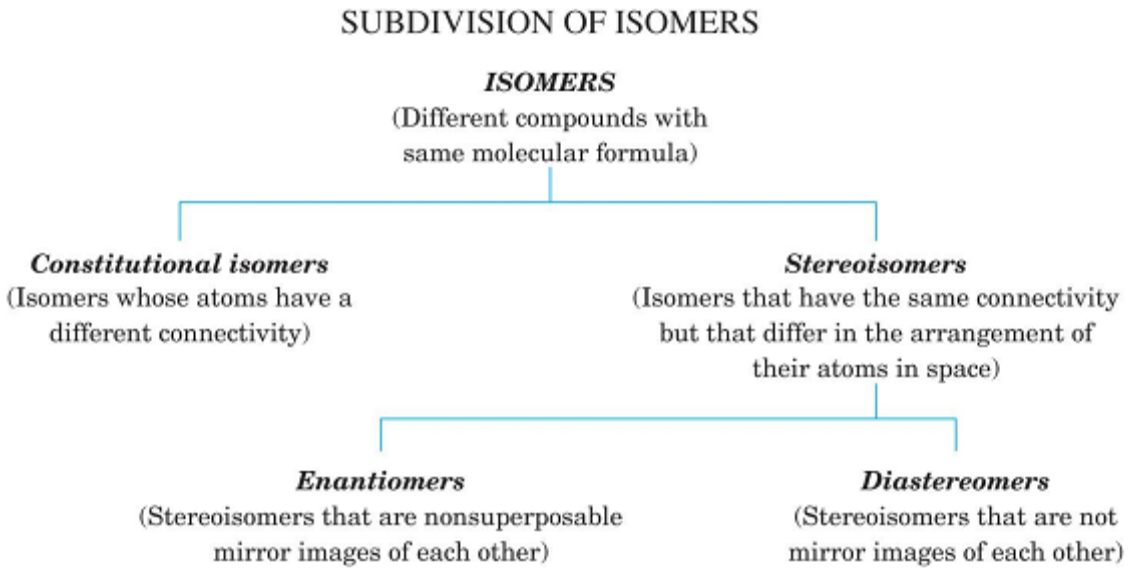
Organic chemistry

Chapter I *Lecture 1 by Prof. Dr. Dawood Salim Abid*

Stereochemistry

- isomerism: constitutional isomers and stereoisomers
- chirality, stereogenic center
- *R,S* nomenclature of enantiomers
- optical activity
- chiral drugs
- molecules with more stereogenic centers
- *threo, erythro* and *meso* compounds
- Fischer projection formulas
- D,L nomenclature of enantiomers
- relative and absolute configuration

The isomerism of organic compounds

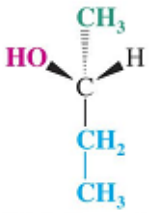


Constitutional isomers

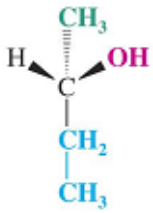
MOLECULAR FORMULA	CONSTITUTIONAL ISOMERS		
C_4H_{10}	$CH_3CH_2CH_2CH_3$ **Butane**	and	$CH_3CH(CH_3)CH_3$ **Isobutane**
C_3H_7Cl	$CH_3CH_2CH_2Cl$ **1-Chloropropane**	and	$CH_3CH(Cl)CH_3$ **2-Chloropropane**
C_2H_6O	CH_3CH_2OH **Ethanol**	and	CH_3OCH_3 **Dimethyl ether**

Stereoisomers

ENANTIOMERS

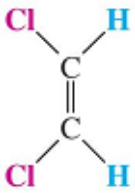


(*R*)-2-Butanol
$[\alpha]_D^{25} = -13.52°$

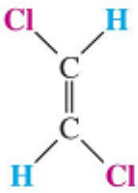


(*S*)-2-Butanol
$[\alpha]_D^{25} = +13.52°$

DIASTEREOMERS



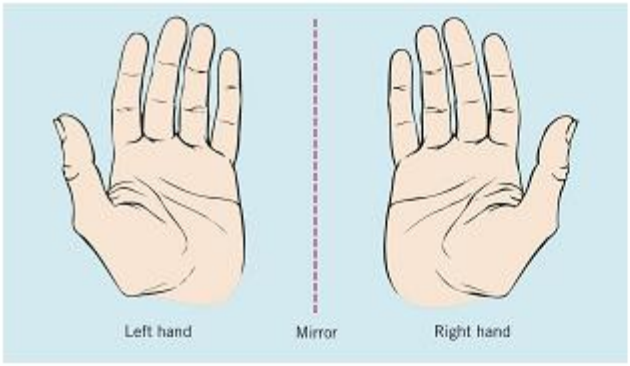
***cis*-1,2-Dichloroethene**
($C_2H_2Cl_2$)

