Organic Chemistry II

2nd Year Students – Biology Group

Faculty of Education

First Term – 2022/2023

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Isomerism

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- 2nd year students - Biology group – Faculty of Education
- First term – 2021/2022
- Dr/ Ibrahim Abdul-Motaleb Mousa

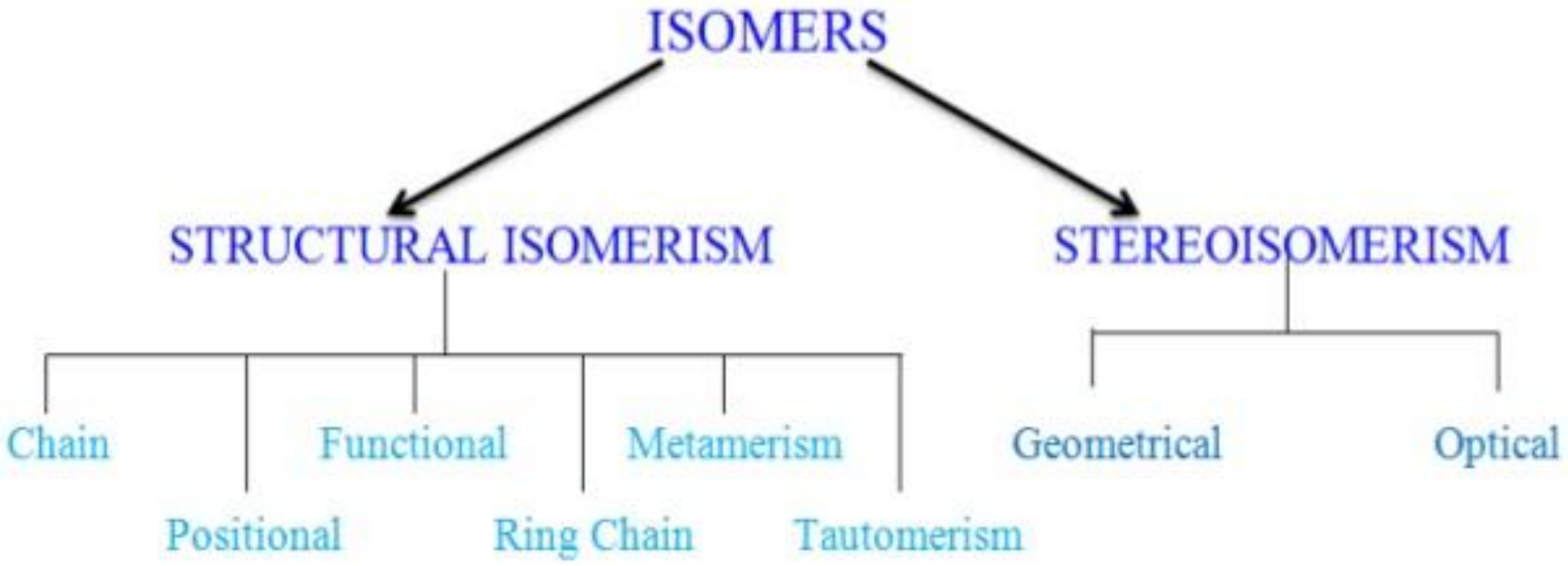
Contents

What is Isomerism?

The organic compounds having the same molecular formula but different structures are known as Isomers. This phenomenon is known as Isomerism.

In other words, the organic compounds having the same molecular formula but different arrangements of carbon atoms in them, are known as Isomers.

CLASSIFICATION OF ISOMERISM



- ISOMERS
  - STRUCTURAL ISOMERISM
    - Chain
    - Positional
    - Functional
    - Ring Chain
    - Metamerism
    - Tautomerism
  - STEREOISOMERISM
    - Geometrical
    - Optical

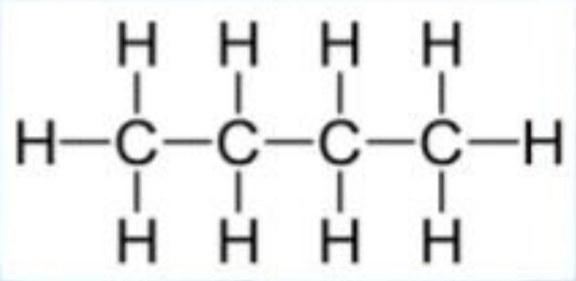
STRUCTURAL ISOMERISM

This type of Isomerism is classified into 6 types-

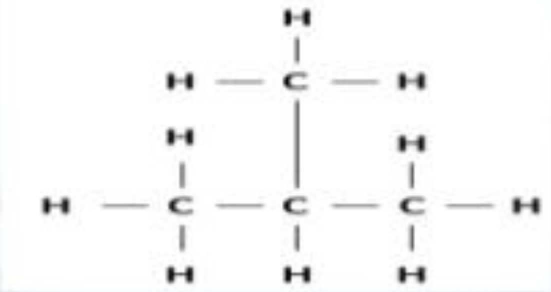
1. Chain Isomerism.
2. Positional Isomerism.
3. Functional Isomerism.
4. Ring Chain Isomerism.
5. Metamerism Isomerism.
6. Tautomerism Isomerism

1. CHAIN ISOMERISM

- The same molecular formula represents two or more compounds.
- It differs in the nature of carbon chain(straight or branched)
- Example, C_4H_{10} (Butane) has two isomers namely butane and 2-methylpropane.



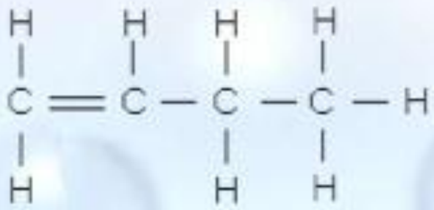
BUTANE



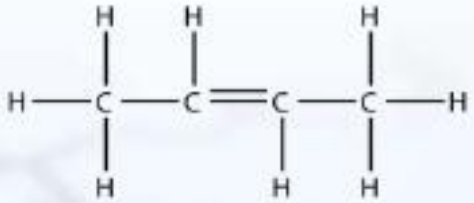
2-METHYLPROPANE

2. POSITIONAL ISOMERISM

- The same molecular formula represents two or more compounds.
- It differs in the position of the same functional group
- Example, Butene has two isomers namely But-1-ene and But-2-ene.



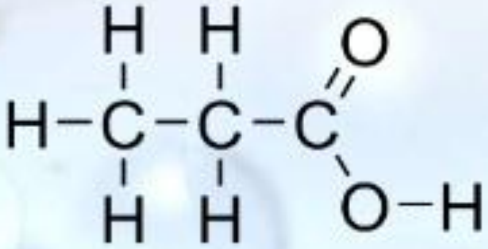
BUT-1-ENE



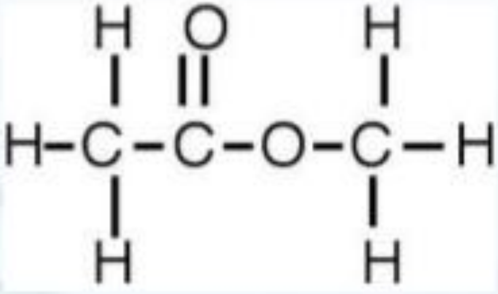
BUT-2-ENE

3. FUNCTIONAL ISOMERISM

- The same molecular formula represents two or more compounds.
- It differs in the nature of the functional group.
- Example, $C_3H_60_2$ has two isomers namely Propanoic acid and Methyl ethanoate.



PROPANOIC ACD

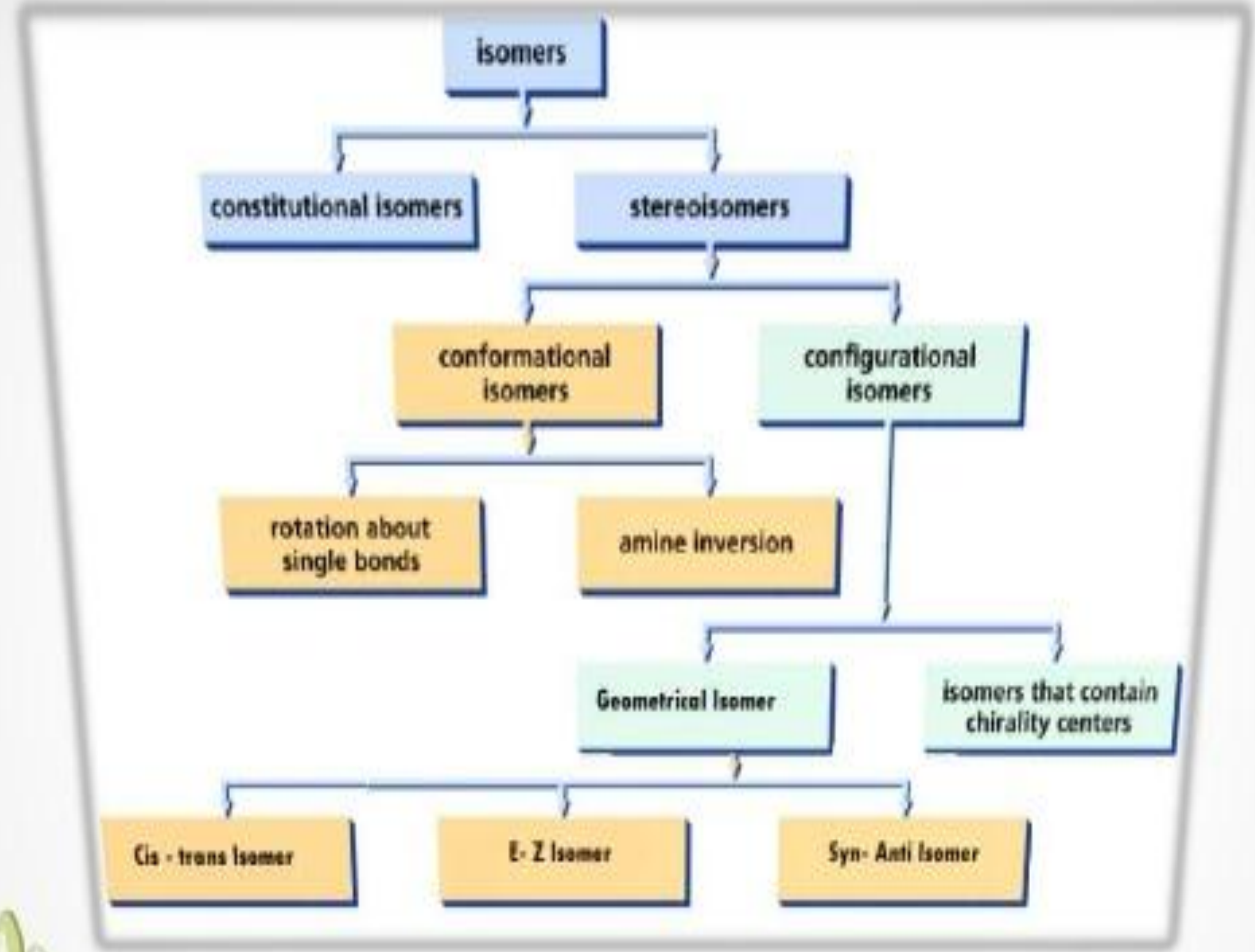


METHYL ETHANOATE

Geometrical isomerism

Objective

- What is isomer
- Geometrical isomer
- Cis-trans isomer
- E-Z Isomer
- Syn – anti Isomer



- isomers
  - constitutional isomers
  - stereoisomers
    - conformational isomers
      - rotation about single bonds
      - amine inversion
    - configurational isomers
      - Geometrical Isomer
        - Cis - trans Isomer
        - E- Z Isomer
        - Syn- Anti Isomer
      - isomers that contain chirality centers

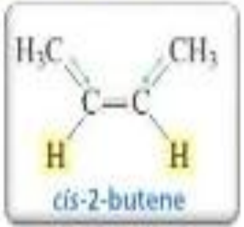
Geometrical Isomer

These isomers occur where you have restricted rotation somewhere in a molecule. At an introductory level in organic chemistry, examples usually just involve the carbon-carbon double bond

✓ ***Geometric Isomers***

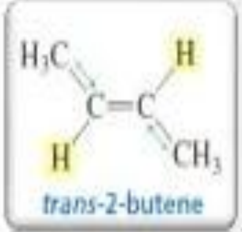
- ✓ ***Different physical properties – Different arrangement***
- ✓ ***(Different density, polarity, solubility, melting point /boiling point)***

Cis- trans isomer



cis isomer

the isomer with the hydrogens on the same side of the double bond

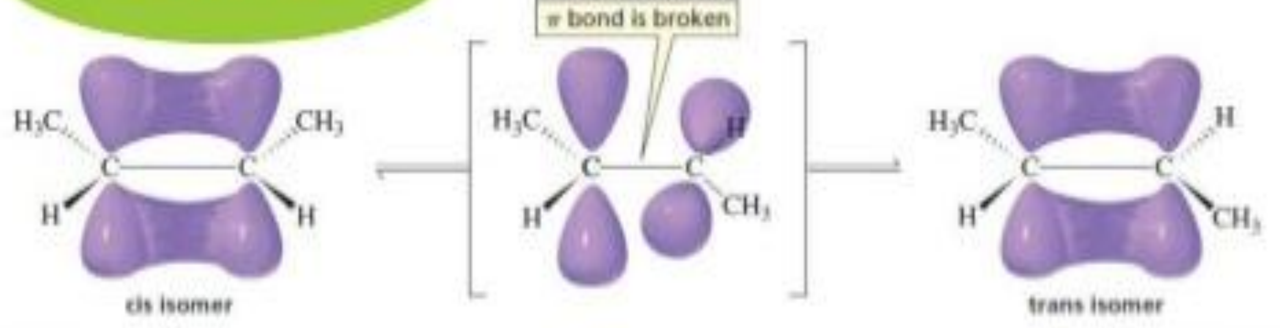


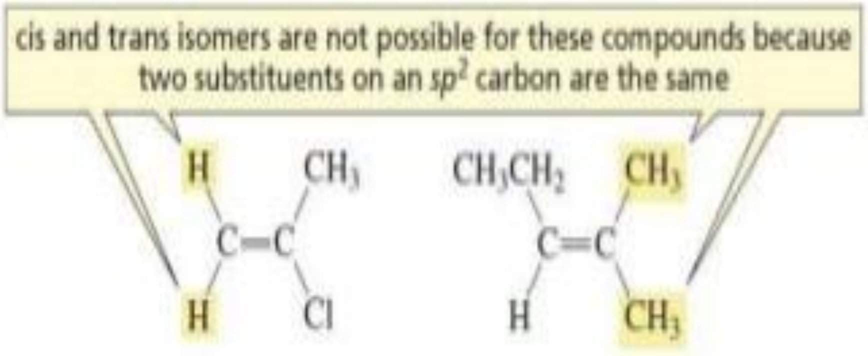
trans isomer

the isomer with the hydrogens on opposite sides of the double bond

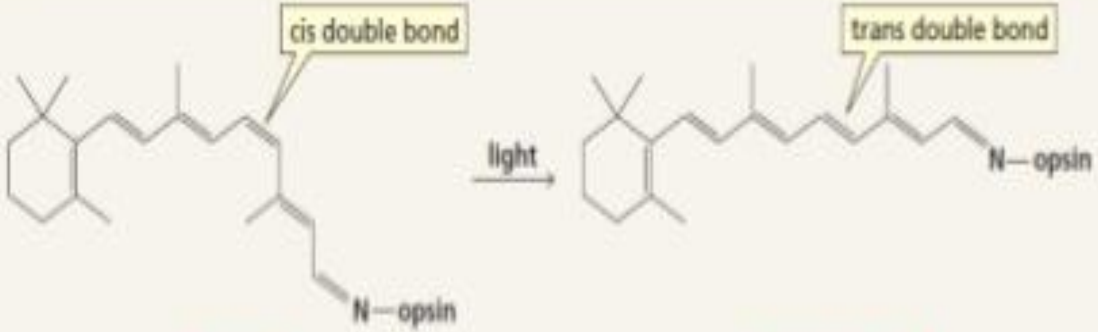
Cis-trans isomer

In alkene





cis and trans isomers are not possible for these compounds because two substituents on an *sp*² carbon are the same



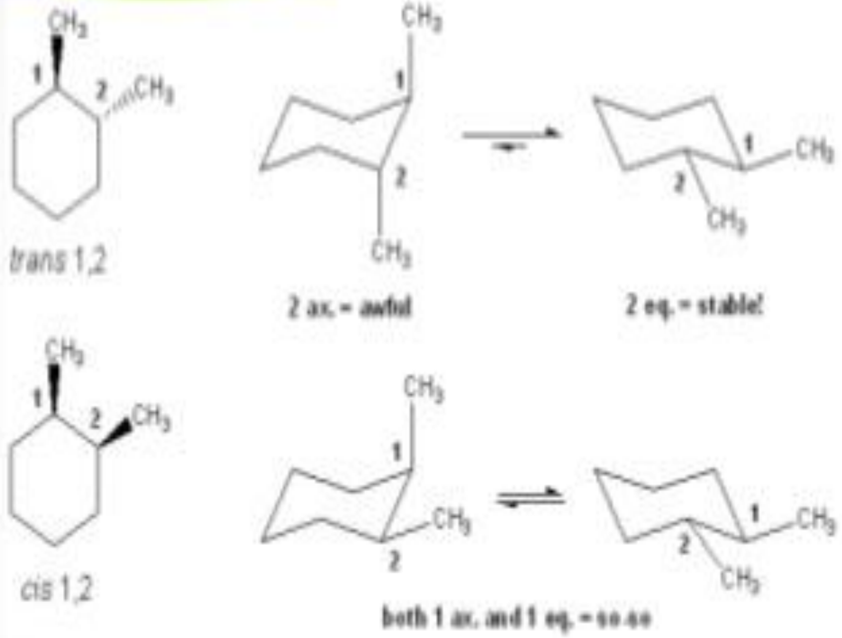
cis double bond

trans double bond

rhodopsin

metarhodopsin II
(*trans*-rhodopsin)

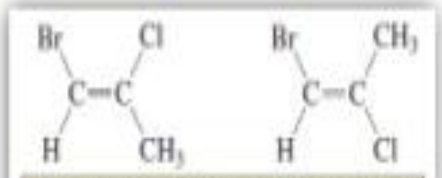
Cyclo alkane



cis-1-bromo-3-chlorocyclobutane

trans-1-bromo-3-chlorocyclobutane

E-Z system



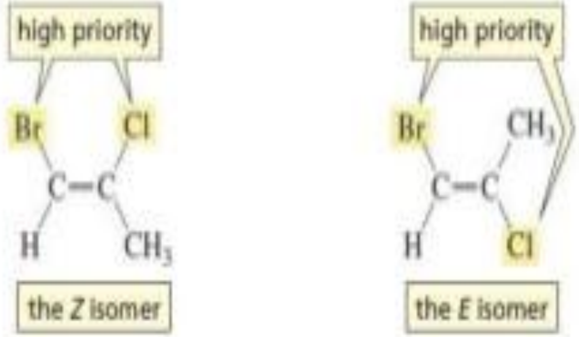
Which isomer is cis and which is trans?

- The *Z isomer has the high-priority* **groups on the SAME side.**
- The *E isomer has the high-priority* **groups on the OPPOSITE side.**

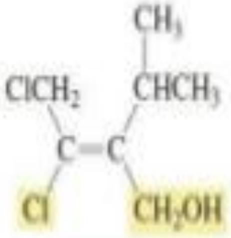
If the high-priority groups are on the same side of the double bond, the isomer has the *Z* configuration (Z is for *zusammen*, German for "together").
If the high-priority groups are on opposite sides of the double bond, the isomer has the *E* configuration (*E* is for *entgegen*, German for "opposite").

Rules

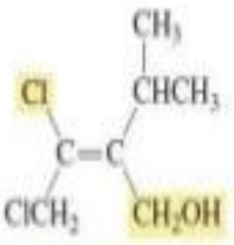
Rule 1: high atomic number high priority



Rule 2: If the two substituents bonded to an carbon start with the same atom , move to the next attached group

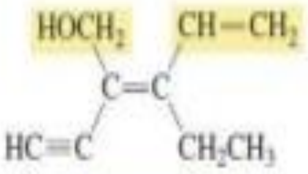


the *Z* isomer

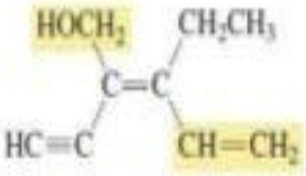


the *E* isomer

Rule 3: If an atom is doubly bonded to another atom, the priority system treats it as if it were singly bonded to two of those atoms. If an atom is triply bonded to another atom, the priority system treats it as if it were singly bonded to three of those atoms.

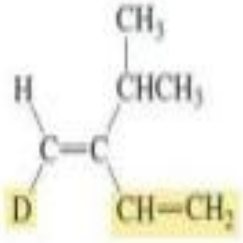


the *Z* isomer

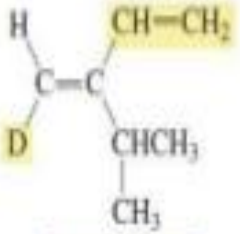


the *E* isomer

Rule 4. In the case of isotopes (atoms with the same atomic number, but different mass numbers), the mass number is used to determine the relative priorities.



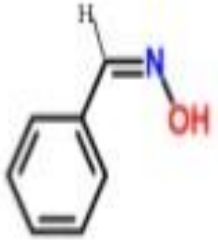
the *Z* isomer



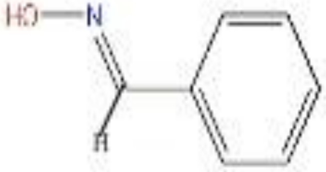
the *E* isomer

Syn-anti isomer

This type used for sterioisomeric oxime



Anti isomer
Where H and OH is trans



syn isomer
Where H and OH is ciz

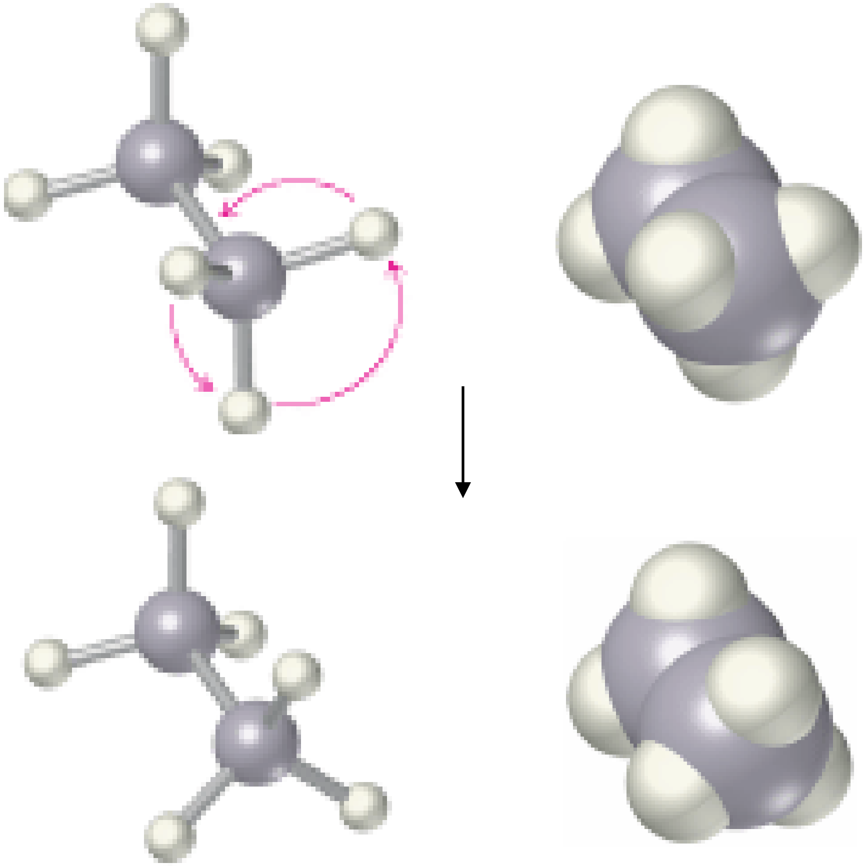
Stereochemistry of Alkanes and Cycloalkanes

The Shapes of Molecules

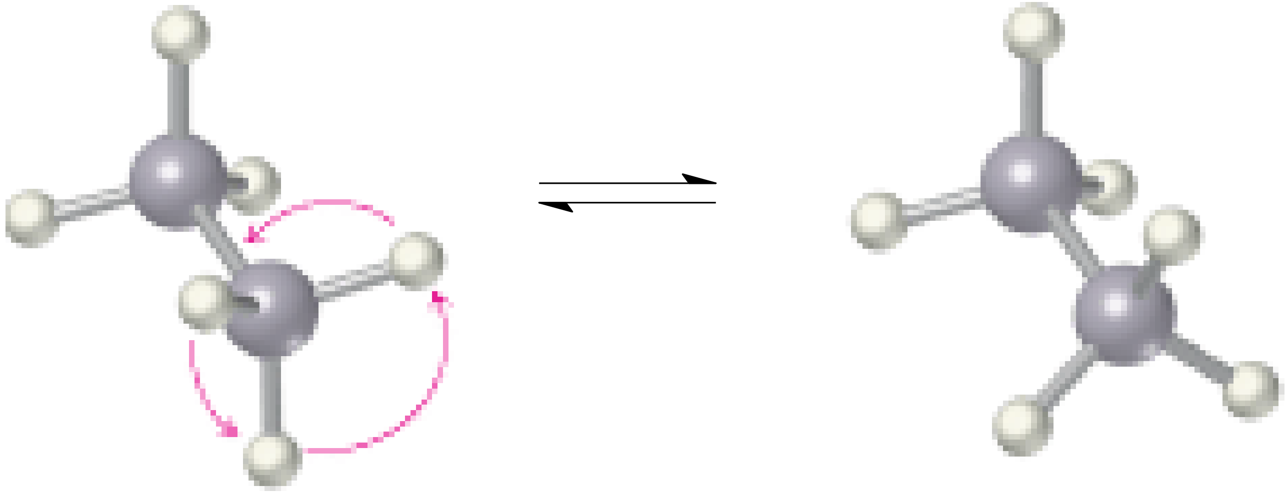
- The three-dimensional shapes of molecules result from many forces
- A molecule may assume different shapes, called **conformations**, that are in equilibrium at room temperature (*the conformational isomers are called **conformers***, emphasis on the first syllable)
- The systematic study of the shapes molecules and properties from these shapes is **stereochemistry**
- The field of stereochemistry is one of the central parts of organic chemistry and includes many important topics

Conformations of Ethane

- Conformers interconvert rapidly and a structure is an average of conformers
- Molecular models are three dimensional objects that enable us to visualize conformers
- Representing three dimensional conformers in two dimensions is done with standard types of drawings



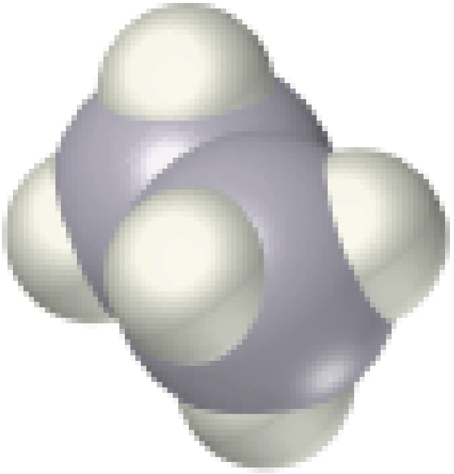
Conformations of Ethane



staggered conformation

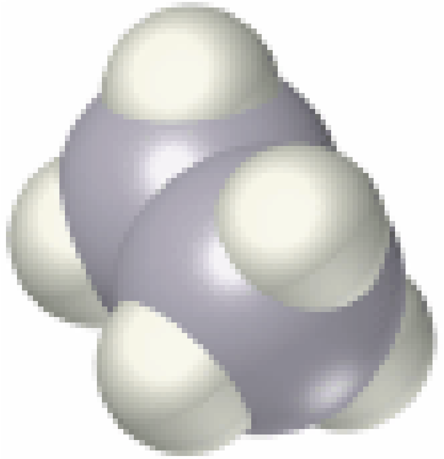
eclipsed conformation

Conformations of Ethane



staggered conformation

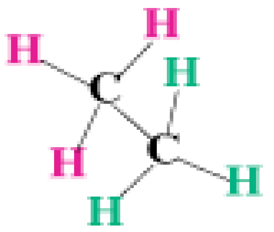
$\rightleftharpoons$



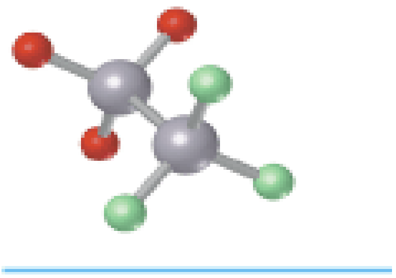
eclipsed conformation

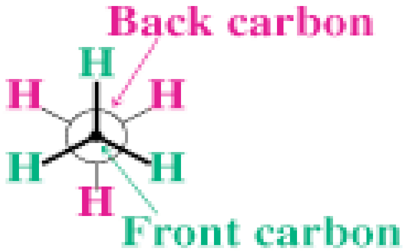
Representing Conformations

- **Sawhorse representations** show molecules at an angle, showing a molecular model
  - C-C bonds are at an angle to the edge of the page and all C-H bonds are shown
- **Newman projections** show how the C-C bond would project end-on onto the paper
  - Bonds to front carbon are lines going to the center
  - Bonds to rear carbon are lines going to the edge of the circle

