

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

ISOMERISM

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4th lecture in Medical Chemistry
Faculty of Medicine
University of Diyala

ISOMERS



INTRODUCTION

Isomerism

Occurs when certain compounds, having the same molecular formula, exist in different forms each form called isomer.

Isomers

Compounds having the same molecular formula but different linkages or spatial arrangements of atoms

Classification Isomerism

Two main types of isomerism

1. Structural isomerism

Different linkages of atoms.

Same molecular formula.

Different structural formula.

2. Stereoisomerism

Different spatial arrangements of atoms

Same molecular formula

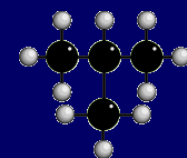
& structural formulae

Isomerism

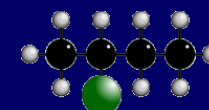
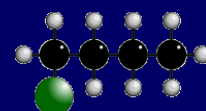
STRUCTURAL ISOMERISM

Same molecular formula
but different structural
formulae

CHAIN ISOMERISM



POSITION ISOMERISM

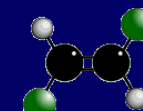
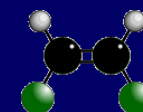
FUNCTIONAL GROUP
ISOMERISM

STEREoisomerism

Same molecular
formula but atoms
occupy different
positions in
space.

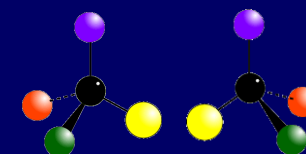
GEOMETRICAL ISOMERISM

Occurs due to the restricted
rotation of C=C double
bonds... two forms - CIS and
TRANS



OPTICAL ISOMERISM

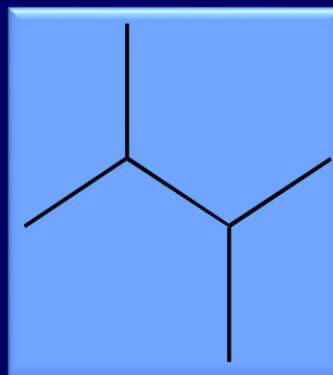
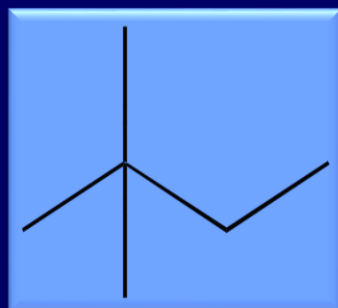
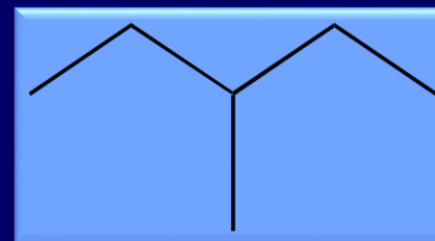
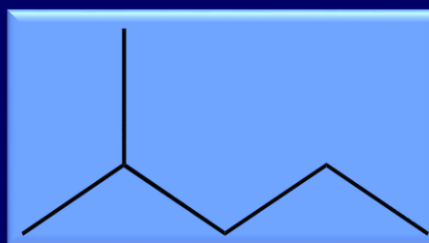
Occurs when molecules
have a chiral centre. Get
two non-superimposable
mirror images.



Structural Isomerism

Due to the presence of different carbon skeletons.

1. Chain isomerism C_6H_{14}



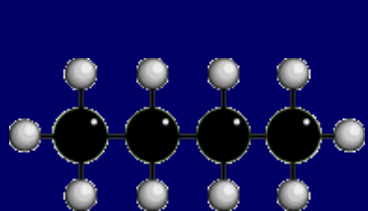
Properties

Different physical properties

e.g : Boiling point

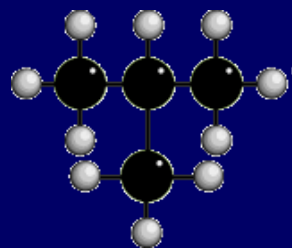
Straight-chain > branched-chain

Because the larger surface area and thus stronger van der Waals force



Butane (b.p= -0.5 °C)

>



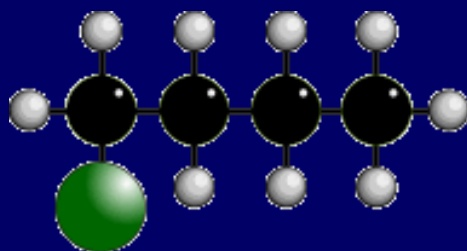
Methylpropane (b.p= -11 °C)

Same Chemical properties

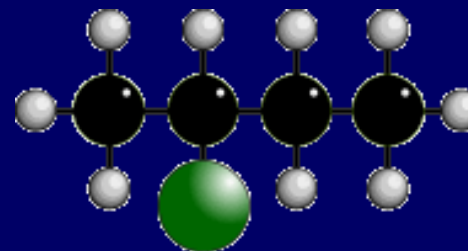
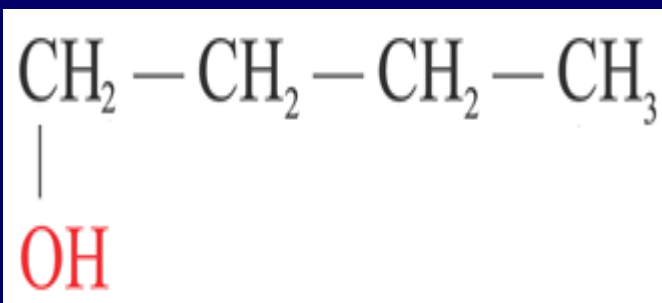
Chain isomers have similar chemical properties because they have the same functional groups.

Position isomerism

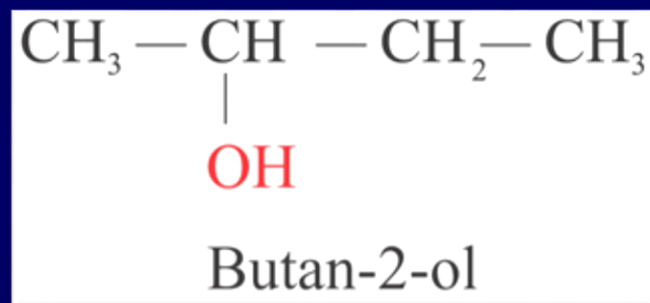
e.g. Butan-1-ol and butan-2-ol
(molecular formula: $C_4H_{10}O$)



Butan-1-ol



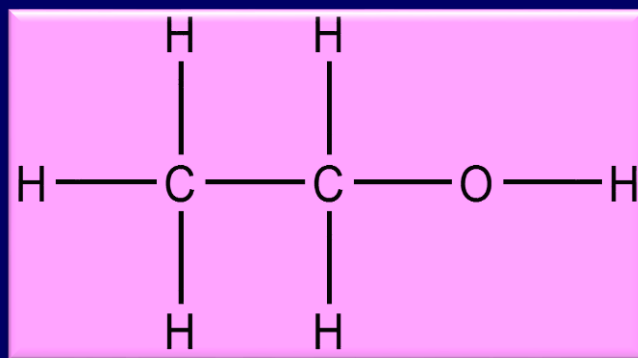
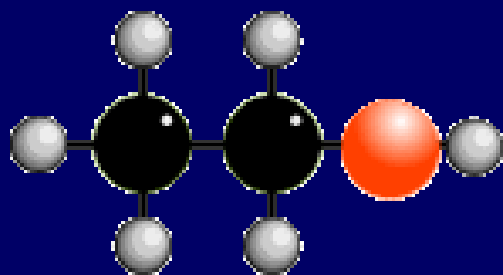
butan-2-ol



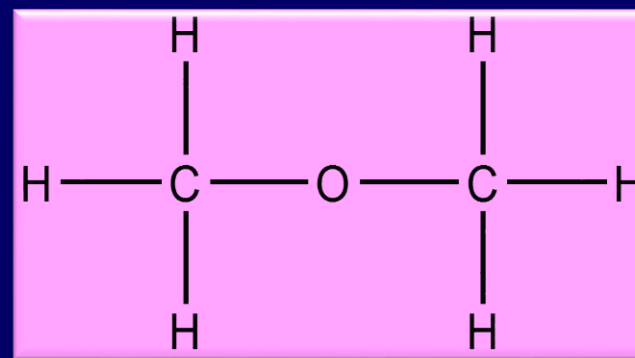
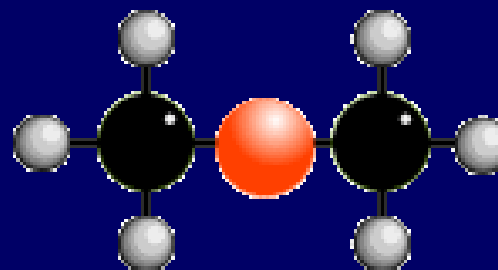
Functional Group Isomerism

Due to the presence of different functional groups

e.g. C_2H_6O

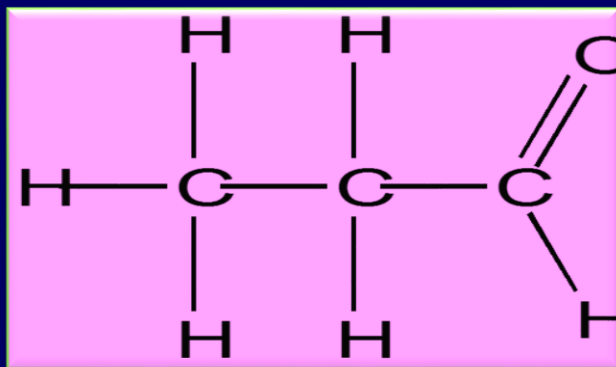


Alcohol

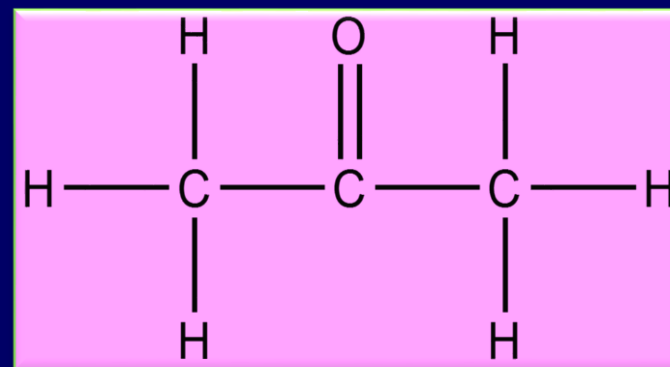


Ether

e.g. C_3H_6O

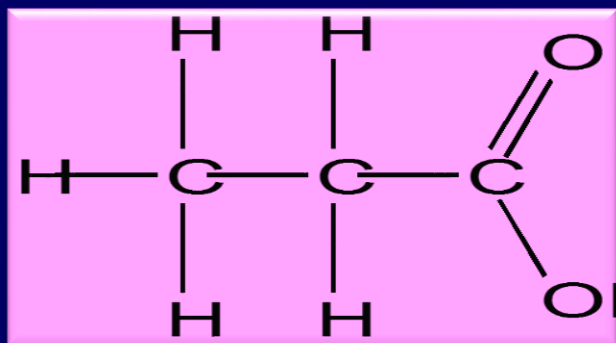


Aldehyde

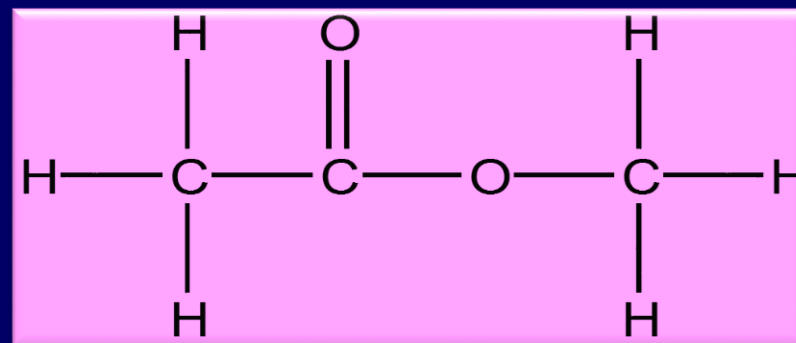


Ketone

e.g. $C_3H_6O_2$



Carboxylic acid

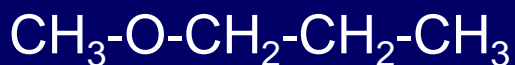


Ester

Metamerism

Occurs when the functional group (-oxy or -carbonyl) **interrupts** the main carbon skeleton at different positions.

e.g. Methoxypropane and ethoxyethane
(molecular formula: $C_4H_{10}O$)



Methoxypropane



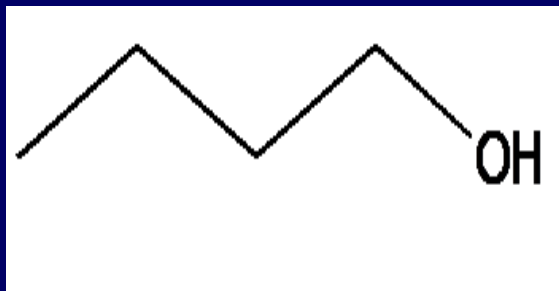
Ethoxyethane

Position
Isomers

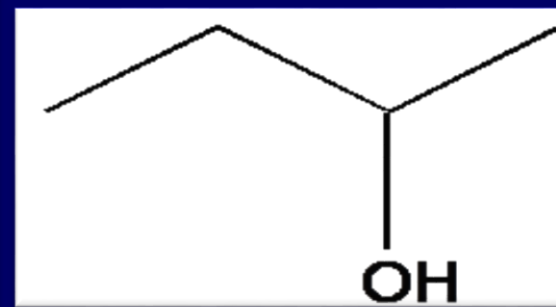


e.g. Pentan-2-one and pentan-3-one
(molecular formula: $C_5H_{10}O$)

Write the chemical structure?