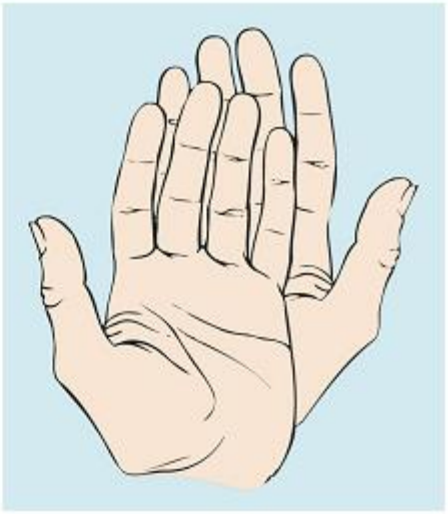


***trans*-1,2-Dichloroethene**
($C_2H_2Cl_2$)

Chirality

Left and right hand are not superposable - are **chiral**





Chiral and achiral molecules

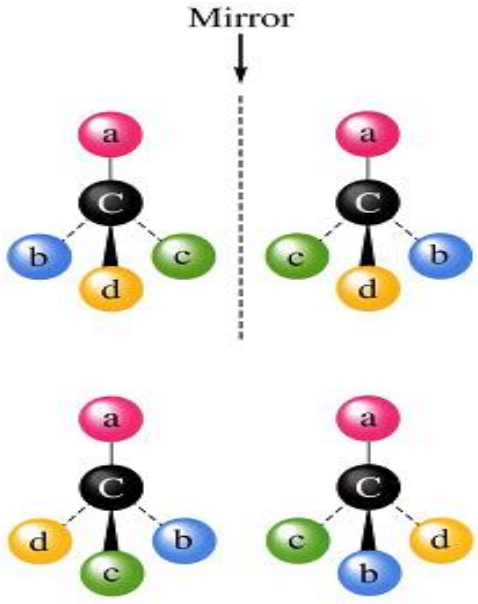
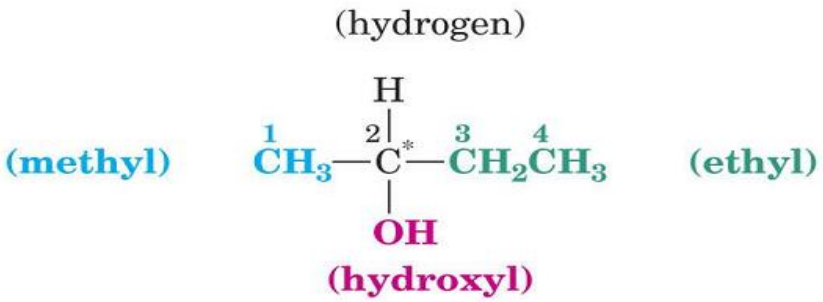


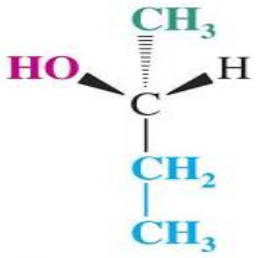
Figure 23.15
Optical isomerism for carbon with four different substituents
Steven S. Zumdahl, *Chemistry*, Third Edition, © 1993 by D. C. Heath and Company

Stereogenic center

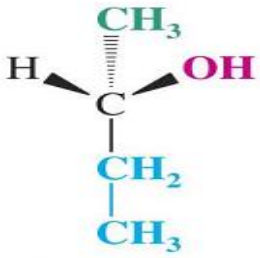
tetrahedral stereogenic center
tetrahedral stereogenic carbon
(asymmetric carbon)



The pair of enantiomers



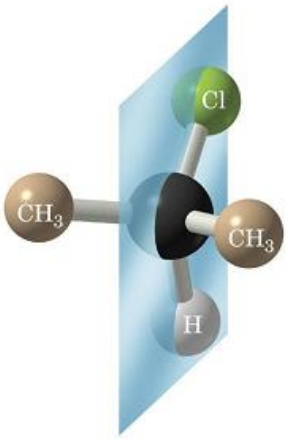
(*R*)-2-Butanol
$[\alpha]_D^{25} = -13.52°$



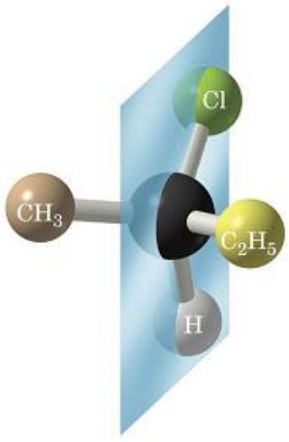
(*S*)-2-Butanol
$[\alpha]_D^{25} = +13.52°$