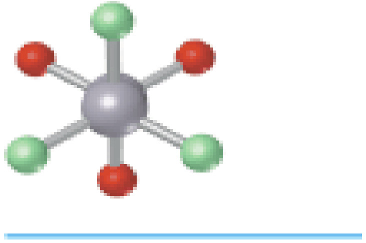


Sawhorse representation

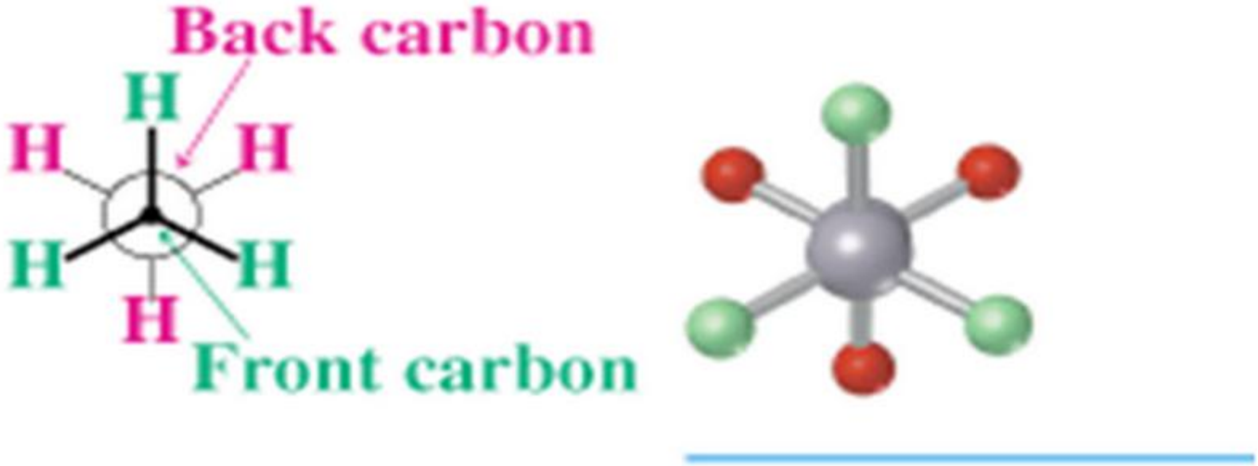




Newman projection

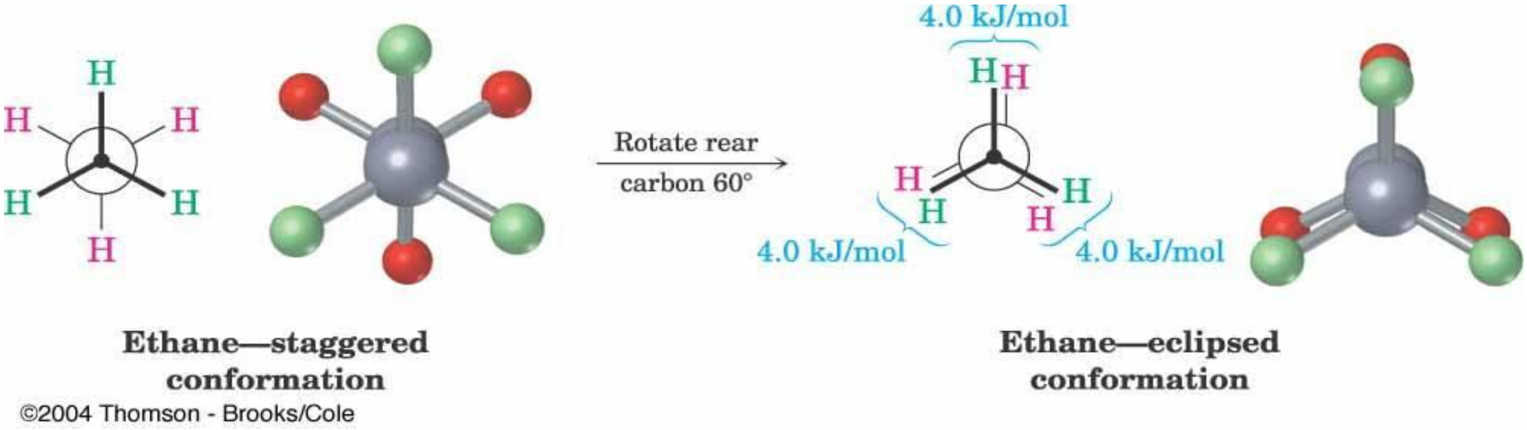


Newman Projections



Newman projection

Ethane's Conformations

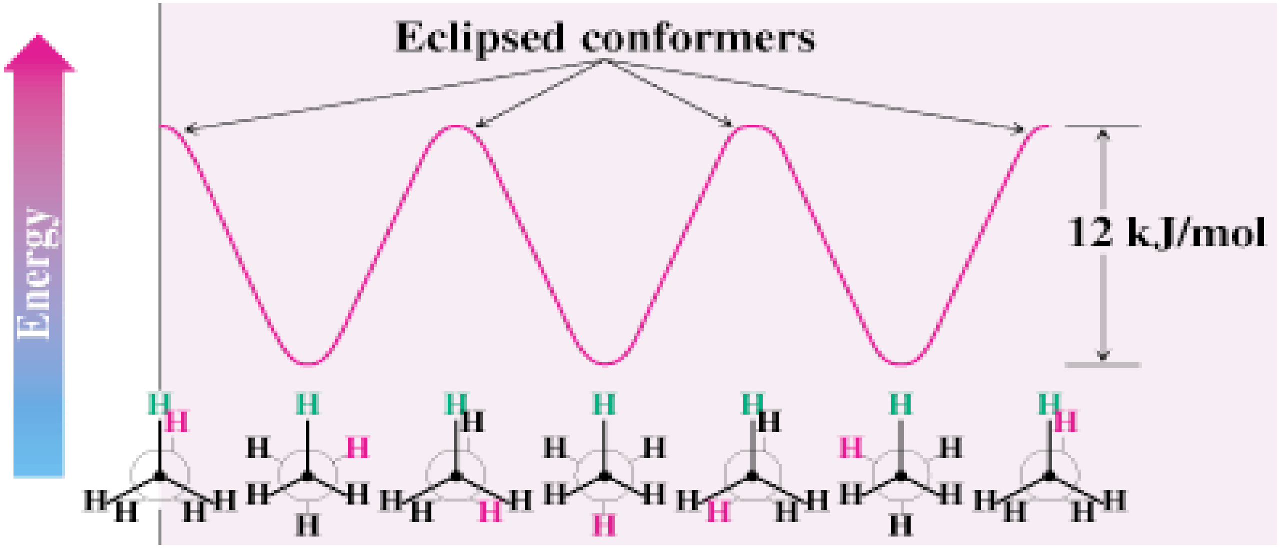


Ethane—staggered conformation

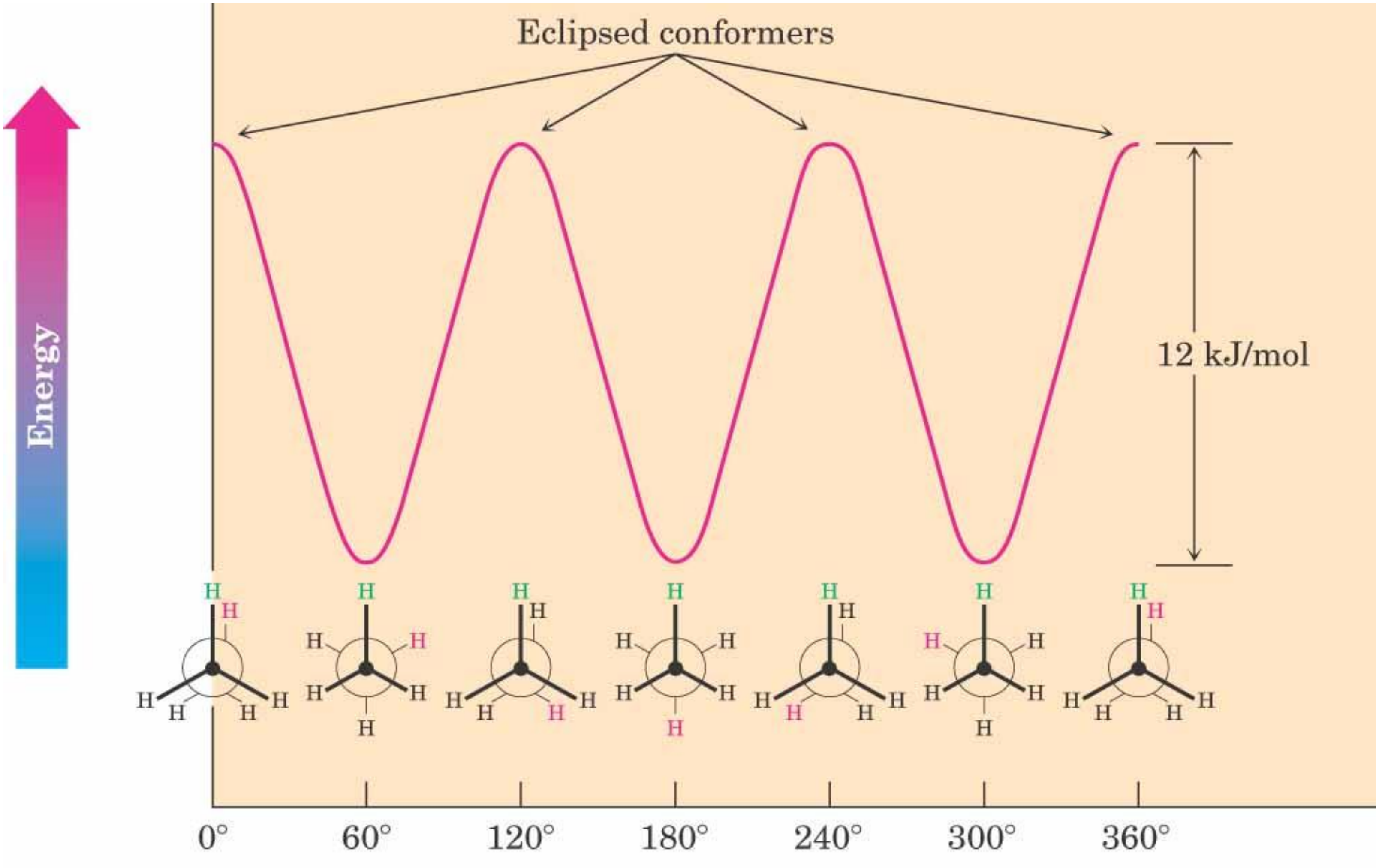
Ethane—eclipsed conformation

Ethane’s Conformations

- There barrier to rotation between conformations is small (12 kJ/mol; 2.9 kcal/mol) The most stable conformation of ethane has all six C–H bonds away from each other (**staggered**)
- The least stable conformation has all six C–H bonds as close as possible (**eclipsed**) in a Newman projection – energy due to torsional strain



Ethane's Conformations



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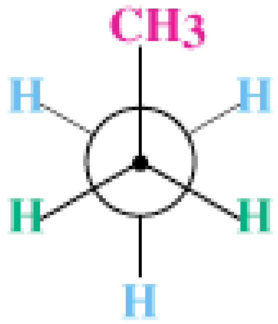
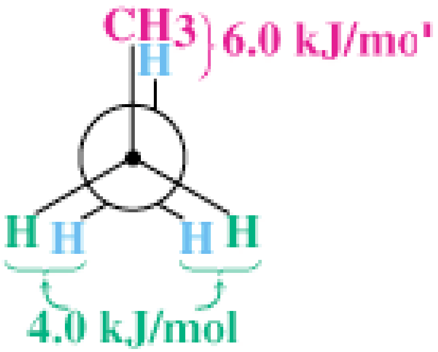
Conformations of Propane

- Propane (C_3H_8) torsional barrier around the carbon–carbon bonds 14 kJ/mol
- Eclipsed conformer of propane has two ethane-type H–H interactions and an interaction between C–H and C–C bond

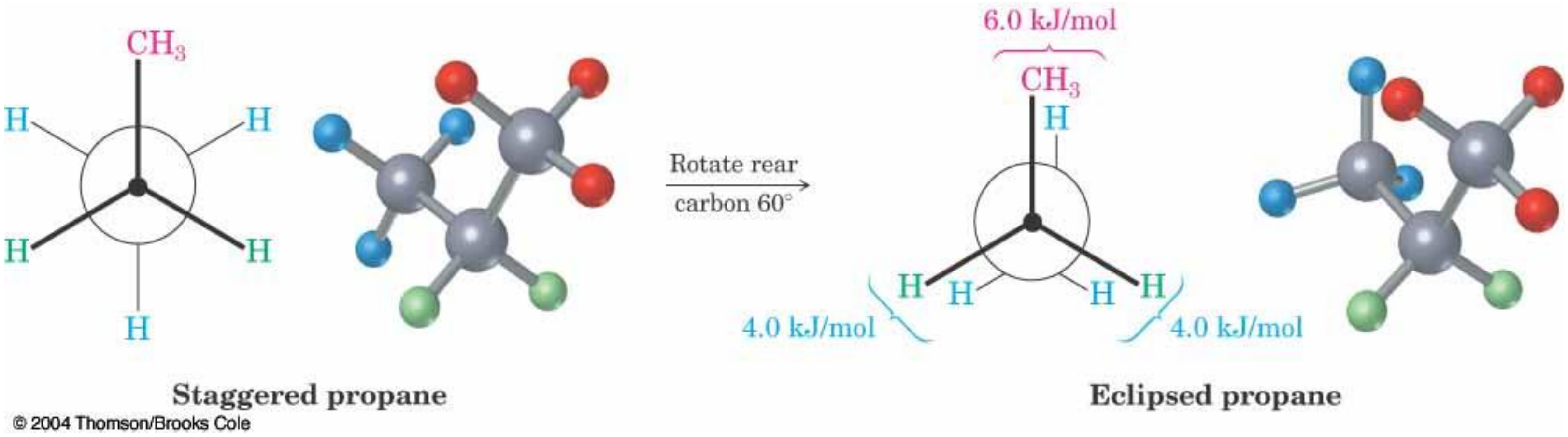


Staggered propane



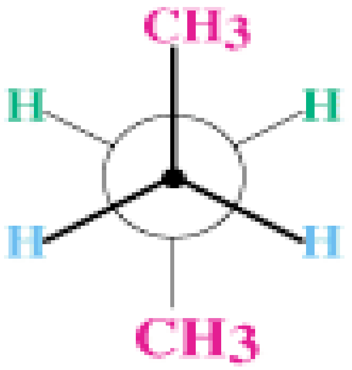
Eclipsed propane

Propane conformations

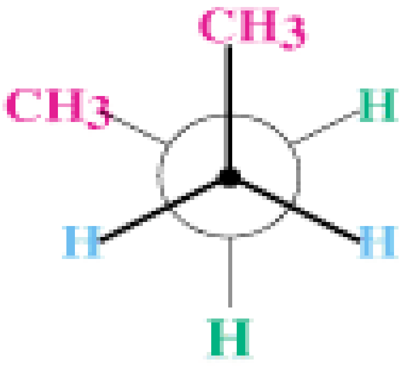


Conformations of Butane

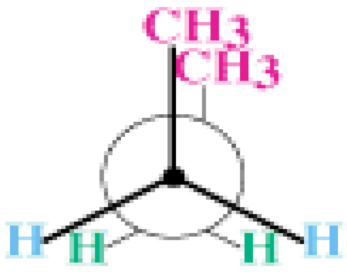
- **anti conformation** has two methyl groups 180° away from each other
- Rotation around the C2–C3 gives eclipsed conformation
- Staggered conformation with methyl groups 60° apart is **gauche conformation**



Anti

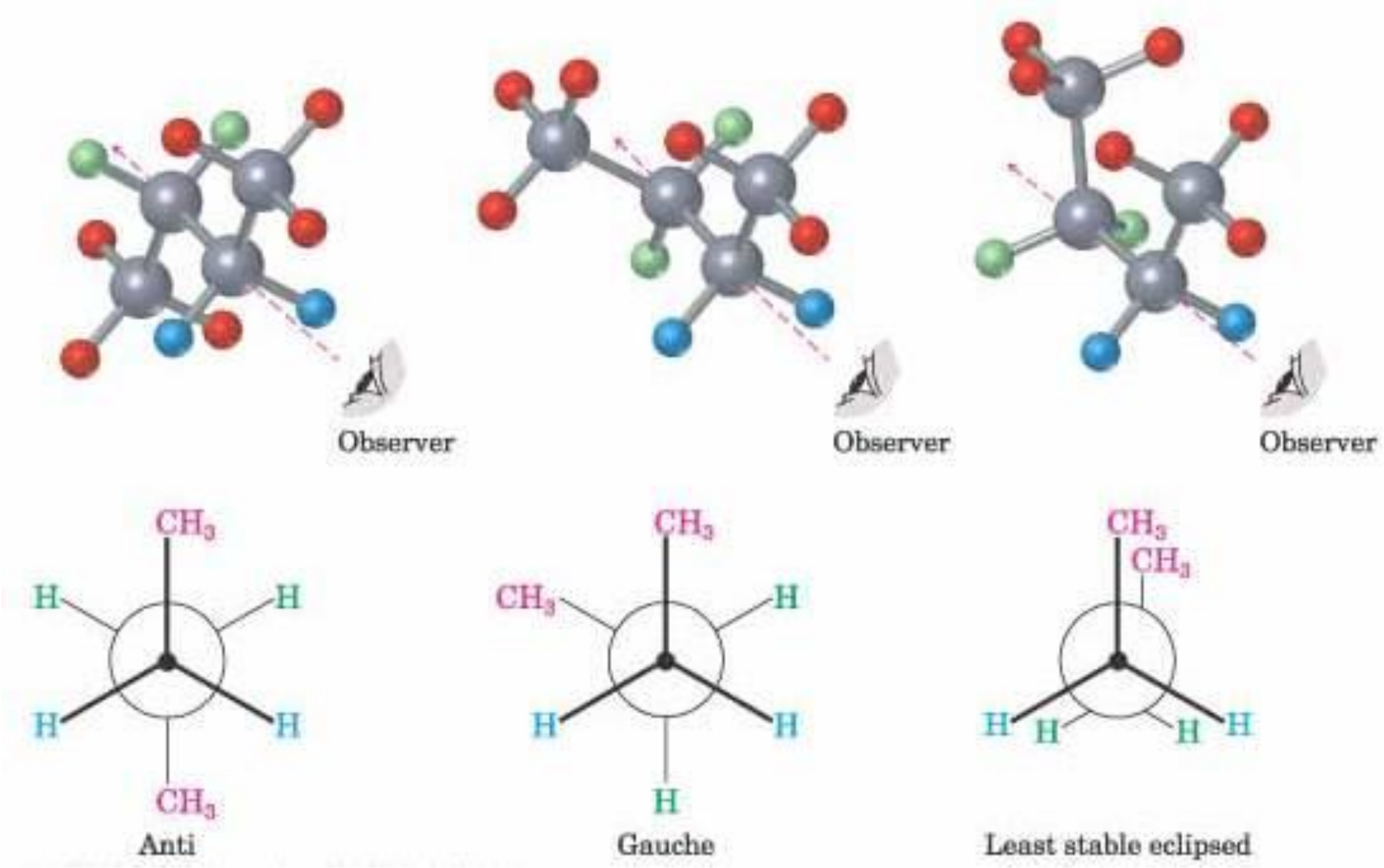


Gauche

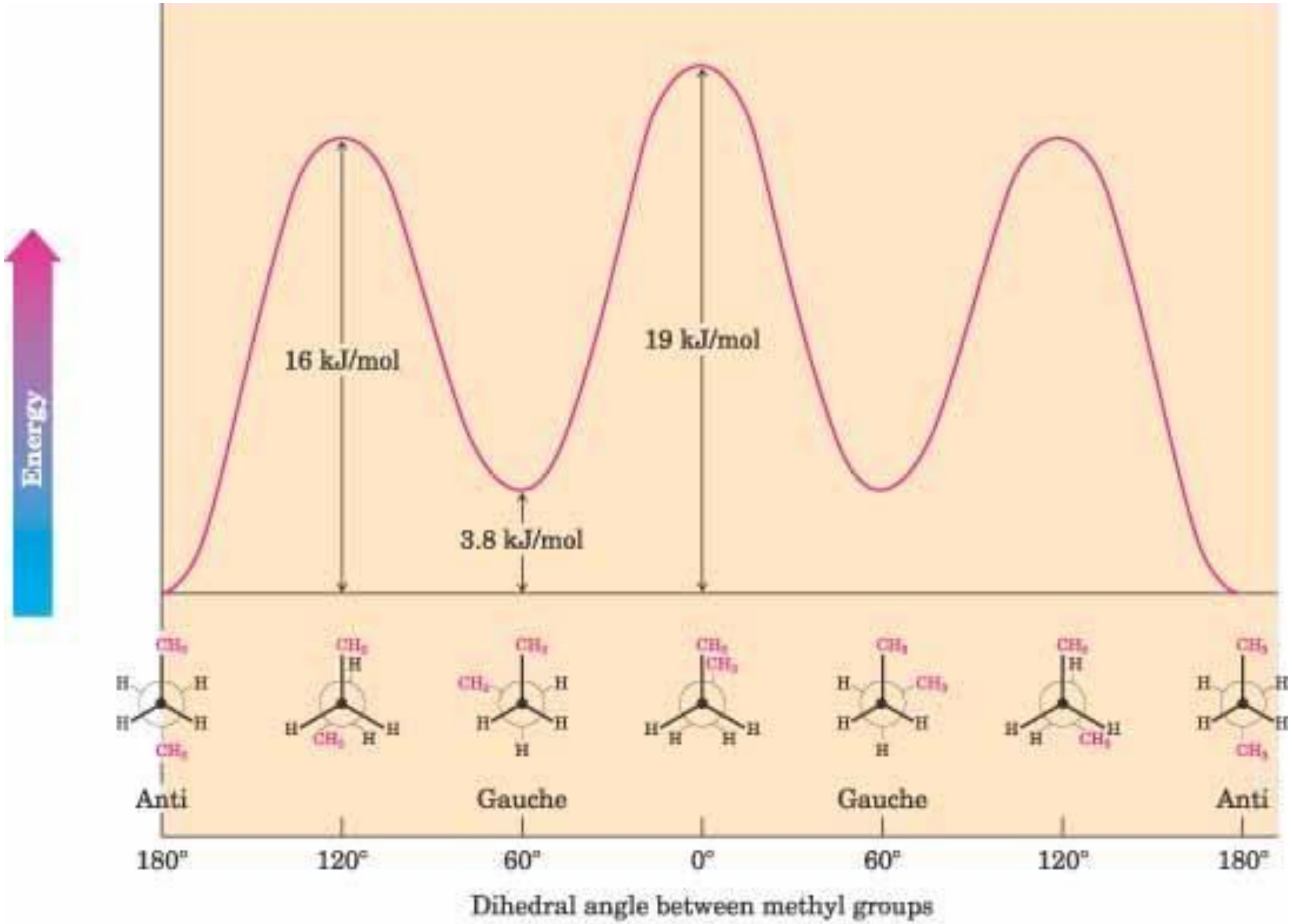


Least stable eclipsed

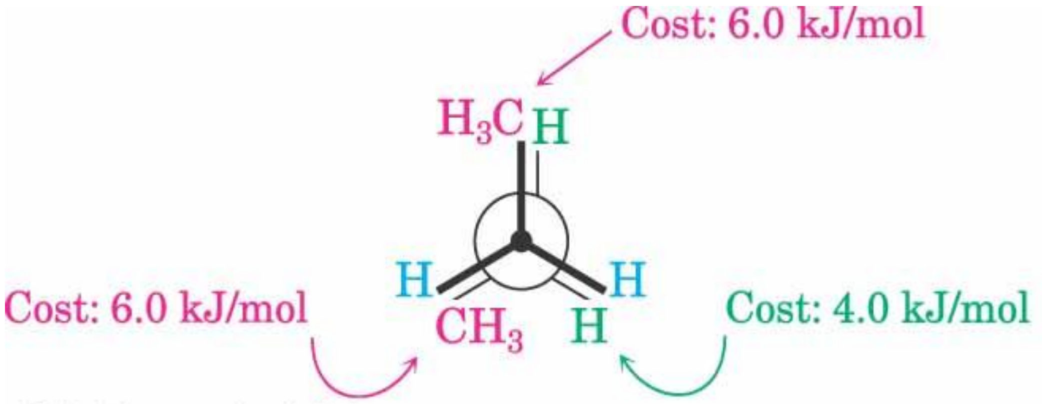
Conformations of Butane



Conformations of Butane



Eclipsed Conformations of Butane



Cost: 6.0 kJ/mol

Cost: 6.0 kJ/mol

Cost: 4.0 kJ/mol

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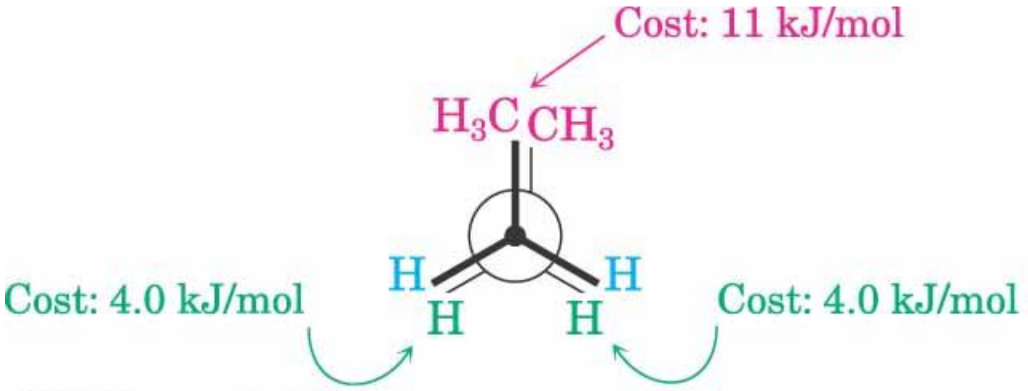
Total cost: 16 kJ/mol



Cost: 11 kJ/mol

Cost: 4.0 kJ/mol

Cost: 4.0 kJ/mol

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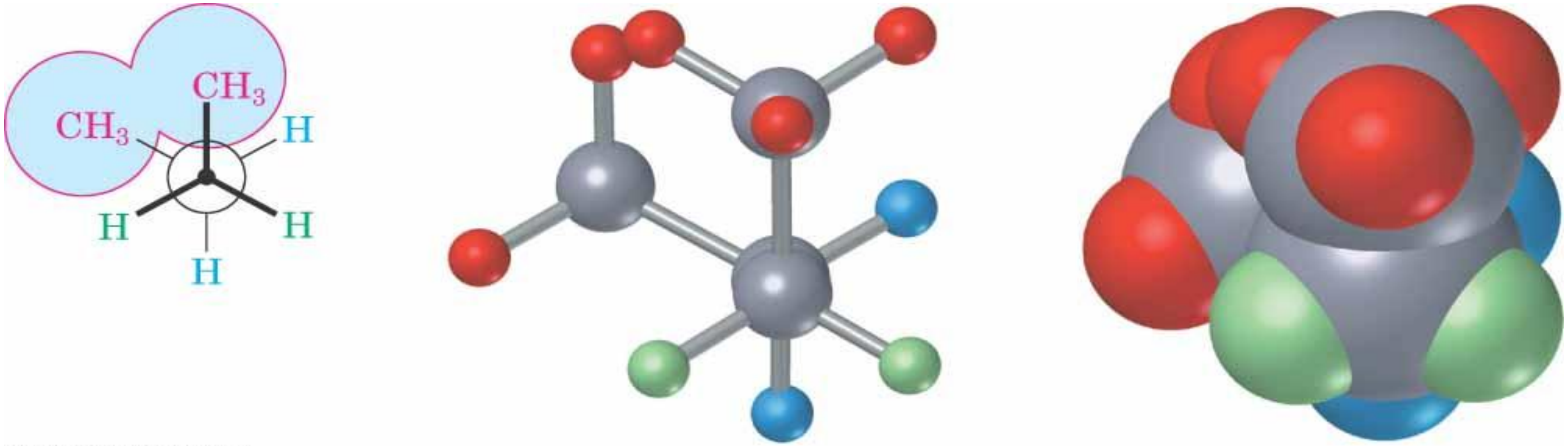
Total cost: 19 kJ/mol

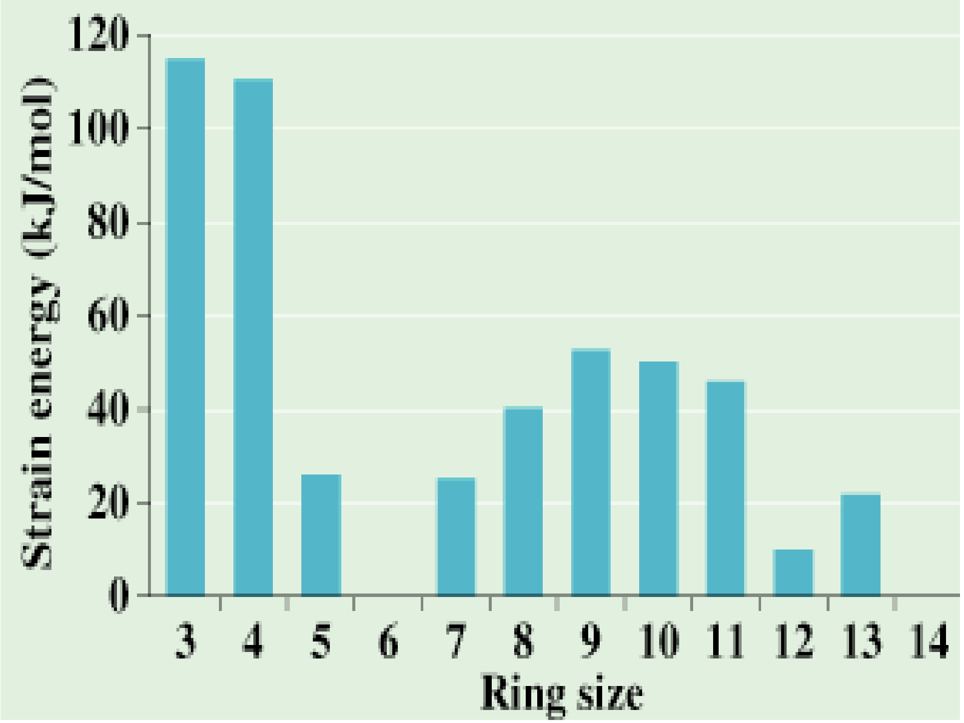
Gauche conformation: steric strain



Stability of Cycloalkanes: The Baeyer Strain Theory

- **Baeyer (1885): since (sp^3) carbon prefers to have bond angles of approximately 109°, ring sizes other than five and six may be too *strained* to exist**

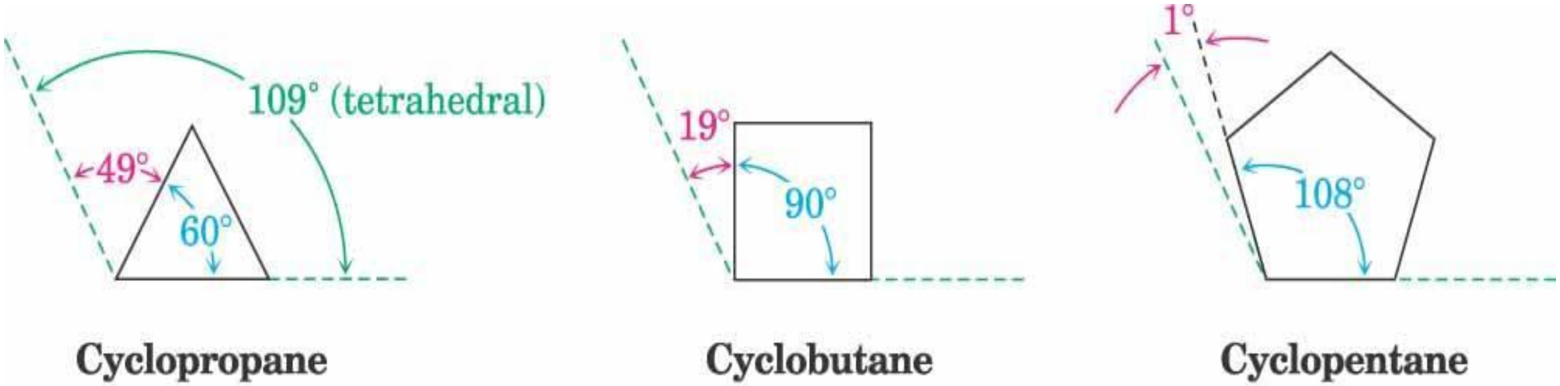
- **Rings from 3 to 30 C's do exist but are strained due to bond bending distortions and steric interactions**



The Nature of Ring Strain

- Rings larger than 3 atoms are not flat (planar)
- Cyclic molecules can assume nonplanar conformations to minimize angle strain and torsional strain by ring-puckering
- Larger rings have many more possible conformations than smaller rings and are more difficult to analyze

Angle Strain



Cyclopropane **Cyclobutane** **Cyclopentane**

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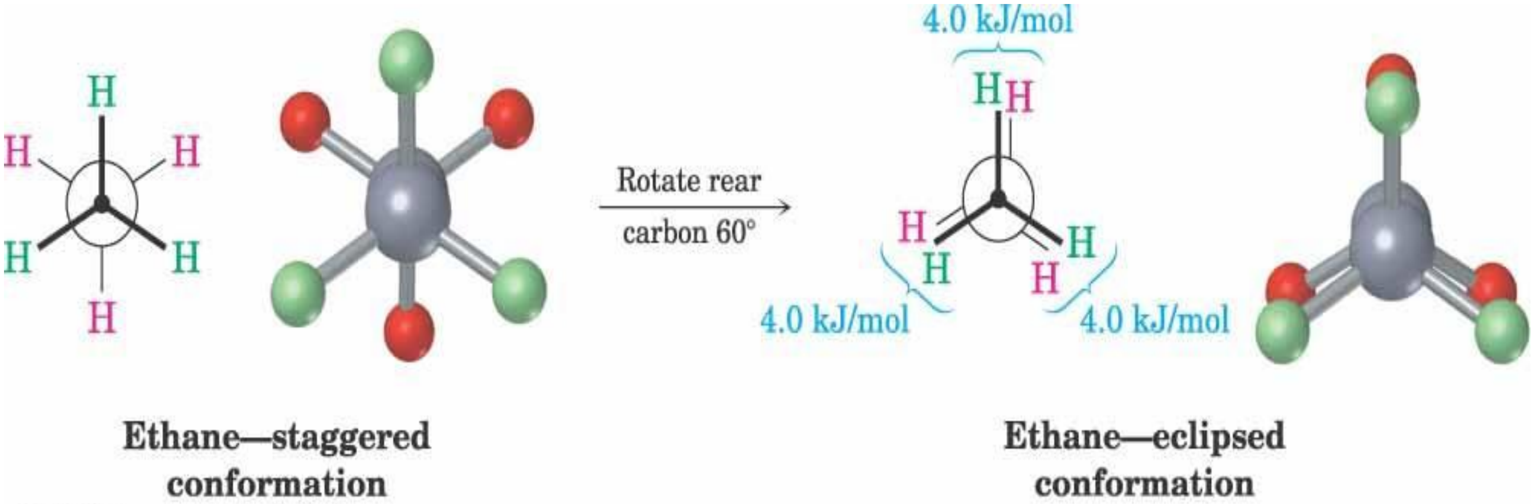
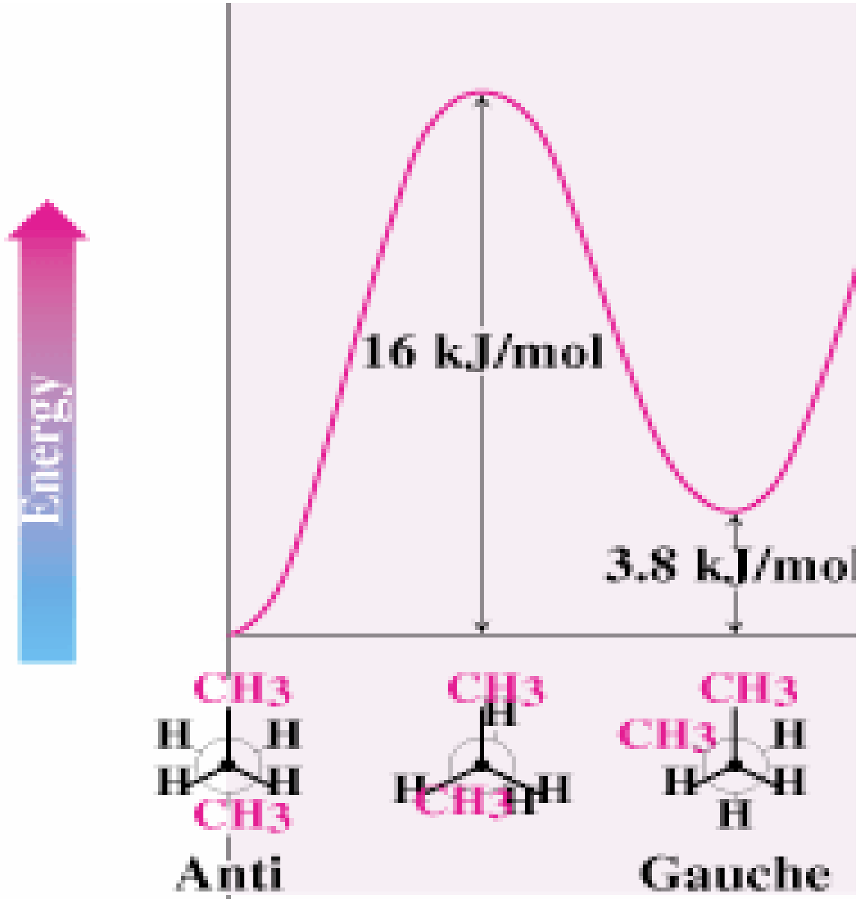
Types of Strain