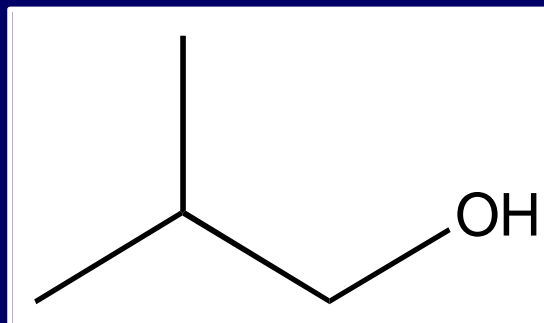
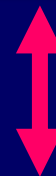
Position isomers



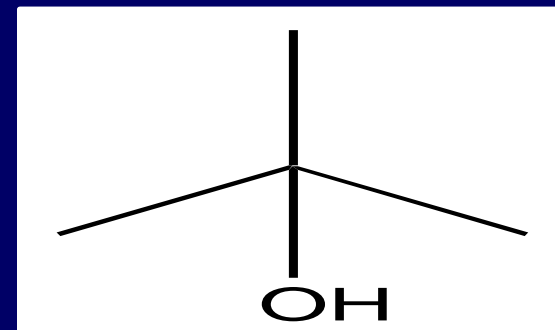
Chain isomers

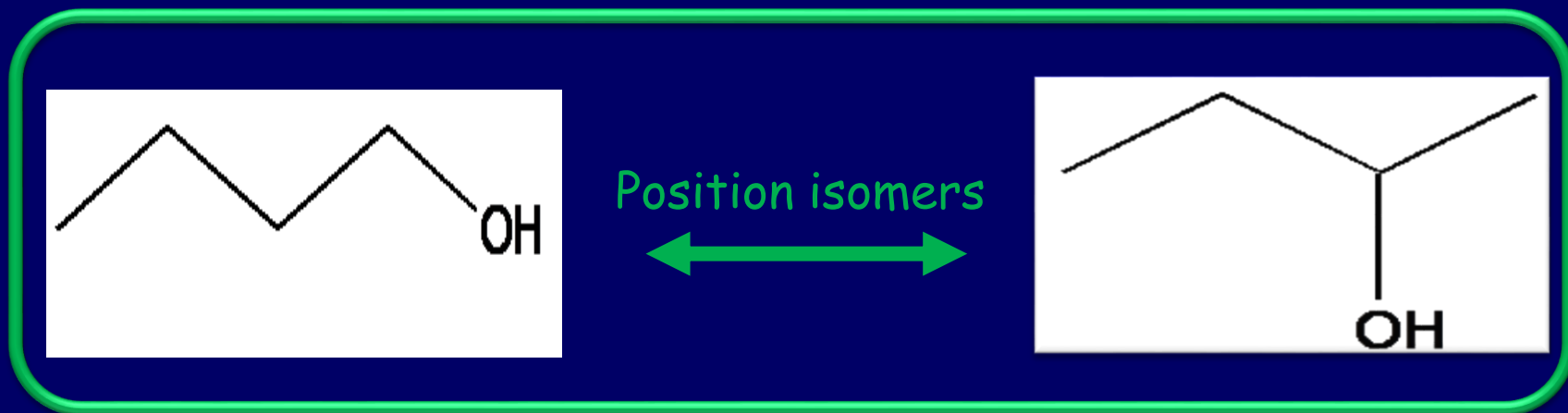


Chain isomers



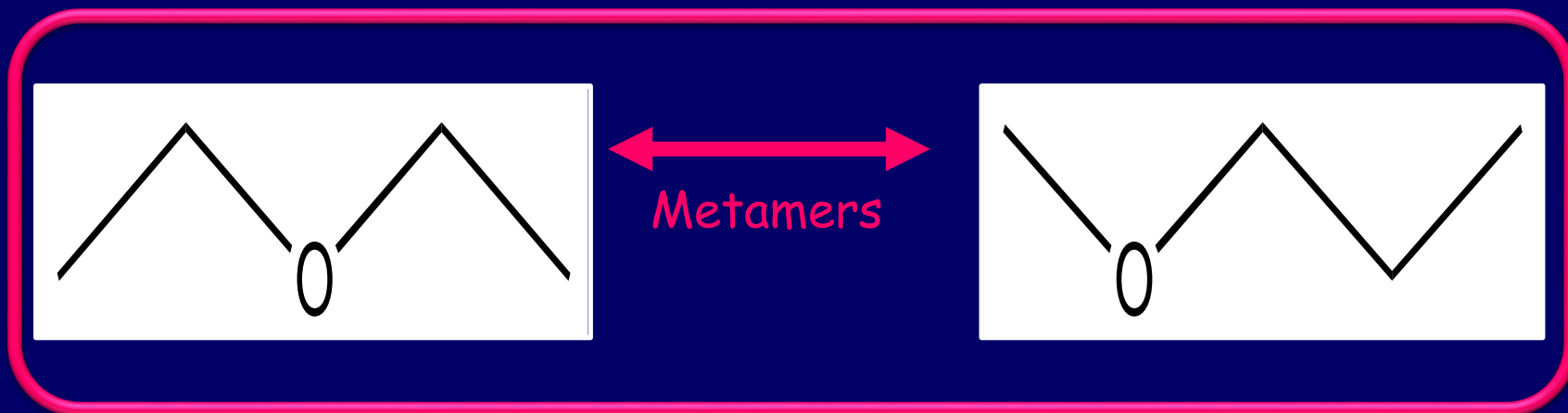
Position isomers





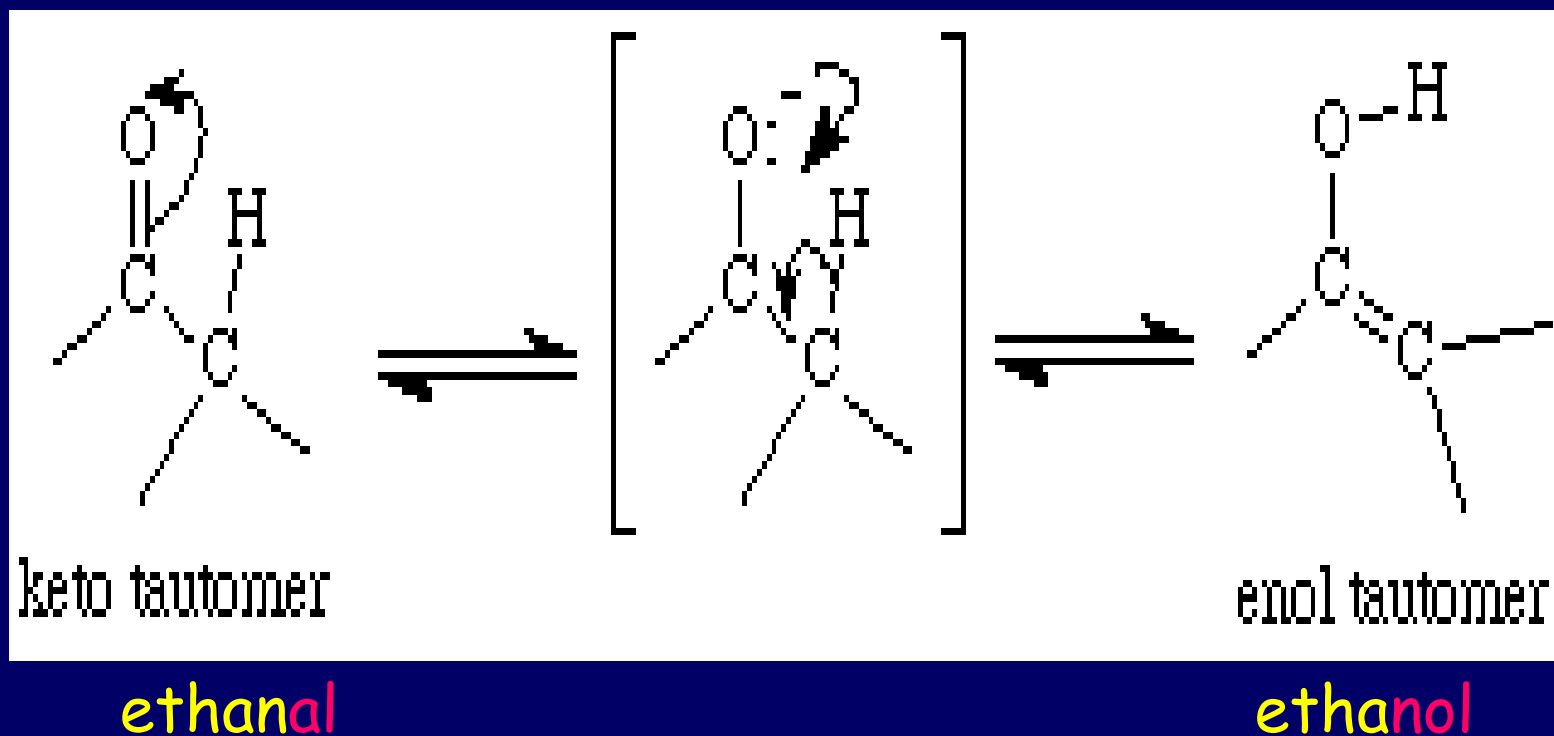
functional group isomers

$C_4H_{10}O$



Tautomerism

Occurs when functional group isomers are in dynamic equilibrium with each other.



Stereoisomerism

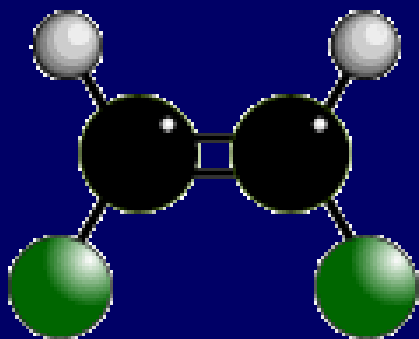
Stereoisomerism occurs when compounds having the same structural formula show different spatial arrangements of atoms in the space .

Two categories of stereoisomerism:

1. Geometrical isomerism
2. Optical isomerism

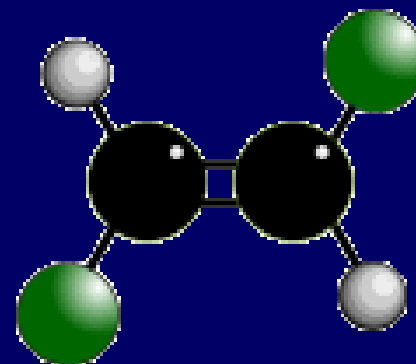
GEOMETRICAL ISOMERISM

- An example of geometrical isomerism found in some, but not all, alkenes.
- Occurs due to the restricted rotation of C=C bonds
- Get two forms....



