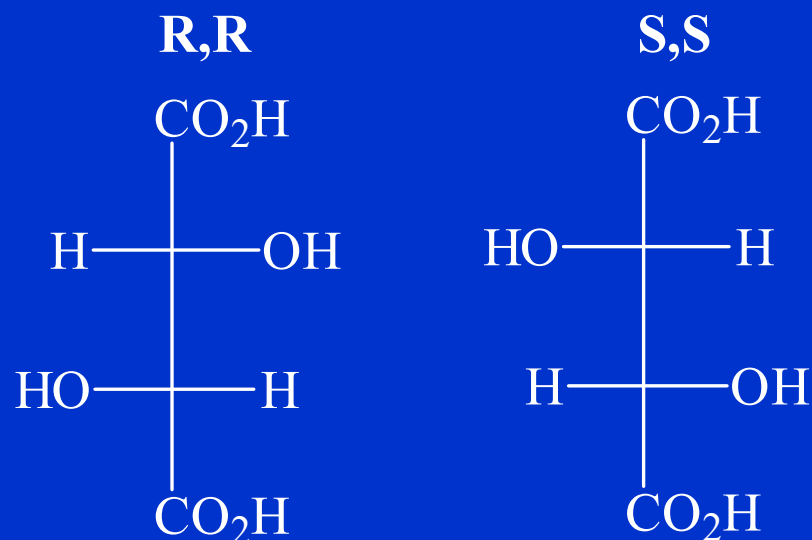
**R,S**



**S,R**



# Racemic Mixture



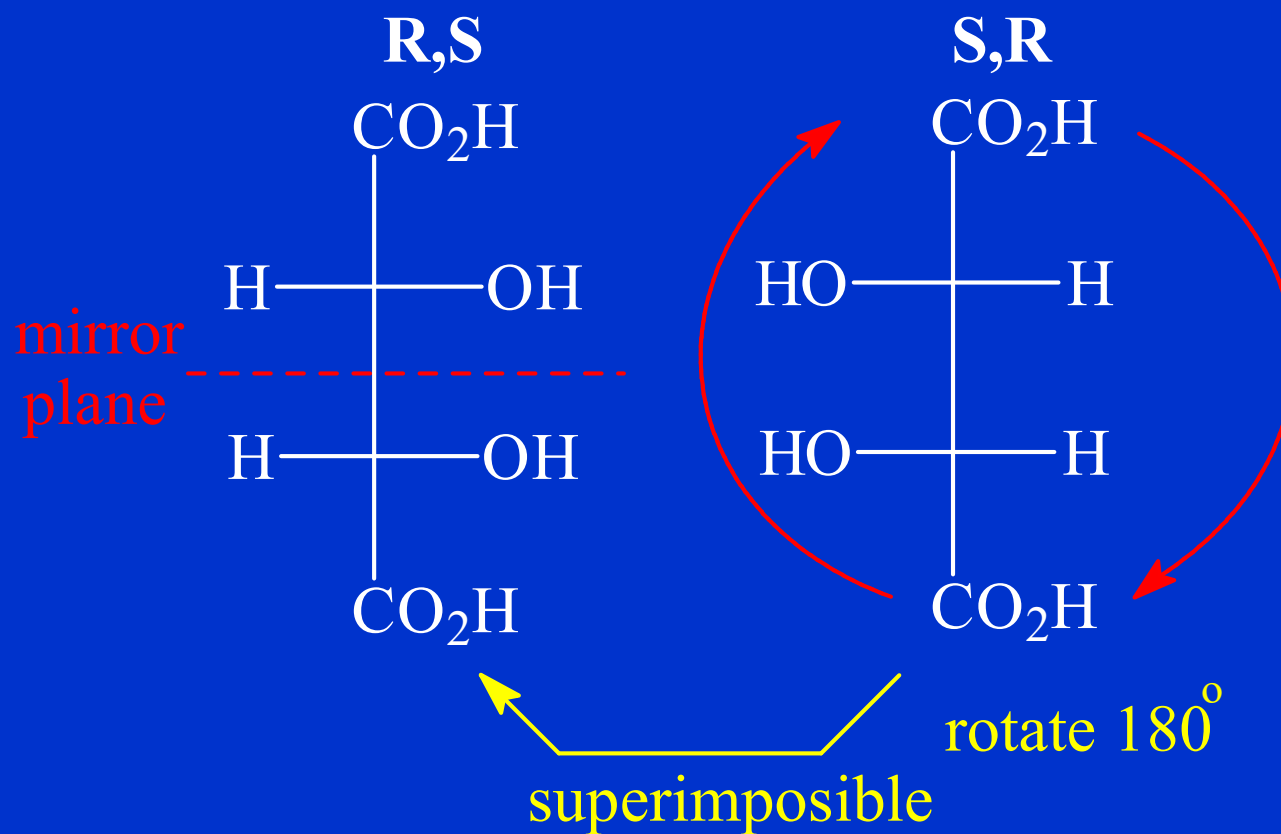
Racemic Mixture (Racemate): 50/50 mixture of enantiomers