Test for chirality: plane of symmetry

2-chloropropane vs. 2-chlorobutane



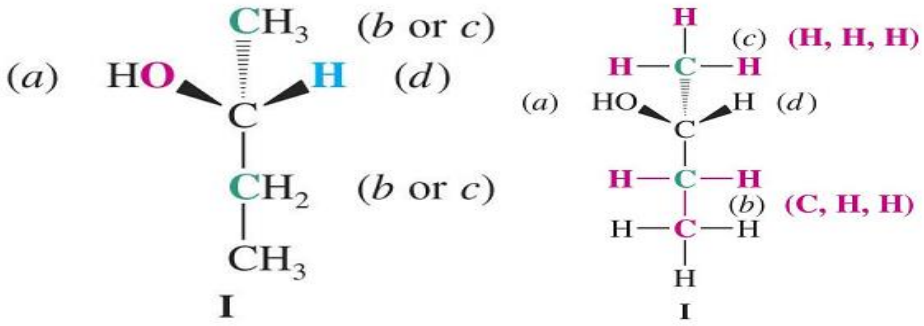
(*a*)



(*b*)

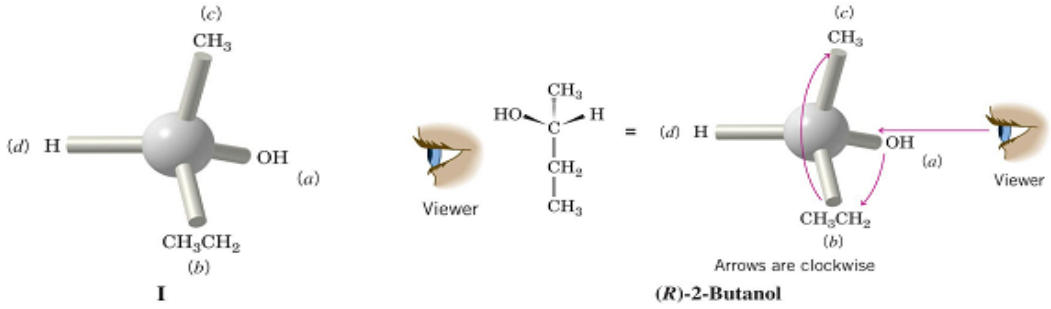
Nomenclature of enantiomers

The ***R,S*-system** I



Nomenclature of enantiomers

The ***R,S*-system** II



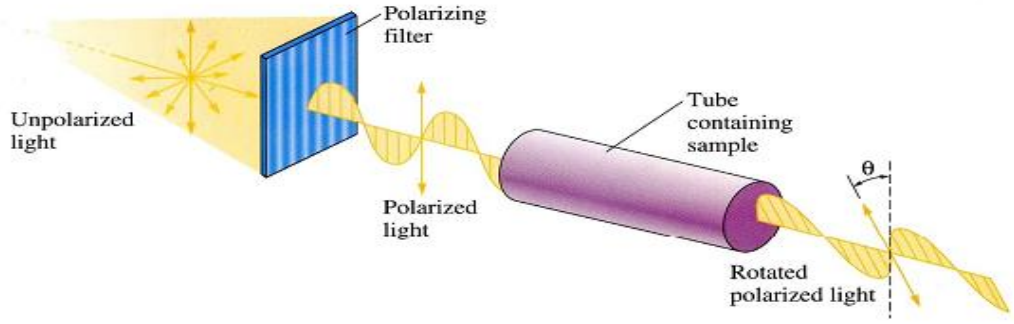
Properties of enantiomers: optical activity

Physical Property	(*R*)-2-Butanol	(*S*)-2-Butanol
Boiling point (1 atm)	99.5°C	99.5°C
Density (g mL^{-1} at 20°C)	0.808	0.808
Index of refraction (20°C)	1.397	1.397