CIS

Groups/atoms are on the
SAME SIDE of the double bond



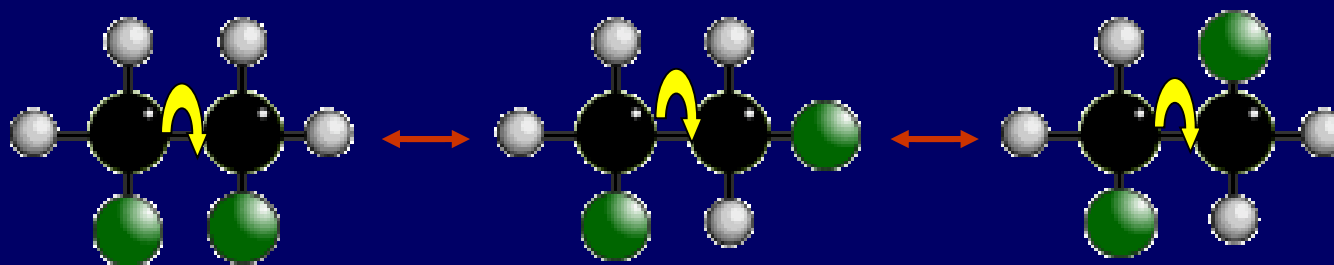
TRANS

Groups/atoms are on OPPOSITE SIDES
across the double bond

GEOMETRICAL ISOMERISM

FREE ROTATION OF C-C BONDS

Single covalent bonds can easily rotate.

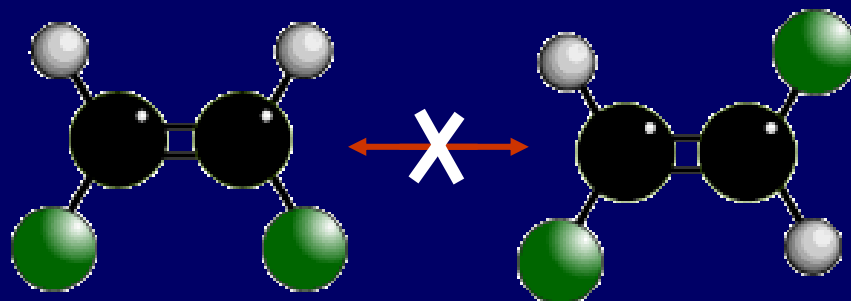


All these structures are the same because C-C bonds have free rotation

GEOMETRICAL ISOMERISM

RESTRICTED ROTATION OF C=C BONDS

C=C bonds have restricted rotation so the groups on either end of the bond are 'frozen' in one position; it isn't easy to flip between the two.

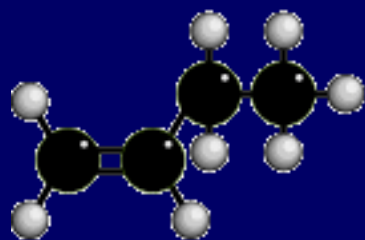


This produces two possibilities.. The two structures cannot interchange easily so the atoms in the two molecules occupy different positions in space.

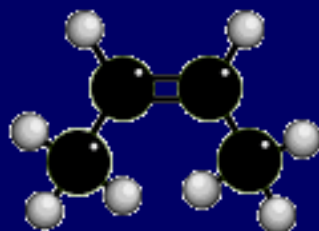
GEOMETRICAL ISOMERISM

Isomerism in butane

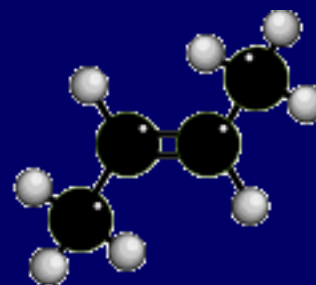
There are 3 structural isomers of C_4H_8 that are alkenes*. Of these **ONLY ONE** exhibits geometrical isomerism



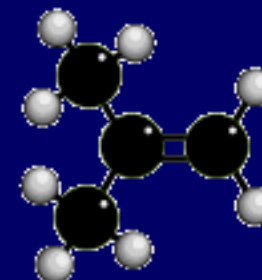
BUT-1-ENE



cis BUT-2-ENE



trans BUT-2-ENE

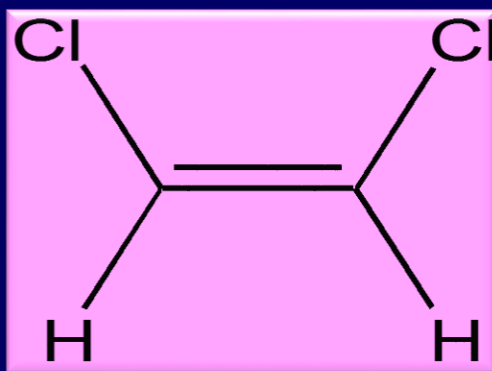


2-METHYLPROPEN

Properties of Geometrical Isomers

Have similar chemical properties - in most cases

They have significantly different physical properties

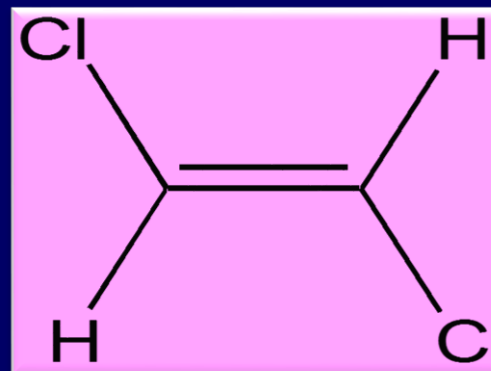


m.p.

-80°C

b.p.

60°C

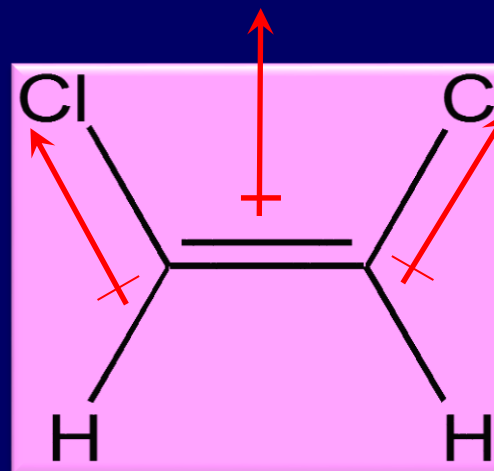
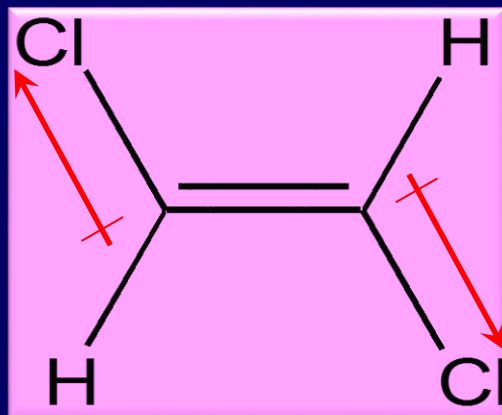


-50°C

48°C

b.p. depends on van der Waals' forces ONLY

Zero net
dipole moment



van der Waals' forces : $\text{cis} > \text{trans}$
 \Rightarrow b.p. : $\text{cis} > \text{trans}$

Stereoisomers

Isomers with same connectivity but differ in the arrangement of atoms in space

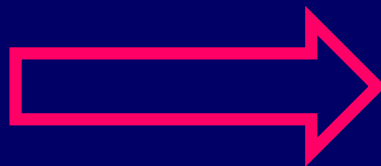
stereoisomers subdivided into:

1. *Enantiomers* non superposable mirror images
2. *Diastereomers* non mirror images

Geometric isomers cis/trans-isomers are diastereomers

Enantiomers (Optical Isomers)

- Enantiomers occur when compounds have non-superimposable mirror images



- The two different forms are known as optical isomers or , Chiral molecules enantiomer
- They occur when molecules have a chiral centre

A chiral centre contains an asymmetric carbon atom

An asymmetric carbon has four different atoms (or groups) arranged tetrahedrally around it.

A chiral \neq Achiral

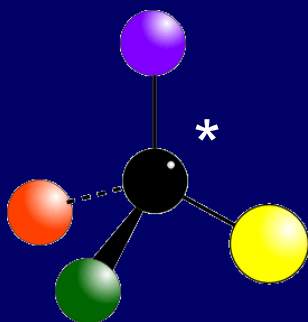
Asymmetric \neq symmetric

Achiral (not chiral) if object and its mirror image are identical (symmetry element)

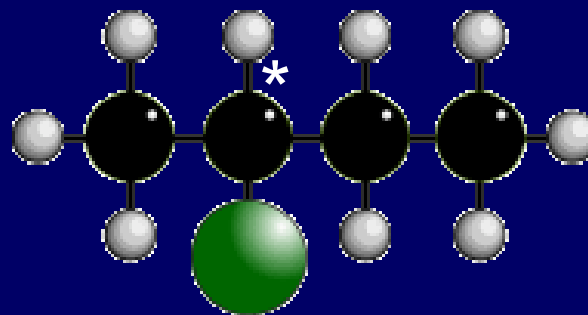


Optical activity arises from asymmetry or chirality

Any molecule with an sp^3 carbon atom bonded to FOUR different groups arranged tetrahedrally show optical activity



There are four different colours arranged tetrahedrally about the carbon atom



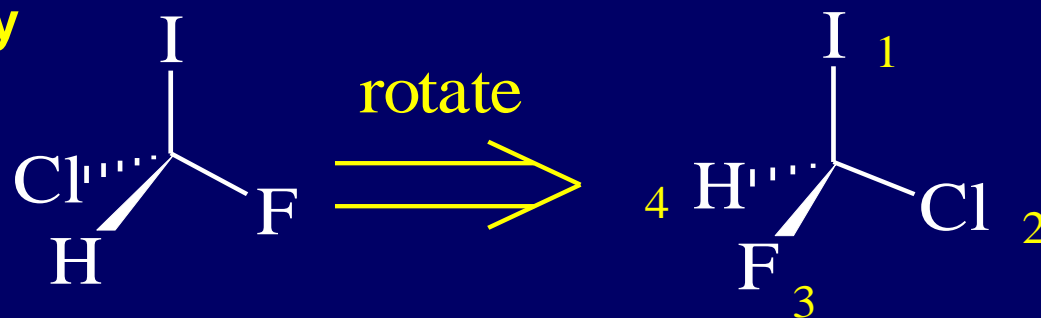
2-chlorobutane exhibits optical isomerism because the second carbon atom has four different atoms/groups attached

In compounds with n chiral centers, the maximum number of stereoisomers is 2^n .

(R) And (S) Nomenclature

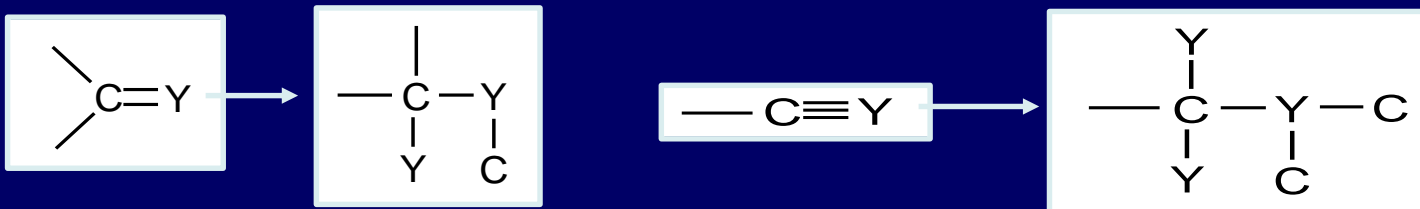
Assign a numerical priority to each group bonded to the asymmetric carbon:

group 1 = highest priority
group 4 = lowest priority



focus down C-4 bond

Atoms with higher atomic numbers have higher priority



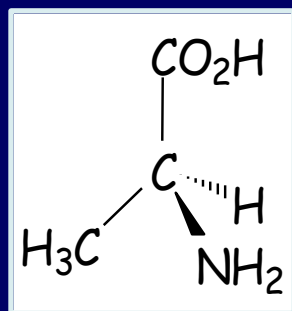
Draw an arrow from the 1st priority group to the 2nd group to the 3rd group.