	<u>(R,R) Tartaric acid</u>	<u>(S,S) Tartaric Acid</u>	<u>(+/-) Tartaric acid</u>
m.p. °C	168-170	168-170	<b>210-212</b>
[α] (degrees)	- 12	+ 12	<b>0</b>
ρ (g/mL)	1.7598	1.7598	<b>1.7723</b>

# Meso Compound

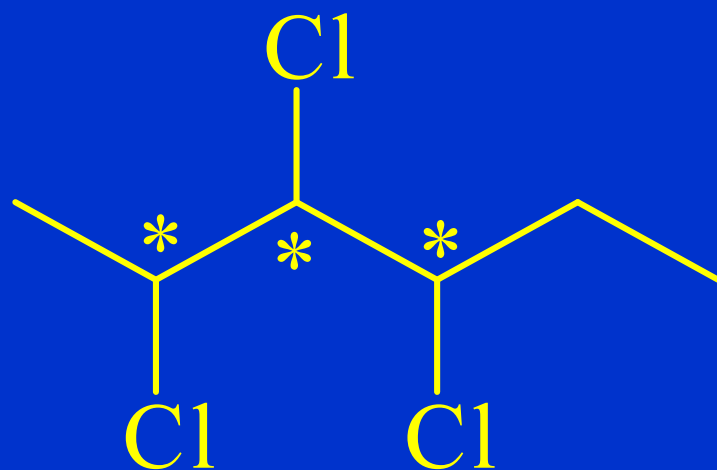
## Internal Plane of Symmetry

### Optically Inactive



# 2,3,4-trichlorohexane

## How many stereoisomers?



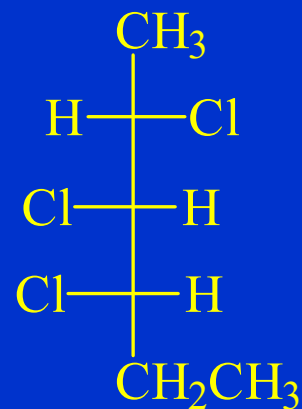
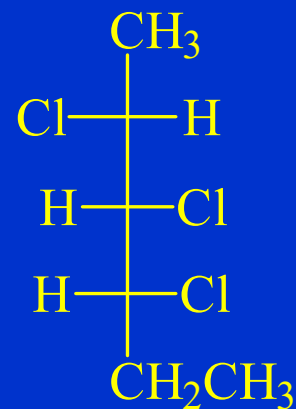
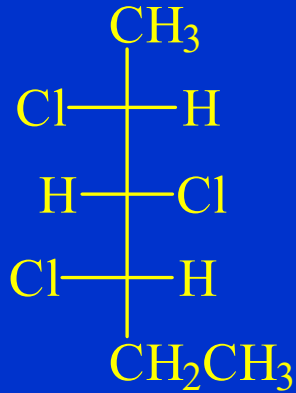
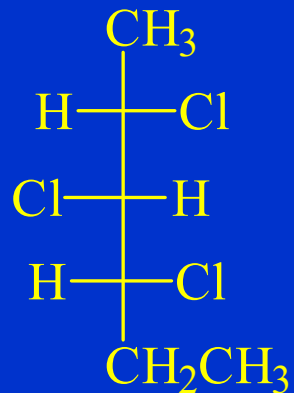
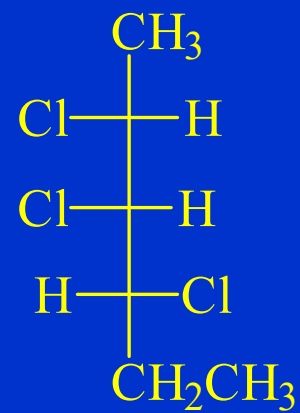
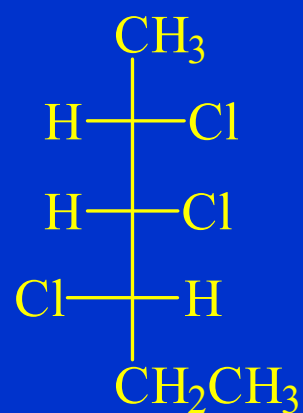
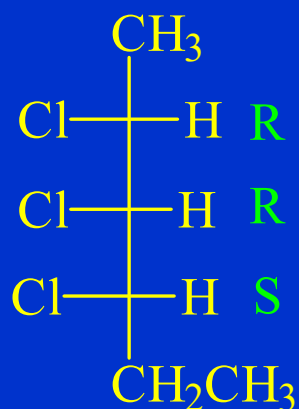
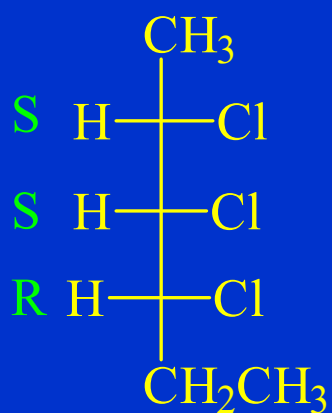
3 asymmetric centers

$2^n$ ,  $n = \#$  asymmetric centers (3)