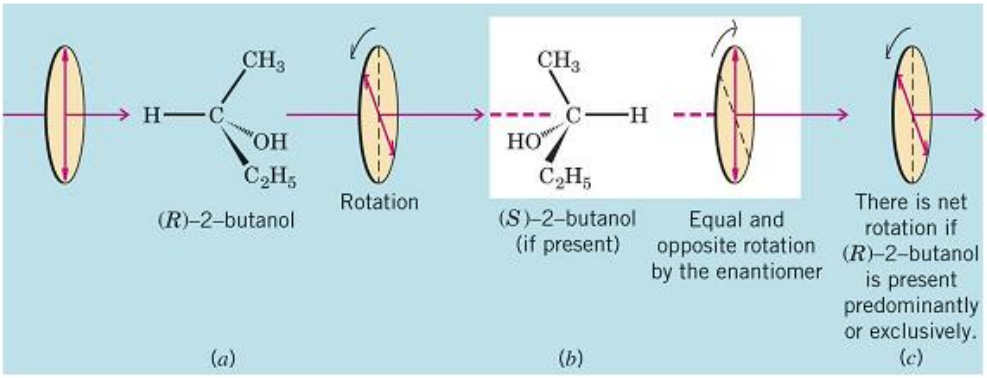
The behavior of enantiomers toward plane-polarized light ⇨

optically active compounds

Passing the plane-polarized light through an optically active compound



The origin of optical activity



Specific rotation [α]

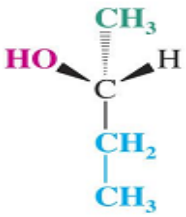
$$[\alpha] = \frac{\alpha}{c \cdot l}$$

where $[\alpha]$ = the specific rotation

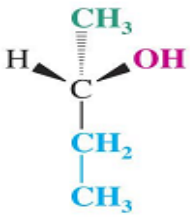
α = the observed rotation

c = the concentration of the solution in grams per milliliter of solution (or density in g mL^{-1} for neat liquids)

l = the length of the tube in decimeters (1 dm = 10 cm)

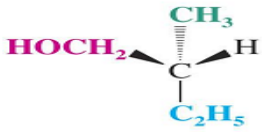


(*R*)-2-Butanol
$[\alpha]_D^{25} = -13.52°$

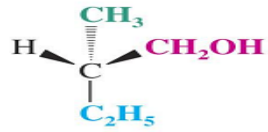


(*S*)-2-Butanol
$[\alpha]_D^{25} = +13.52°$

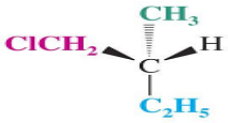
Correlation between the configurations of enantiomers and the direction ± [α]



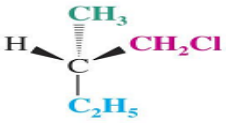
(*R*)-(+)-2-Methyl-1-butanol
$[\alpha]_D^{25} = +5.756°$



(*S*)-(−)-2-Methyl-1-butanol
$[\alpha]_D^{25} = -5.756°$



(*R*)-(−)-1-Chloro-2-methylbutane
$[\alpha]_D^{25} = -1.64°$

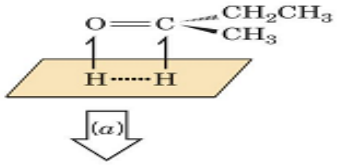


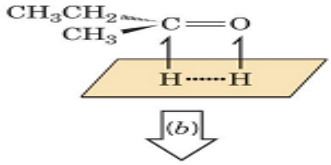
(*S*)-(+)-1-Chloro-2-methylbutane
$[\alpha]_D^{25} = +1.64°$