Clockwise arrow

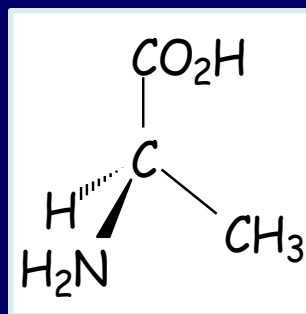
(R) configuration

Counterclockwise arrow

(S) configuration

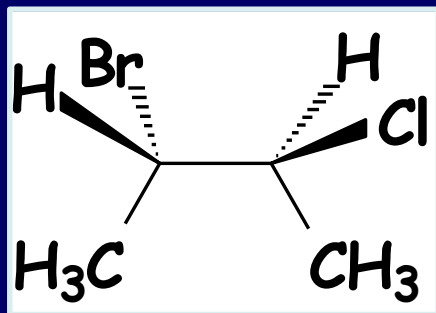


(S)-alanine

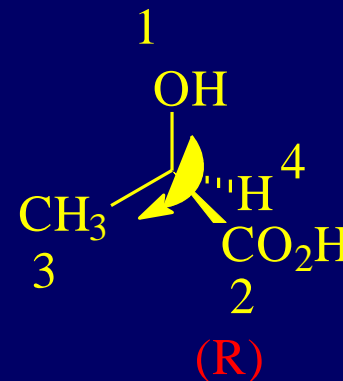
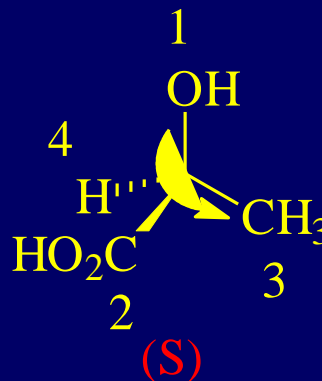


(R)-alanine

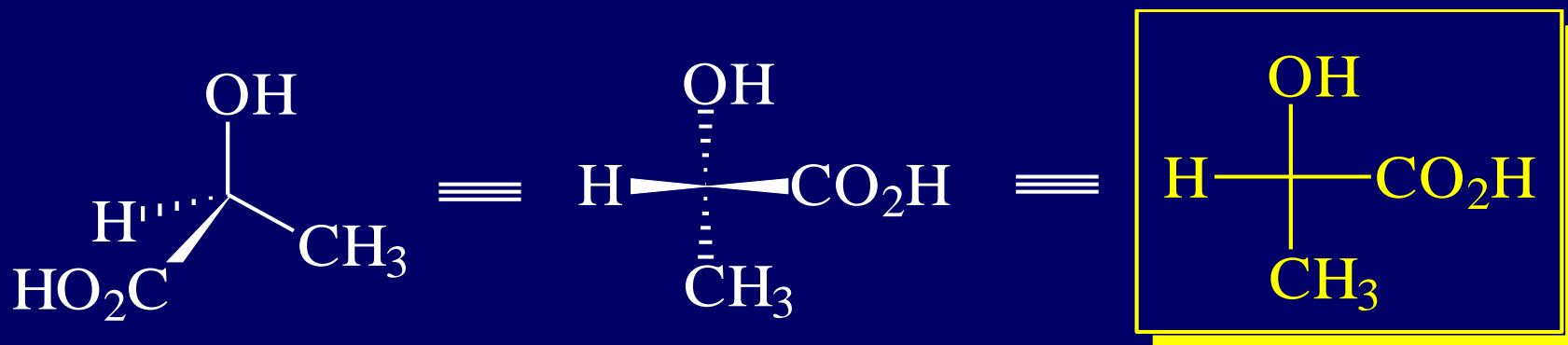
When naming compounds containing multiple chiral atoms, you must give the configuration around each chiral atom:



(2S, 3S)-2-bromo-3-chlorobutane

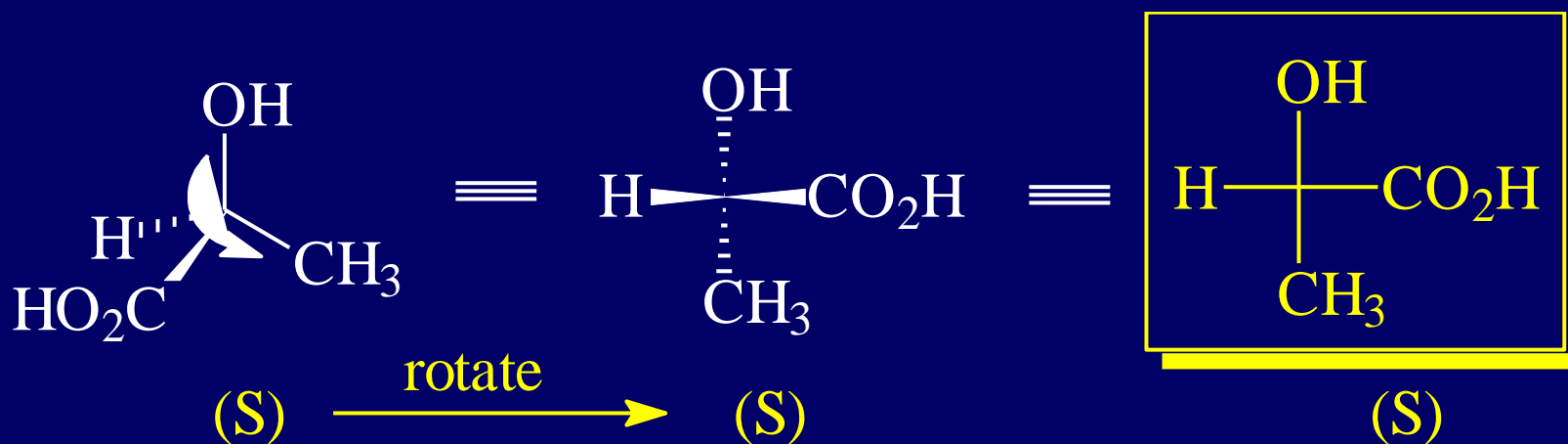


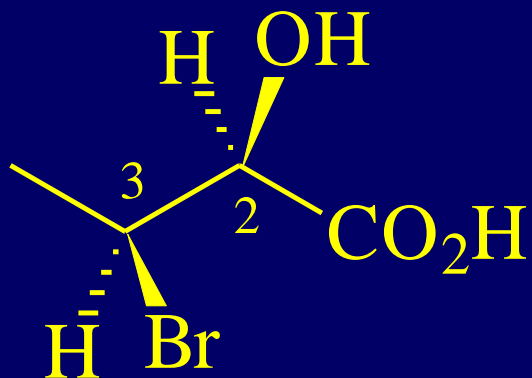
Fischer Projections



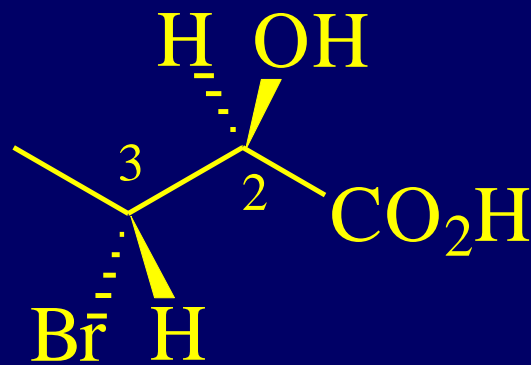
Horizontal bonds approach you (wedge bonds)

Vertical bonds move away (dashed bonds)





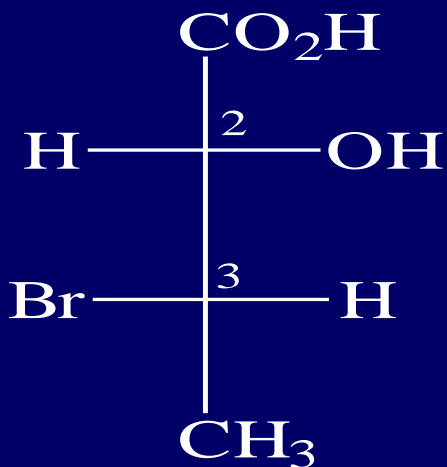
(2S,3S)



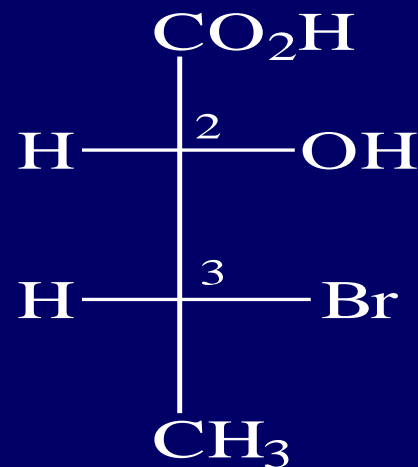
(2S,3R)

same stereochemistry at C₂ (S)

opposite stereochemistry at C₃



(2S,3S)

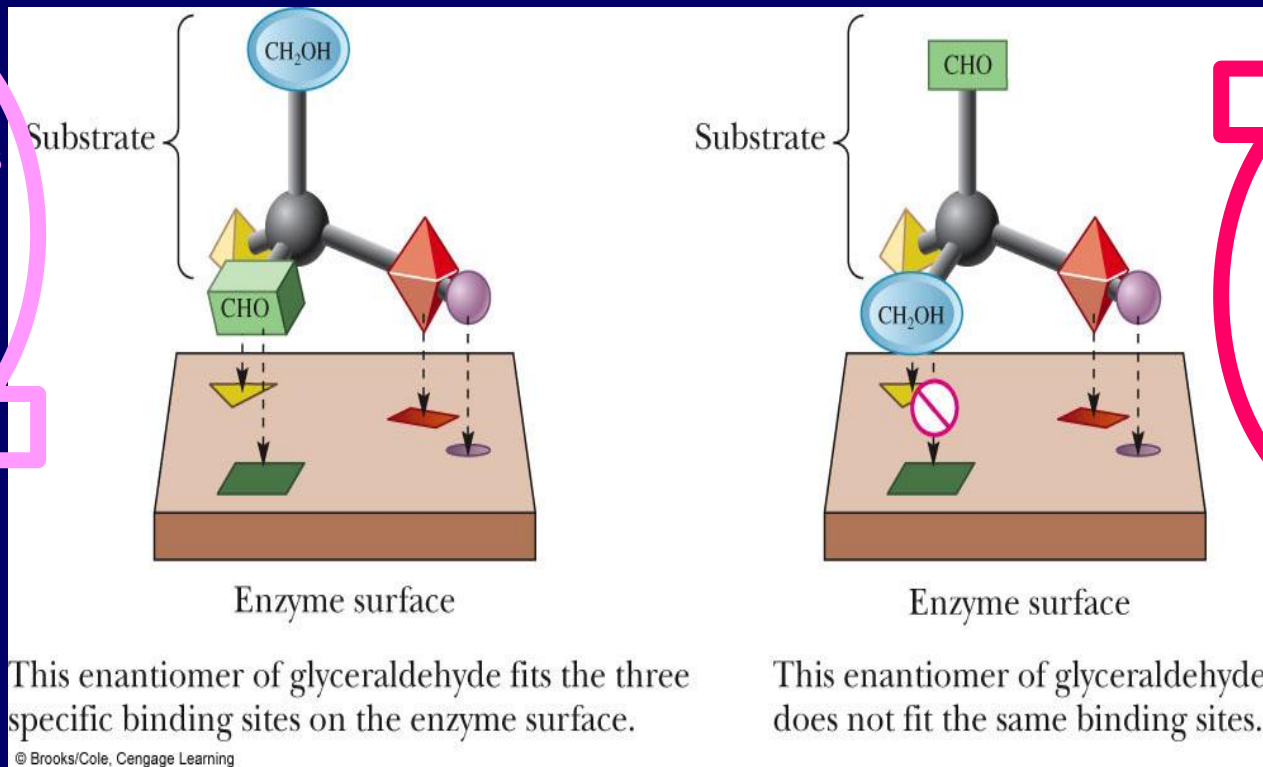


(2S,3R)

Chirality in the Biological World

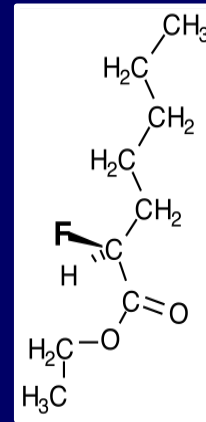
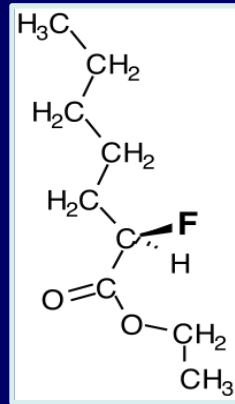
1. An enzyme distinguishes between a molecule and its enantiomer
A schematic diagram of an enzyme surface capable of binding with (*R*)-glyceraldehyde but not with (*S*)-glyceraldehyde.