- **Angle strain** - expansion or compression of bond angles away from most stable
- **Torsional strain** - eclipsing of bonds on neighboring atoms
- **Steric strain** - repulsive interactions between nonbonded atoms in close proximity

Torsional Strain

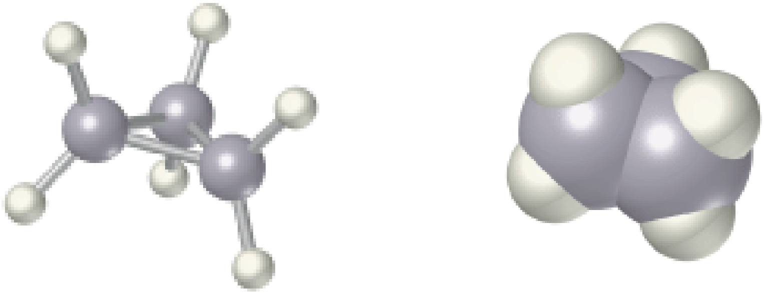


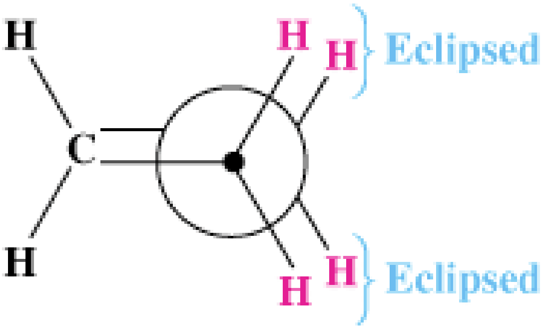
Steric Strain



Cyclopropane: An Orbital View

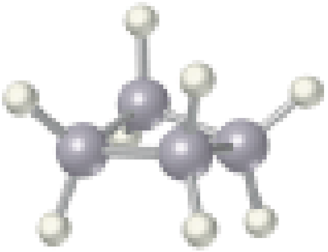
- 3-membered ring must have planar structure
- Symmetrical with C–C–C bond angles of 60°
- Requires that sp^3 based bonds are bent (and weakened)
- All C-H bonds are eclipsed

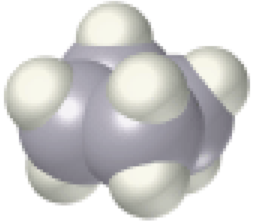


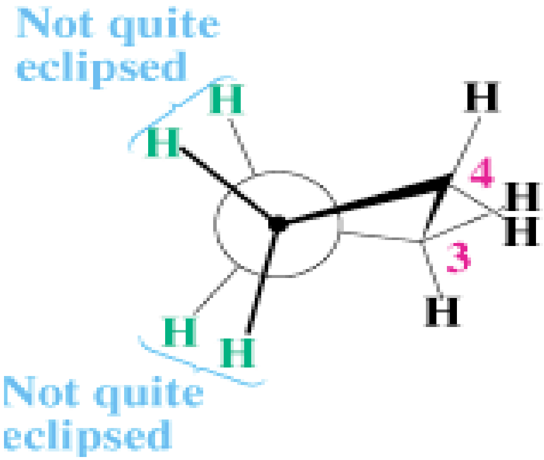


Conformations of Cyclobutane and Cyclopentane

- Cyclobutane has less angle strain than cyclopropane but more torsional strain because of its larger number of ring hydrogens
- Cyclobutane is slightly bent out of plane - one carbon atom is about 25° above
  - **The bend *increases* angle strain but *decreases* torsional strain**

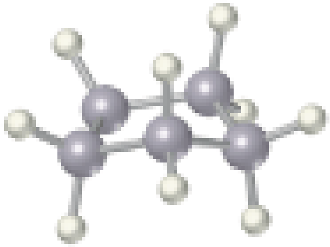


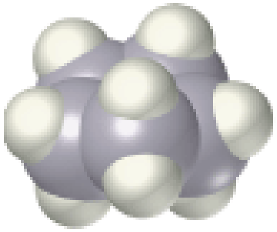


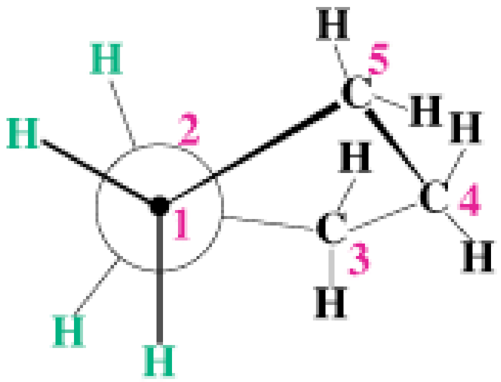


Cyclopentane

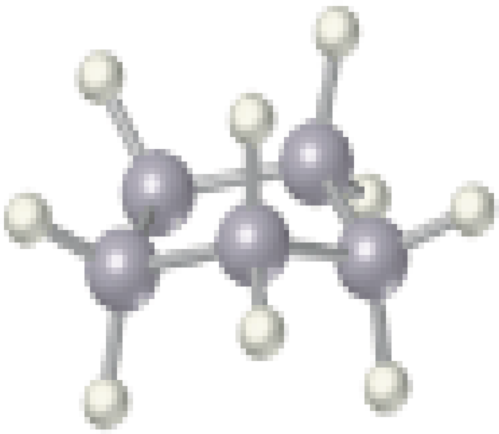
- Planar cyclopentane would have no angle strain but very high torsional strain
- Actual conformations of cyclopentane are nonplanar, reducing torsional strain
- Four carbon atoms are in a plane
  - The fifth carbon atom is above or below the plane – looks like an envelope

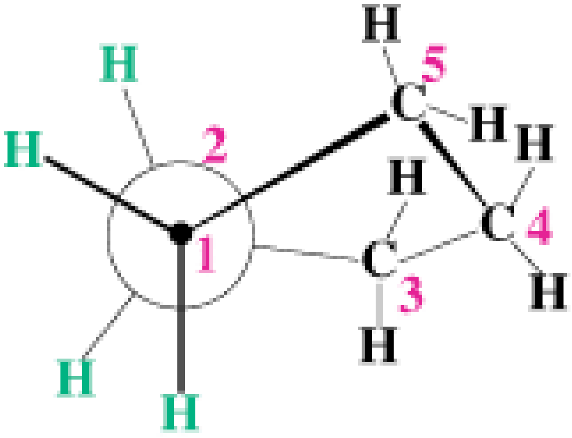






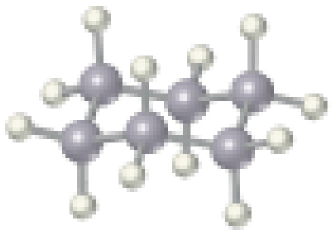
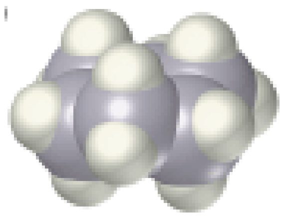
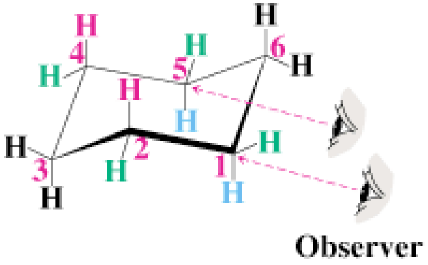
Cyclopentane

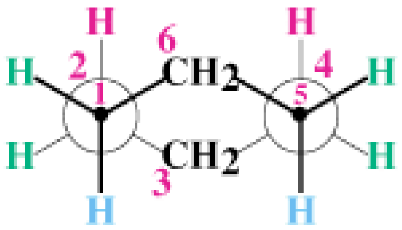




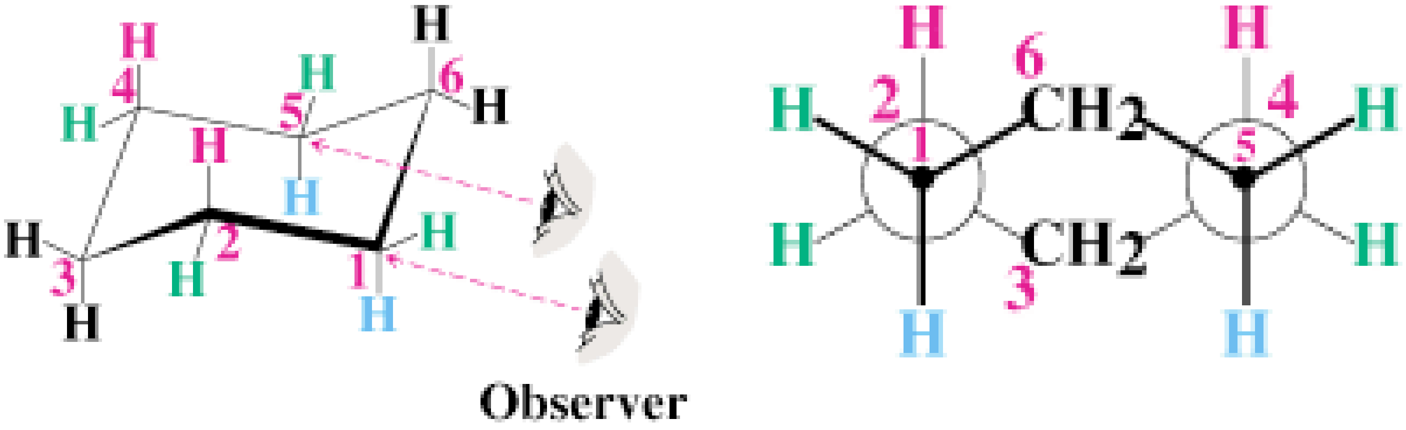
Conformations of Cyclohexane

- Substituted cyclohexanes occur widely in nature
- The cyclohexane ring is free of angle strain and torsional strain
- The conformation is has alternating atoms in a common plane and tetrahedral angles between all carbons
- This is called a **chair conformation**



Chair Conformations

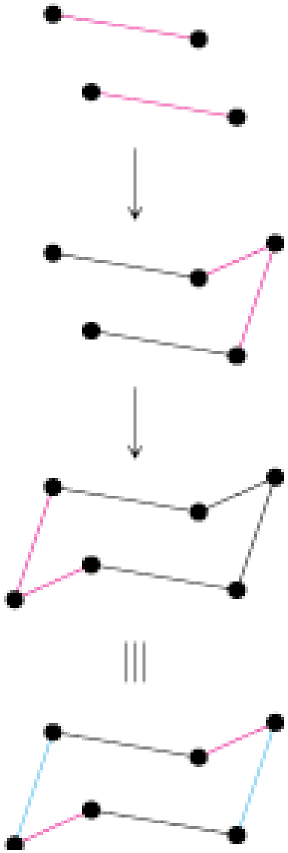


How to Draw Cyclohexane

STEP 1 Draw two parallel lines, slanted downward and slightly offset from each other. This means that four of the cyclohexane carbon atoms lie in a plane.

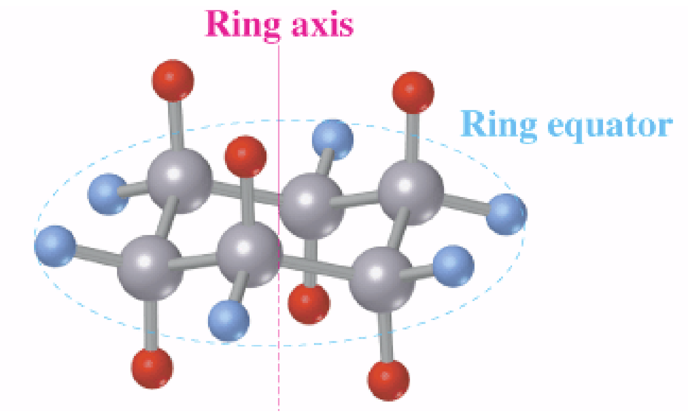
STEP 2 Locate the topmost carbon atom above and to the right of the plane of the other four and connect the bonds.

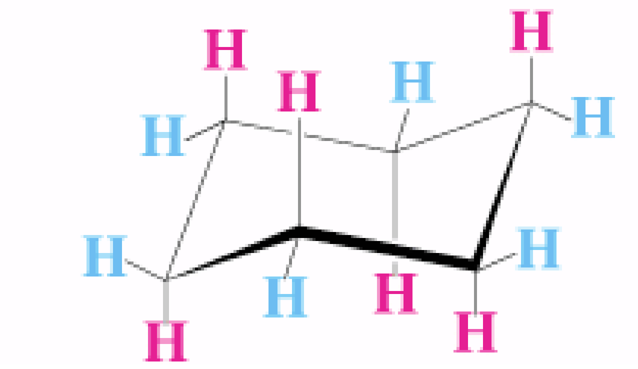
STEP 3 Locate the bottommost carbon atom below and to the left of the plane of the middle four and connect the bonds. Note that the bonds to the bottommost carbon atom are parallel to the bonds to the topmost carbon.



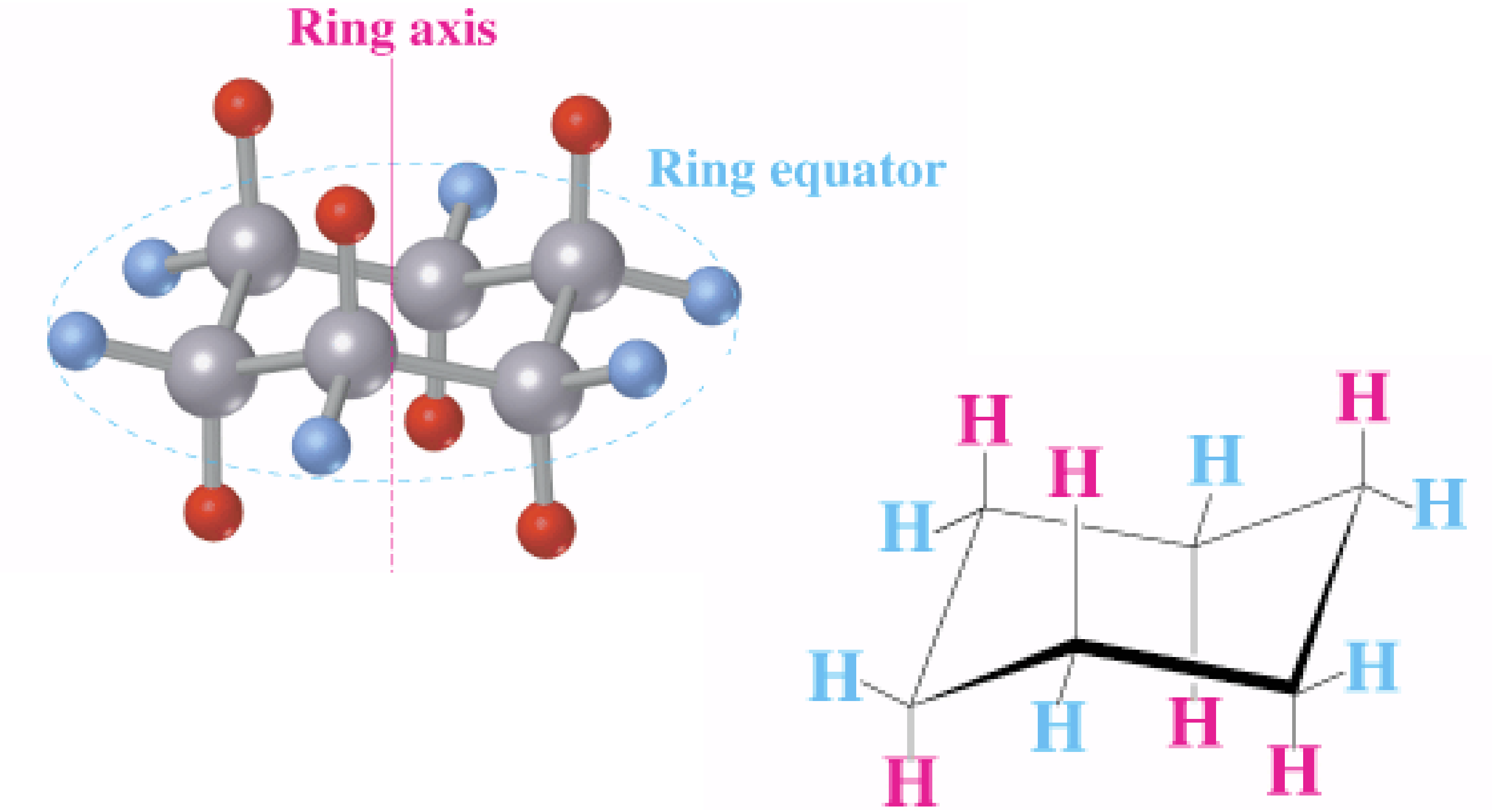
Axial and Equatorial Bonds in Cyclohexane

- The chair conformation has two kinds of positions for substituents on the ring: *axial* positions and *equatorial* positions
- Chair cyclohexane has six **axial** hydrogens perpendicular to the ring (parallel to the ring axis) and six **equatorial** hydrogens near the plane of the ring



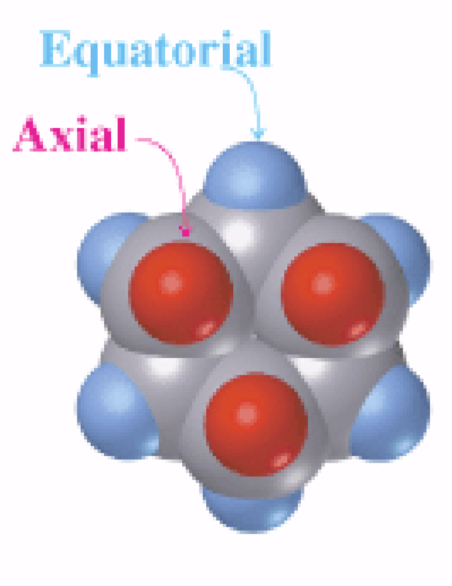


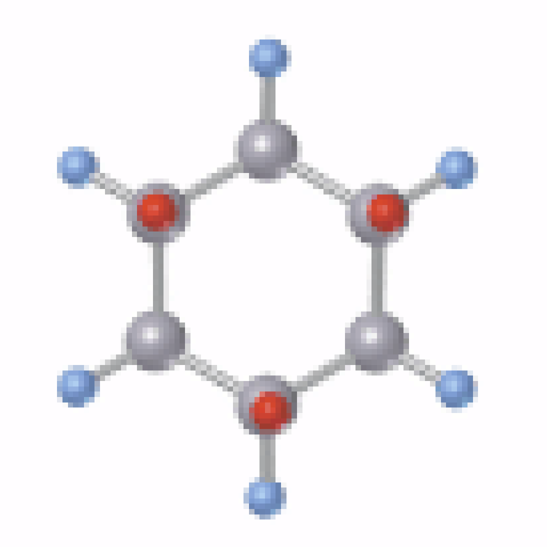
Axial and Equatorial Bonds



Axial and Equatorial Positions

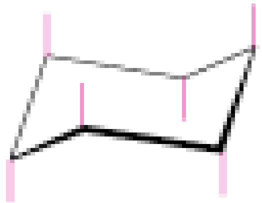
- Each carbon atom in cyclohexane has one axial and one equatorial hydrogen
- Each face of the ring has three axial and three equatorial hydrogens in an alternating arrangement



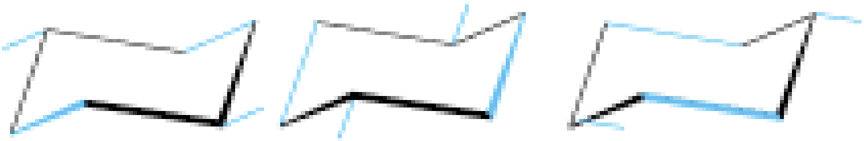


Drawing the Axial and Equatorial Hydrogens

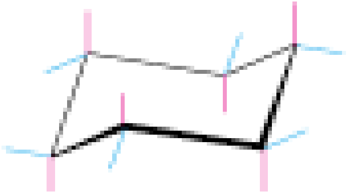
Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up–down.



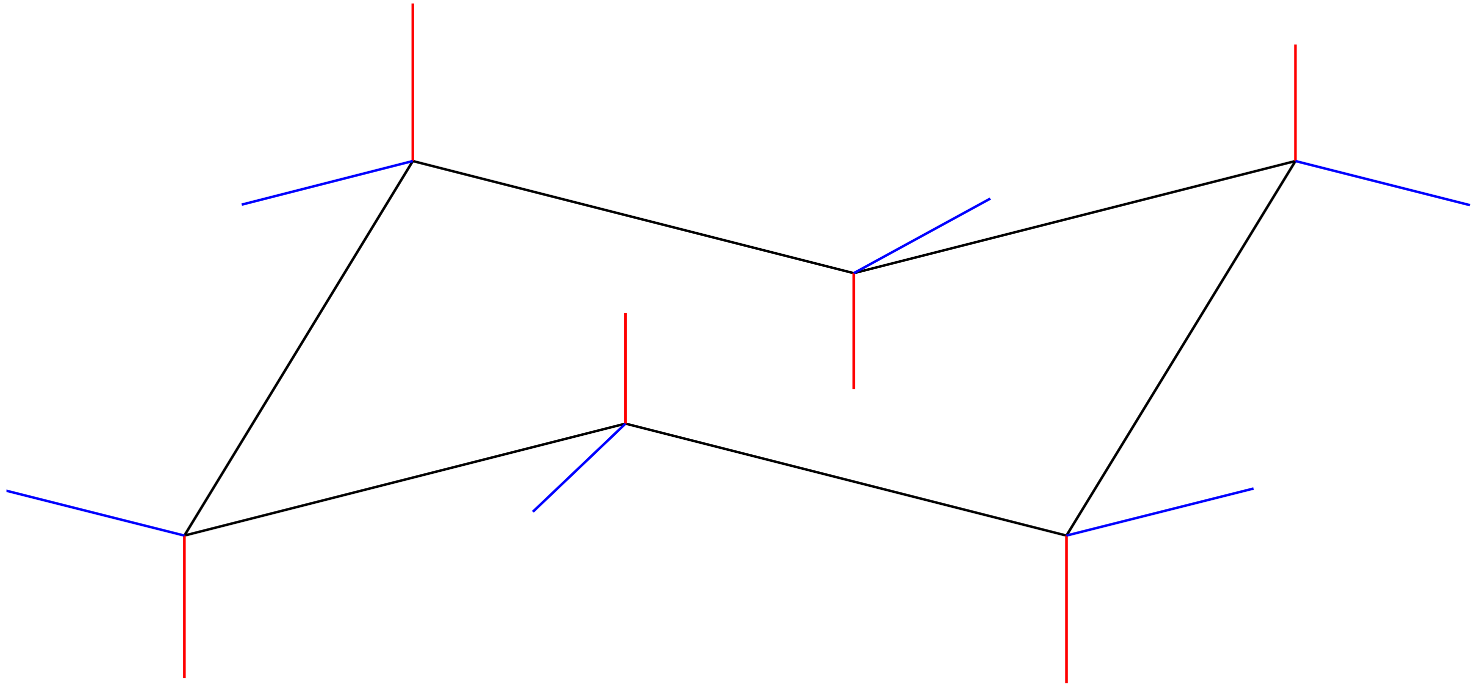
Equatorial bonds: The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alter- nate between sides around the ring.



Completed cyclohexane



Axial and Equatorial Hydrogens

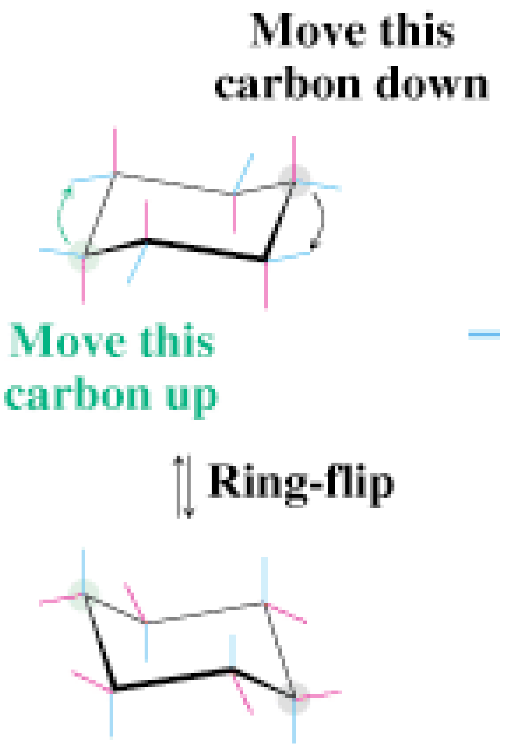


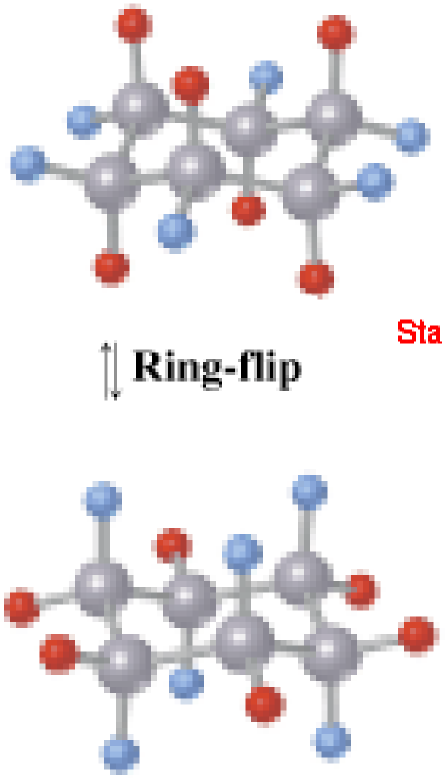
Conformations of Cyclohexane

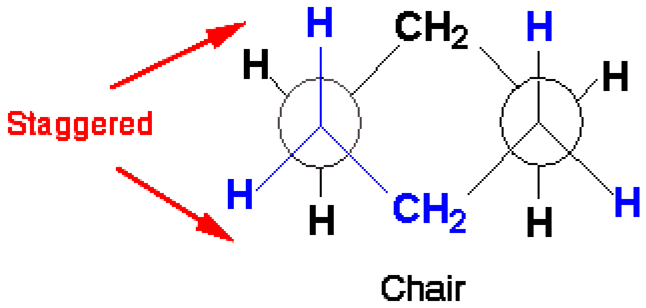
- Chair Conformation
- Boat Conformation
- Twisted Boat Conformation
- Half Chair Conformation

Chair Conformation of Cyclohexane

- Chair conformations readily interconvert, resulting in the exchange of axial and equatorial positions by a **ring-flip**

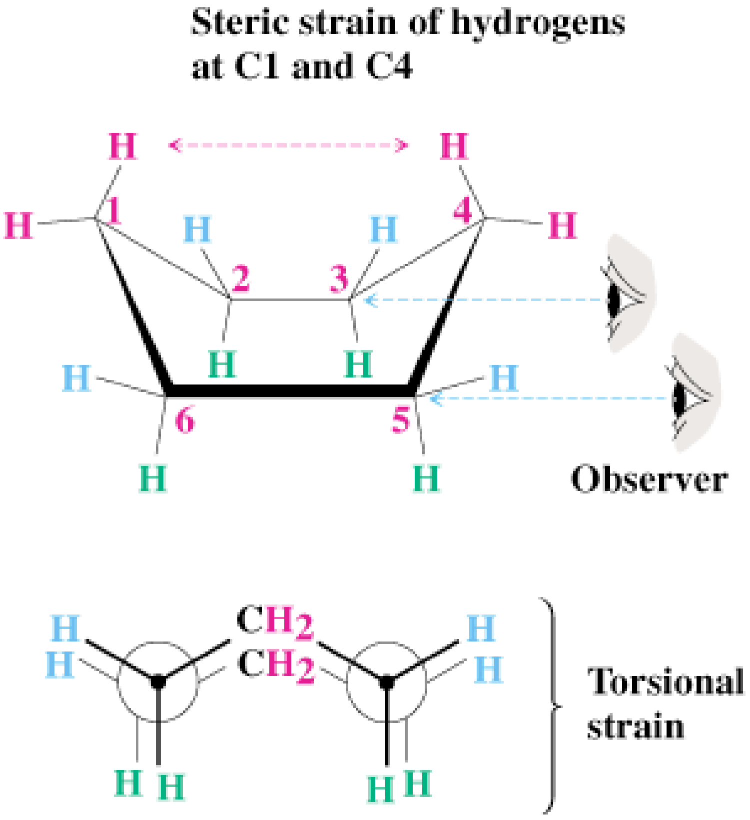






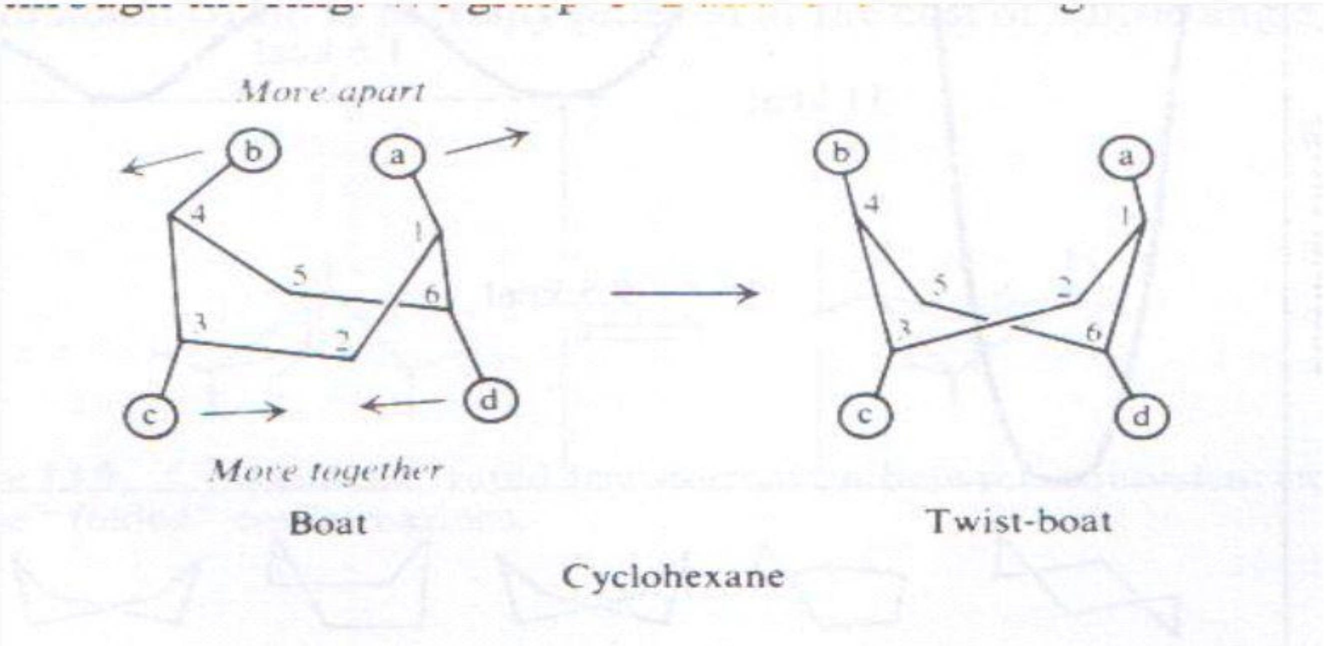
Boat Cyclohexane

- Cyclohexane flips through a **boat conformation**
- Less stable than chair cyclohexane due to steric and torsional strain
- C-2, 3, 5, 6 are in a plane
- H on C-1 and C-4 approach each other closely enough to produce considerable steric strain
- Four eclipsed H-pairs on C-2, 3, 5, 6 produce torsional strain
- ~29 kJ/mol (7.0 kcal/mol) less stable than chair