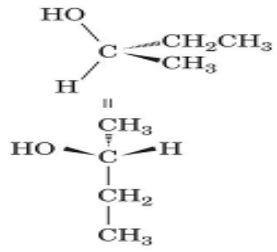
Racemic mixture

⇨ an equimolar mixture of two enantiomers

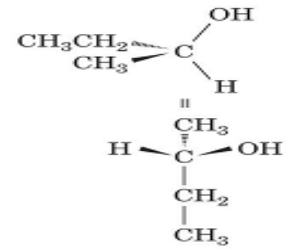
(±)-2-butanol





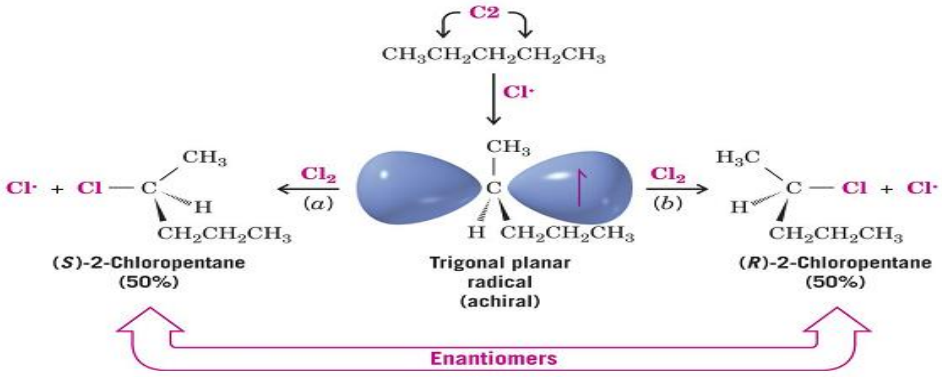


(*R*)-(−)-(2)-Butanol

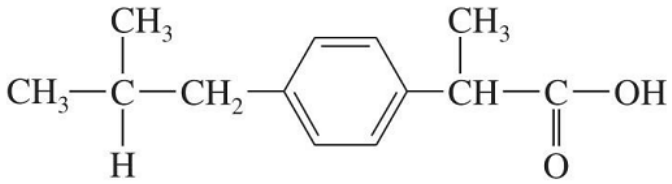


(*S*)-(+)-(2)-Butanol

The stereochemistry of chlorination at C2 of pentane



Chiral drugs I



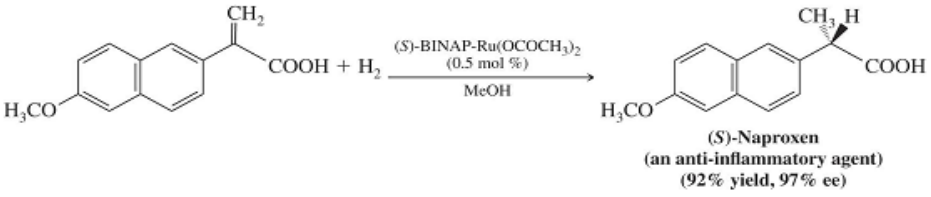
Ibuprofen

Generally the (±)-ibuprofene racemate is used (Brufen, Ibalgin), but only (*S*)-enantiomer has the anti-inflammatory action

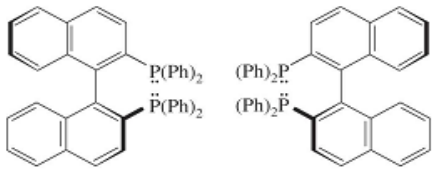
Chiral drugs II

Stereoselective synthesis of (*S*)-Naproxene

[Nalgesin *S*]

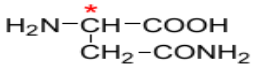


(*S*)-Naproxen
(an anti-inflammatory agent)
(92% yield, 97% ee)



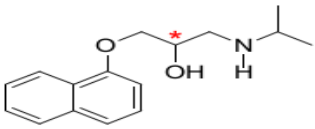
(*S*)-BINAP **(*R*)-BINAP**

Absolute configuration vs. biological activity I



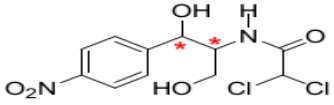
Asparagine

R- sweet
S- bitter



Propranolol

R- contraceptive
S- antihypertensive



Chloramfenikol

R,R- antibiotic
S,S- inactive

Molecules with more than one stereogenic center

the total number of stereoisomers = 2^n

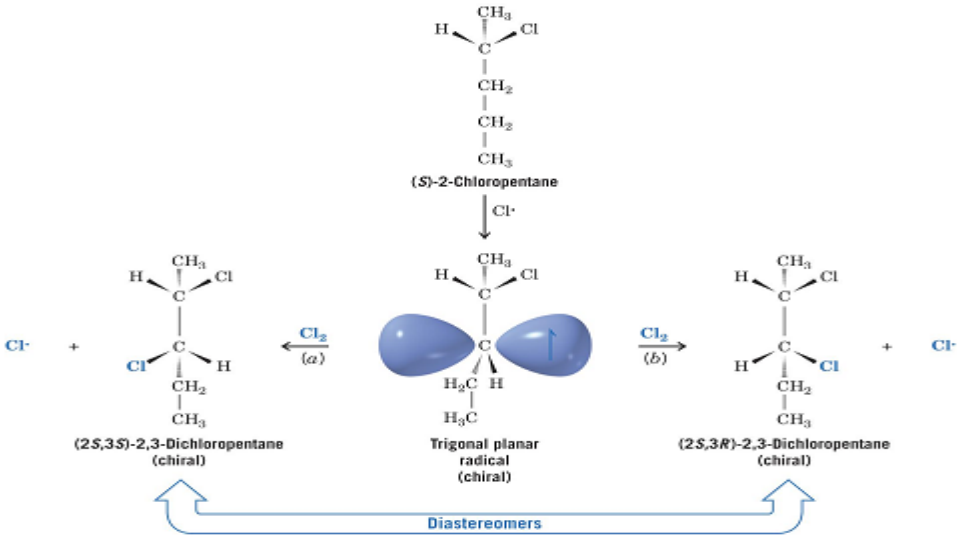
where **n** is equal to the number of tetrahedral stereogenic centers