All three substituents match up with sites on the enzyme.

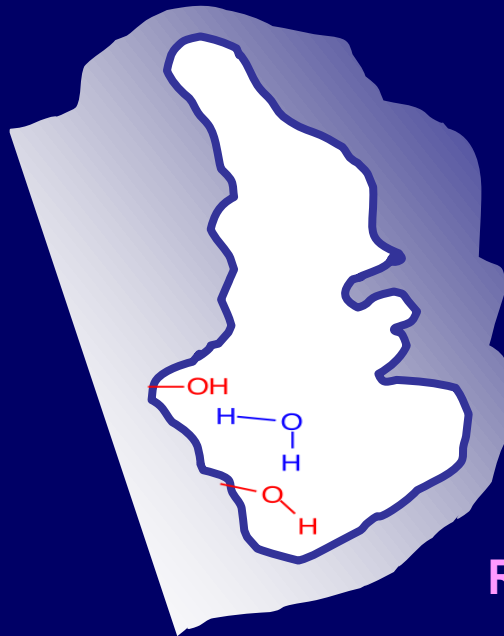


If two are matched up then the third will fail!

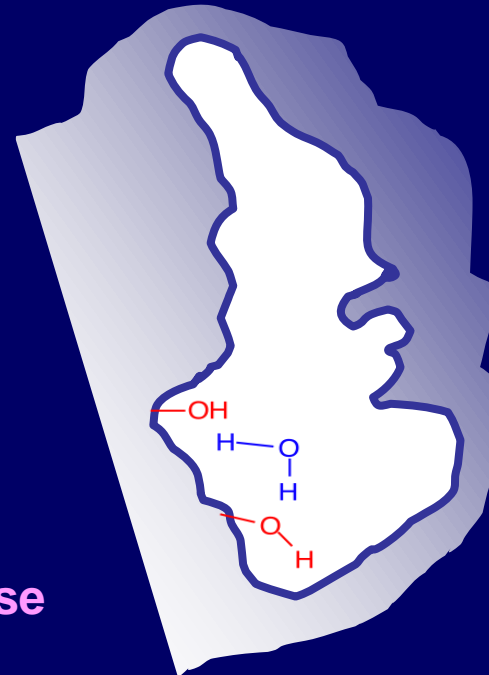
mirror



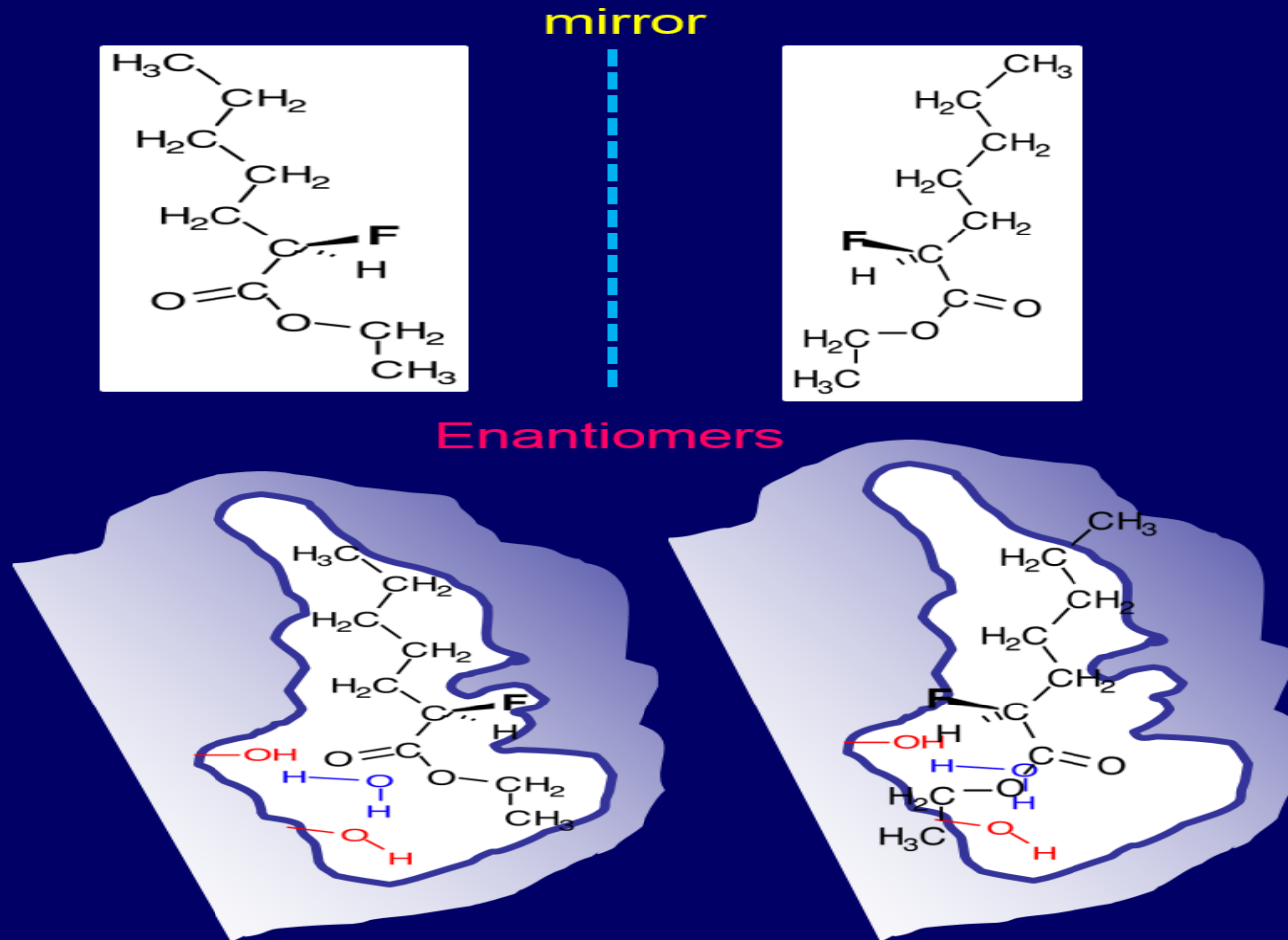
Enantiomers

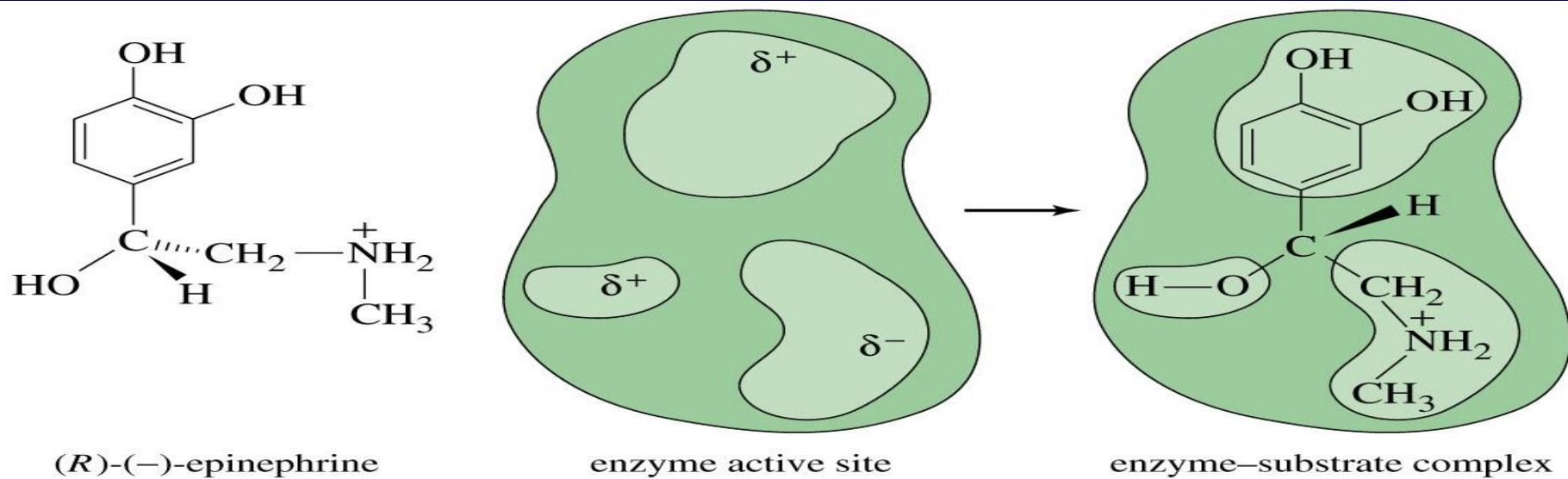


R-lipase



Enzymes are like hands in a handshake the substrate fits into a binding site on the enzyme surface

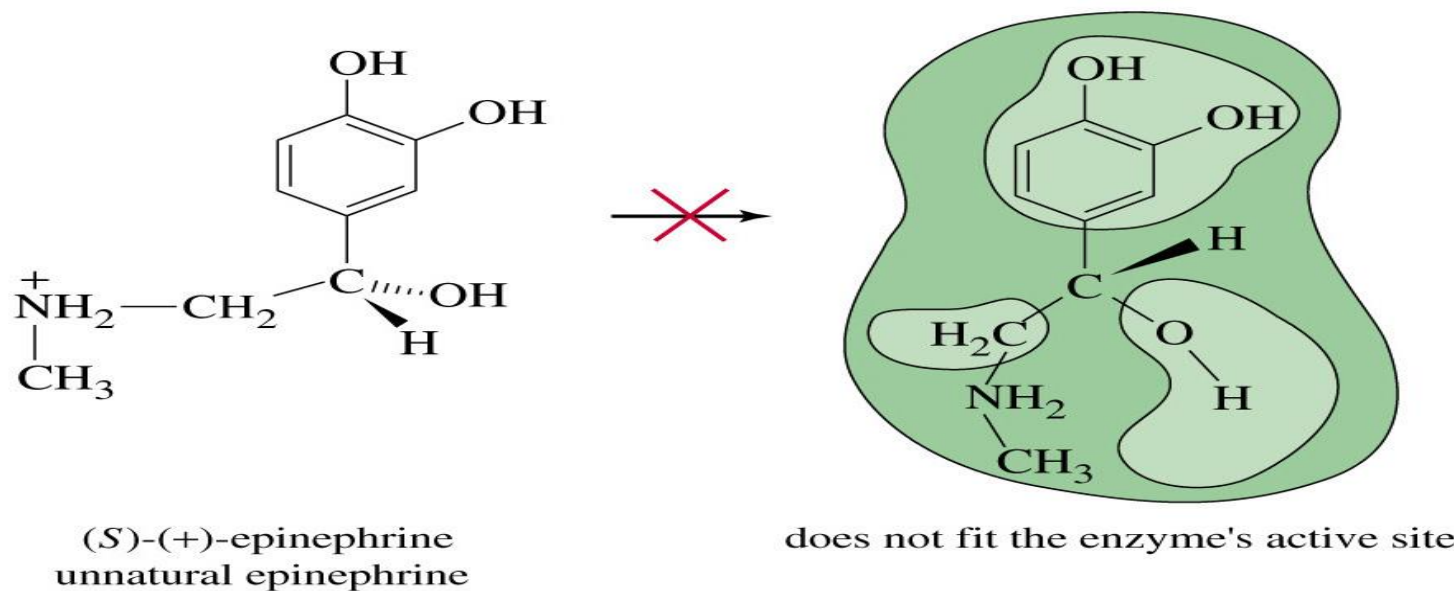




(*R*)-(-)-epinephrine
natural epinephrine

enzyme active site

enzyme-substrate complex



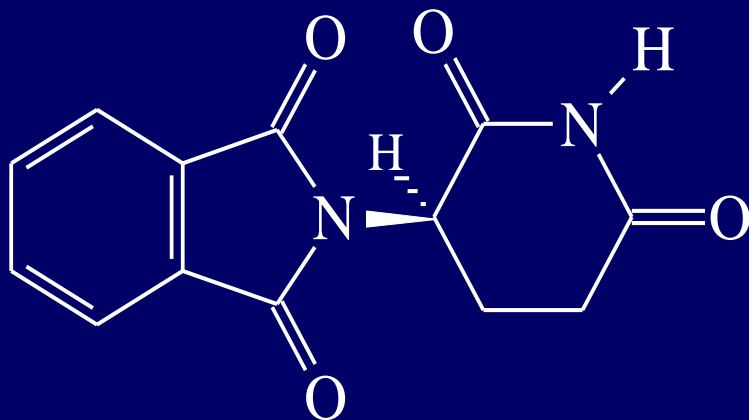
(*S*)-(+)-epinephrine
unnatural epinephrine