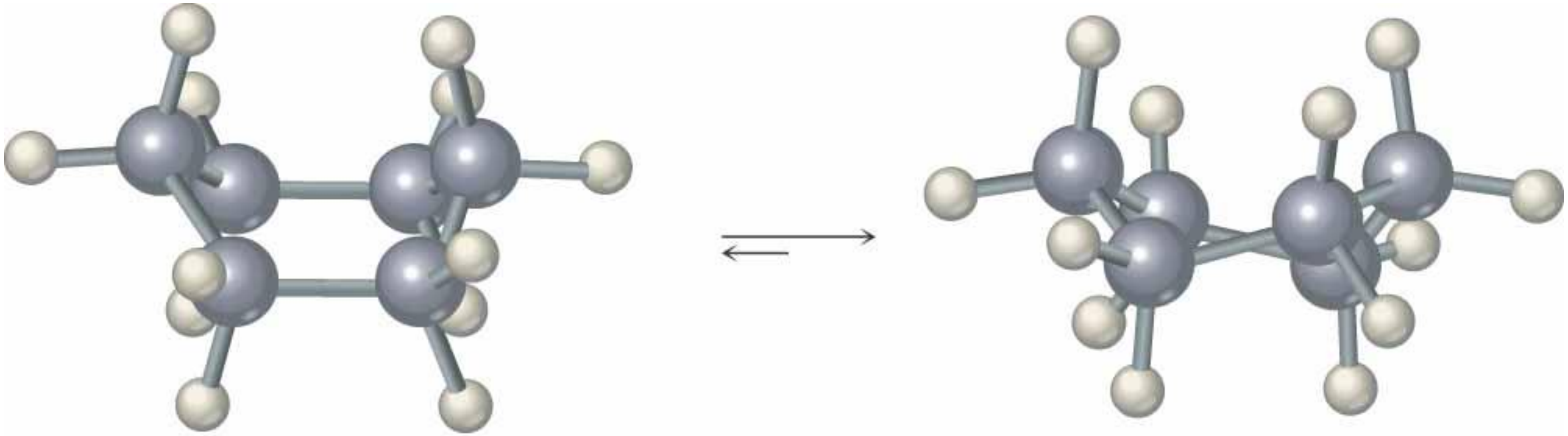


Twisted Boat Conformation

Twist boat is more stable than the boat conformation



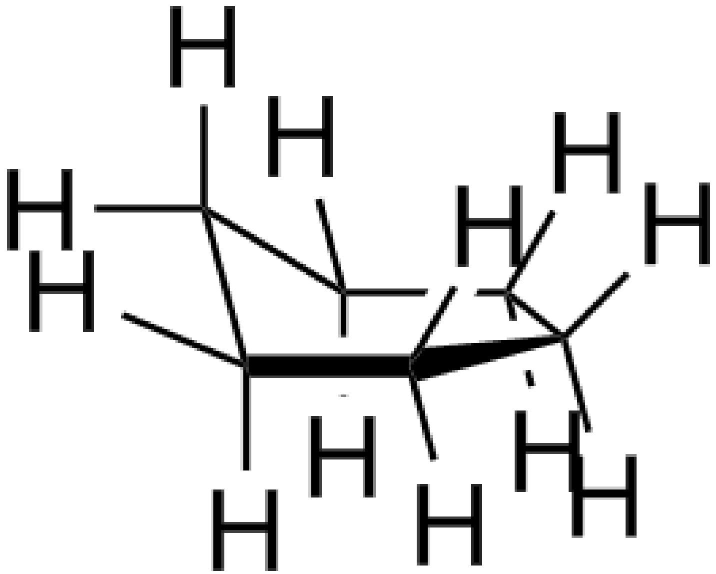
Boat & Twist-boat conformations:



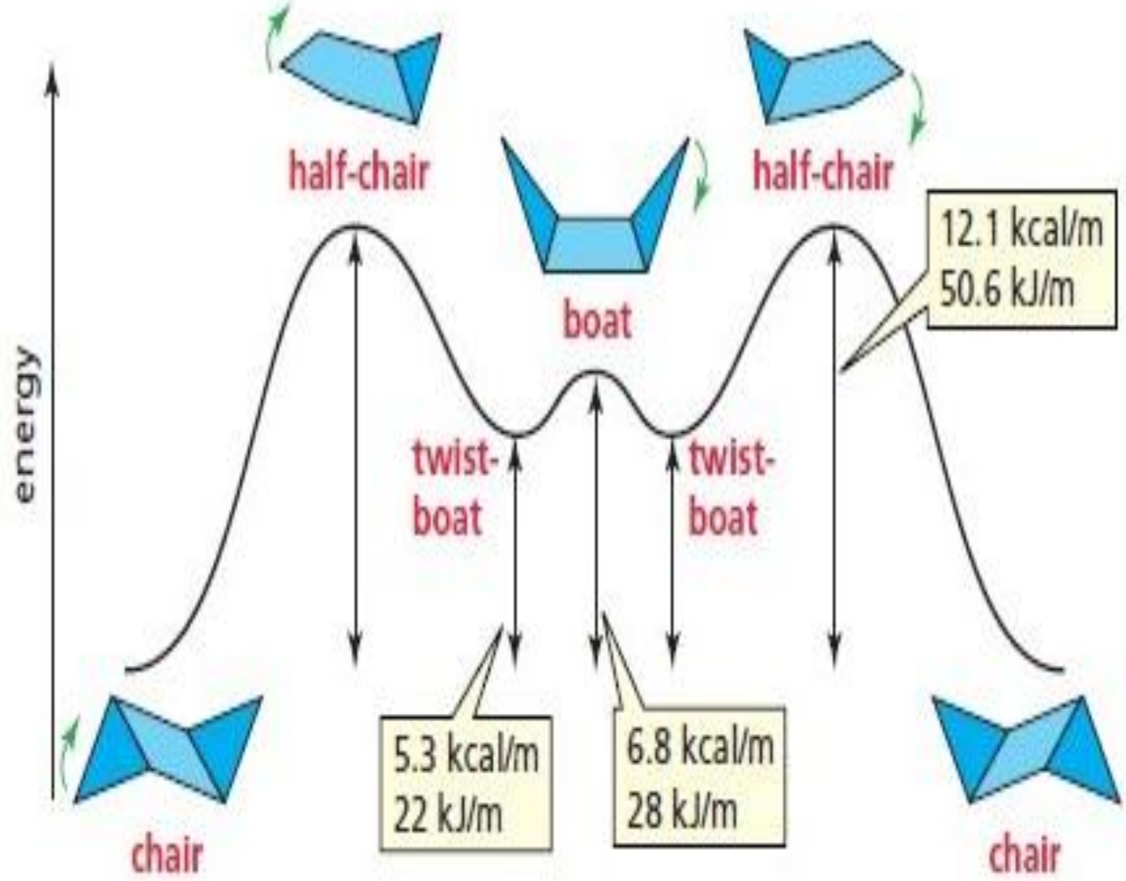
Boat cyclohexane
(29 kJ/mol strain)

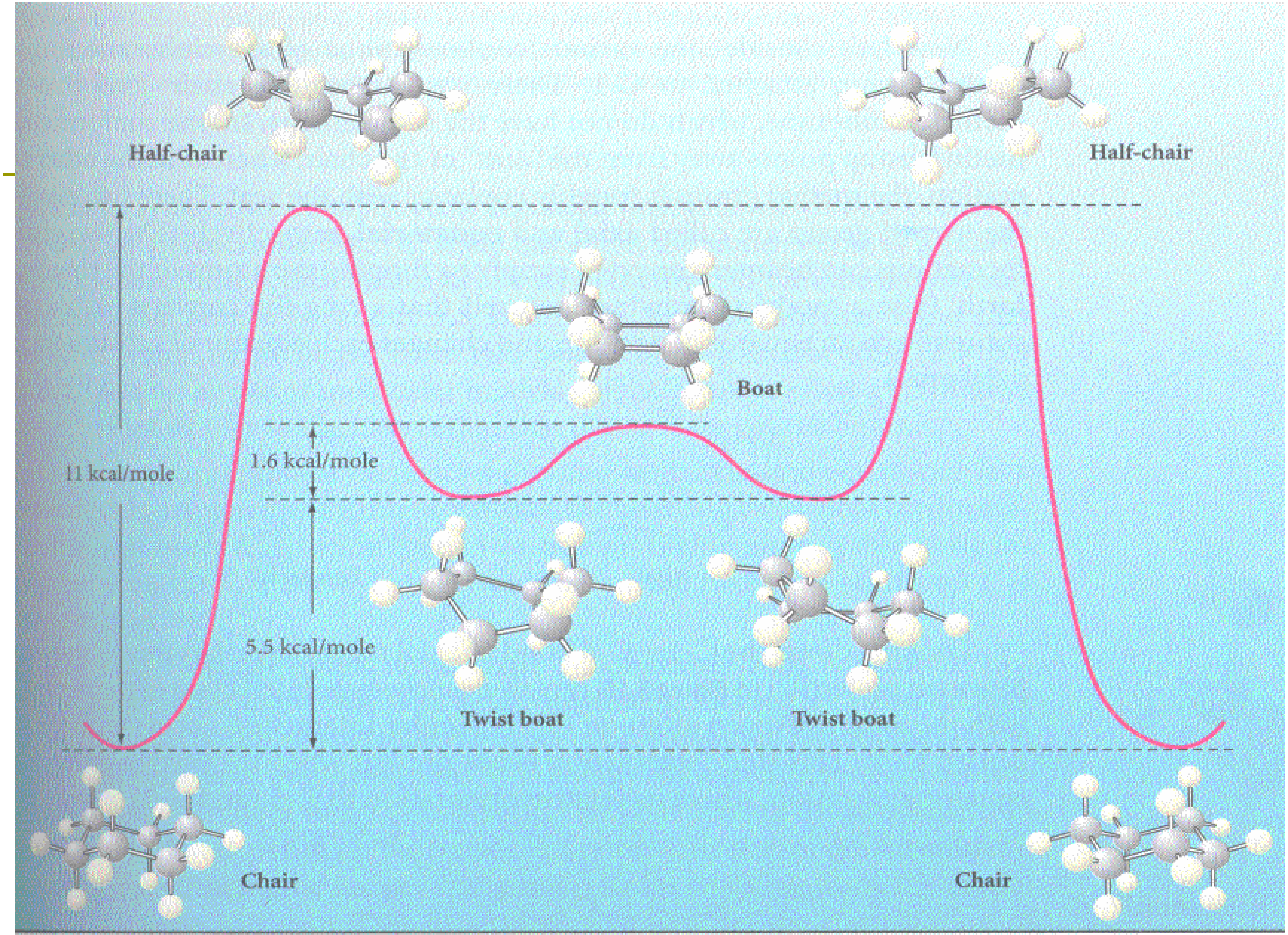
Twist-boat cyclohexane
(23 kJ/mol strain)

Half Chair Conformation



Stability of Cyclohexane



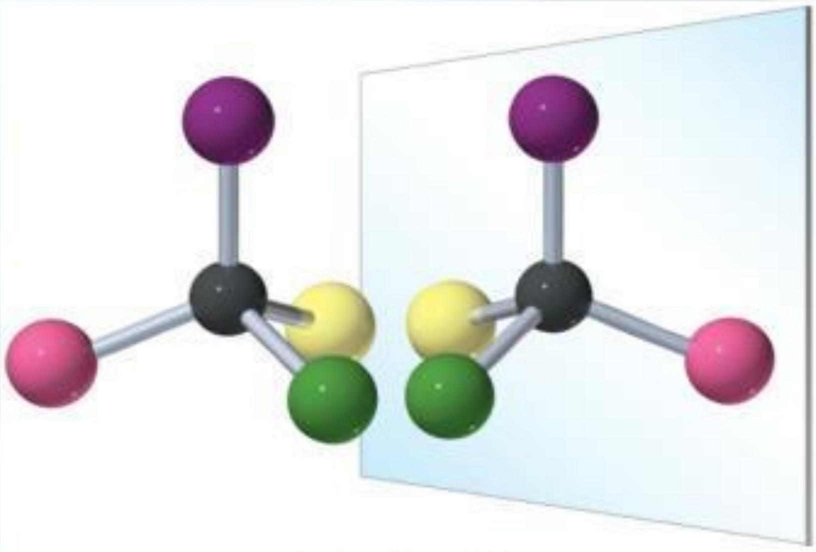

Half-chair
Half-chair
Boat
11 kcal/mole
1.6 kcal/mole
5.5 kcal/mole
Twist boat
Twist boat
Chair
Chair

STEREO CHEMISTRY

Stereochemistry:

Arrangement of Atoms in Space;

Stereochemistry of Addition Reactions

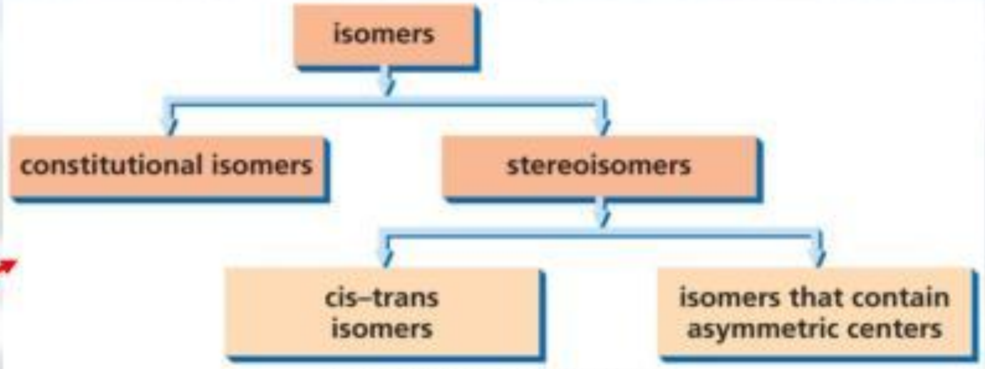


nonsuperimposable mirror images

enantiomers

Isomers

Isomers - compounds with the same molecular formula but different structures


isomers

constitutional isomers

stereoisomers

cis–trans isomers

isomers that contain asymmetric centers

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constitutional isomers

CH_3CH_2OH and CH_3OCH_3

ethanol — dimethyl ether

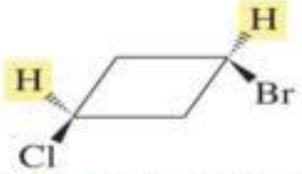
$CH_3CH_2CH_2CH_2CH_3$ and


$CH_3\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2CH_3$

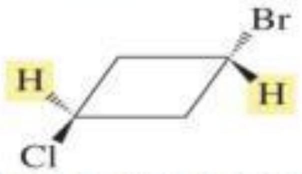
pentane — isopentane

Stereoisomers – different 3D structures

cis-trans are one example



cis-1-bromo-3-chlorocyclobutane



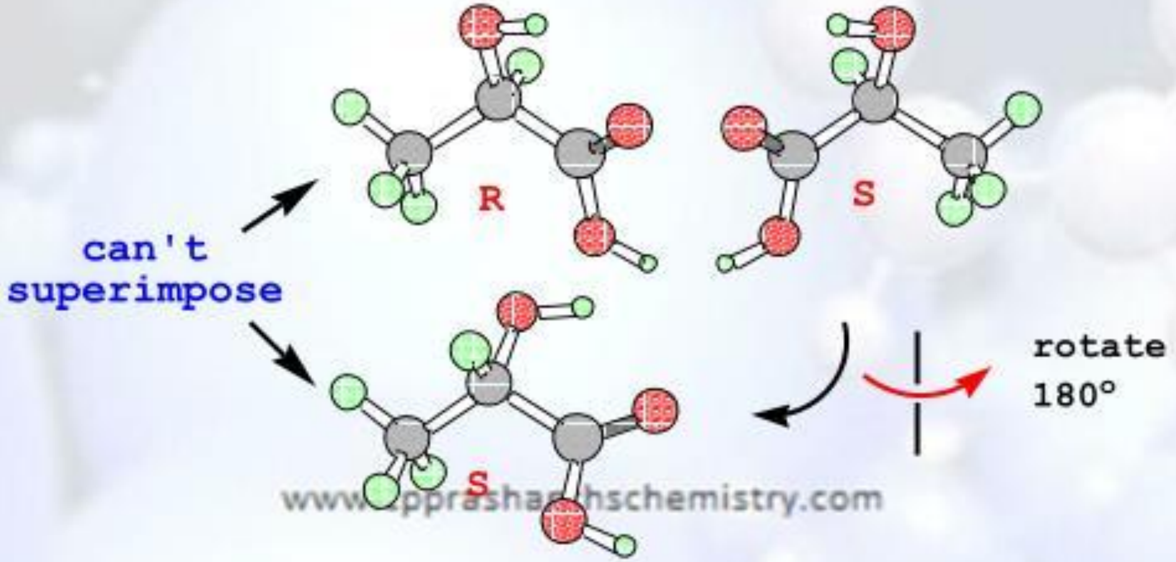
trans-1-bromo-3-chlorocyclobutane

stereo isomers = isomers which differ only in their 3D structures;
eg, cis & trans isomers, **enantiomers and diastereomers**

enantiomers = **non-superimposable** (different) mirror images;
majority of chemical and physical properties are identical

(R)-(-)-lactic acid (S)-(+)-lactic acid

enantiomers



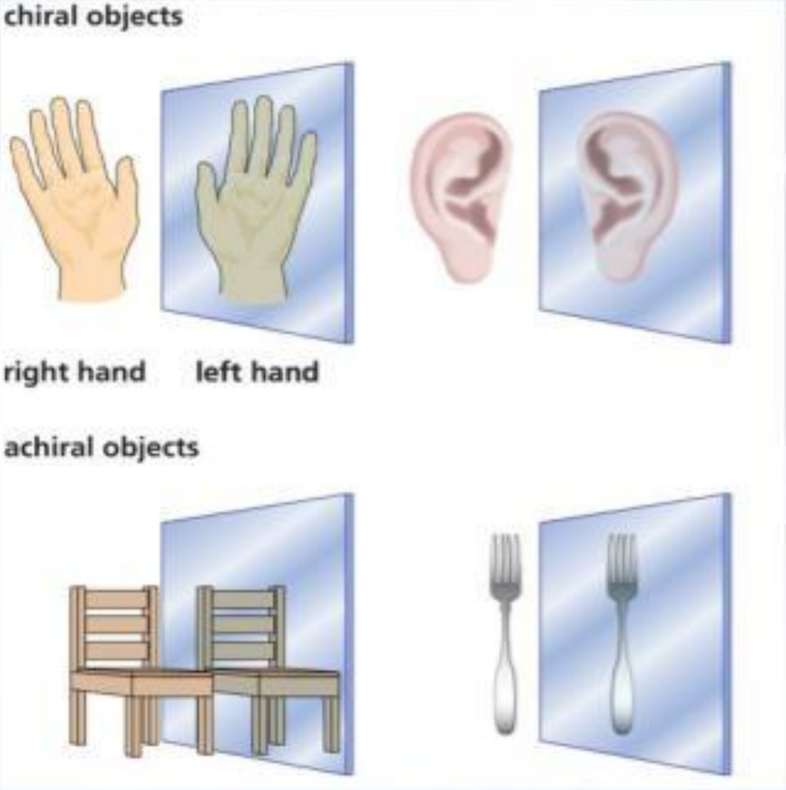
can't superimpose

rotate 180°

chiral = describes a molecule that is **different** from its mirror image;

enantiomers are chiral

achiral = describes a molecule that is the **same** as its mirror image



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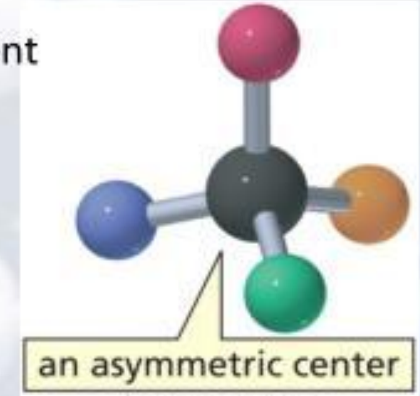
Asymmetric Centers

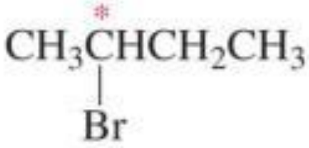
Chiral molecules – usually contain an asymmetric (chiral, stereo, stereogenic) center

Asymmetric center - tetrahedral atom bonded to four different groups - indicated with an *asterisk (*)*


an asymmetric center

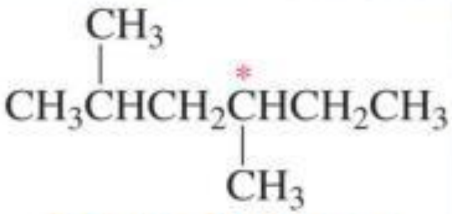
$$CH_3CH_2CH_2\underset{\overset{|}{OH}}{\overset{*}{C}}HCH_2CH_2CH_2CH_3$$

4-octanol



$$CH_3\underset{\overset{|}{Br}}{\overset{*}{C}}HCH_2CH_3$$

2-bromobutane



$$CH_3\overset{\underset{|}{CH_3}}{C}HCH_2\underset{\overset{|}{CH_3}}{\overset{*}{C}}HCH_2CH_3$$

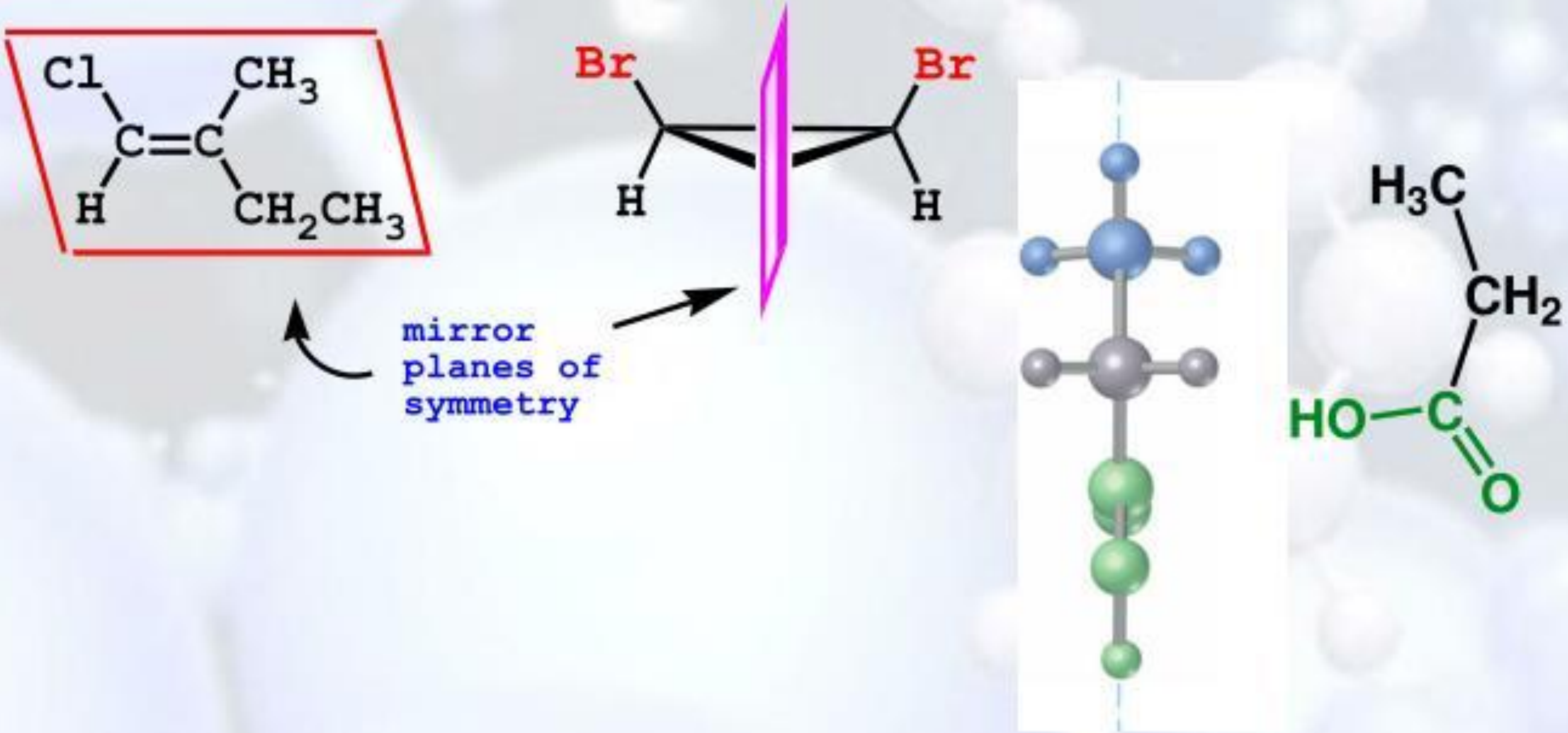
2,4-dimethylhexane

achiral molecules have either one or both of the following…

- → plane of symmetry
- → center of symmetry ← **see next two slides**

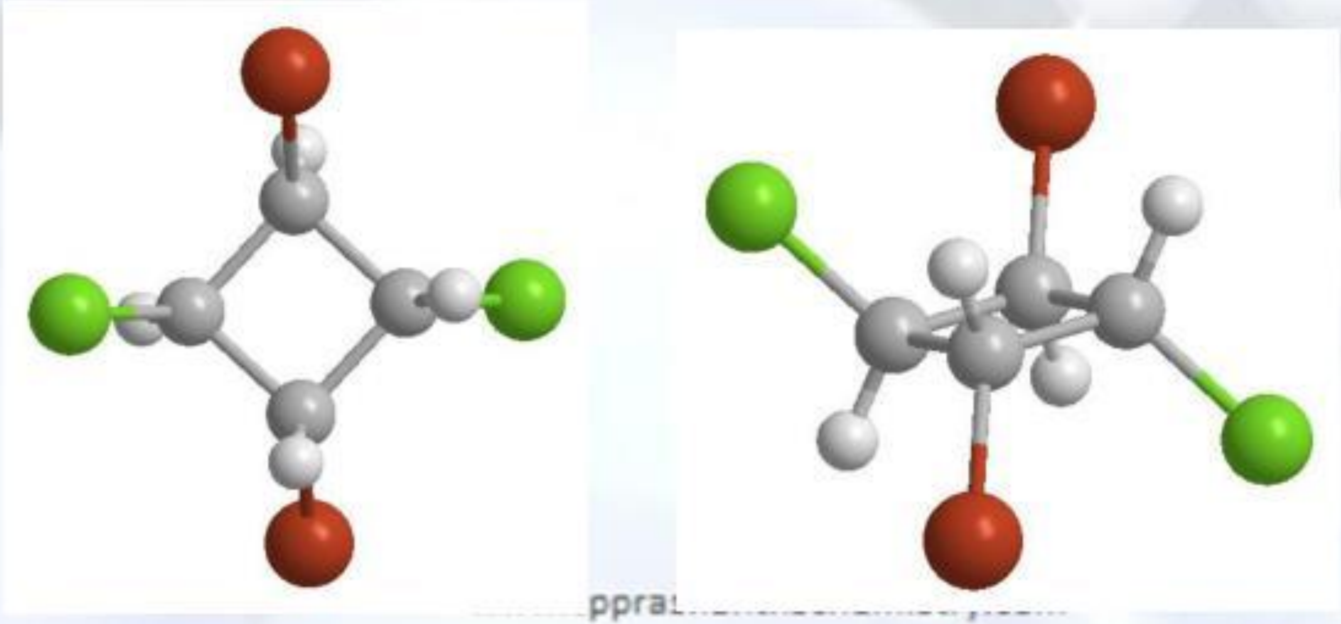
chiral molecule → (R)-lactic acid (no symmetry)

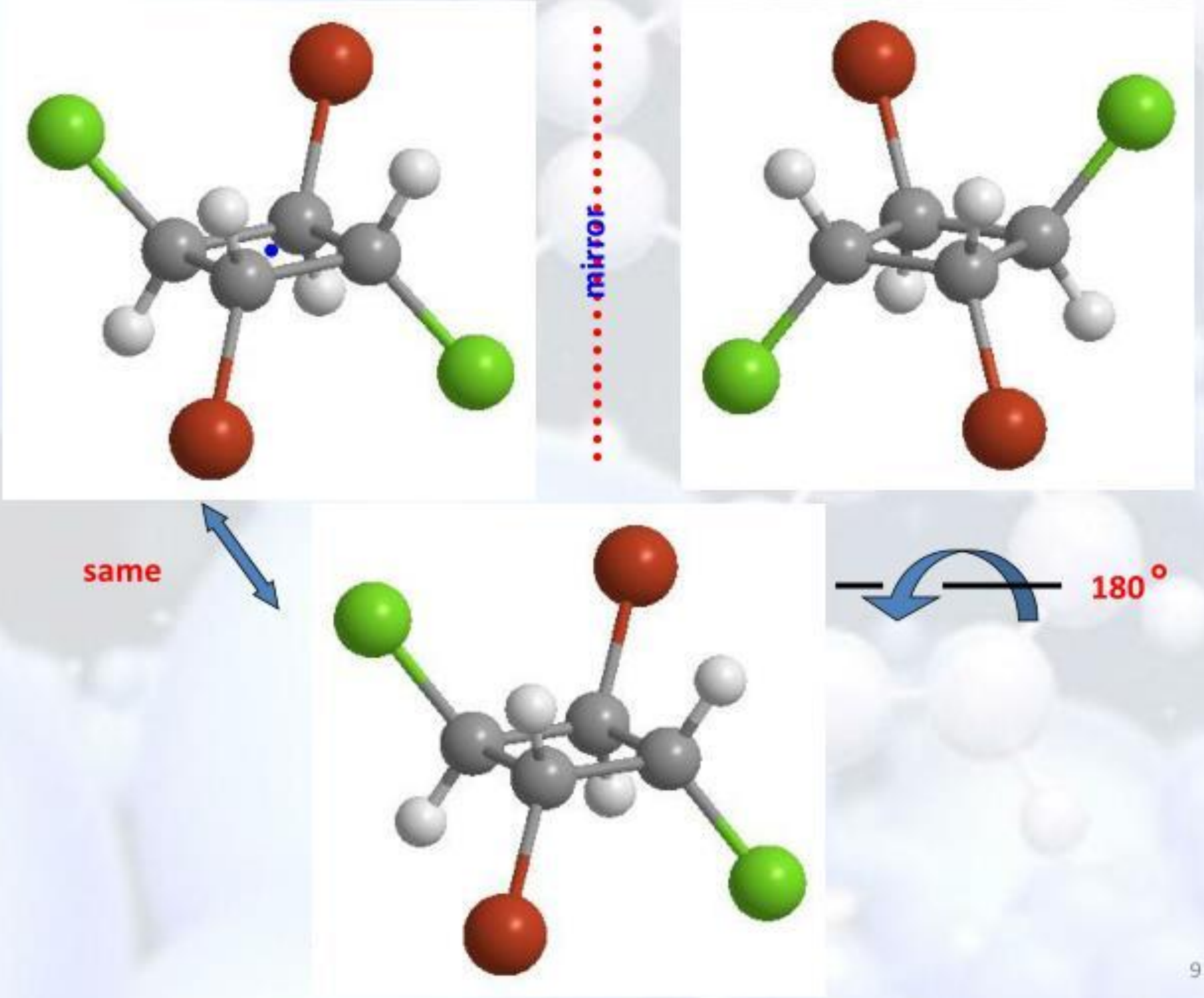
achiral molecule → water (plane of symmetry)



mirror planes of symmetry

* = center of symmetry in geographical middle of the molecule





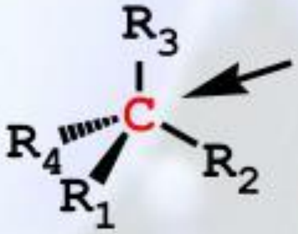
mirror

same

180 °

chiral center (stereo, stereogenic, asymmetric center) ➔

an atom attached to 4 different atoms or groups

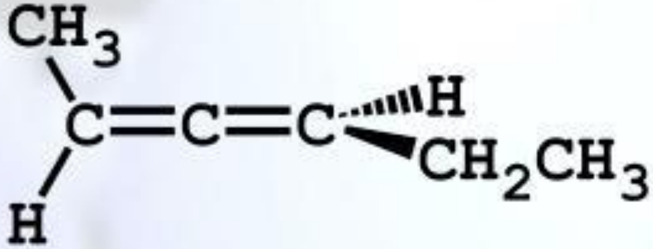


chiral center

most chiral molecules contain chiral centers →

but a molecule can be chiral and **not** contain a chiral center

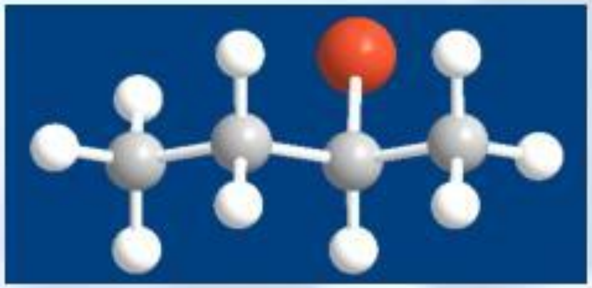
How about 2,3-hexadiene? … chiral / achiral…which??

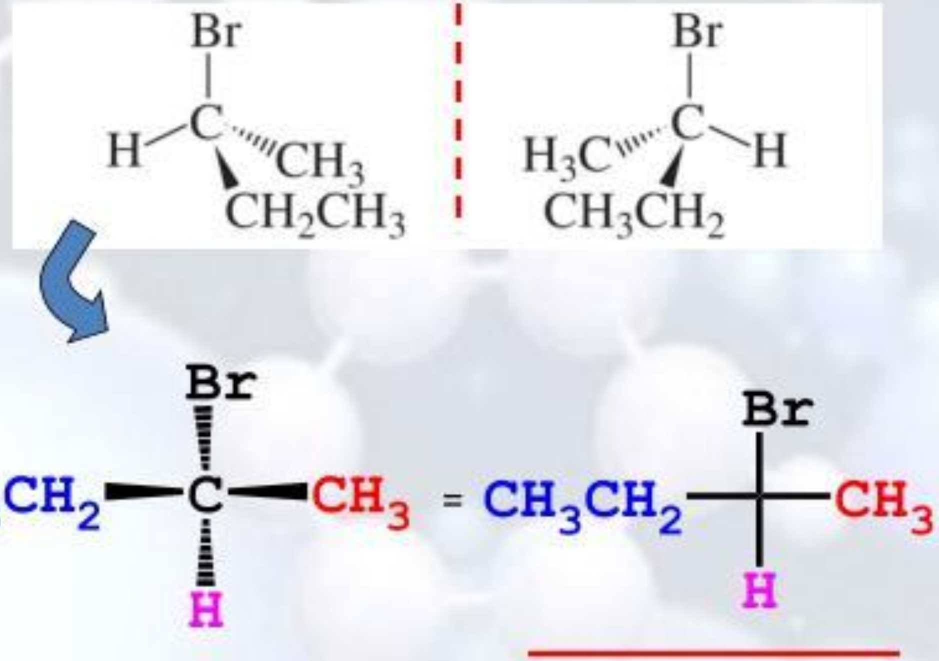


Also…molecule with 2
or more chiral centers
can be
achiral

Drawing Enantiomers

3D, prospective drawings





*Horizontal bonds are out of paper toward viewer and
*Vertical bonds are into the paper away from the viewer.