2,3-Dibromopentane

erythro ***threo***

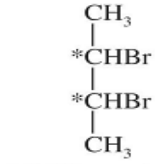
The stereochemistry of chlorination at C_3 of (*S*)-2-chloropentane

⇨ The two diastereomers are **not** produced in equal amounts

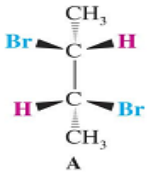


Meso compounds

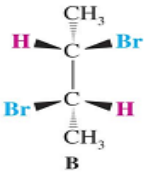
The achiral molecules even though they contain stereogenic centers
⇨ they have a **plane of symmetry**



2,3-Dibromobutane

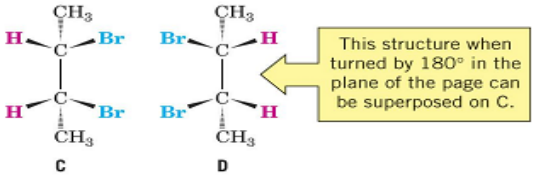


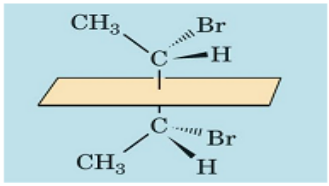
A



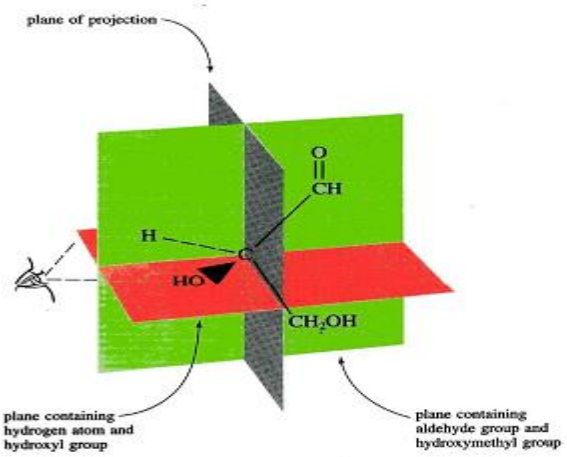
B

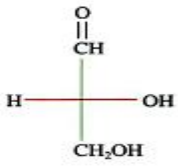
threo





erythro* ≡ *meso



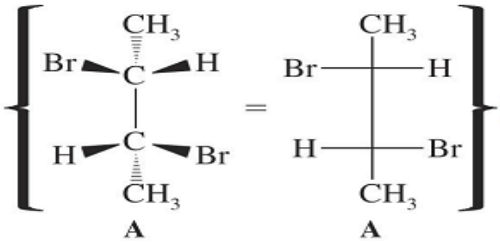


Fischer projection formula

(*R*)-(+)-glyceraldehyde

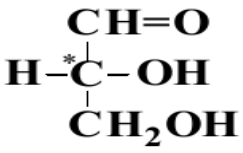
Fischer projection formulas II

Three-dimensional formula



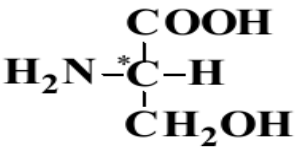
Fischer projection formula

Nomenclature of enantiomers
The D,L-system



D-(+)-Glyceraldehyde

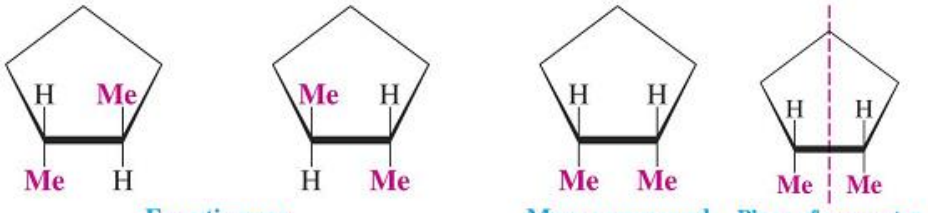
(R)-(+)-Glyceraldehyde



L-(-)-Serine

(S)-(-)-Serine

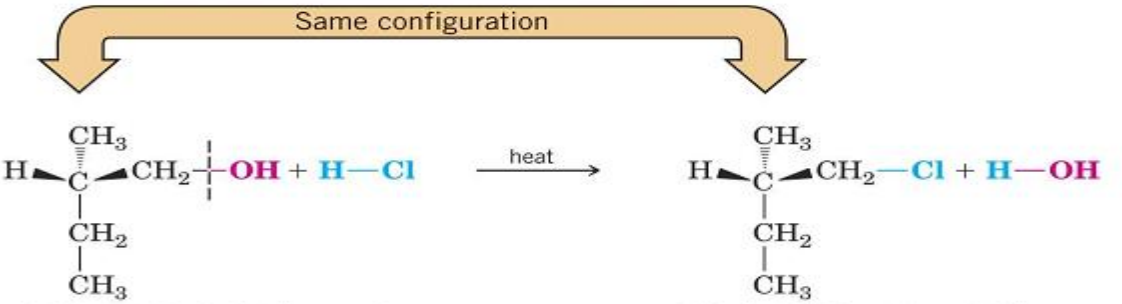
Stereoisomerism of cyclic compounds



Relative configuration I

When **no bonds** to the stereogenic carbon are broken
⇨ the reaction proceed with **retention of configuration**