does not fit the enzyme's active site

2. The properties of many drugs depends on their stereochemistry

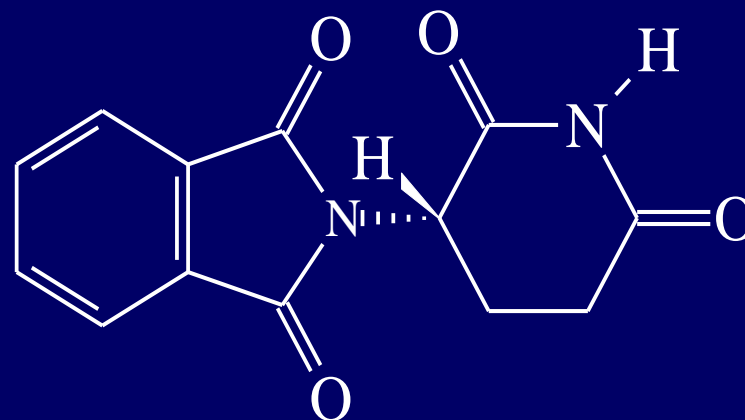
e.g. **Thalidomide** one mirror image causes birth defects the other cures morning sickness

(R)(+) Thalidomide



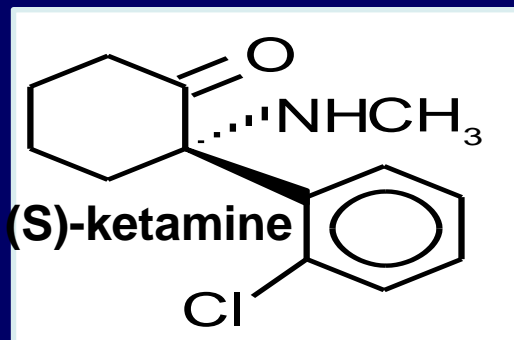
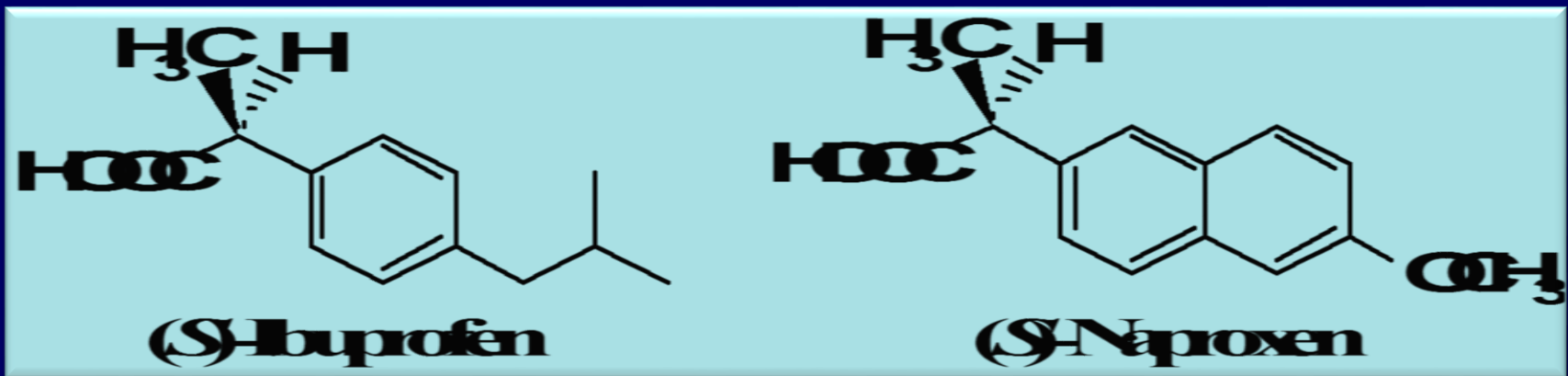
a sedative and hypnotic

(S)(-) Thalidomide

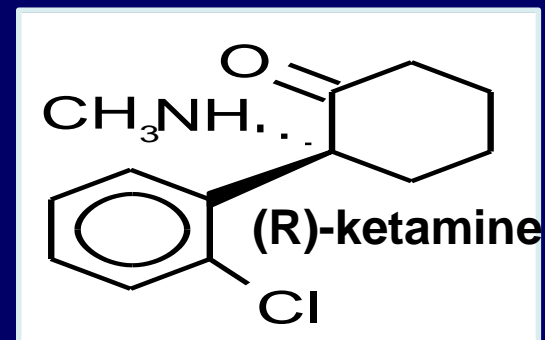


a teratogen

Enantiomers elicit different physiological responses
 (*S*)-ibuprofen is active as a pain and fever reliever, while its
 R enantiomer is inactive
 S enantiomer of naproxen active as pain reliever, but R
 enantiomer is a liver toxin!



anesthetic



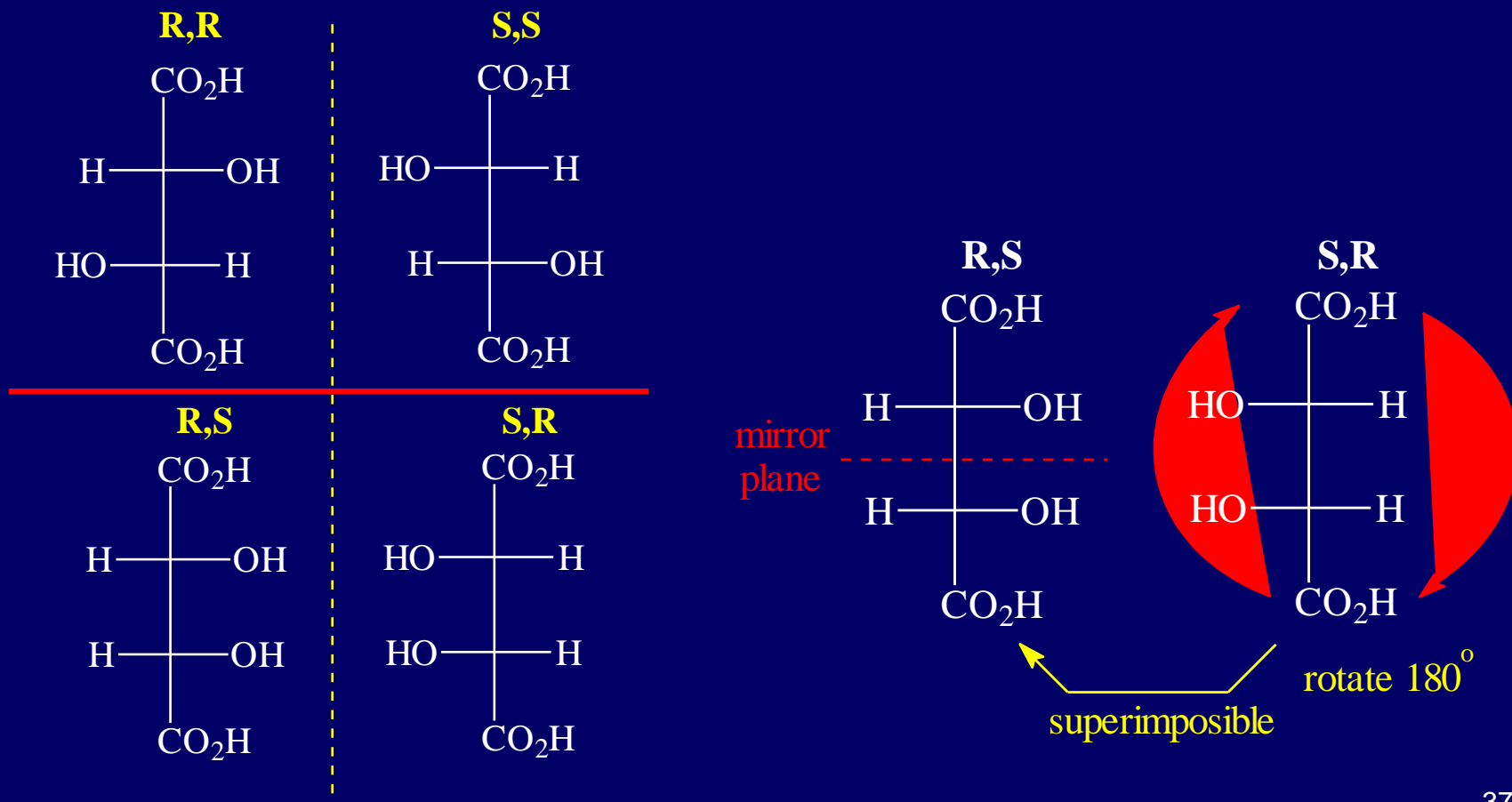
hallucinogen

Meso Compounds

Compounds with 2 stereocenters do not always have 4 stereoisomers
($2^2 = 4$)

Some stereoisomers are achiral, even though they contain stereocenters

Example: tartaric acid has two stereocenters, but only has 3 stereoisomers

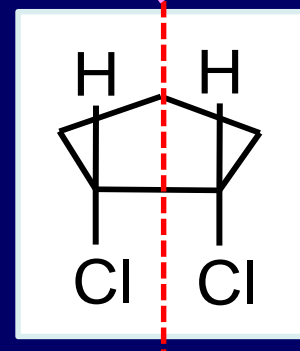
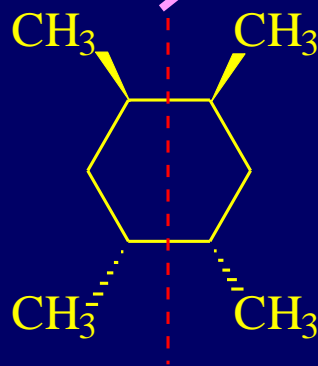
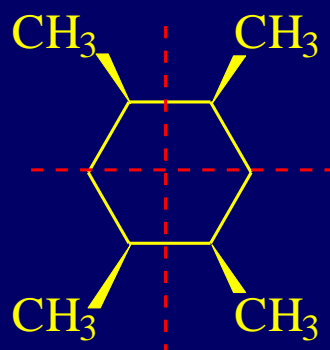


Internal Plane of Symmetry

Cis-1,2-dichlorocyclopentane contains two asymmetric carbons but is achiral.