⇐ **Fisher projection (short-hand)…**

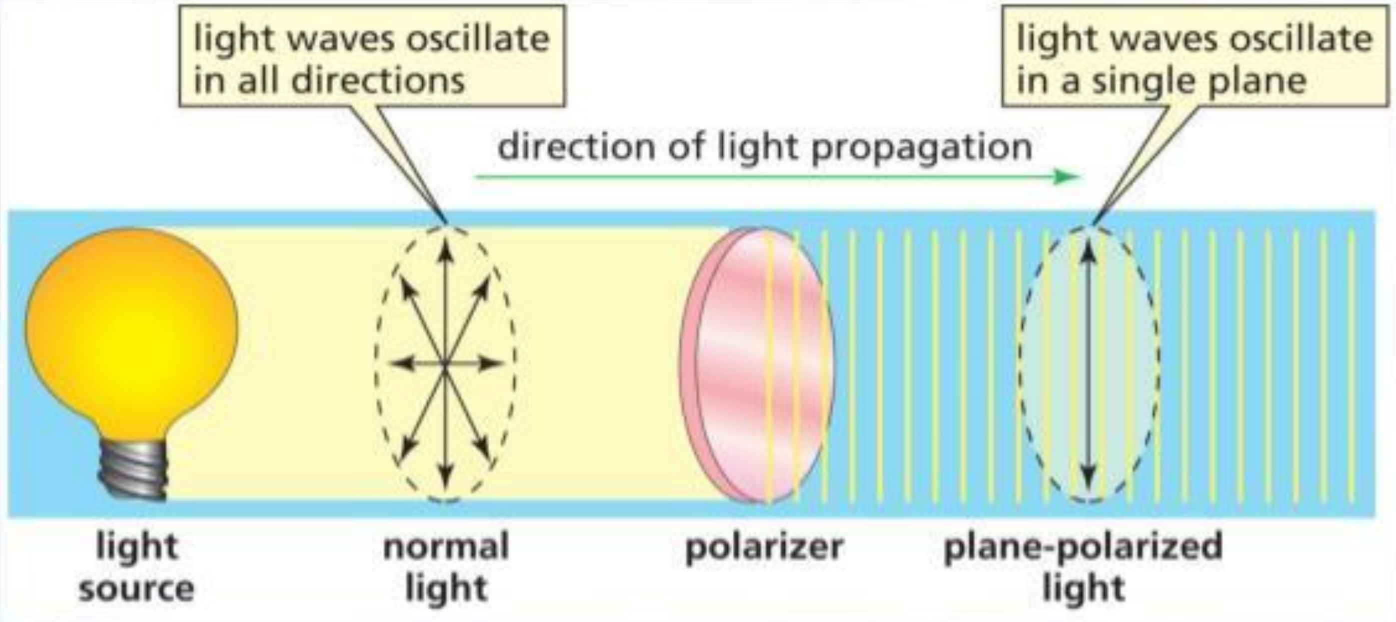
Optical Activity

What properties are ***the same*** with chiral compounds…enantiomers?

*Boiling point, melting point, solubility & cannot be easily separated (if at all)

What properties are ***different*** with chiral compounds?

*Interaction with **plane-polarized light** - light in which all the rays/waves oscillate in a single plane (normal light has ray oscillations in all directions)

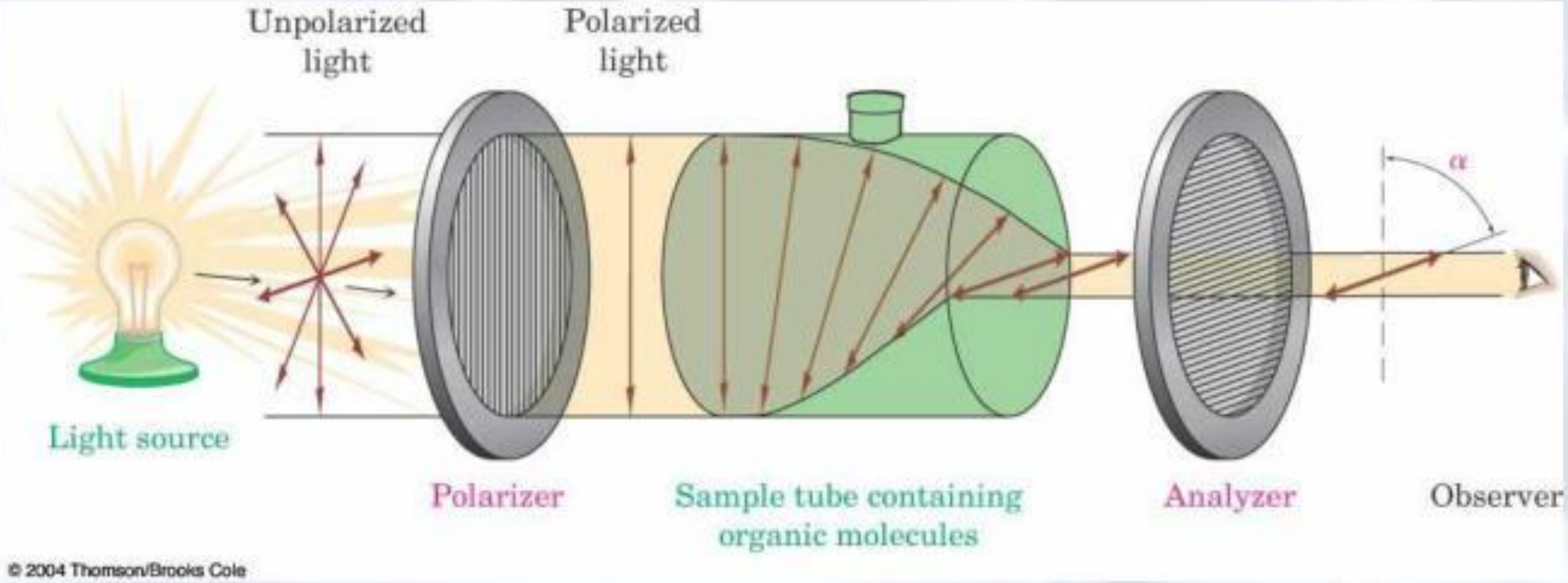


How do we get plane-polarized light? *Passing normal light through a polarizer*

Chiral compounds rotate ppl →

polarimeter = instrument used to measure the amount (in °) by which materials rotate **plane-polarized light**

Schematic diagram of a **polarimeter**…



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optical activity = a substance that **rotates** plane polarized light is **chiral** and said to be **"optically active"**

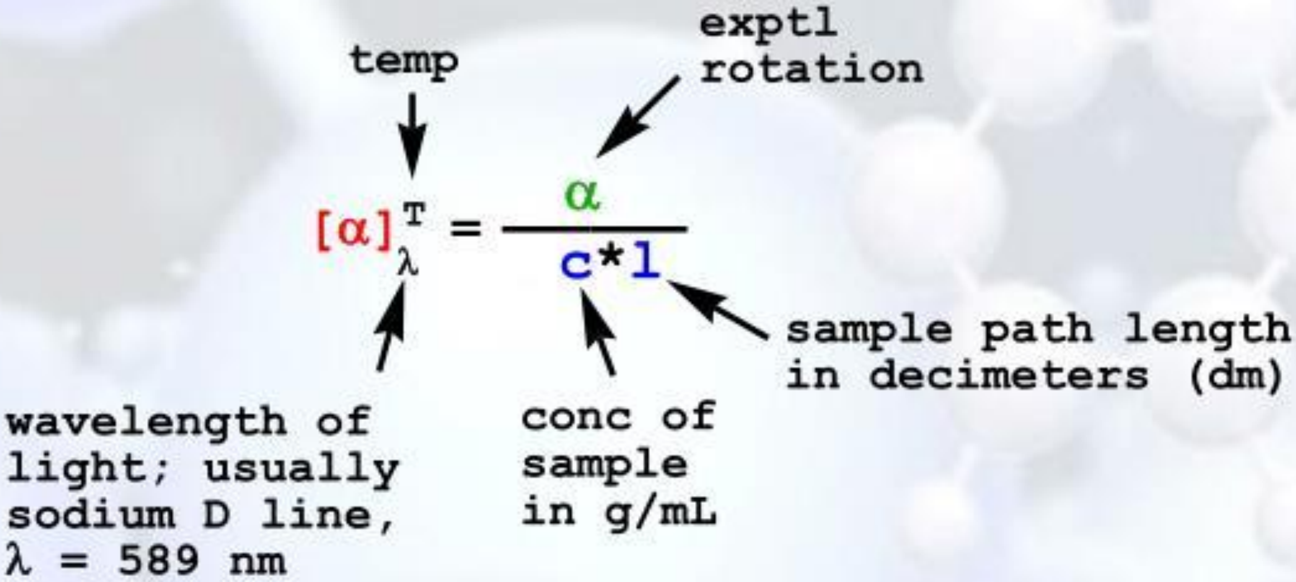
Specific rotation, $[\alpha]$ = amount (degrees) that a substance rotates ppl expressed in a standard form…

It accounts for variables such as…

(1) concentration (c)

(2) length (l) of the light path through the sample solution

(3) α is the experimental (measured) rotation



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

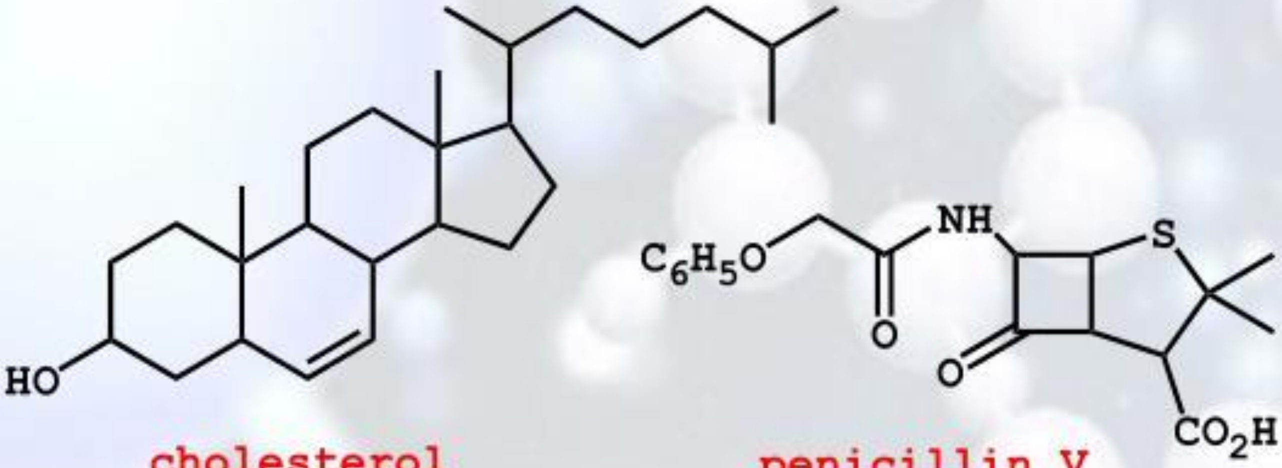
temp

exptl rotation

wavelength of light; usually sodium D line, λ = 589 nm

conc of sample in g/mL

sample path length in decimeters (dm)

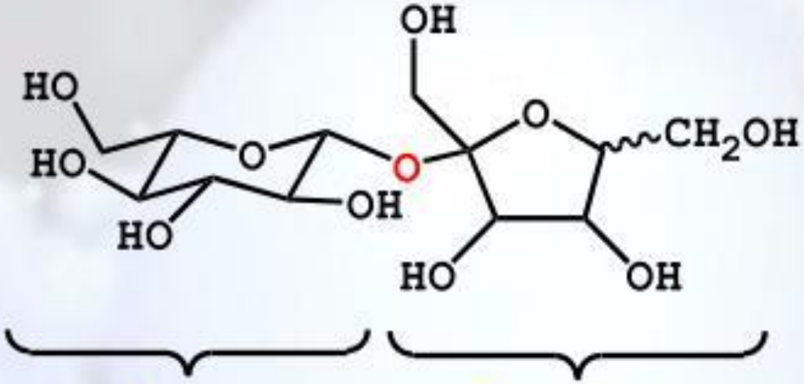


cholesterol

$[\alpha] = -31.5^\circ$

penicillin V

$[\alpha] = +223^\circ$



sucrose

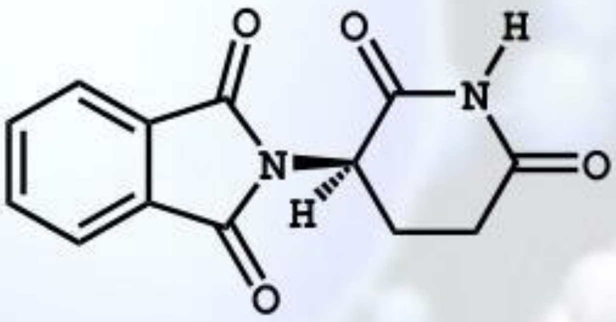
$[\alpha] = +66.4^\circ$

glucose

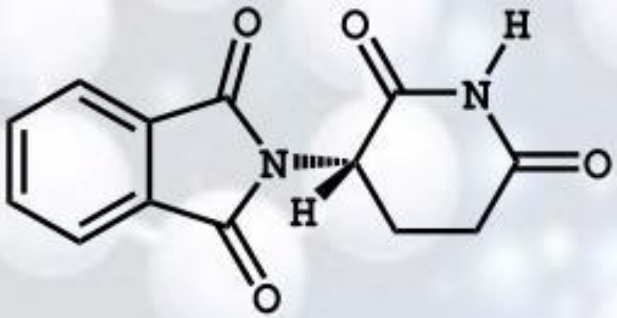
$[\alpha] = +53^\circ$

fructose

$[\alpha] = -92^\circ$



(R)-thalidomide
(antidepressant)



(S)-thalidomide
(mutagenic and
antiabortive)

The thalidomide story and tragedy…..

- 1959-62, prescribed as an analgesic for morning sickness
- used extensively in Europe and Canada despite strong warnings that it not be given to pregnant women.
- FDA had not approved its use in U. S. at the time!
- By 1961, it was recognized as the cause for numerous birth defects (~7- 10,000 in 28 countries).
- Presently being evaluated for the treatment of
  AIDS CANCER LEPROSY ARTHRITIS

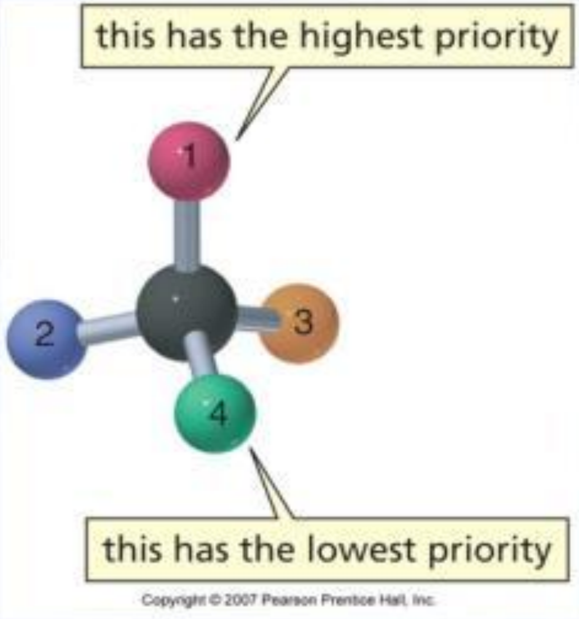
Naming enantiomers - *R,S* system (Cahn-Ingold-Prelog)

Enantiomers with one asymmetric center….one member has ***R* configuration**

the other has ***S* configuration**.

Visualize molecule in 3D and assign R/S priorities;

1->2->3 = R if clockwise, S = if counter clockwise


this has the highest priority

this has the lowest priority

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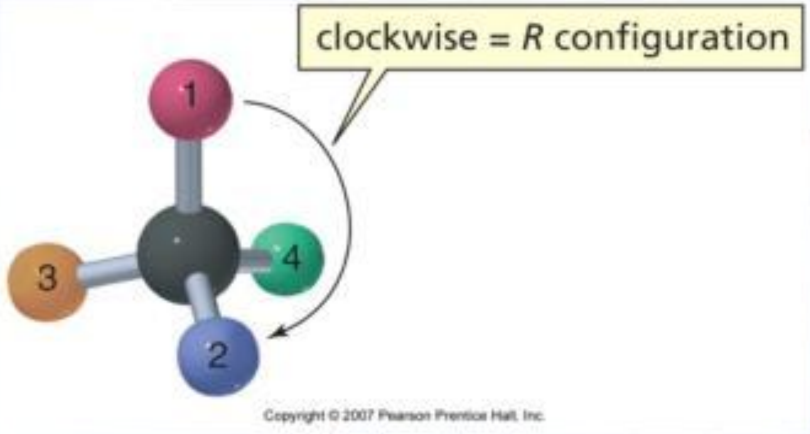
clockwise = *R* configuration

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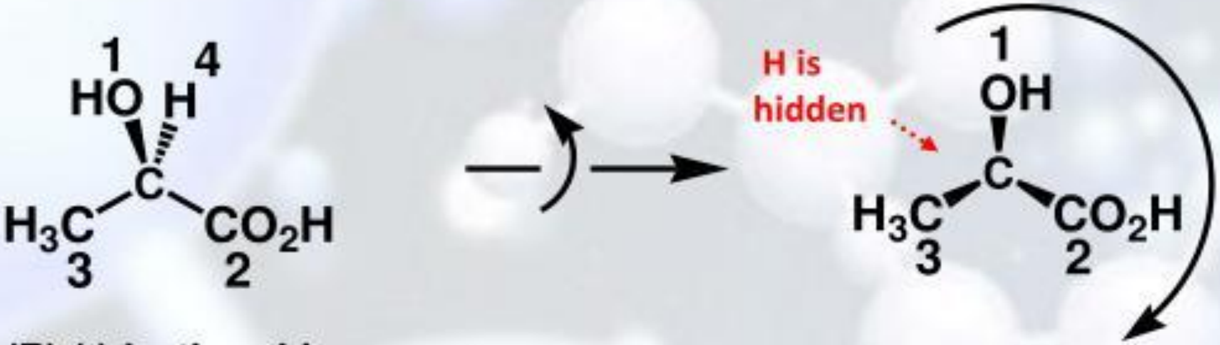
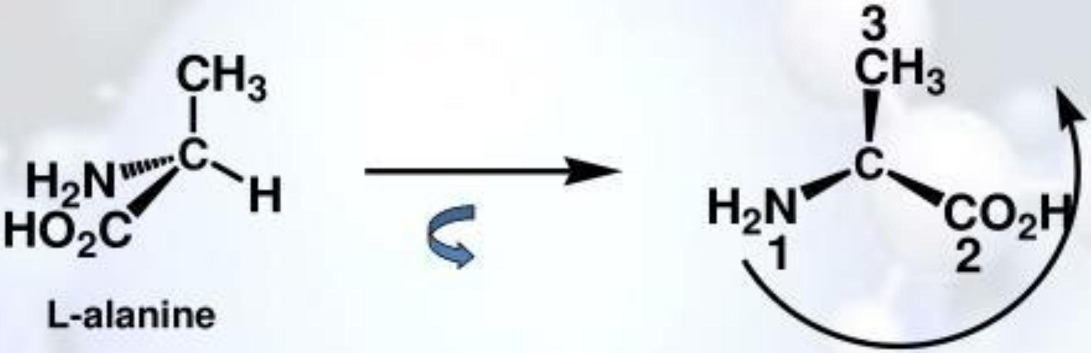
R/S notation = specifies absolute configuration of a chiral center; there is **no** correspondence between R and + or S and –



(R)-(-)-lactic acid

m.i. = (S)-(+)-lactic acid

clockwise = R



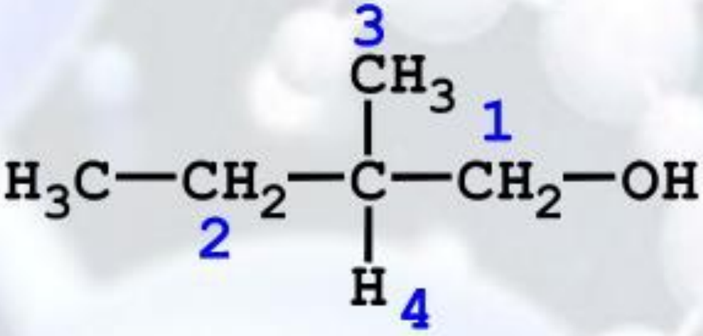
L-alanine

2-aminopropanoic acid

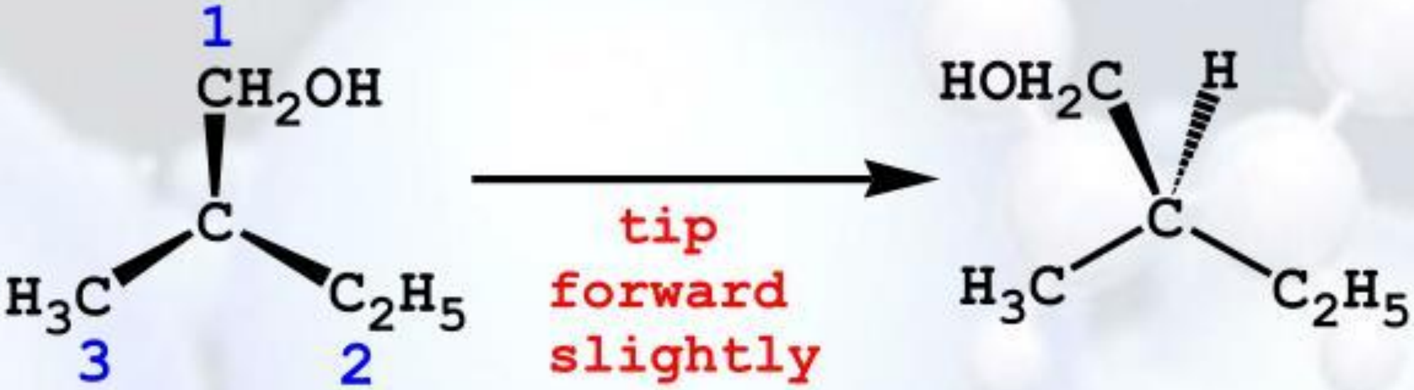
counter-clockwise = S

Draw a 3D structure for

(R)-2-methyl-1-butanol

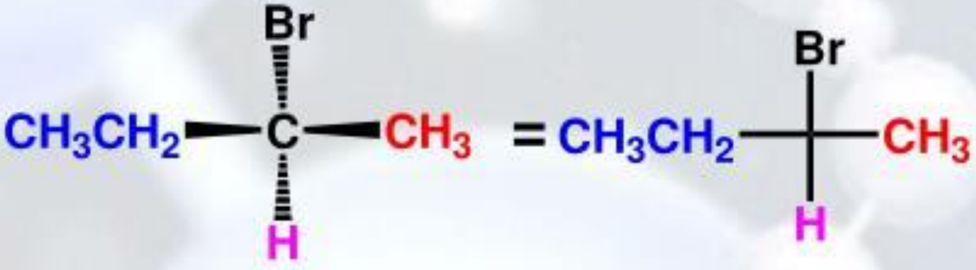


$$H_3C-CH_2-\overset{CH_3}{\underset{H}{C}}-CH_2-OH$$



Fischer projections = short hand for displaying molecules with stereogenic centers

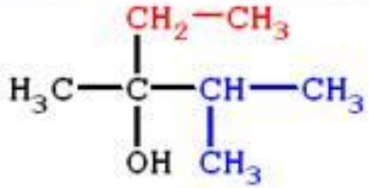
*Horizontal bonds are out of paper toward viewer and vertical bonds are into the paper away from the viewer.



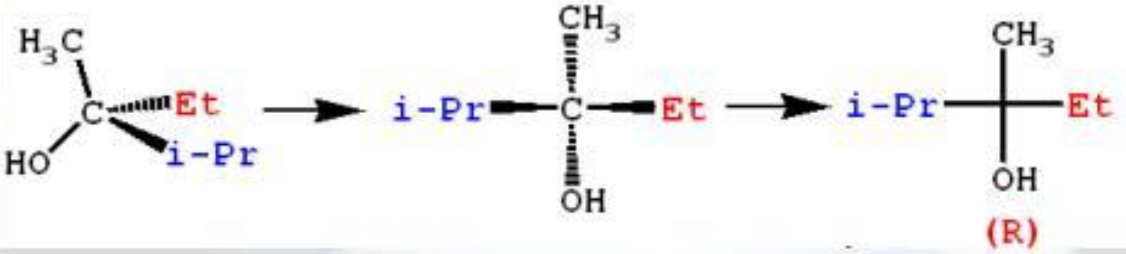
*90 ° rotation -> inverts the configuration (R -> S and *vice versa*).

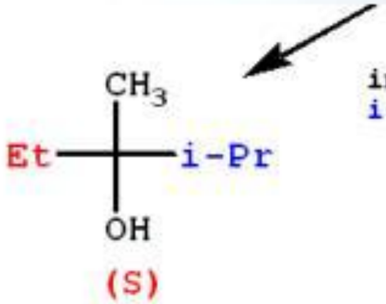
*Can be rotated 180 ° about an axis perpendicular to the paper without altering the configuration.

*If the projection is rotated in a way that lifts some groups out of the paper, the absolute configuration will be reversed.



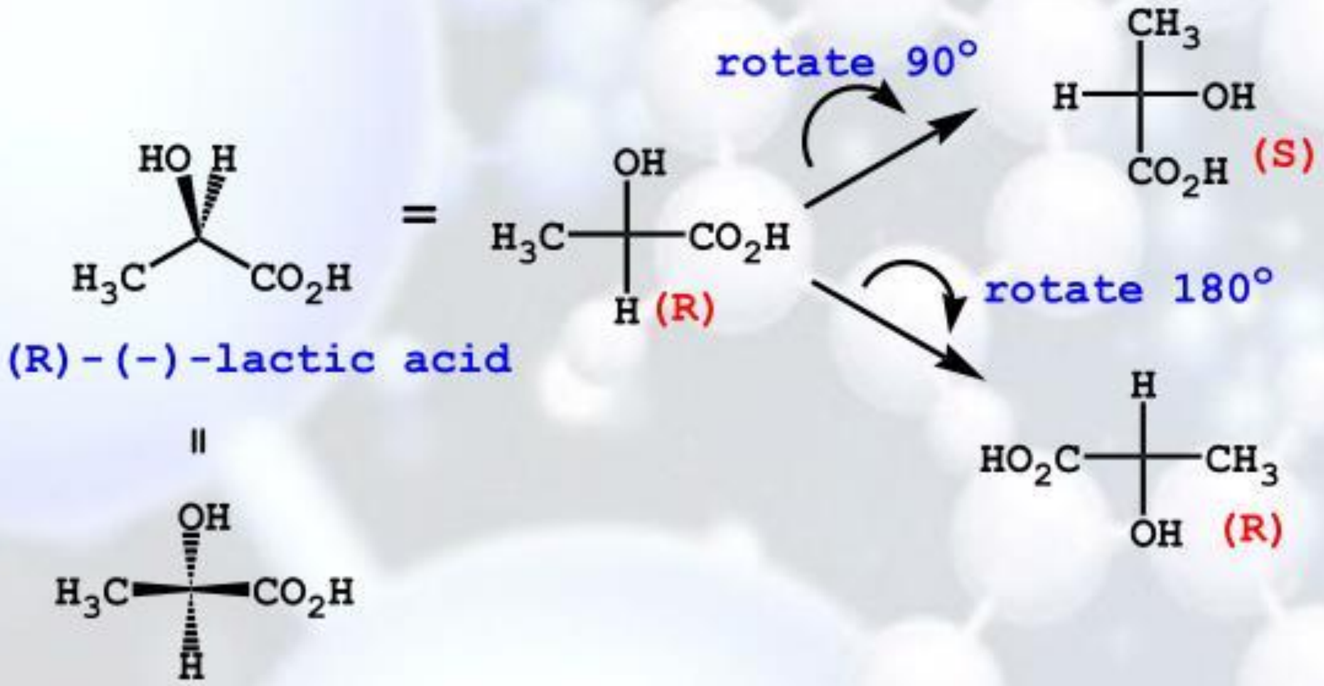
2,3-dimethyl-3-pentanol





interchange
i-Pr and Et

R -> S

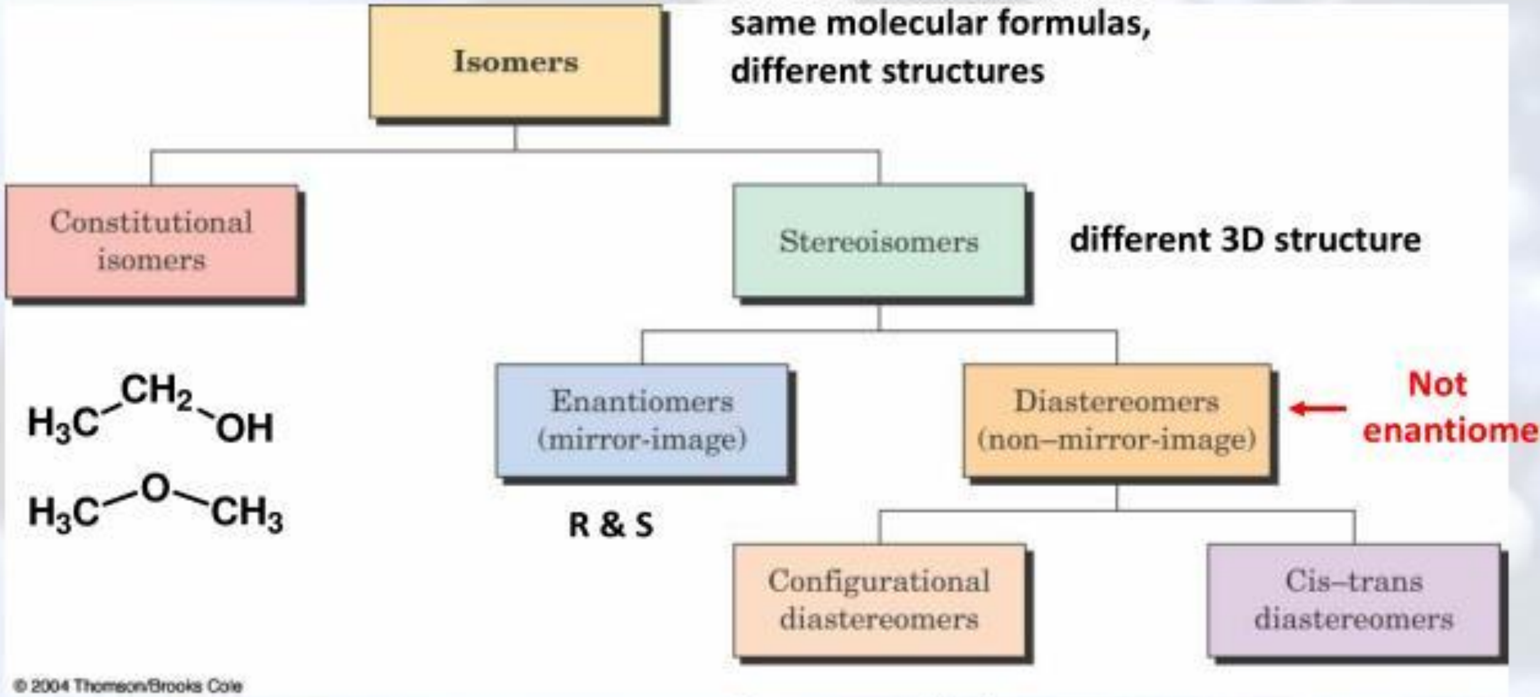


Note: Interchange two of the groups attached to a chiral center, the molecule → mirror image.

Odd number of interchanges → the mirror image.

Even number → absolute configuration unchanged.