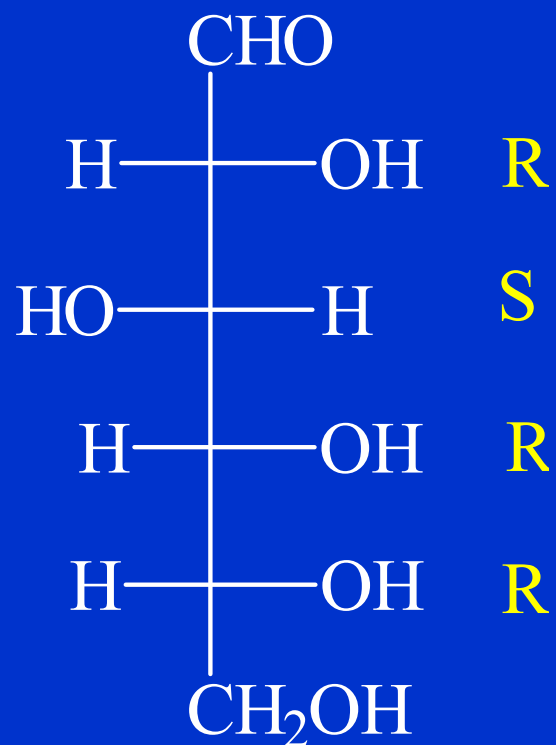
**8 stereoisomers**



$$\underline{n = 3; 2^n = 8}$$



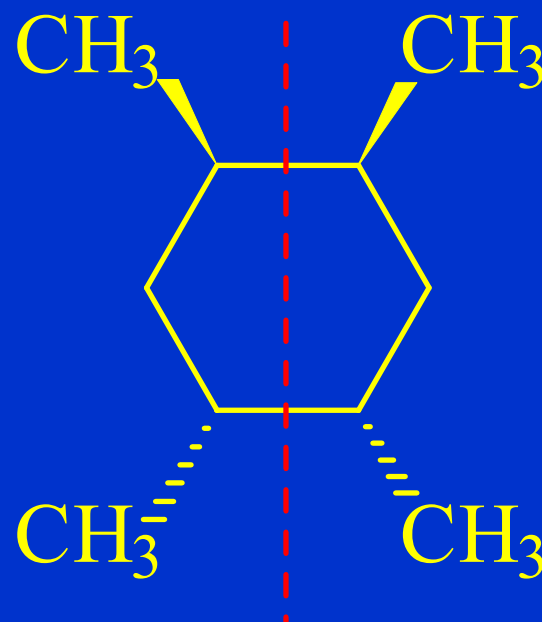
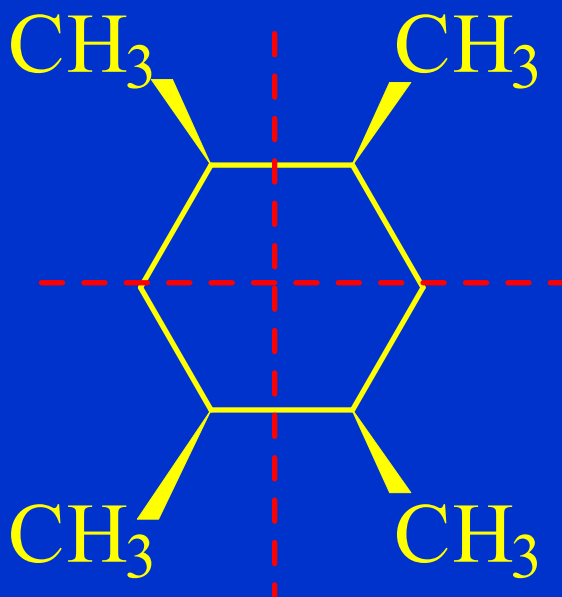
# A Carbohydrate



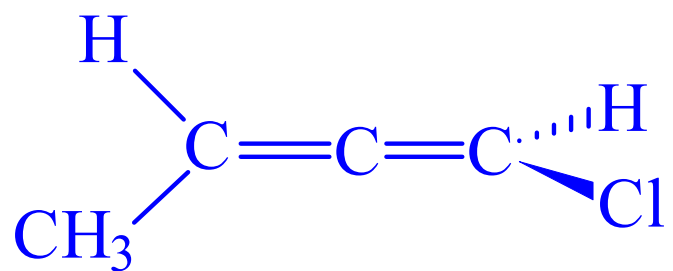
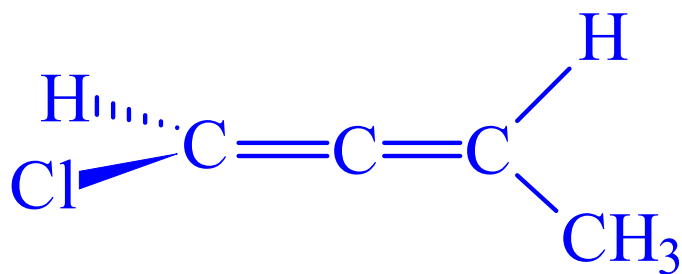
**(+) D-Glucose**