contains an internal mirror **plane of symmetry**

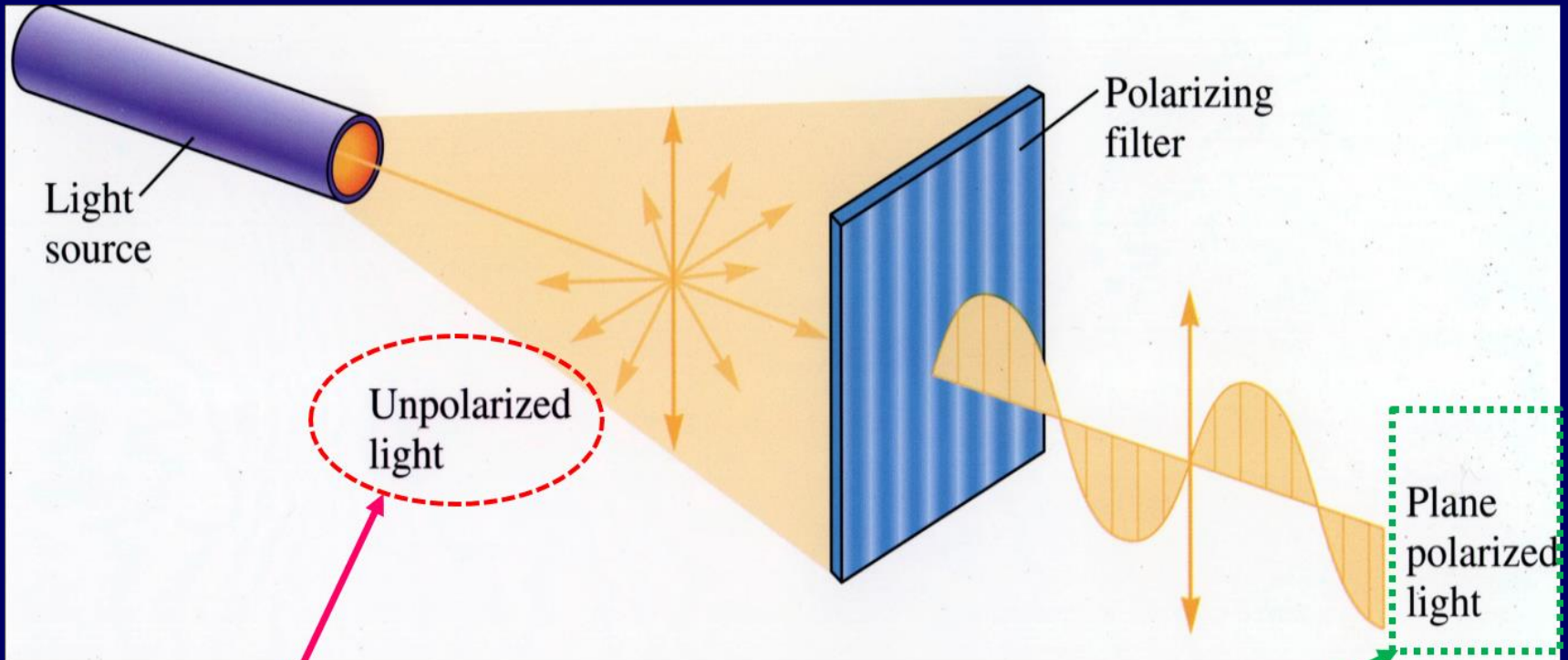
Both are Meso



Any molecule that has an internal mirror plane of symmetry is achiral even if it contains asymmetric carbon atoms.

Cis-1,2-dichlorocyclopentane is a **meso compound**

plane-polarized light



Light vibrating in ALL possible planes

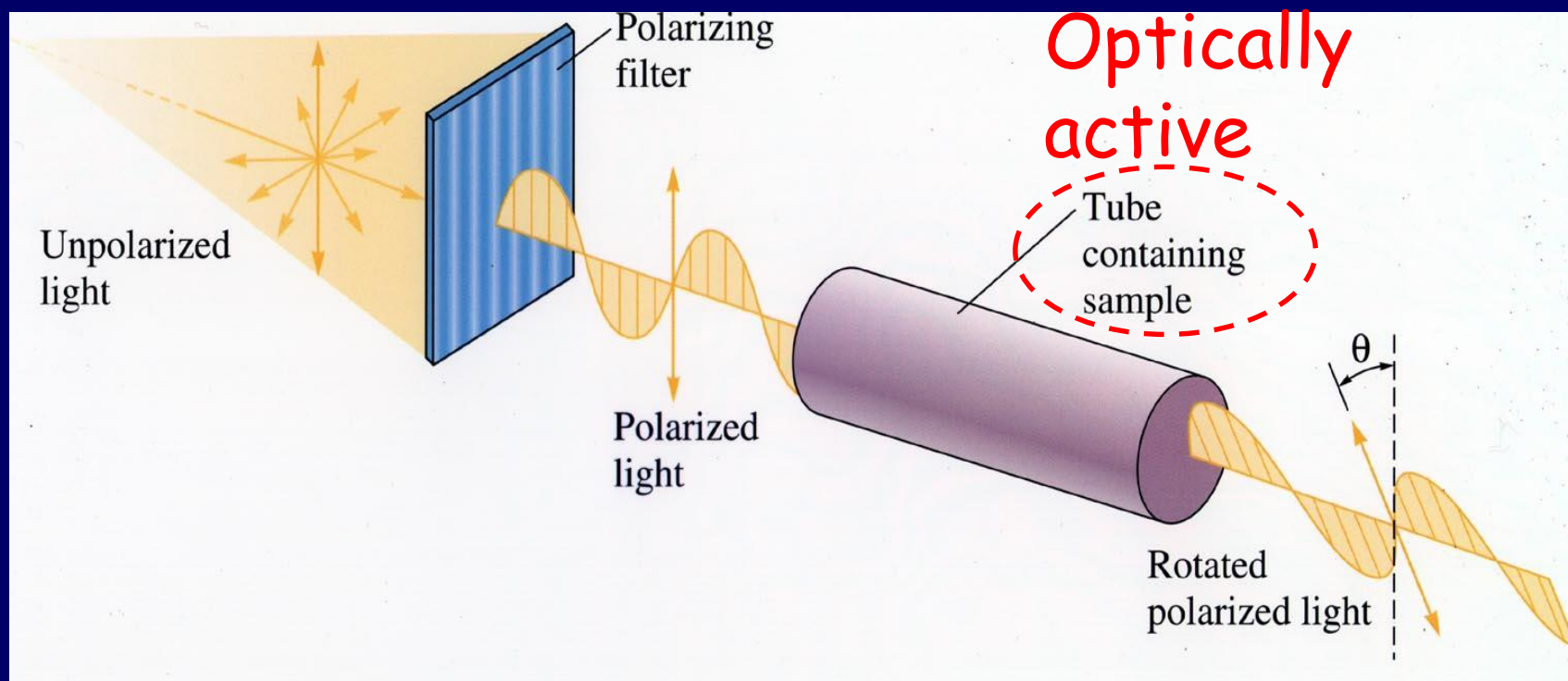
Light vibrating in ONE plane

Optically active substance can rotate the plane of polarization of plane-polarized light

Measured by a **polarimeter**.

Dextrorotatory(+) : clockwise (to the right)

Laevorotatory(-): anti-clockwise (to the left)



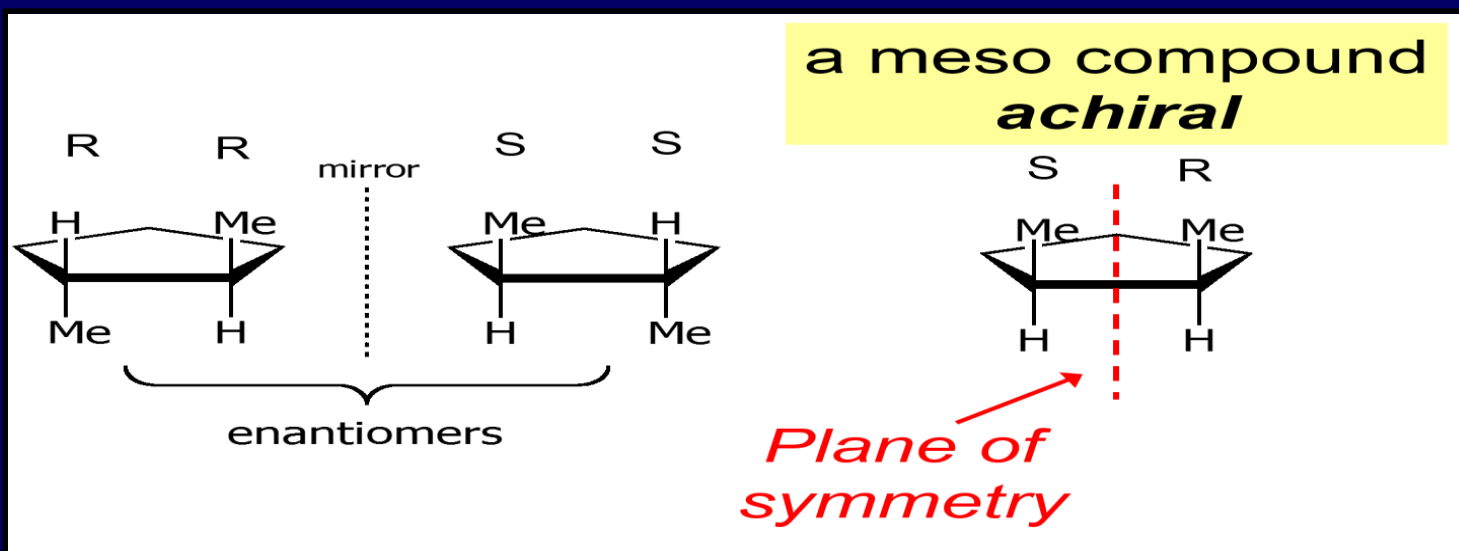
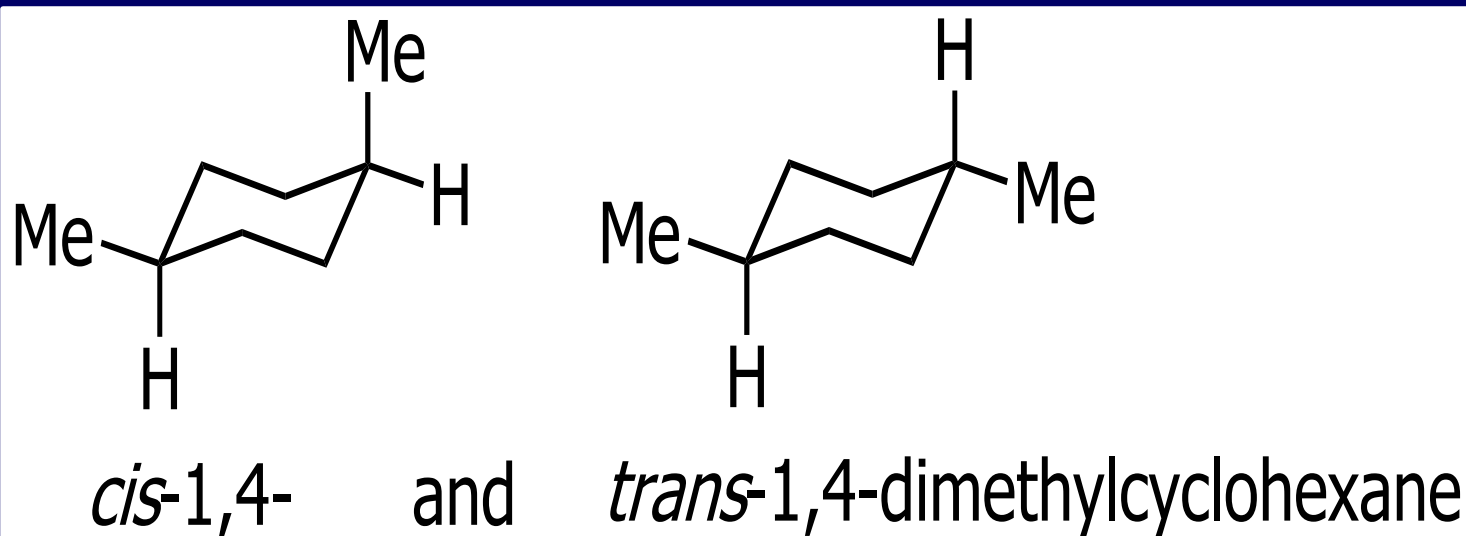
Properties of enantiomers

- Identical physical properties except their optical activities.
- Identical chemical properties except their reactions with optically active substances.