A slightly expanded chart of isomers…



Isomers

same molecular formulas, different structures

Constitutional isomers

H_3C-CH_2-OH

$H_3C-O-CH_3$

Stereoisomers

different 3D structure

Enantiomers (mirror-image)

R & S

Diastereomers (non–mirror-image)

← **Not enantiomers**

Configurational diastereomers

2 or more chiral centers

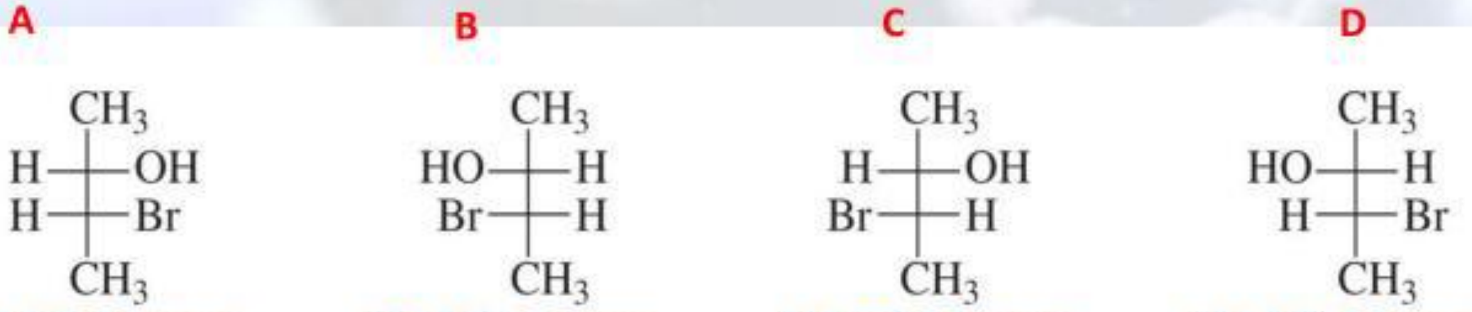
Cis–trans diastereomers

More than 1 Asymmetric Center…

A compound can have a ***maximum*** of 2^n stereoisomers,

where *n* = the number of asymmetric centers

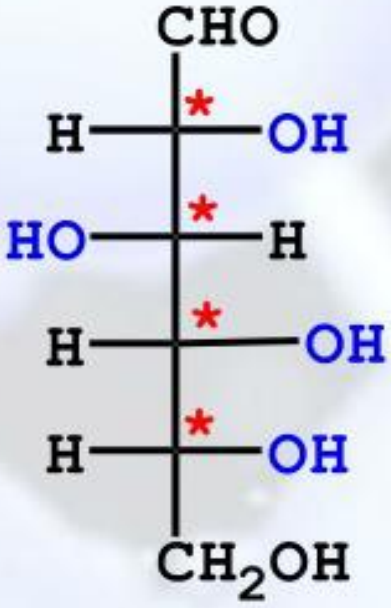
3-bromo-2-butanol - 2 asymmetric centers = 4 stereoisomers:



(2*S*,3*R*)-3-bromo-2-butanol **(2*R*,3*S*)-3-bromo-2-butanol** **(2*S*,3*S*)-3-bromo-2-butanol** **(2*R*,3*R*)-3-bromo-2-butanol**

Fischer projections of the stereoisomers of 3-bromo-2-butanol

Enantiomers = A/B and C/D….what are A/C, A/D, B/C, B/D?



(+)-glucose

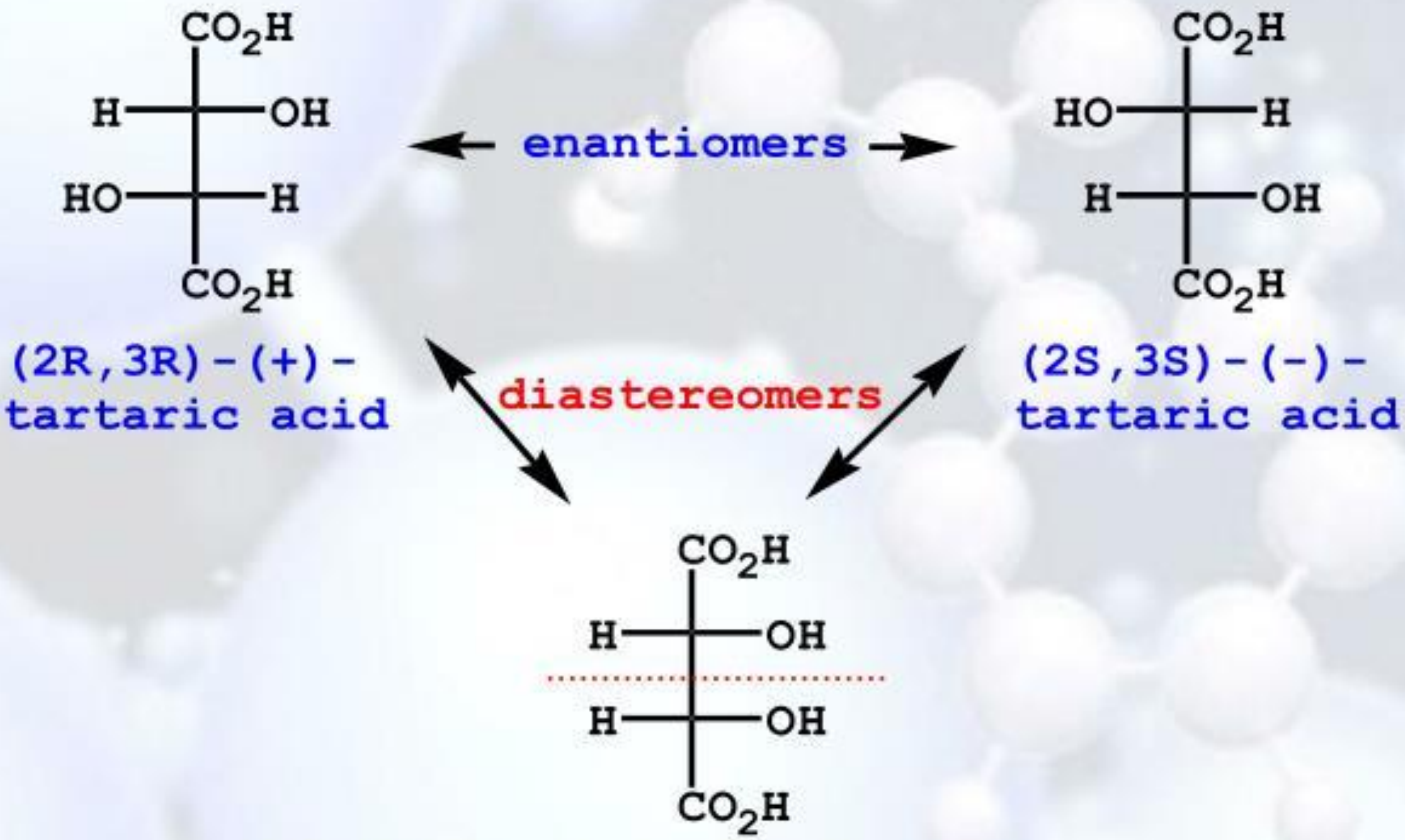
# of chiral centers = 4

total # of stereoisomers =

$2^4 = 16$

Diastereomers = stereoisomers that are <u>not</u> enantiomers;

have **different** chemical and physical properties



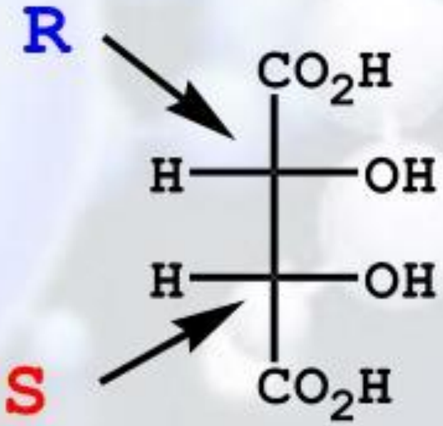
enantiomers

(2R,3R)-(+)-tartaric acid

(2S,3S)-(-)-tartaric acid

diastereomers

(2R,3S)-tartaric acid (meso isomer)



(2R,3S)-tartaric acid (meso isomer)

meso isomer = an achiral molecule with 2 or more chiral centers + an internal plane of symmetry; the molecule is achiral

Note absolute configurations of the two chiral centers in meso-tartaric acid are opposite, R and S

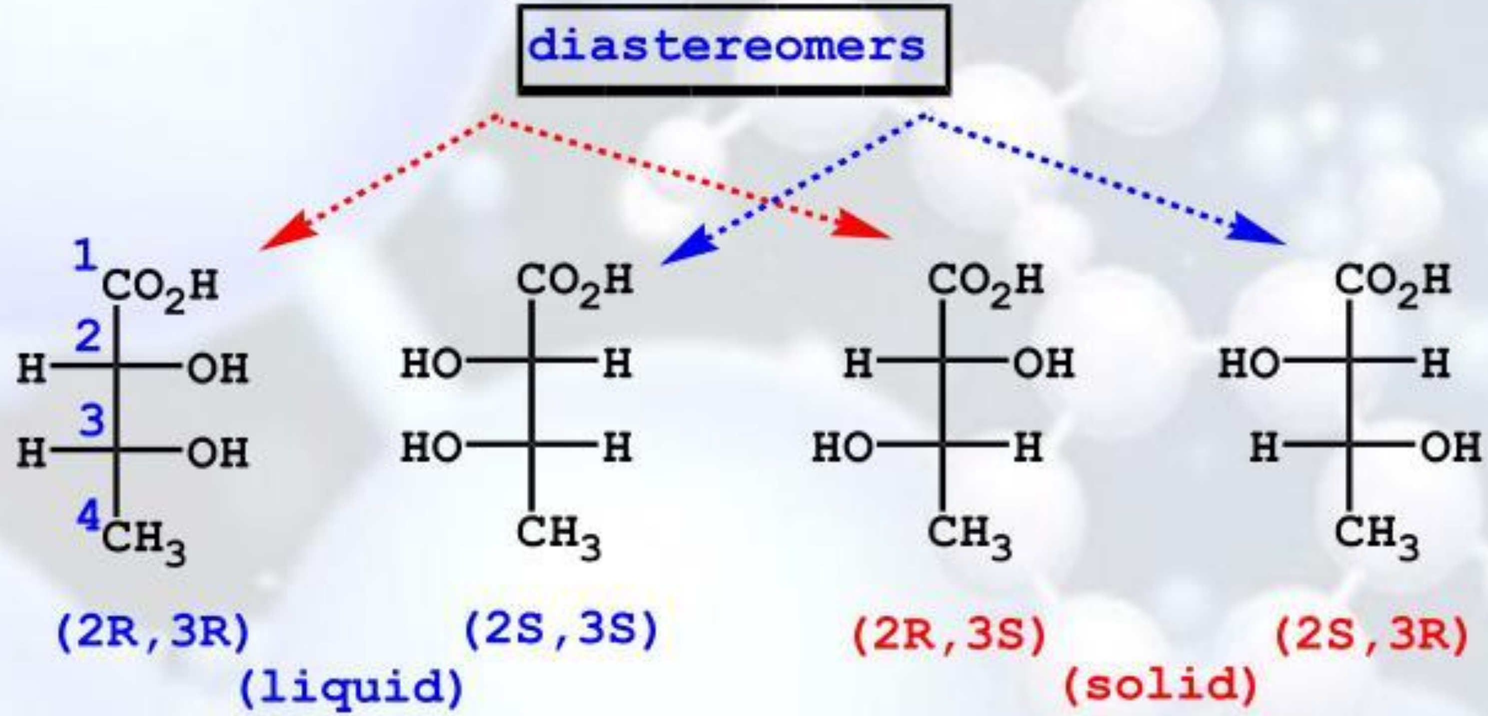
Tartaric acid properties....

3 stereo isomers → 4 crystal forms

Stereo-isomer	Mp (°C)	$[\alpha]^{20}_{D}$ (°)	ρ (gm/ml)	H_2O solubility (gm/100 ml)
(+)	168-170	+12	1.760	139
(-)	168-170	-12	1.760	139
meso	146-8	0	1.660	125
(+-)	206	0	1.788	20.6

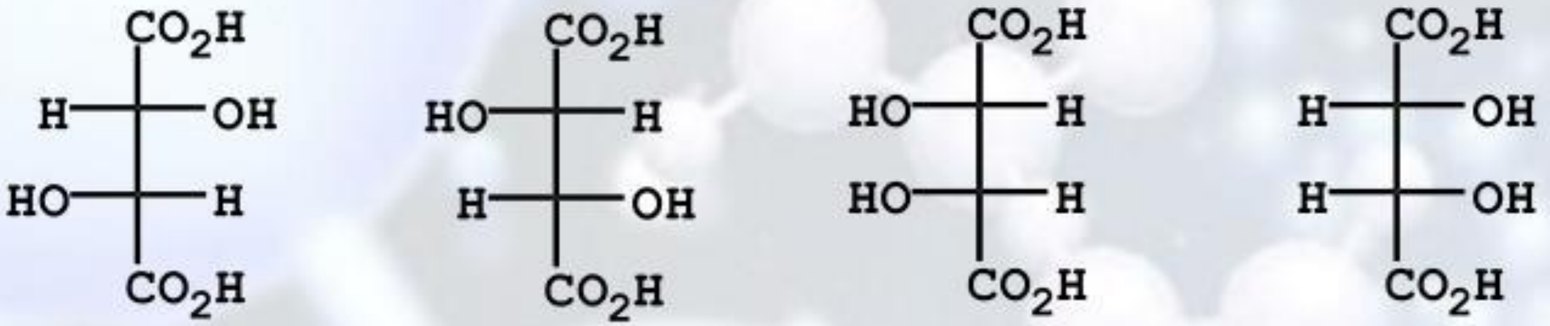
	pK_a # 1	pK_a # 2
(+) or (-)	2.98	4.34
meso	3.23	4.82

*<u>Chiral</u> molecules with 2 stereogenic centers…



various 2,3-dihydroxybutanoic acids

***Achiral molecules** with 2 stereogenic centers…



(2R,3R) (2S,3S) (2S,3R) (2R,3S)

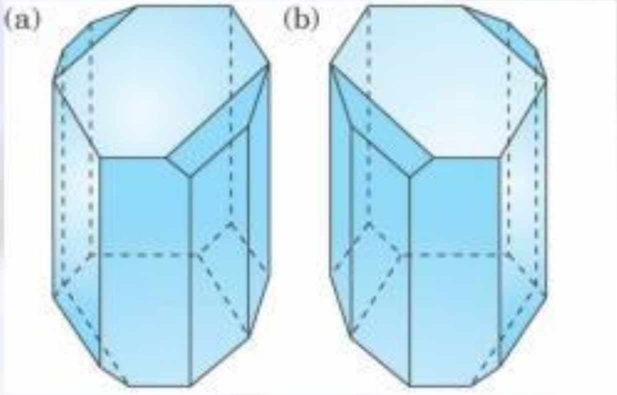
various tartaric acids

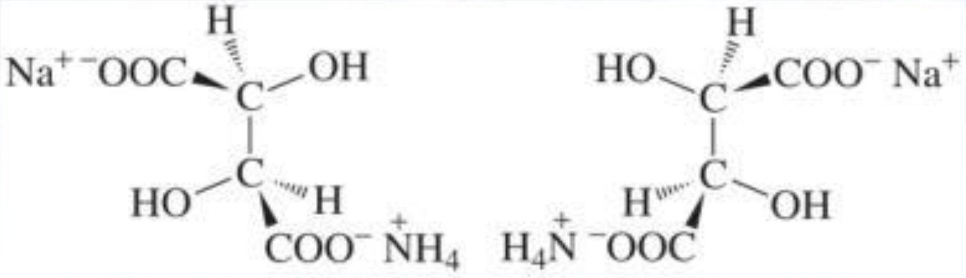
identical

meso isomer

racemic mixture = **1:1 mixture of enantiomers;**
has <u>no</u> optical activity

Louis Pasteur, ~1860 ➔ crystallized racemic mixture of sodium ammonium tartrate
➔ mirror image crystals.

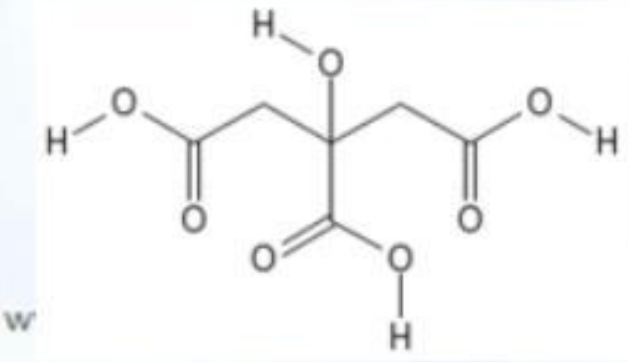




left-handed crystals **right-handed crystals**

sodium ammonium tartrate

Citric acid most
common in fruits



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2- Stereochemistry of organic compounds, Emest L. Eliel, Samuel H. Wilen (2015).

3- Stereochemistry conformation and mechanism, eighth edition, P. S. Kalsi (2020).

4- Stereochemistry of organic compounds principles and applications, D. Nasipure (2019).

5- Guide to stereochemistry, A Detailed Guide, Bishal Bashya, (2014).

Heterocyclic Chemistry

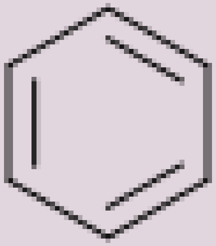
2nd year students Biology group Faculty of Education
Hurghada univeristy
2021/2022
Dr/ Ibrahim Abdul-Motaleb Mousa

Contents

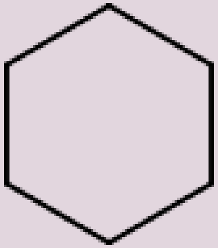
- Introduction to heterocyclic compounds
- Aromatic properties
- Nomenclature of heterocyclic compounds
- Furan
- Pyrrole
- Thiophene
- Pyridine
- Indole

WHAT IS HETEROCYCLIC CHEMISTRY?

What are carbocyclic compounds?

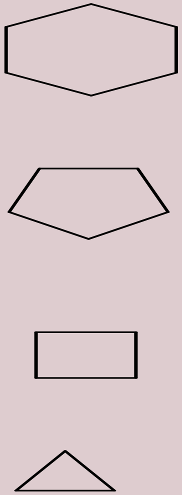
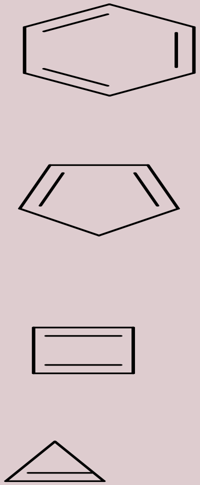


benzene



cyclohexane

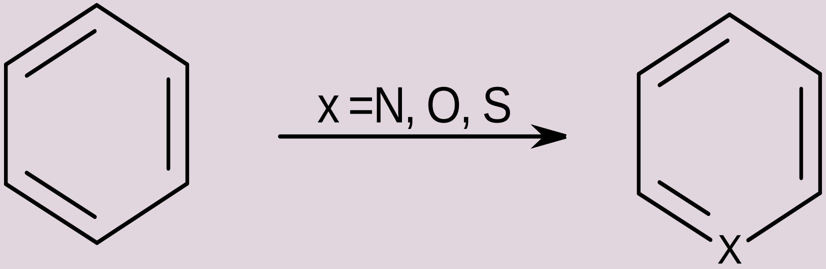
Carbocyclic Compound

<table>
<tr><th colspan="2">Carboxylic Compound</th></tr>
<tr><th>Cyclic Compound</th><th>Aromatic Compound</th></tr>
<tr><td></td><td></td></tr>
</table>

What’s aheterocyclic compound?

If the ring system is made up of carbon atoms and at least one other element, the compound can be classified as hetero cyclic.

The elements that are found most commonly together with carbon in a ring system are Nitrogen (N), Oxygen(O), and Sulfur(S).



Heterocyclic Chemistry

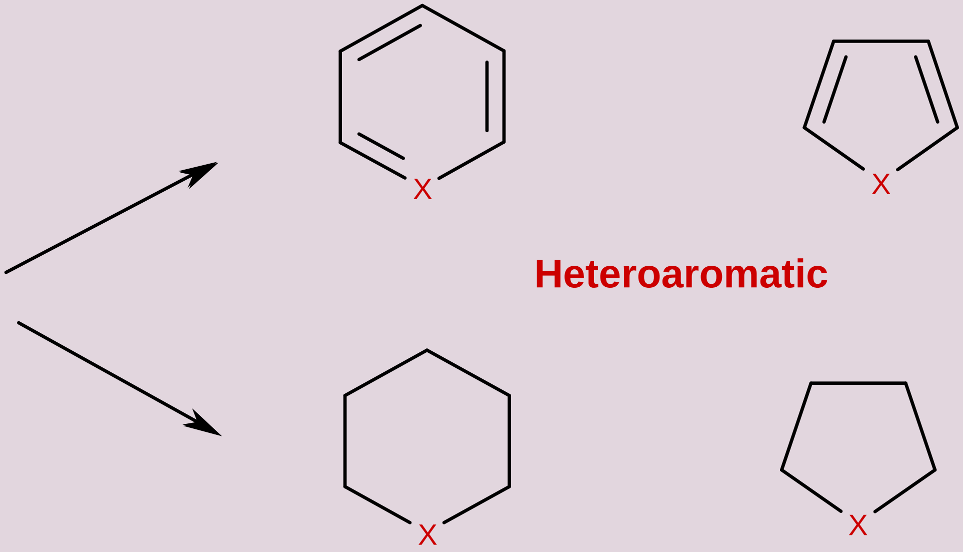
Heterocyclic compounds

are organic compounds that contain a ring structure containing atoms in addition to carbon, such as sulfur, oxygen or nitrogen, as the heteroatom.

Heterocyclic Chemistry

Heterocyclic classification

It can be classified into



Heterocyclic compounds

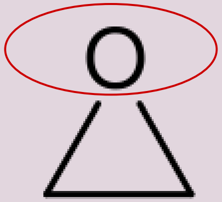
Heteroaromatic

Heteroalicyclic

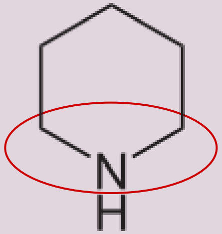
Heterocyclic Chemistry

Heterocyclic classification

1- Aliphatic heterocycles :-



Oxirane

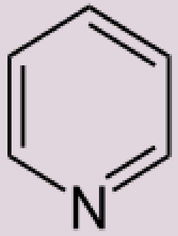


Piperidine

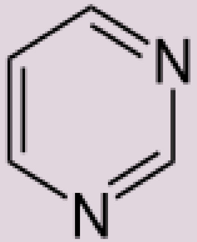
Heterocyclic Chemistry

2- Aromatic heterocycles :-

a- six-membered aromatic hetrocycles



Pyridine

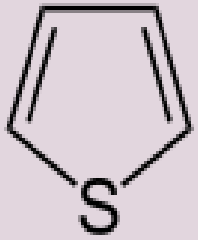


Pyrimidine

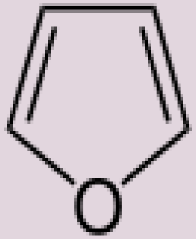
Heterocyclic Chemistry

2- <u>Aromatic heterocycles</u> :-

b- five-membered aromatic hetrocycles



Thiophen

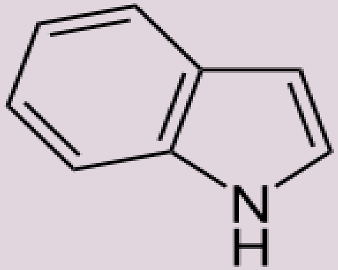


Furan

Heterocyclic Chemistry

2- <u>Aromatic heterocycles</u> :-

c- bicyclic heteroaromatic compounds



Indol

Quinoline

Heterocyclic Chemistry

Importantce and uses of Heterocyclic compounds:-

- *Biosynthesized*
- *Essential for life (haem, chlorophyll)*
- *Their metabolitis used as*
  - *toxin towords off predators*
  - *colouring agents to attact mates*

In general various important compounds such as:- alkaloids, vitamins, antibiotics, essential amino acids, hormones, drugs and dyes contain heterocyclic structure.

Heterocyclic Chemistry

- in general: nucleic acids, amino acids (proteins),
- feeding: proteins, carbohydrates, vitamins
- alkaloids: nicotine, caffeine

Application:

- antibiotics (penicillins, sulfonamides)
- insecticides (triazoles)
- herbicides (triazines, pyridines)

HETEROCYCLIC NOMENCLAUTURE

Nomenclature of heterocyclic compounds

- There are three systems for naming heterocylic compounds:

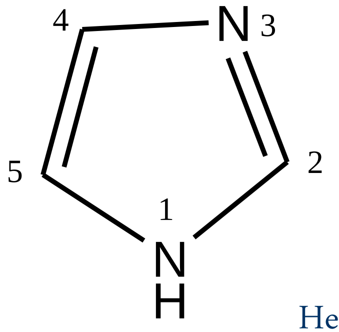
1) **The common nomenclature:** which convey little or no structural information but it still widely used.

2) **The Hantzsch-Widman (IUPAC or Systematic)** method which in contrast is designed so that one may deduce from it the structure of the compound.

I-Common Nomenclature

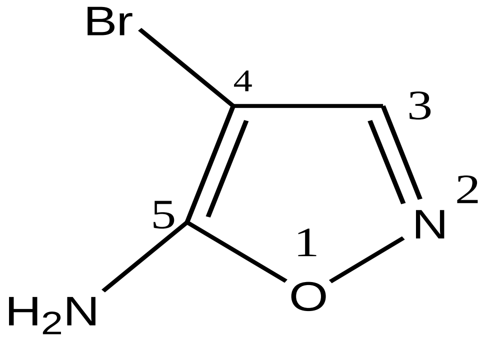
1) Each compound is given the corresponding trivial name (which should be memorized, see the following slides). This usually originates from the compounds occurrence, its first preparation or its special properties.

2) If there is more than one hetroatom of the same type numbering starts at the saturated one, e.g. imidazole.



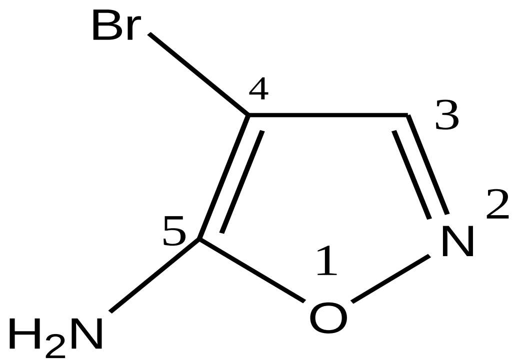
Common Nomenclature

3) If there is more than one type of the heteroatoms, the ring is numbered starting at the hetroatom of the higher priority (O>S>N) and it continues in the direction to give the other hetroatoms the lower numbers as possible.



Common Nomenclature

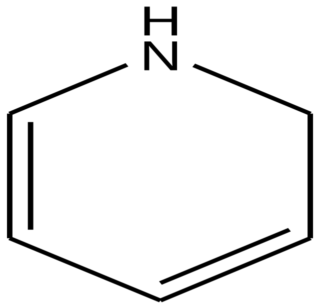
4) If substituents are present, their position should be identified by the number of the atoms bearing them and then they should be listed in alphabetical order.



5-Amino-4-bromoisoxazole

Common Nomenclature

5) The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated trivial name.

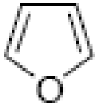


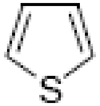
1,2-Dihydro-pyridine

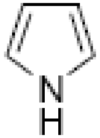
Trivial names

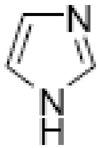
1) 5-membered heterocycles with one or two heteroatoms

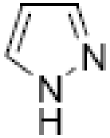
common azoles - five-membered aromatic nitrogen heterocycles


furan


thiophene


pyrrole


imidazole


pyrazole

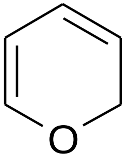

isoxazole

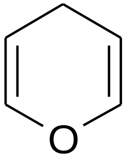

oxazole


thiazole

2) 6-membered heterocycles with one or two heteroatoms

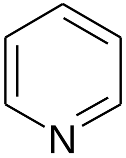
Common azines-six-membered aromatic nitorgrn heterocycles

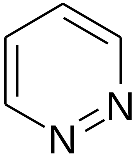

2H-Pyran

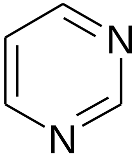

4H-Pyran

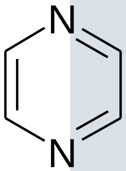
These are tautomers

Both are not aromatic


Pyridine


Pyridazine


Pyrimidine

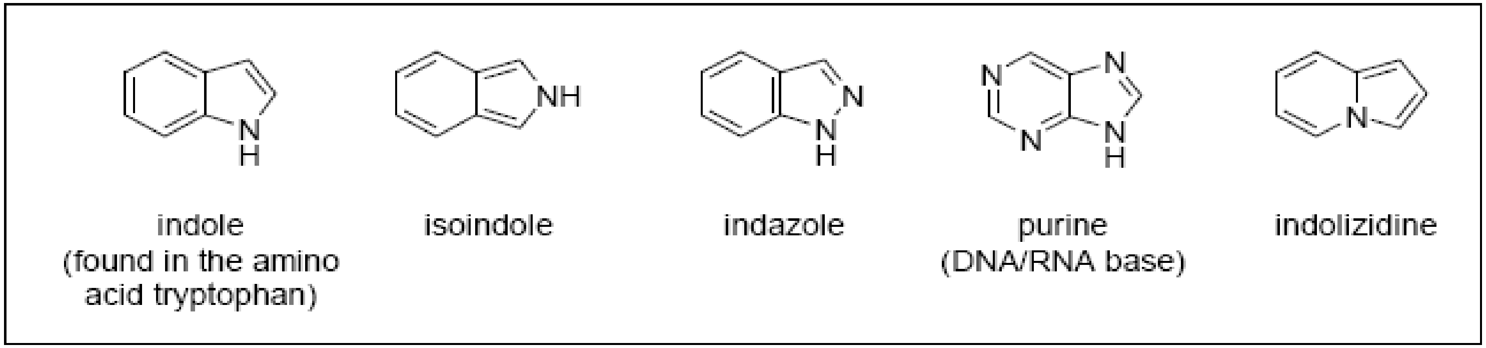

Pyrazine

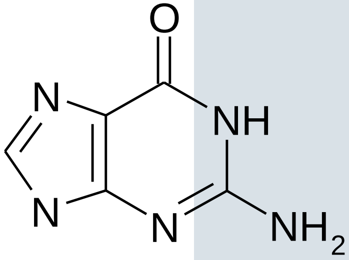
DNA/RNA bases

Trivial Names

3) Fused heterocycles

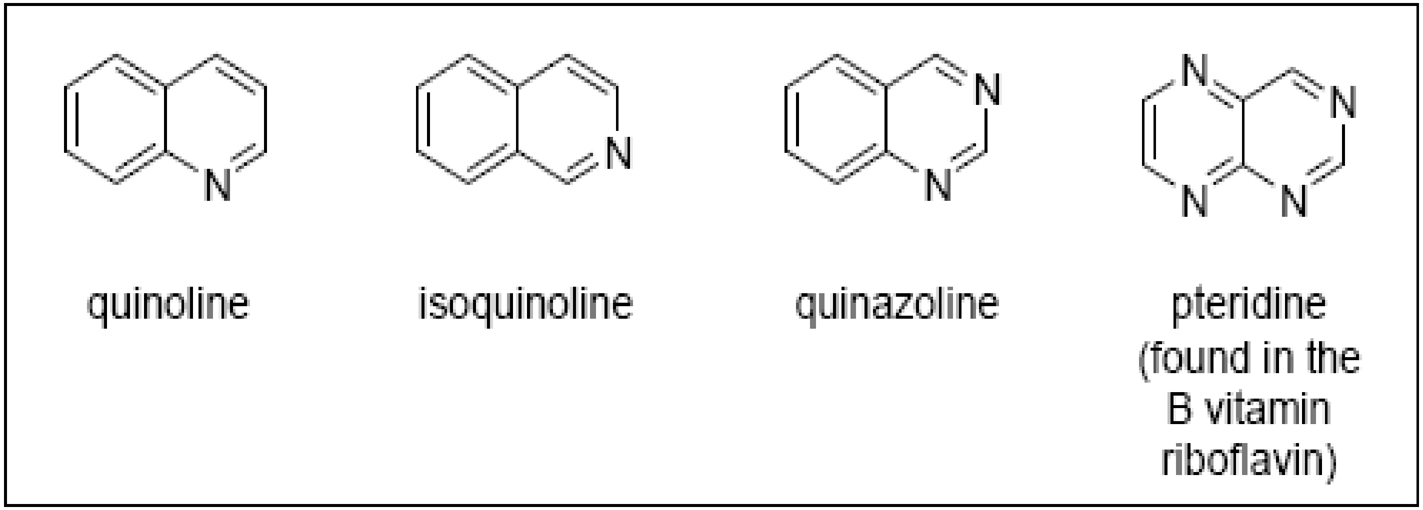
common ring-fused azoles



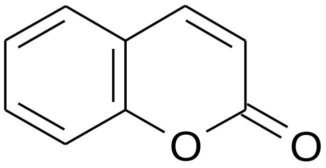


Guanine

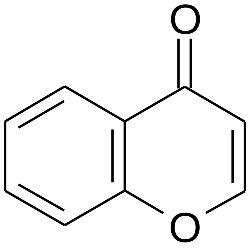
common ring-fused azines



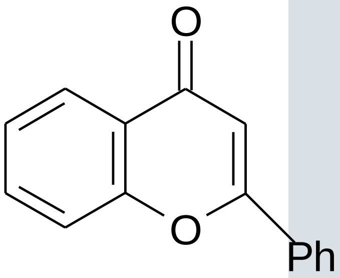
Trivial Names



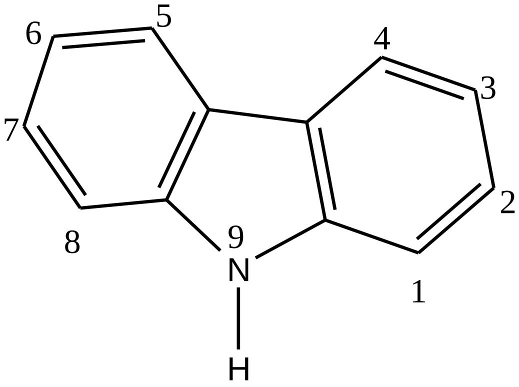
Coumarine
Chromen-2-one



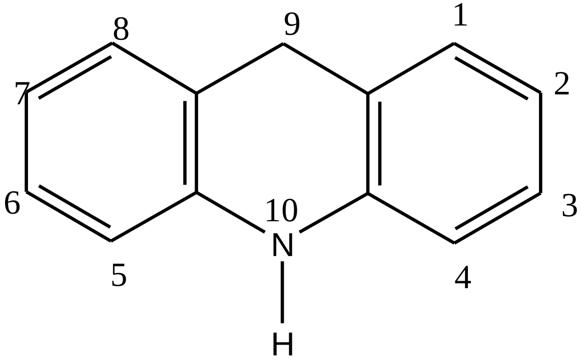
Chromen-4-one



Flavone



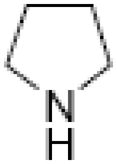
9H-Carbazole



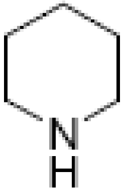
9,10-Dihydro-acridine

Trivial Names

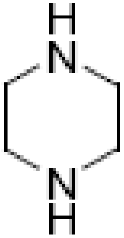
4) Saturated heterocycles



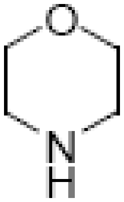
pyrrolidine



piperidine



piperazine



morpholine

II-Hantzsch-Widman nomenclature (IUPAC)

- Hantzsch-Widman nomenclature is named after the German chemists Arthur Hantzsch and Oskar Widman, who proposed similar methods for the systematic naming of heterocyclic compounds in 1887 and 1888 respectively.