# Internal Planes of Symmetry

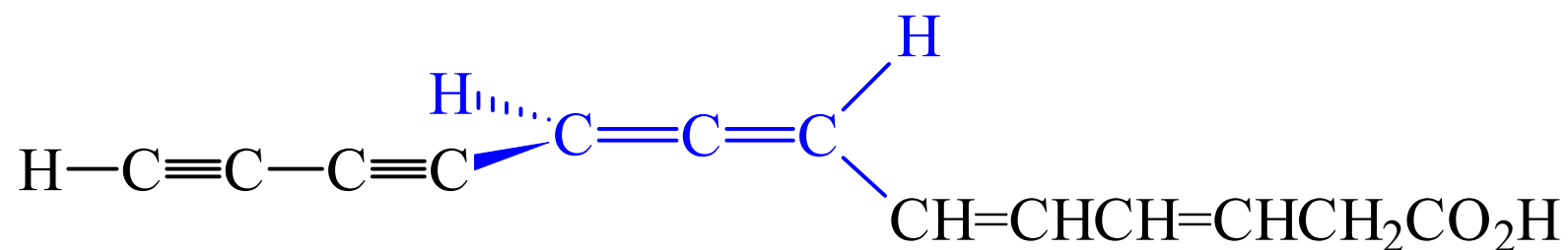
**Both are Meso**



# Allenes can be Chiral

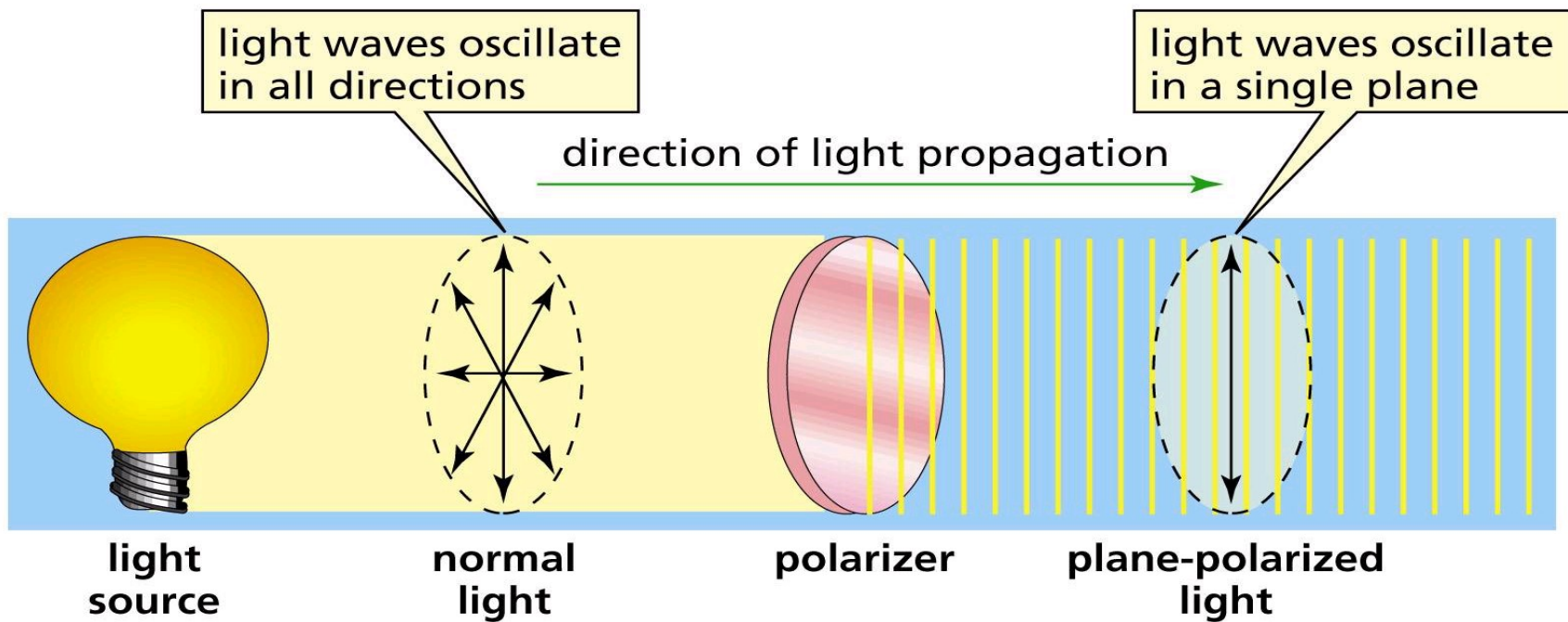


# Mycomycin, an antibiotic

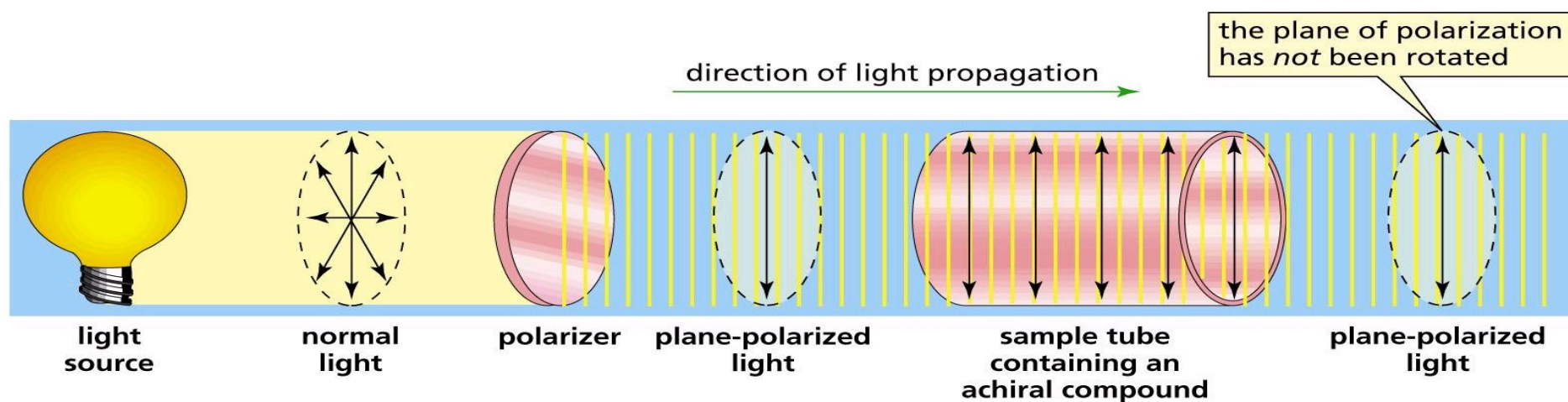


*Nocardia acidophilus*     $[\alpha]_D = -130^\circ$

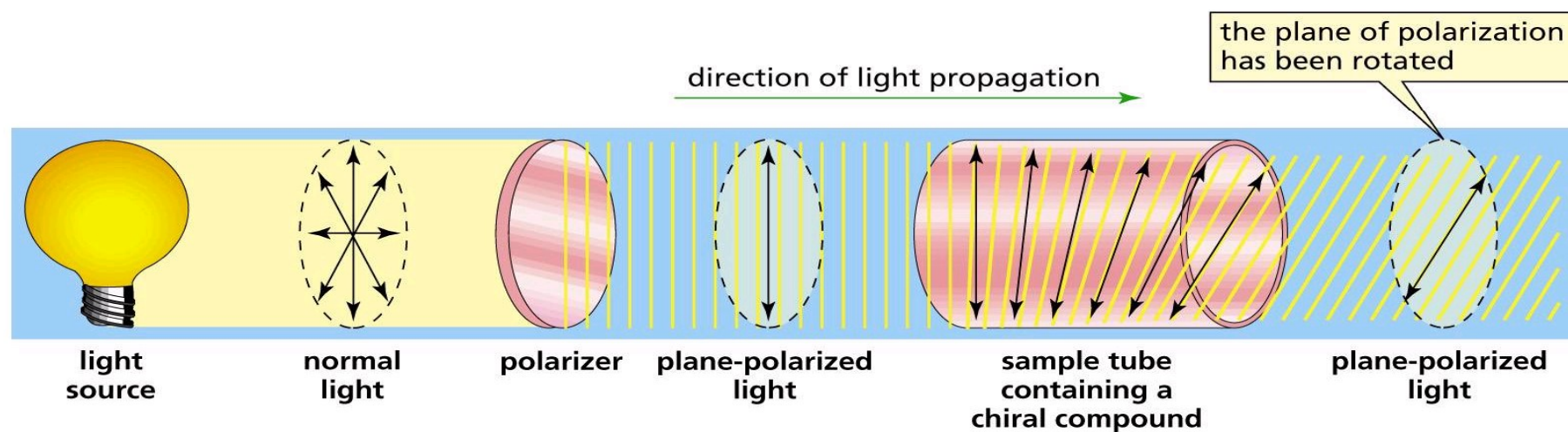