Racemic mixture (racemate)

- The racemic mixture (racemate) is a 50:50 mixture of the two enantiomers.
- The specific rotation is zero.
- The racemic mixture may have different physical properties (m.p., b.p., etc.) than the enantiomers.

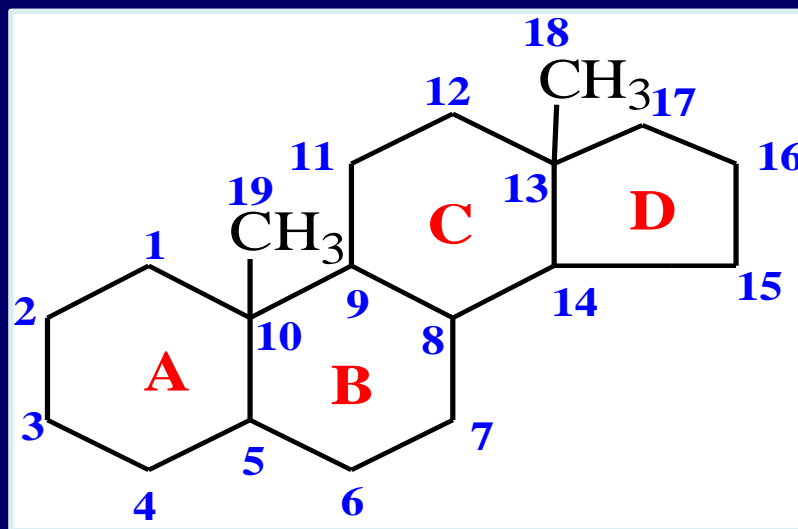
Stereoisomerism of Cyclic system



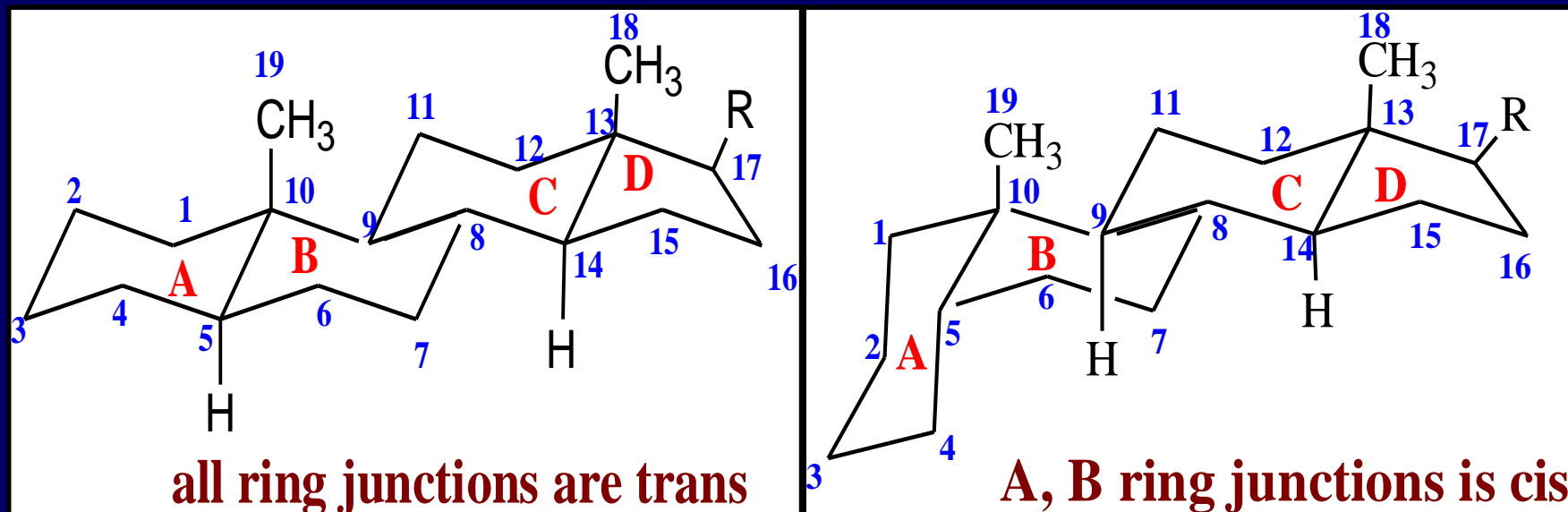
STEROIDS

Steroids are important “biological regulators” that nearly always show dramatic physiological effects when they are administered to living organisms.

Steroids are derivatives of the following ring system

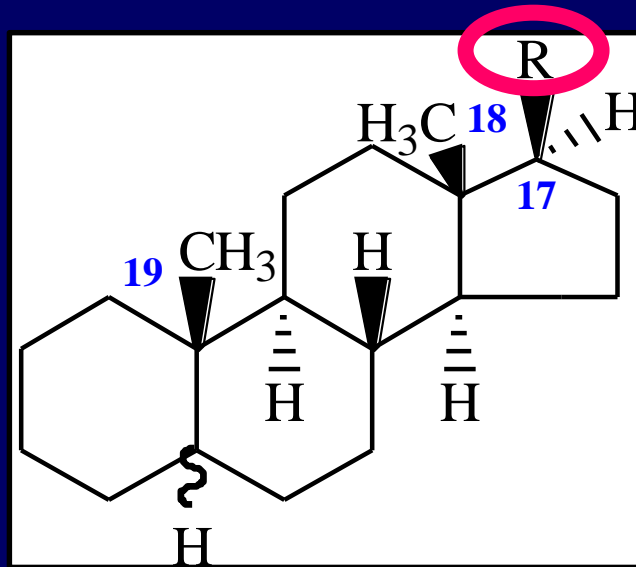


In most steroids the B, C and C, D ring junctions are trans. The A, B ring junction may be either cis or trans.

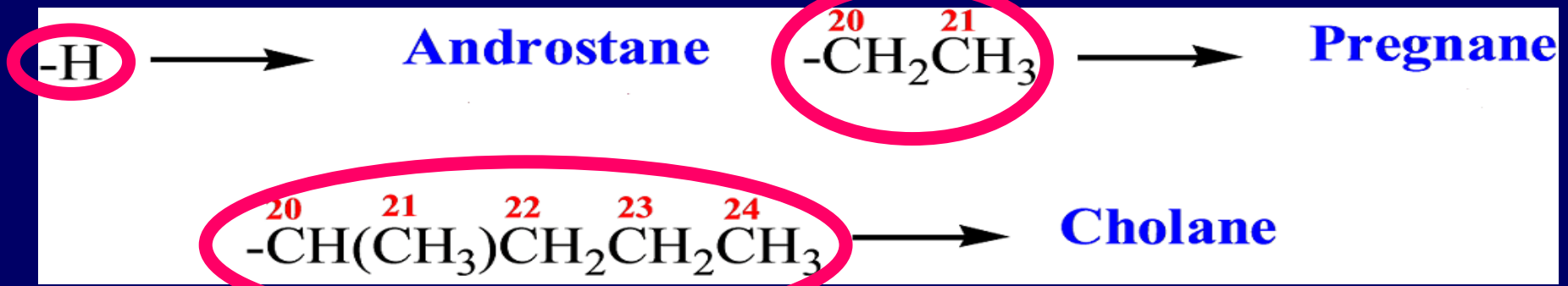


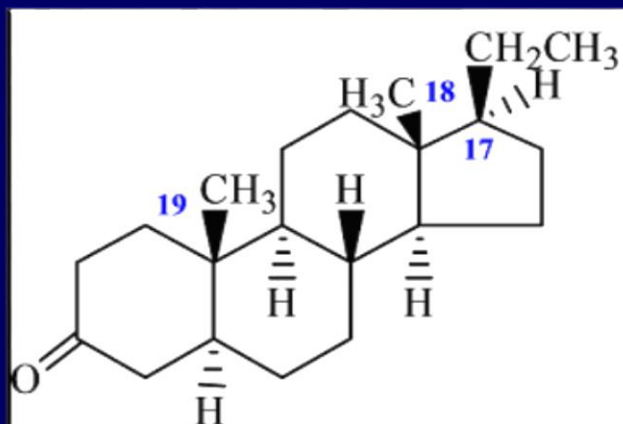
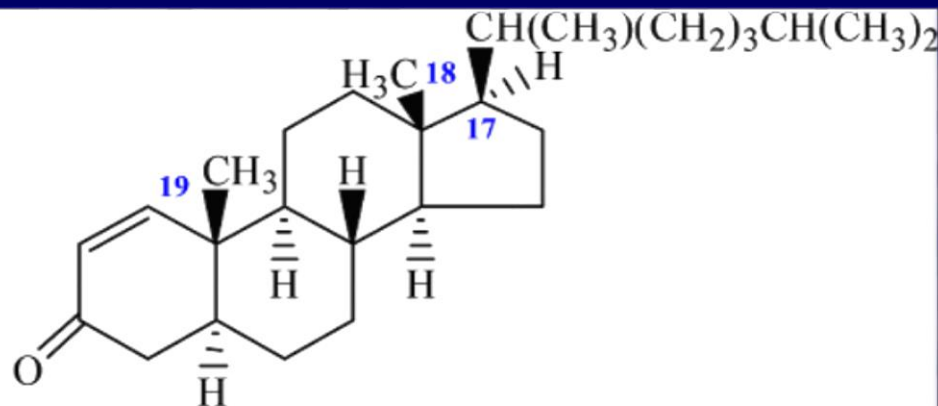
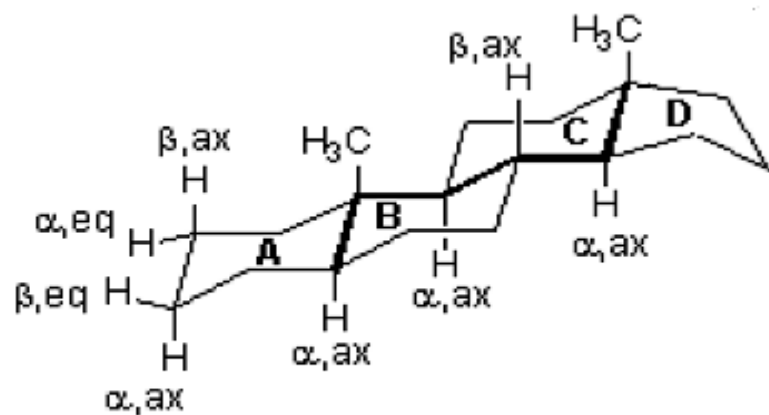
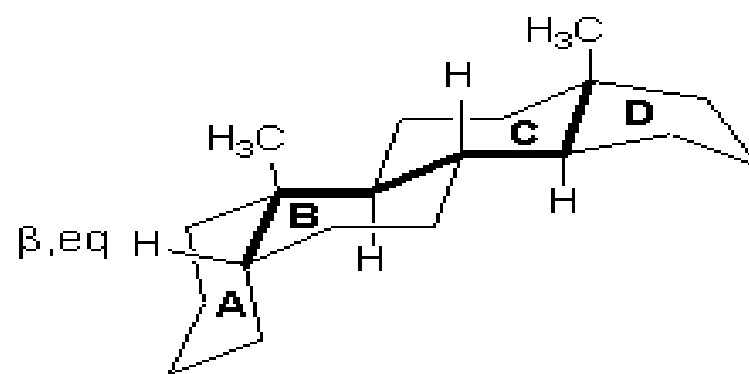
When α and β designation are applied to the hydrogen atom at position 5, the ring system in which the A, B ring junction is trans become the 5 α series; and the ring system in which the A, B ring junction is cis becomes the 5 β series.

In systematic nomenclature of the R group at position 17 determines the base name of an individual steroid.



For example



**5 α -Pregnan-3-one****5 α -Cholest-1-en-3-one****5 α -Androstane****5 β -Androstane**

A magical night landscape featuring a full moon in the upper left, a vibrant aurora borealis in shades of green and blue across the sky, and a field of glowing purple flowers in the foreground. The flowers have a bright, starry center, and the overall scene is illuminated with a soft, ethereal light. The background shows dark, silhouetted mountains under a starry night sky.

Thank you for your attention