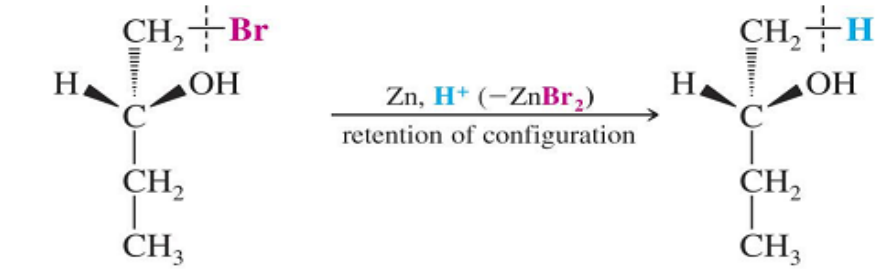
[reaction with **retention of *R,S*- nomenclature**]



Relative configuration II

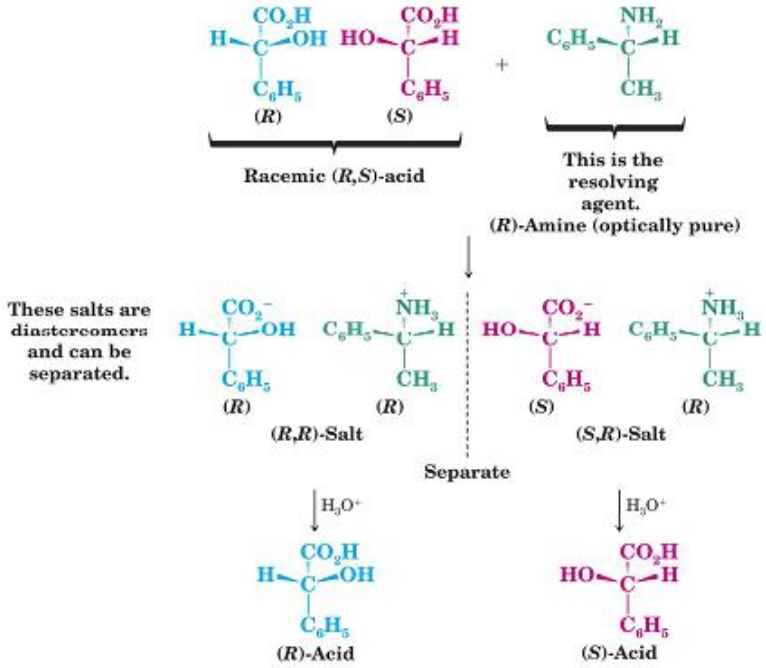
When **no bonds** to the stereogenic carbon are broken
⇨ the reaction proceed with **retention of configuration**

[reaction with **change of *R,S*- nomenclature**]