- According to this system three to ten-membered rings are named by combining the appropriate prefix (or prefixes) that denotes the type and position of the heteroatom present in the ring with suffix that determines both the ring size (depending on the total number of atoms in the ring) and the degree of unsaturation (note that fully saturated and fully unsaturated have certain rules for nomenclature while partially unsaturation will be indicated in certain ways). In addition, the suffixes distinguish between nitrogen-containing heterocycles and heterocycles that do not contain nitrogen

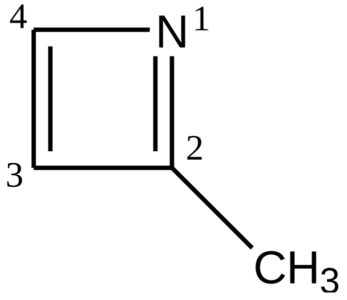
- **IUPAC name = locants +Prefix + suffix**

Hantzsch-Widman rules for fully saturated and fully unsaturated heterocycles

1) Identify the hetroatom present in the ring and choose from (table 1 on slide 11) the corresponding prefix (e.g. thia for sulfur, aza for nitrogen and oxa for oxygen).

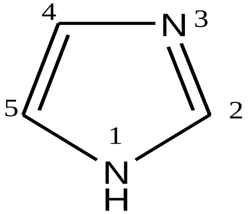
2) The position of a single heteroatom control the numbering in a monocyclic compound. The heteroatom is always assigned position 1 and if substituents present are then counted around the ring in a manner so as to take the lowest possible numbers.

For example:



Hantzsch-Widman rules

3) A multiplicative prefix (di, tri, ect.) and locants are used when two or more similar heteroatoms contained in the ring(two nitrogen indicated by diaza) and the numbering preferably commenced at a saturated rather than an unsaturated atom, as depicted in the following example: 1,3-diaza….



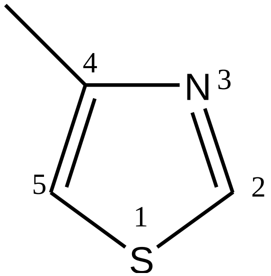
4) If more than one type of hetroatoms present in the ring the name will include more than one prefix with locants to indicate the relative position of the heteroatoms.

- Atom prefixes have a strict order of priority (preference) in which they are to be listed. For example,‘’Oxa’’(for oxygen) always comes before ‘’aza’’ (for nitrogen) in a name (see table 1).

- When combining the prefixes (e.g. oxa and aza) two vowels may end up together, therefore the vowel on the end of the first part should be omitted (oxaza).

Hantzsch-Widman rules

- The numbering is started from the heteroatom of the highest priority in such a way so as to give the smallest possible numbers to the other heteroatoms in the ring (the substituents are irrelevant). For example the prefix corresponding to the following compound is 4-Methyl-1,3-Thiaza….

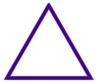
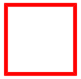
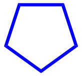
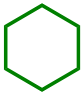
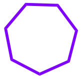
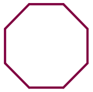


5) Choose the appropriate suffix from (table 2) depending on whether or not nitrogen atom is present in the ring, the size of the ring and presence or absence of any double bonds

6) Combine the prefix(s) and suffix together and drop the first vowel if two vowels came together.

Hantzsch-Widman rules

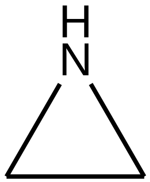
Table 2

Ring size	N-present		N-absent	
	Unsat	sat	Unsat	sat
	irine	iridine	irene	irane
	ete	etidine	ete	etane
	ole	olidine	ole	olane
	ine	a	in	ane
	epine	a	epin	epane
	ocine	a	ocin	ocane
9	onine	a	onin	onane
10	ecine	a	ecin	ecane

a: means use the prefix perhydro followed by the fully unsaturated name

Hantzsch-Widman rules

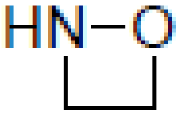
- Examples



- This ring contains (N) ⇨ Prefix is aza
- The ring is 3-membered and fully saturated ⇨ suffix is iridine
- By combining the prefix and suffix, two vowels ended up together (azairidine), therefore the vowel on the end of the first part should be dropped. This gives the correct name: **Aziridine**

III-Hantzsch-Widman nomenclature (IUPAC)

- **Example 2:**



, 1,2-oxazetidine

- **This ring contains nitrogen = aza-**
- **And oxygen = oxa-**
- **And is a fully saturated four-membered**
- **ring = -etidine**
- **Drop the vowels in ox<u>a</u> & az<u>a</u>**
- **The name = 1,2-Oxazetidine**

III-Hantzsch-Widman nomenclature (IUPAC)

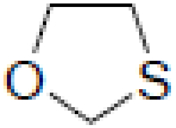
- **Example 3:**

, 1,2,5-oxadiazole

- **This ring contains nitrogen = aza-**
- **And oxygen = oxa-**
- **And Unsaturated five-membered rings with nitrogen = –ole**
- **Oxygen is higher priority than nitrogen, so it is in position 1.**
- **The two nitrogens are therefore at positions 2 and 5**
- **The name = 1,2,5-Oxadiazole**

III-Hantzsch-Widman nomenclature (IUPAC)

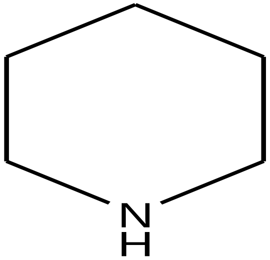
- **Example 4:**



, 1,3-oxathiolane

- **This ring contains sulpher= thia-**
- **And oxygen = oxa-**
- **And saturated five-membered rings without nitrogen = –olane**
- **Oxygen is higher priority than sulpher, so it is in position 1.**
- **Drop the vowel in thia**
- **The name = 1,3-Oxathiolane**

Hantzsch-Widman rules



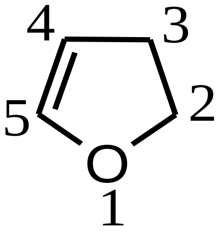
- The ring is 6-membered, fully saturated with N → Prefix perhydro followed by the name of fully unsaturated 6-memberd ring with nitrogen → azine

- Thus the full name is perhydroazine

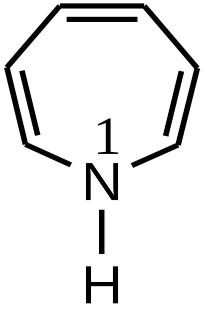
Hantzsch-Widman rules for partially unsaturated heterocycles

- **Partial unsaturation in heterocyclic compounds can be indicated by one of the following methods:**

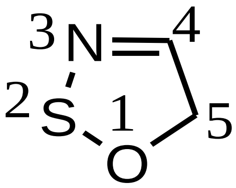
a) The position of nitrogen or carbon atoms which bear extra hydrogen atoms must be indicated by numbers and italic capital H (e.g. 1*H*, 2*H*, etc.) followed by the name of maximally unsaturated ring.



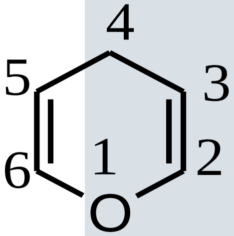
2*H*, 3*H*-Oxole



1*H*-Azepine



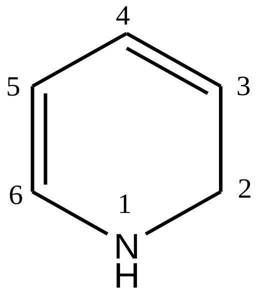
5*H*-1,2,3-Oxathiazole



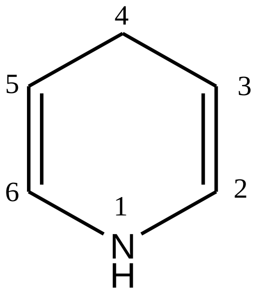
4*H*-Oxin

Hantzsch-Widman rules for partially unsaturated heterocycles

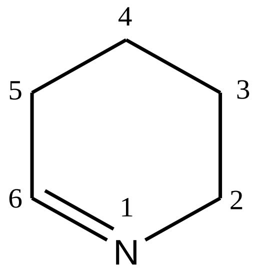
b) The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated Hantzsch-Widman name.



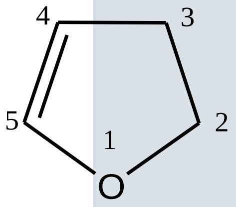
1,2-Dihydroazine



1,4-Dihydroazine



2,3,4,5-Tetrahydroazine



2,3-Dihydrooxole

Isomers have the same M.F.
but differ in the position of
the double bond

Hantzsch-Widman rules for partially unsaturated heterocycles

c) Alternatively, the partially unsaturated 4 and 5 rings (i.e. rings contain one double bond) are given special Hantzsch-Widman suffixes as in table 3 and the double bond is specified as Δ^1, Δ^2, Δ^3, etc.. Which indicates 1 and ; 2 and 3; 3 and 4 atoms respectively have a double bond

(i.e. **Name : Δ^x + Prefix + special suffix)**

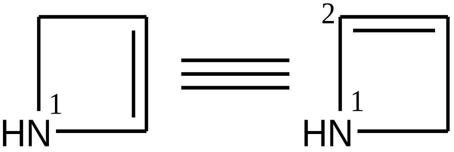
(x= locant of the double bond)

Table 3

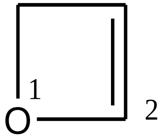
Ring size	**With N**	**Without N**
□	**-etine**	**-etene**
⬠	**-oline**	**-olene**

Hantzsch-Widman rules for partially unsaturated heterocycles

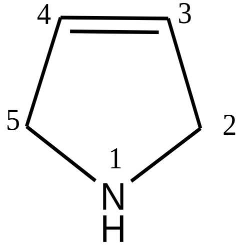
- **Examples**



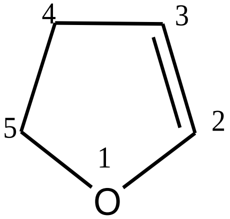
Δ^2 -Azetine



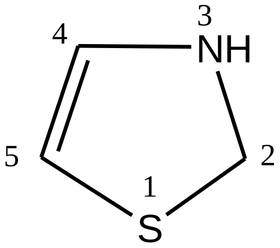
Δ^2 -Oxetene



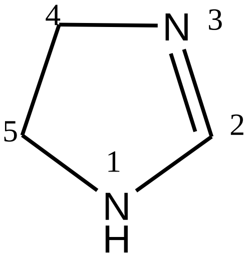
Δ^3 -Azoline



Δ^2 -Oxolene



Δ^4 -1,3-Thiazoline



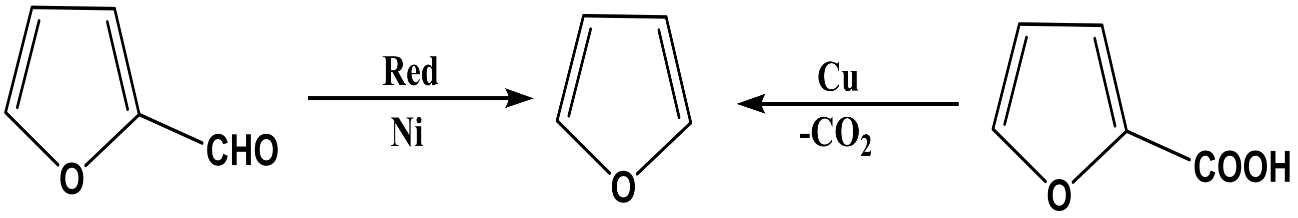
Δ^2 -1,3-Diazoline

Furan

Physical properties

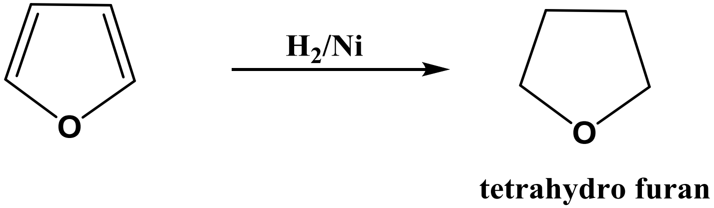
- **Furan may be as ethers but it is aromatic compoud because the lone pair of electrons on oxygen atom contribute in aromaticity.**
- **Furan has low melting point less than pyrrole because there’s no hydrogen bonds.**
- **Furan is a liquid boiled at 31c and has odour as chloroform.**
- **Furan is springily soluble in water but it is miscible with most organic solvents.**

Preparation of furan



Reactions of furan

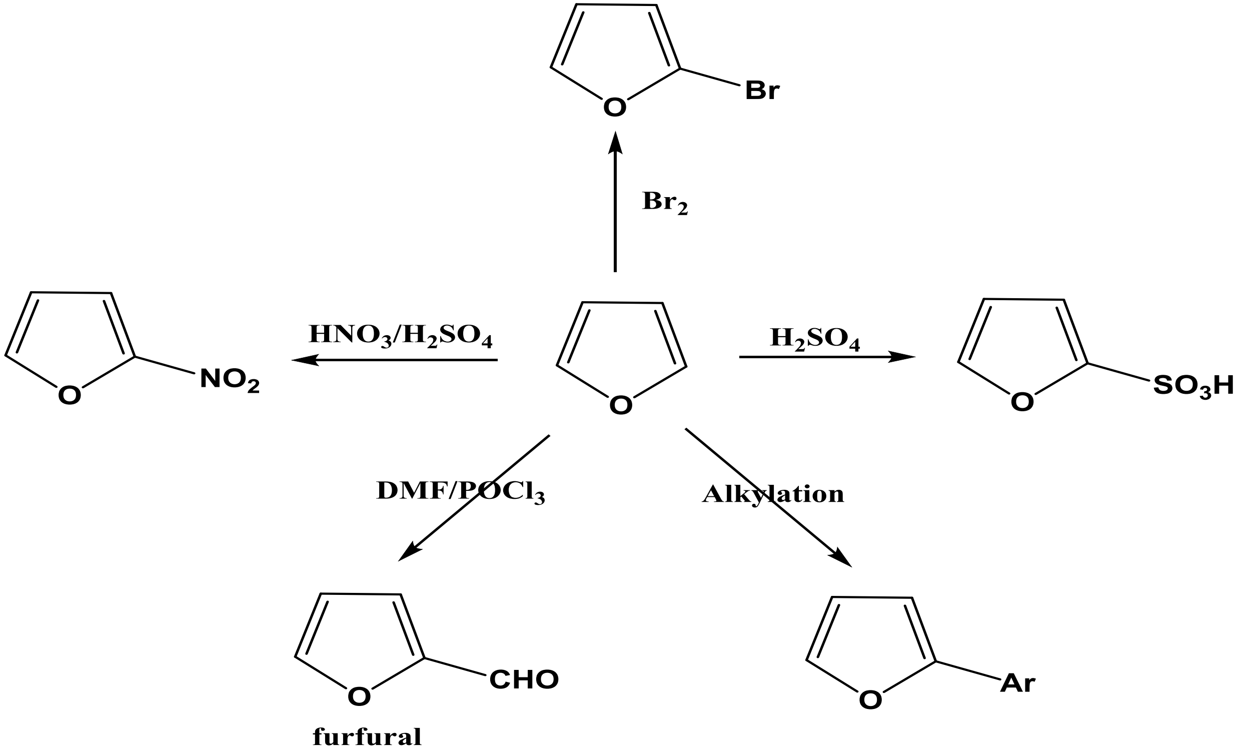
Reduction of furan ❖



Reactions of furan

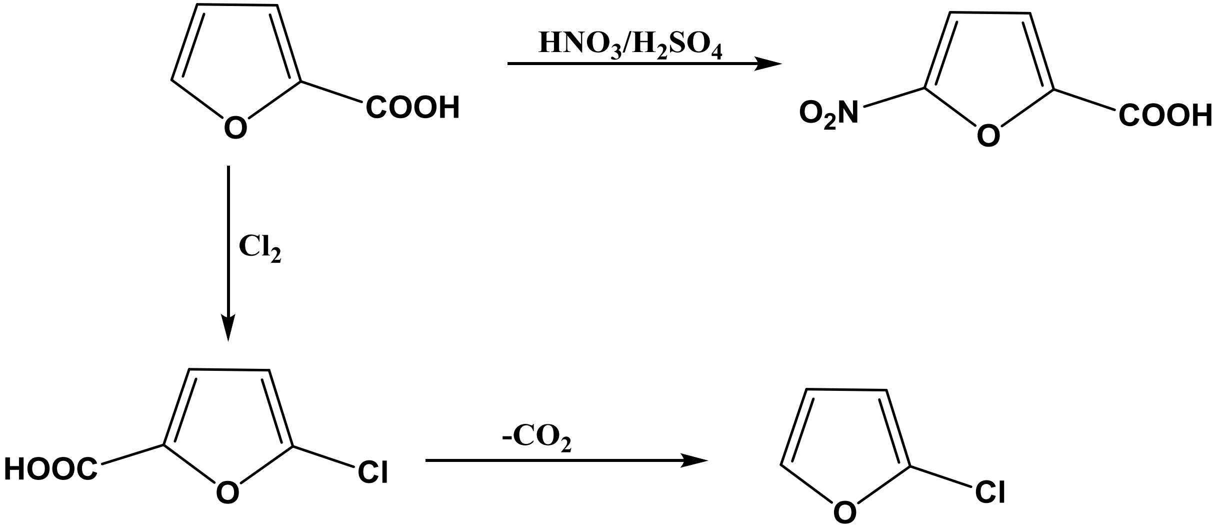
Electrophilic substitution reactions: ❖

The substitution occurred in position 2 ❖



Reactions of furan

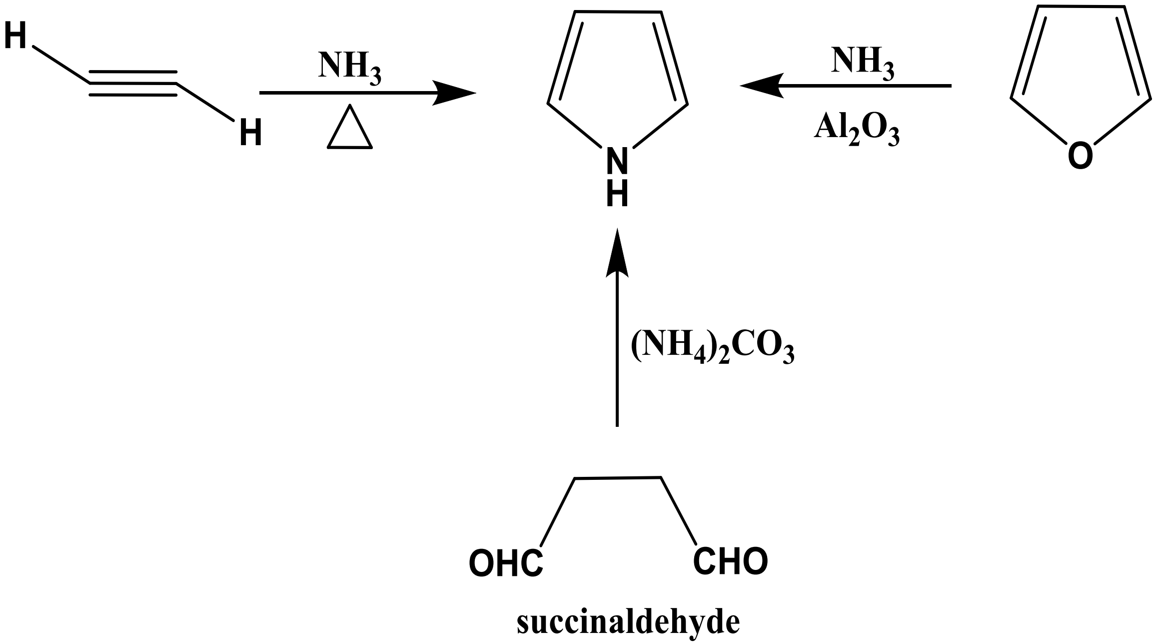
Reactions of furan-2-carboxylic acid:



Pyrrole

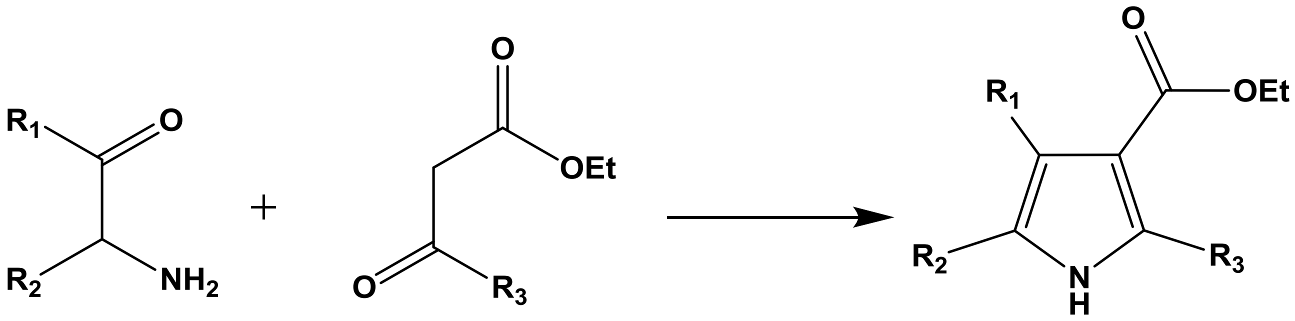
- Pyrrole is a colorless liquid which has an odour as chloroform.
- If it is exposed to air give brown color.
- The lone pairs of electrons on nitrogen atom contribute in aromatic properties.

Preparation of pyrrole



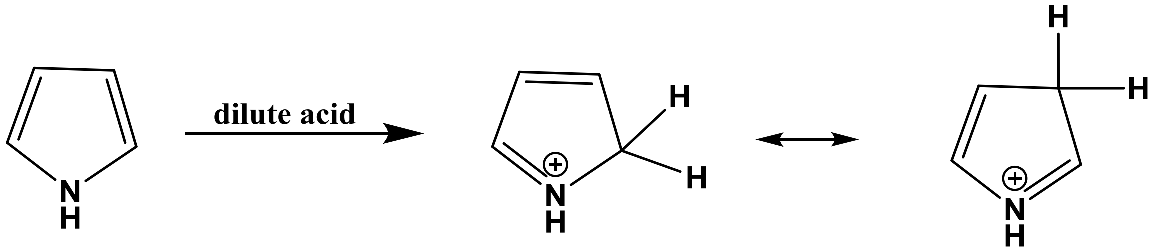
Preparation of pyrrole

Knorr synthesis:



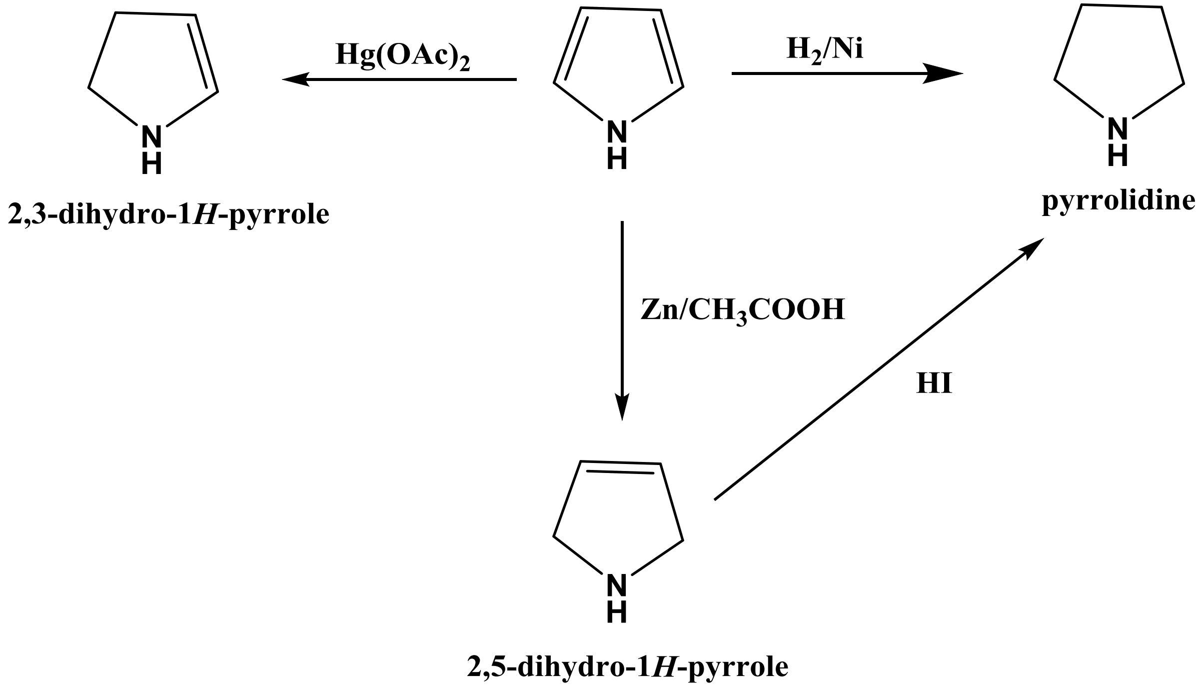
Reactions of pyrrole

Basicity:



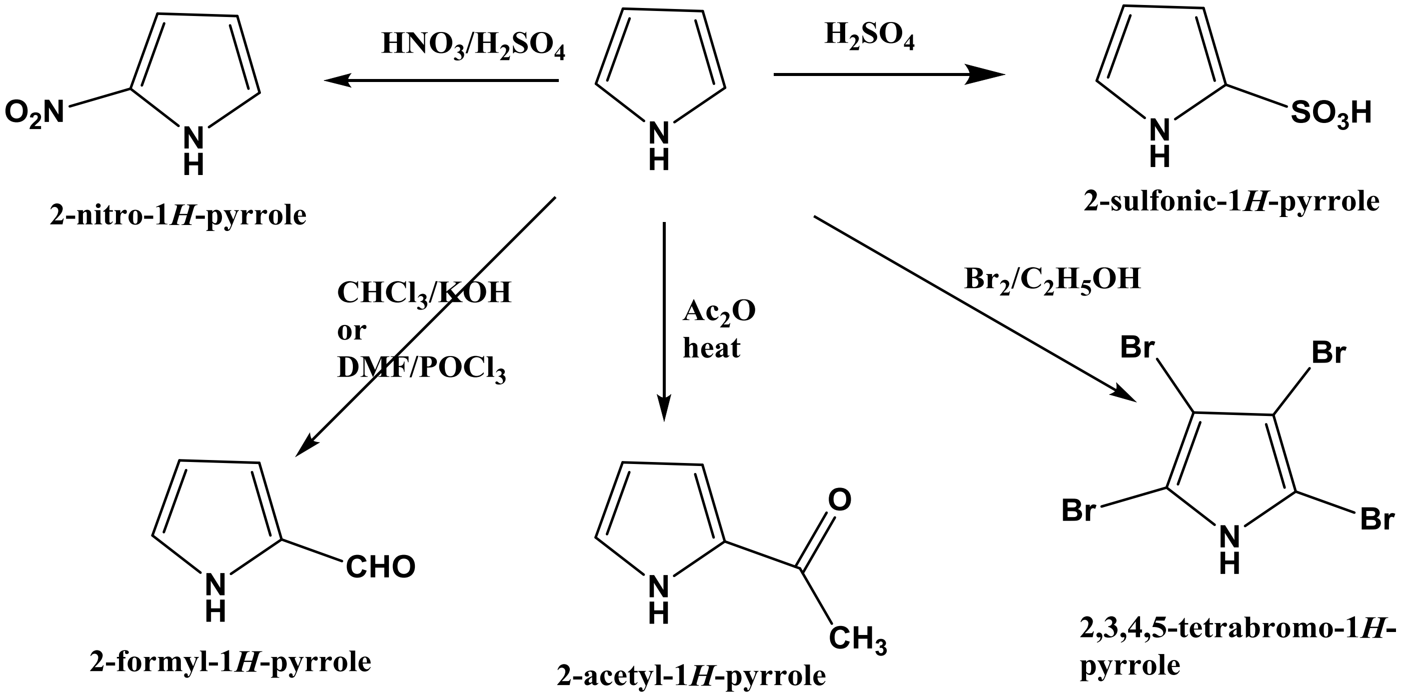
Reactions of pyrrole

Reduction of pyrrole:



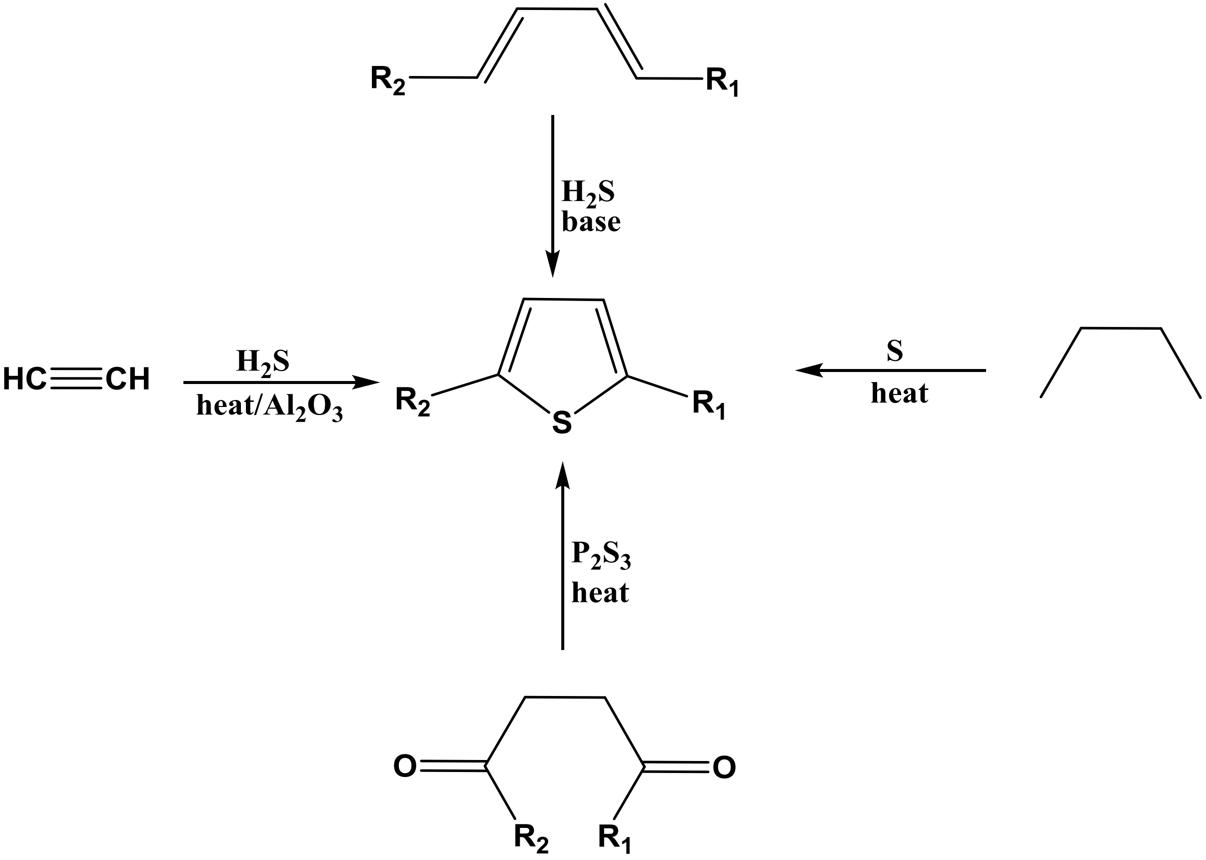
Reactions of pyrrole

Electrophilic substitution:



Thiophene

Preparation of thiophene

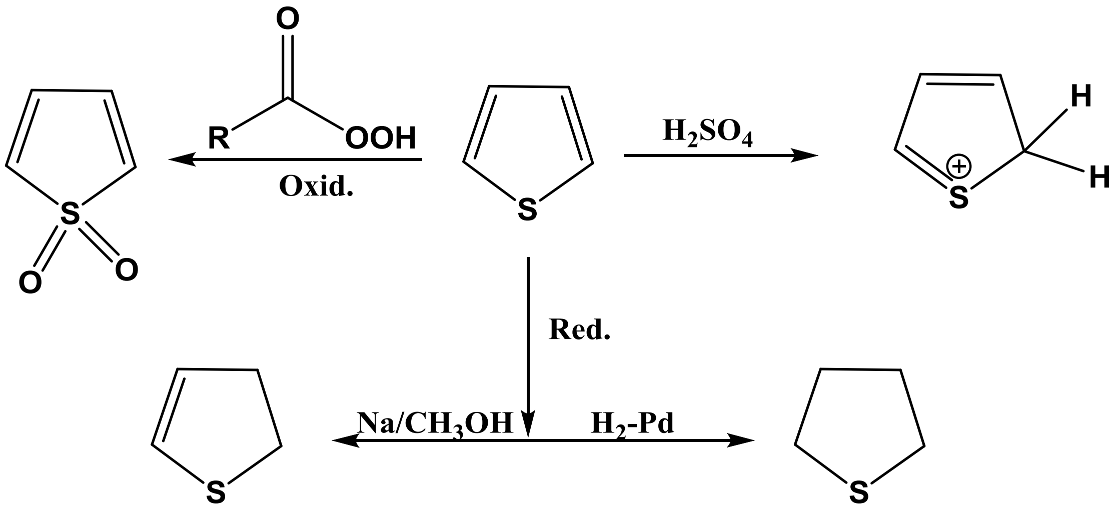


Reactions of thiophene

1- addition reactions.