# Plane-Polarized Light



# Plane-Polarized Light through an Achiral Compound



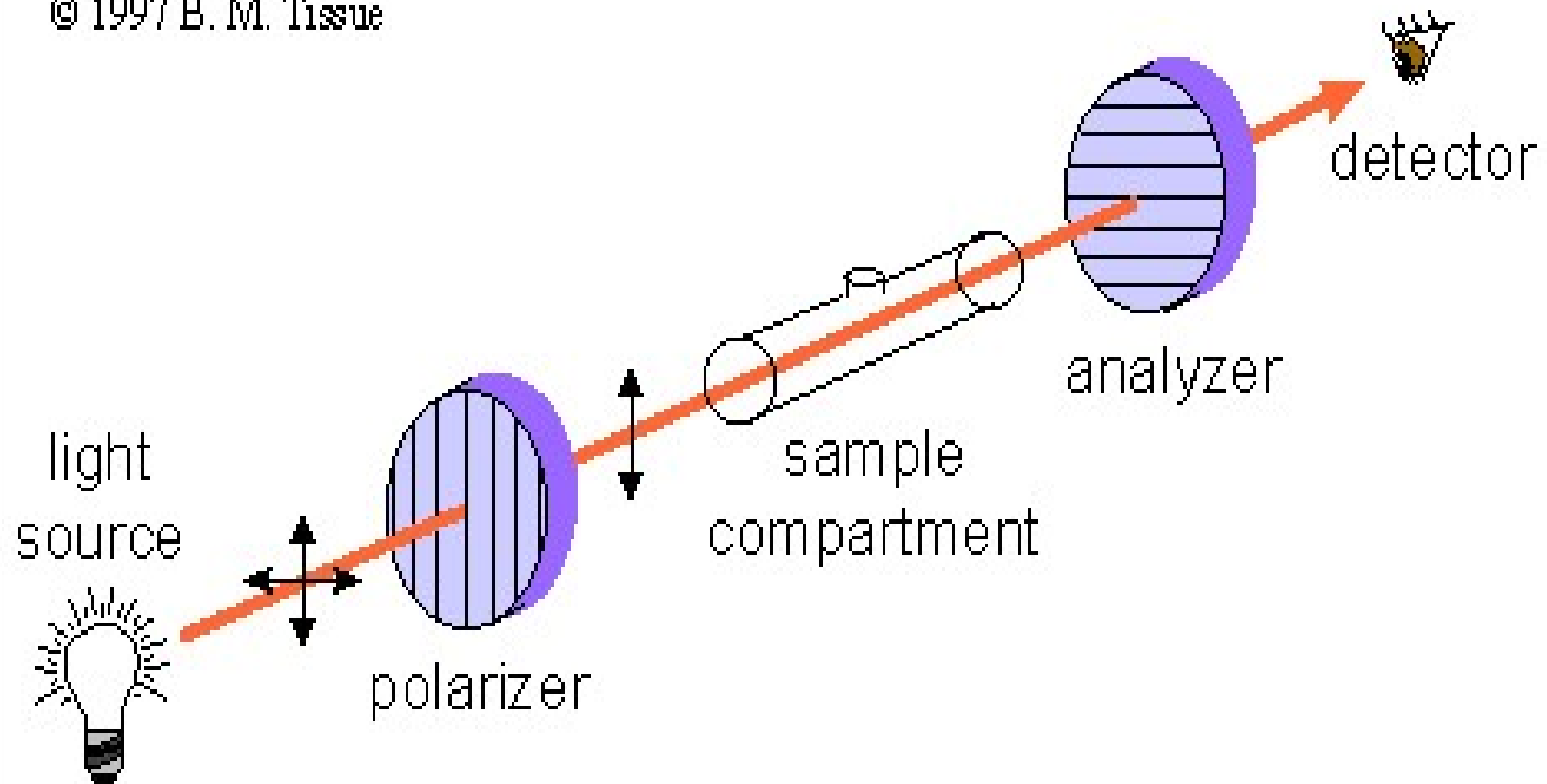
# Plane-Polarized Light through a Chiral Compound





# Polarimeter Measures Optical Rotation

© 1997 B. M. Tissue



## Specific Rotation, $[\alpha]$

$$[\alpha] = \alpha / cl$$

$\alpha$  = observed rotation

$c$  = concentration in g/mL

$l$  = length of tube in dm

**Dextrorotary** designated as  $d$  or (+), clockwise rotation

**Levorotary** designated as  $l$  or (-), counter-clockwise rotation

**Specific rotation** is the number of degrees of rotation caused by a solution of 1.0 g of the compound per mL of solution in a sample tube 1.0 dm long at a specified temperature and wavelength.

$$[\alpha]_{\lambda}^T = \frac{\alpha}{l \times c}$$

# Specific Rotations of some Common Organic Compounds

<u>Compound</u>	<u>[a]</u>	<u># * centers</u>
Sucrose	+66.5	10
Camphor	+44.3	2
MSG	+25.5	1
Cholesterol	-31.3	8
Morphine	-132.0	5