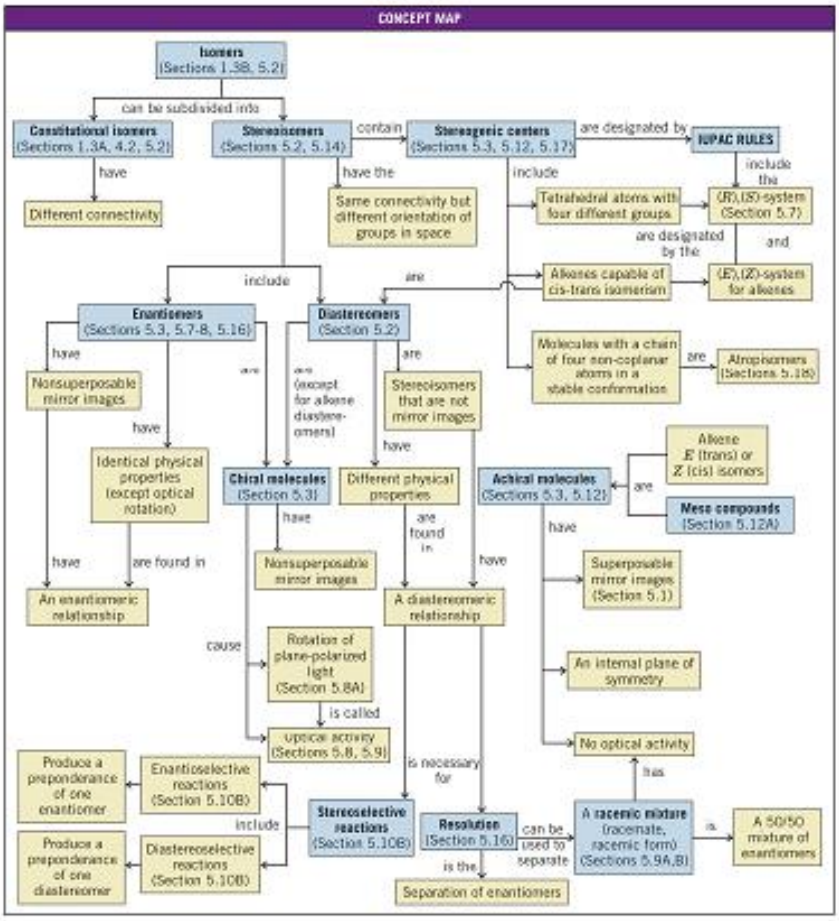


(*R*)-1-Bromo-2-butanol **(*S*)-2-Butanol**

Resolution of enantiomers



Basics of stereochemistry



Stereochemistry of Reactions

This is the study of what happens when chiral compounds react. Studies with chiral compounds can reveal a vast amount of information about a reaction mechanism.

Three general types

1) Reactions that occur at the chiral atom
2) Reactions that do not involve the chiral atom
3) Reactions that generate a new chiral atoms

1) Reactions at a Chiral Atom

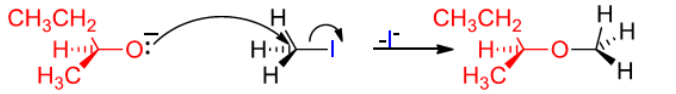
If a reaction occurs at a chiral atom, one of three things can happen.

(a) Inversion of Configuration (R→S)
(b) Racemization of configuration(R→R + S)
(c) Retention of Configuration(R→R)

This depends on the mechanism of reaction.

2) Reactions that do not Involve the Chiral Atom

Typically, if bonds directly to the chiral atom are not broken or formed during the reaction, the configuration will remain unchanged.



(S)-2-butoxide (S)-2-methoxyethane

The four bonds to the chiral C atom are unchanged, and the configuration is the same.

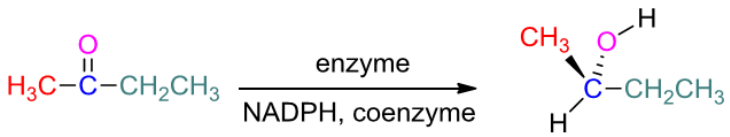
3) Reactions that generate a new Chiral Center

Lots of reactions form new chiral atoms, yet achiral reactants will always produce **racemic** mixtures, since there is no chiral control.

Asymmetric Induction

This is the use of an optically active reagent or catalyst to convert an *achiral* reactant into a *chiral* product.

Enzymes are especially useful for this type of transformation.
Hydrogen is selectively delivered from one face, to give only one enantiomer.



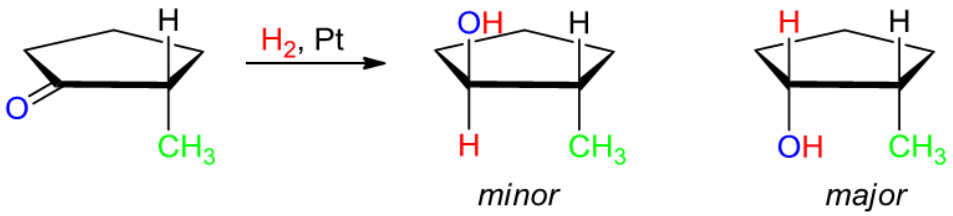
pure (R)

Similar results can be achieved in the lab using chiral catalysts or reagents (which are usually expensive).

Directing Effects of Chiral Carbons

If there is already a chiral atom in the molecule, it is possible that the stereochemistry around that atom can influence or direct a reagent to have a preferred direction of attack.

The platinum catalyzed hydrogenation of 2-methylcyclopentanone gives two products.



minor *major*

The **major** product is *cis*-2-methylcyclopentanol, the **minor** is the *trans* isomer.

The hydrogen attacks from the *least hindered* side.

The two faces of attack are not the same since the methyl group sterically hinders one face.
The chiral carbon atom *communicates* its chirality to the new center.