## (±) Racemic mixture

- A mixture of equal amounts of two enantiomers—such as (R)-lactic acid and (S)-lactic acid—is called a **racemic mixture** or a racemate.
- optically inactive

# Optical Purity

$$\text{optical purity} = \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}}$$

- The specific rotation of (S)-2-bromobutane is  $+23.1^\circ$ . If a sample of 2-bromobutane has an observed specific rotation of  $+9.2^\circ$ . Then optical purity is 0.40

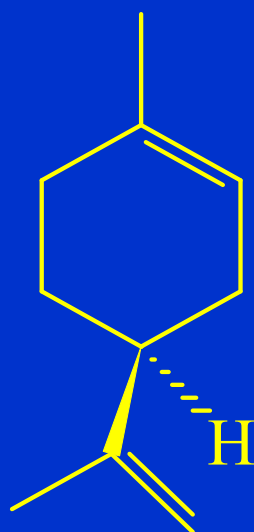
## Enantiomeric Excess

- If the mixture has a 40% enantiomeric excess (S enantiomer is in excess), then 70% of the mixture is the S enantiomer and 30% is the R enantiomer

$$\text{enantiomeric excess} = \frac{\text{excess of a single enantiomer}}{\text{entire mixture}} \times 100\%$$

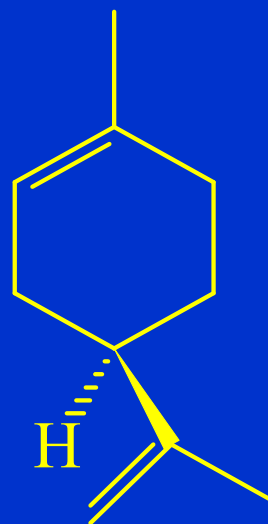
# Enantiomeric Excess (Optical Purity)

$$\frac{\text{observed rotation}}{\text{rotation of pure enantiomer}} \times 100 = \text{enantiomeric excess (e.e.)}$$



(S)-(-) Limonene

$[\alpha] = -123.0^{\circ}$   
from lemons



(R)(+) Limonene

$[\alpha] = +123.0^{\circ}$   
from oranges

observed rotation =  $+109^{\circ}$

$$\text{e.e.} = \frac{109.0}{123.0} \times 100$$

**= 88.6% e.e.**

88.6% (+)

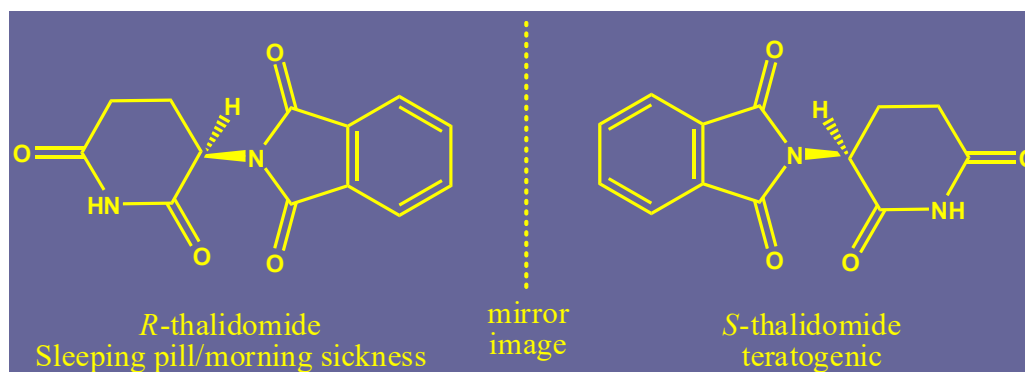
11.4% racemic

actually 94.3% (+)

# Asymmetric Homogeneous Catalysis

- The biggest impact of homogeneous catalysis is in the synthesis of chiral molecules, especially of enantiomerically pure products.
- Most natural products are chiral, and in many cases different enantiomers exhibit radically different properties.
- Different enantiomers can cause completely different effects in vivo.

## Thalidomide and the Role of Enantiomers and FDA approval



S-enantiomer causes  
Phocomelia