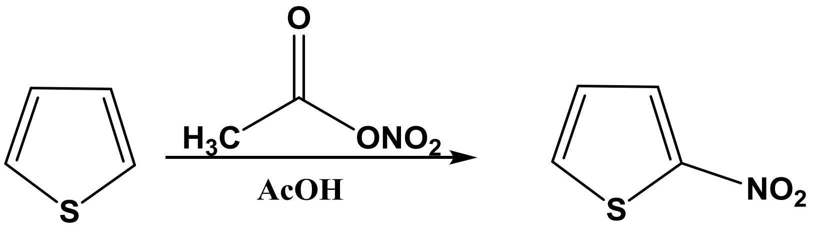
2- reduction reactions.

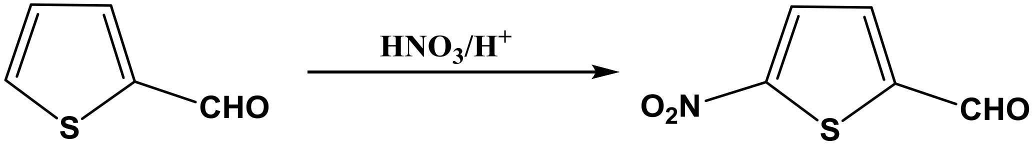
3- oxidation reactions.



Reactions of thiophene

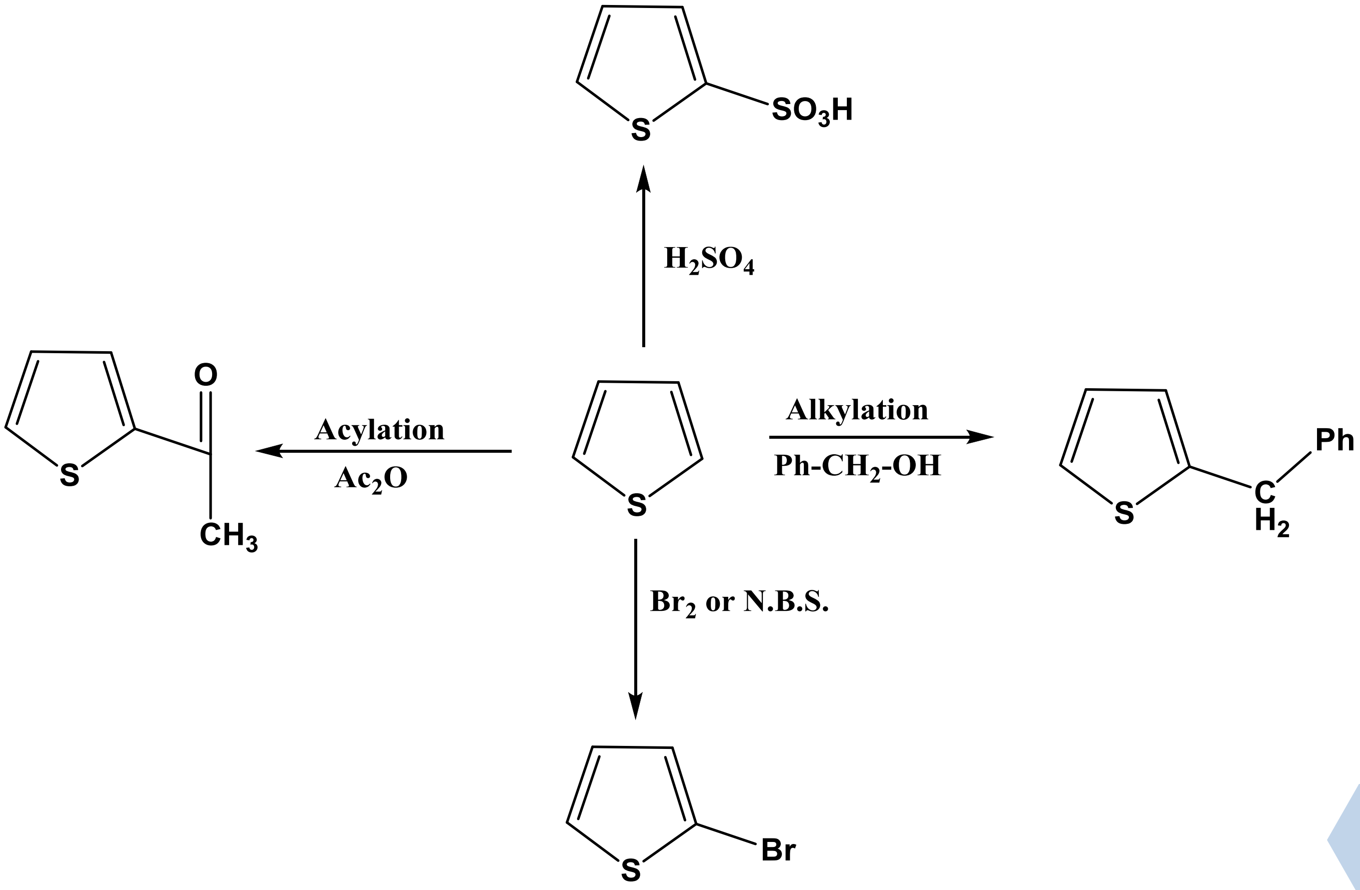
Electron withdrawing groups increase the stability of the ring and rate of reaction.





Reactions of thiophene

Electrophilic substitution reactions:



Pyridine

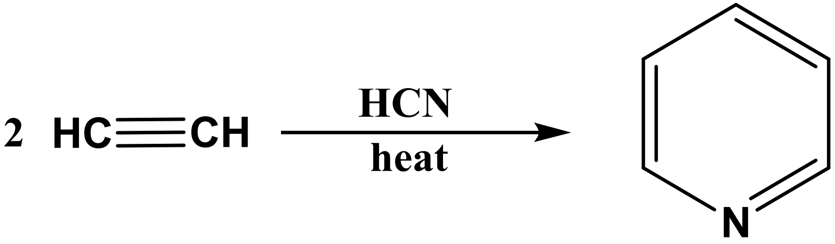
Physical properties

- In case of boiling point pyridine has less boiling point than pyrrole because the presence of hydrogen bonds in pyrrole.

- But in case of basicity pyridine is more basic than pyrrole because the presence of free lone pairs of electrons on nitrogen atom, but in case of pyrrole the lone pairs of electrons contributed in aromaticity.
- Pyridine is used as a solvent in organic synthesis.

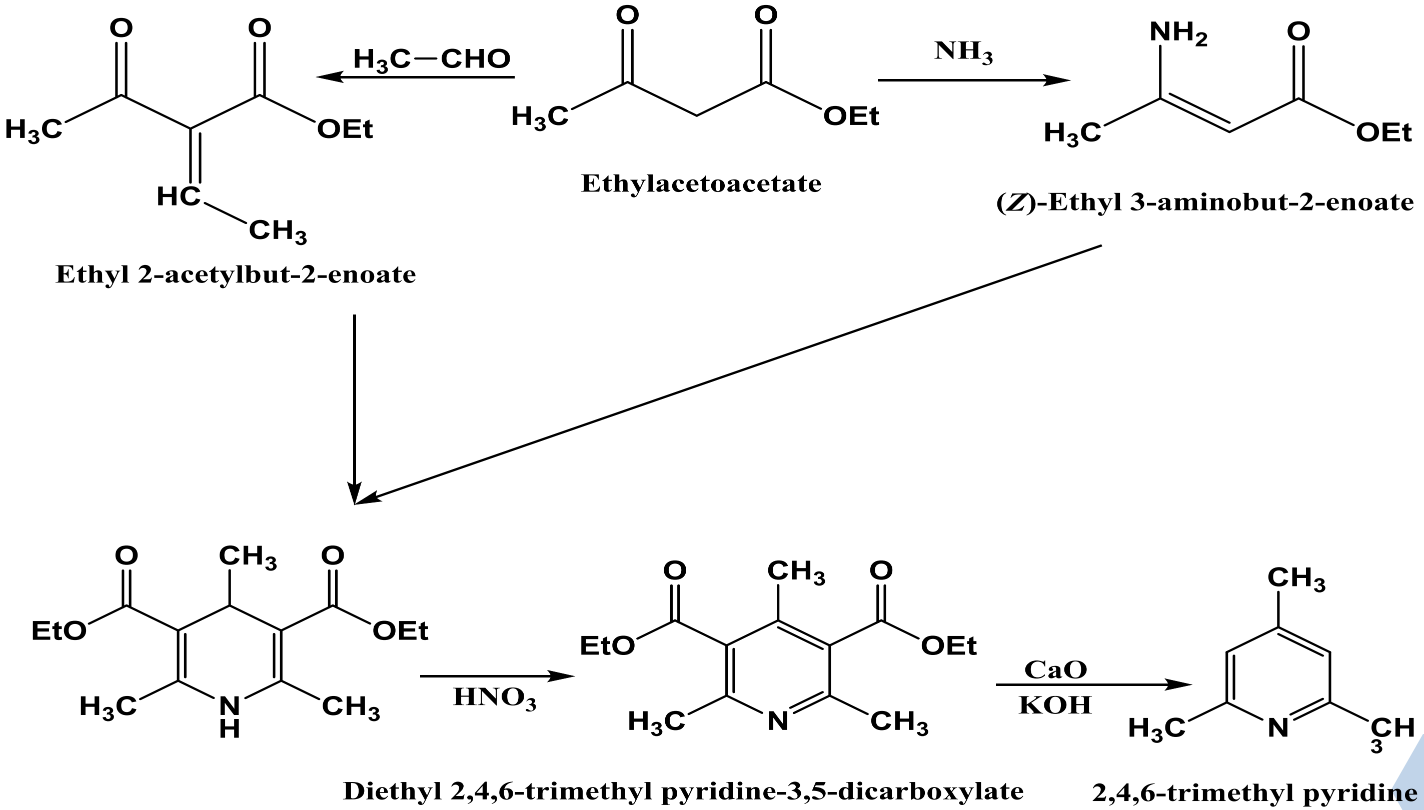
Preparation of pyridine

1- from acetylene:



Preparation of pyridine

2- Hantzch synthesis:

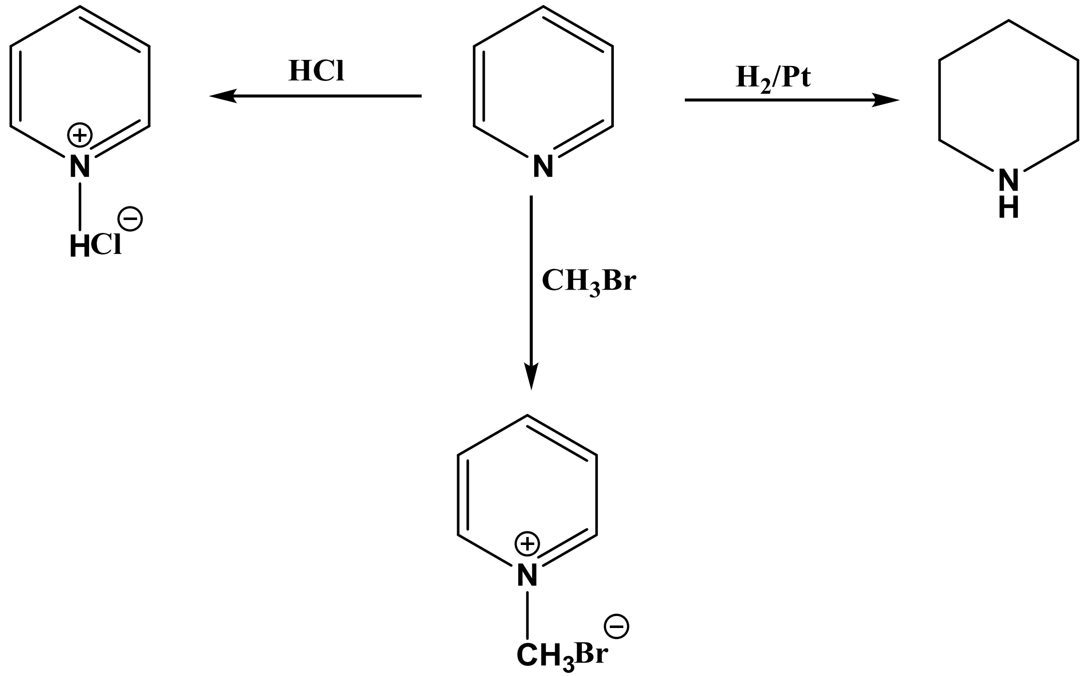


Reactions of pyridine

1- addition reactions:

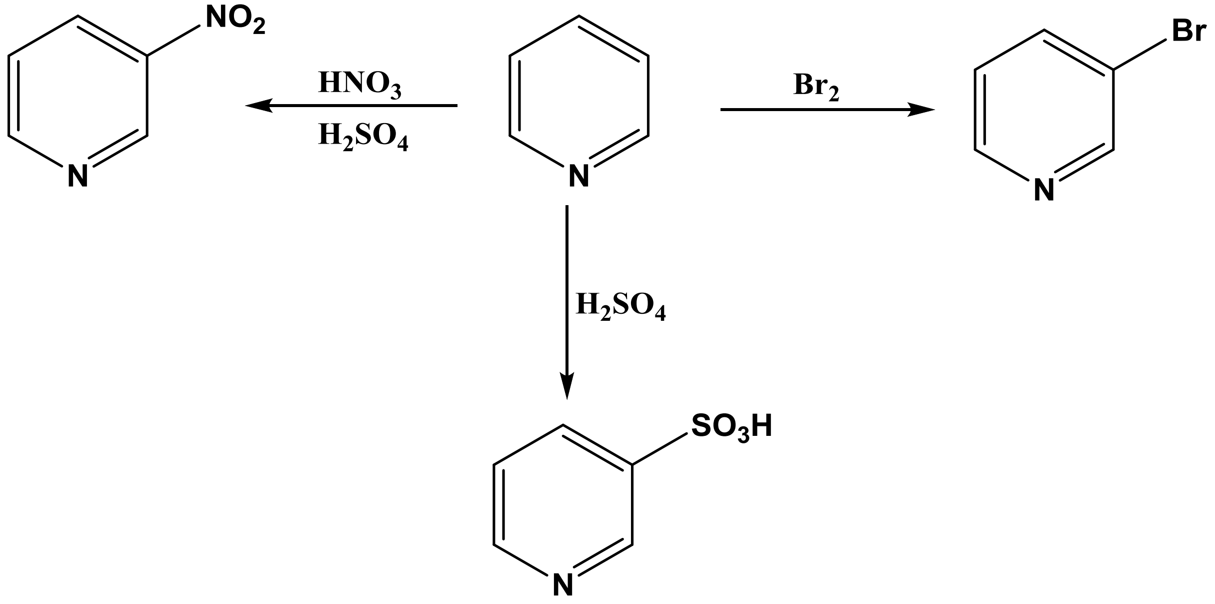
A- reduction

b- salt formation

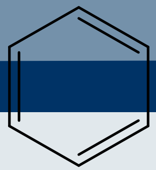


Reactions of pyridine

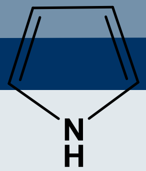
Electrophilic substitution reactions:



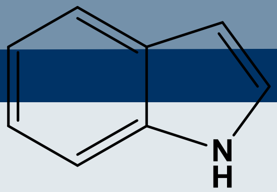
Indole



Benzene



Pyrrole



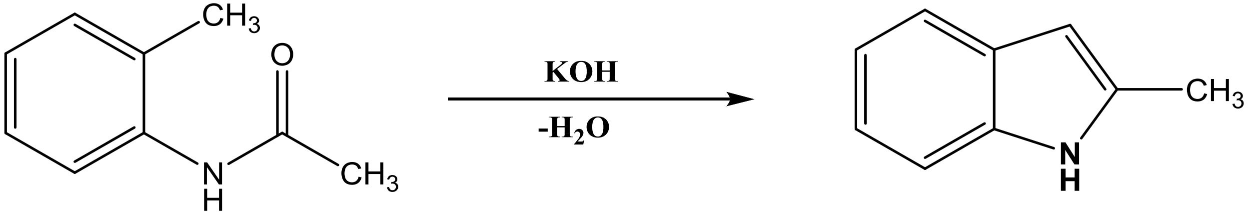
Indole

Physical properties

- Indole is a solid compound has melting point at 52c.
- More stable than pyrrole because of its molecular weight.
- Electrophilic substitution preferred position 3 than position 2.
- It is present in dyes and proteins.

Preparation of indole

1- Madelung Synthesis

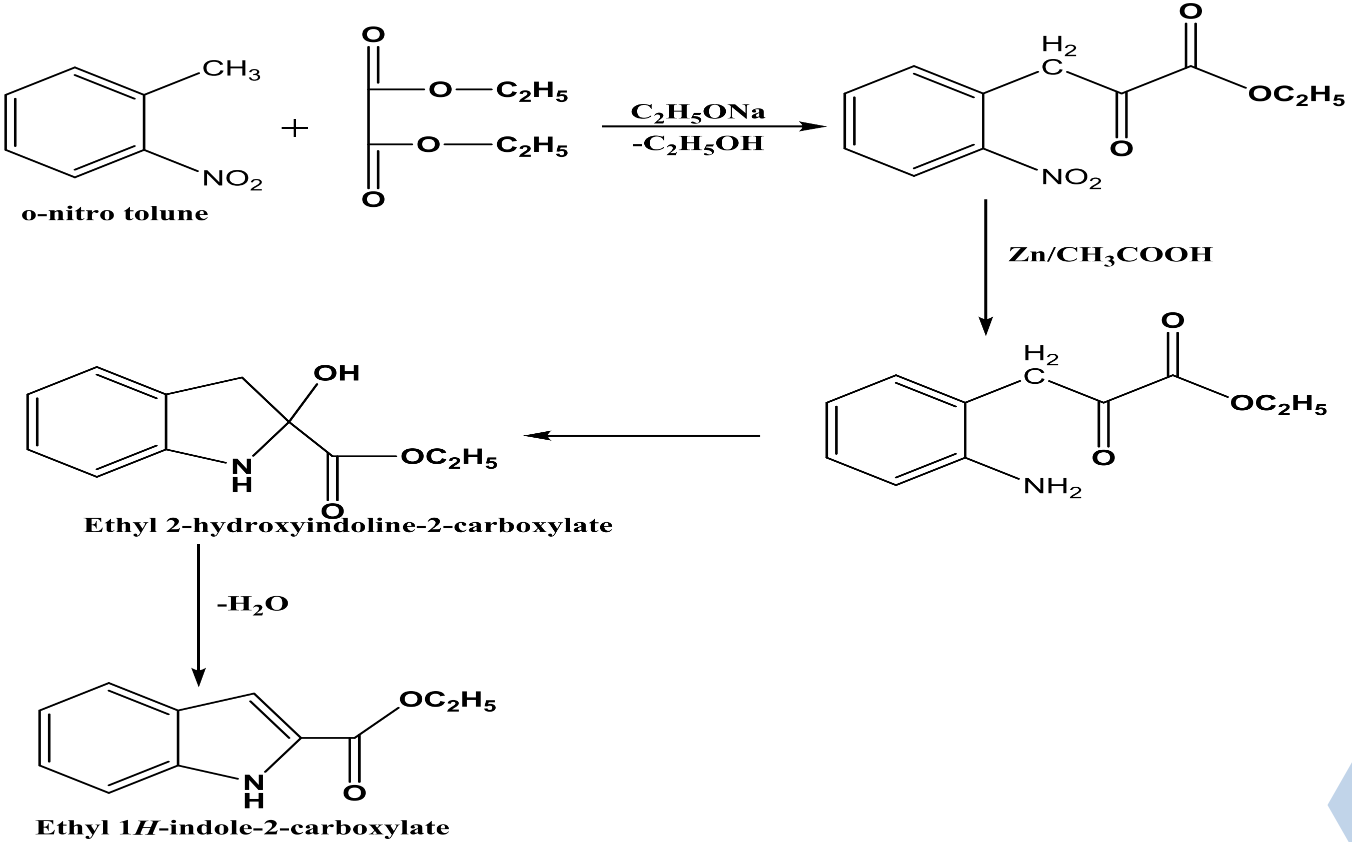


N-o-tolylacetamide

2-methyl indole

Preparation of indole

2- Reissert Synthesis



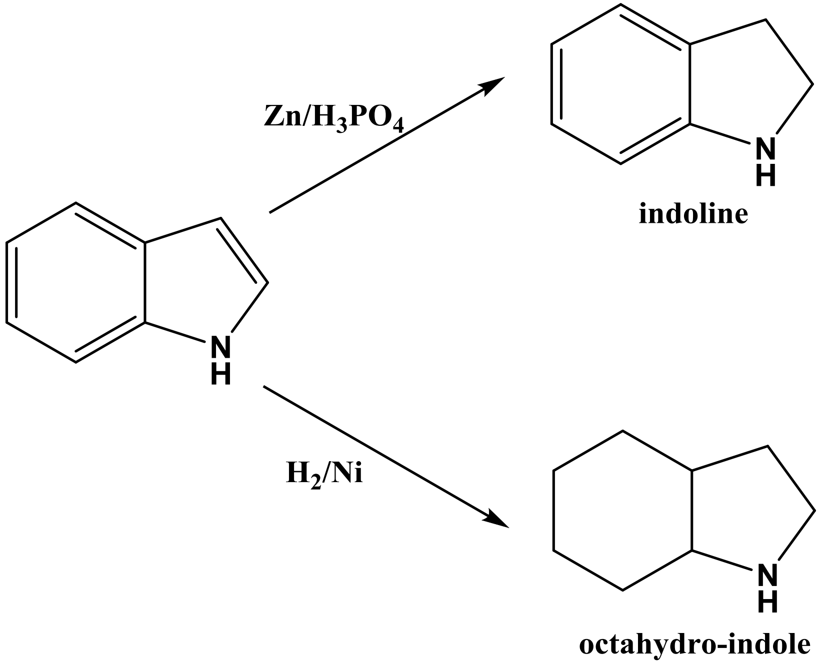
o-nitro tolune

Ethyl 2-hydroxyindoline-2-carboxylate

Ethyl 1*H*-indole-2-carboxylate

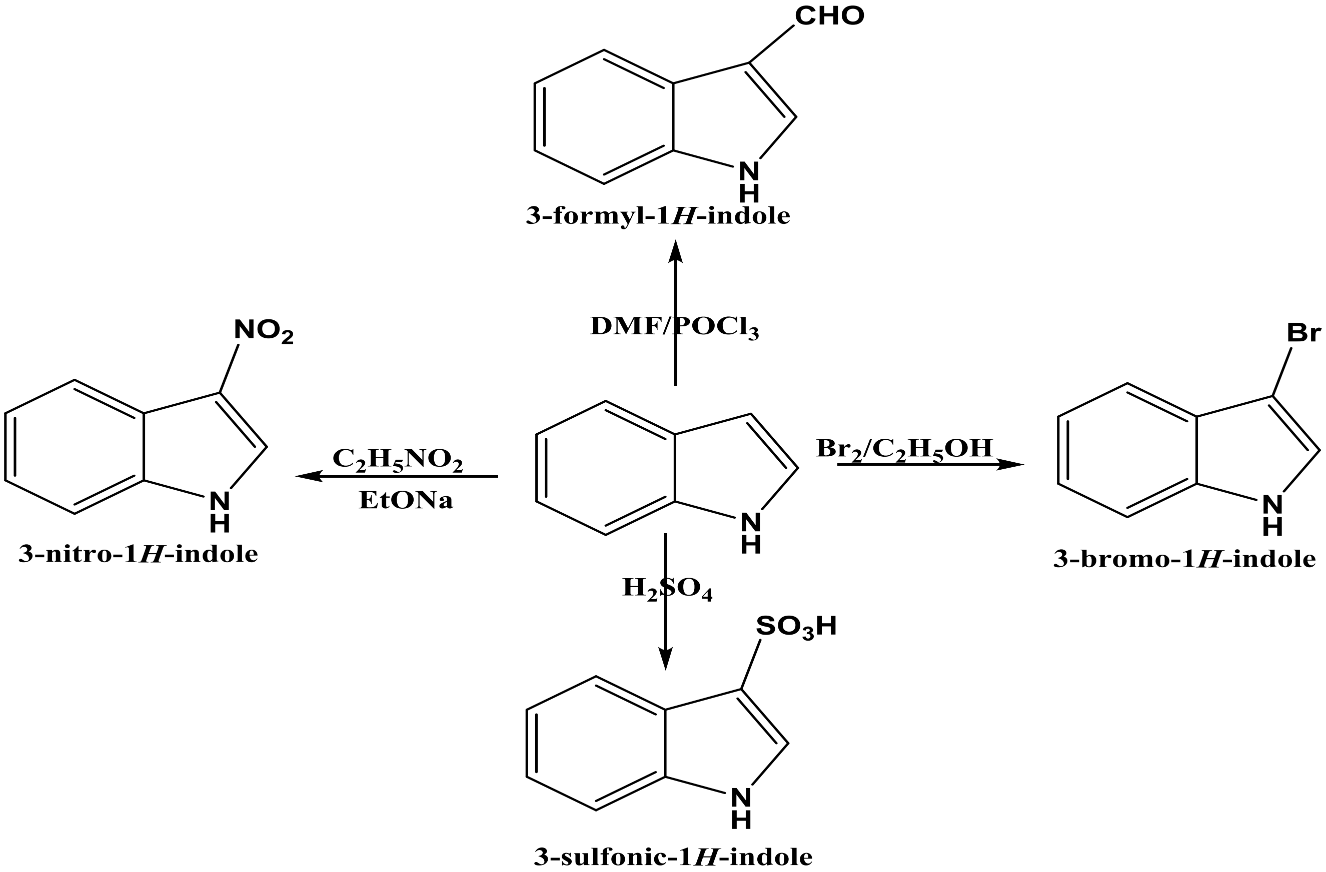
Reactions of indole

Reduction of indole:



Reactions of indole

Electrophilic substitution reactions:



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- **3- Heterocyclic Chemistry I, Mahndra Kumar, Fandana Jupta, Radha Ar. Jupta (2011).**
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Chromatography

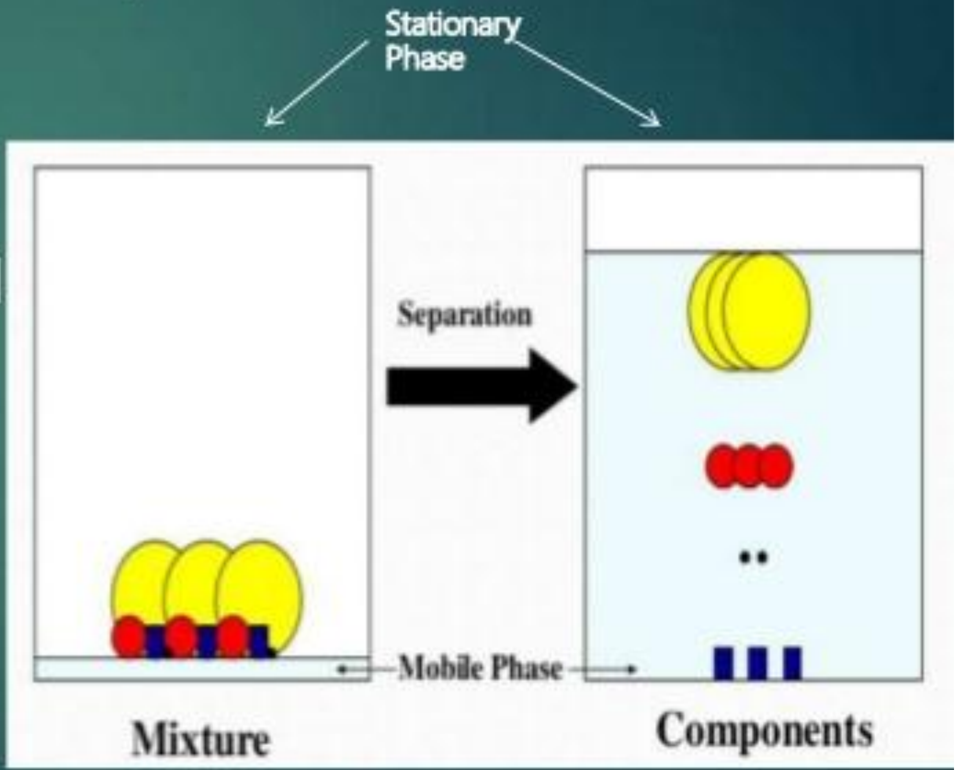
2nd Year Students – Biology Group – Faculty of Education
First Term 2021/2022
Dr/ Ibrahim Abdul-Motaleb Mousa

Contents

- Introduction to chromatographic techniques
- Chromatogram
- Classification of chromatography
- Paper chromatography
- Thin layer chromatography
- Rf value
- Column chromatography
- Gas chromatography
- HPLC chromatography

INTRODUCTION

- Chromatography is a physical process where the components (solutes) of a sample mixture are separated as a result of their differential distribution between stationary and mobile phases.



- Greek *chroma* meaning 'color' and *graphein* meaning 'writing'

HISTORY

- **Tswet**, Russian botanist (referred to *as Father of chromatography*) is credited for the development of chromatography.

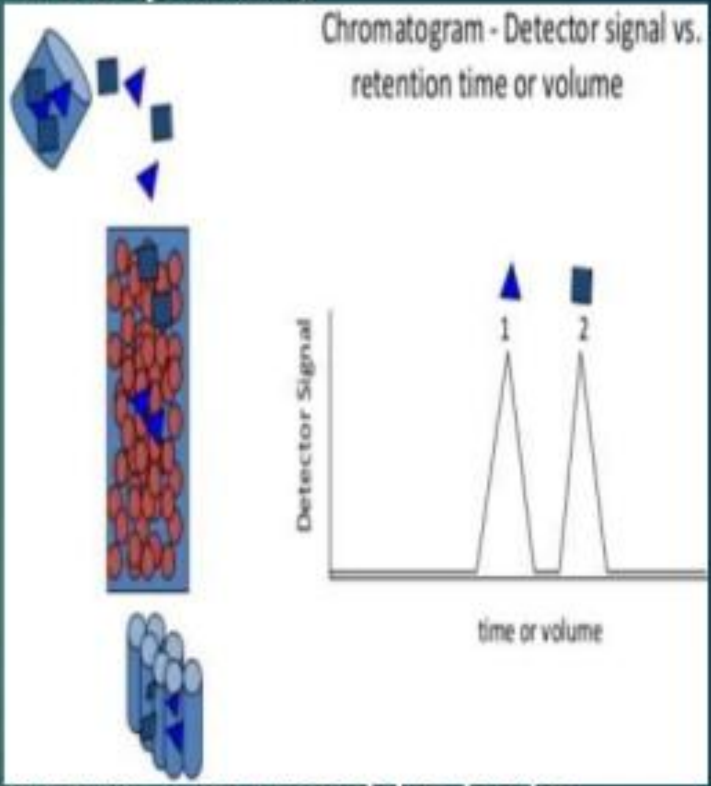
Principle -

- Chromatography is usually based on principle of partition of solute between two phases. It usually consists of a Mobile Phase and a Stationary Phase.

- **The Mobile Phase** usually refers to the mixture of the substances to be separated dissolved in a liquid or a gas .
- **The Stationary Phase** is a porous solid matrix through which the sample contained in the mobile phase percolates.

CHROMATOGRAM

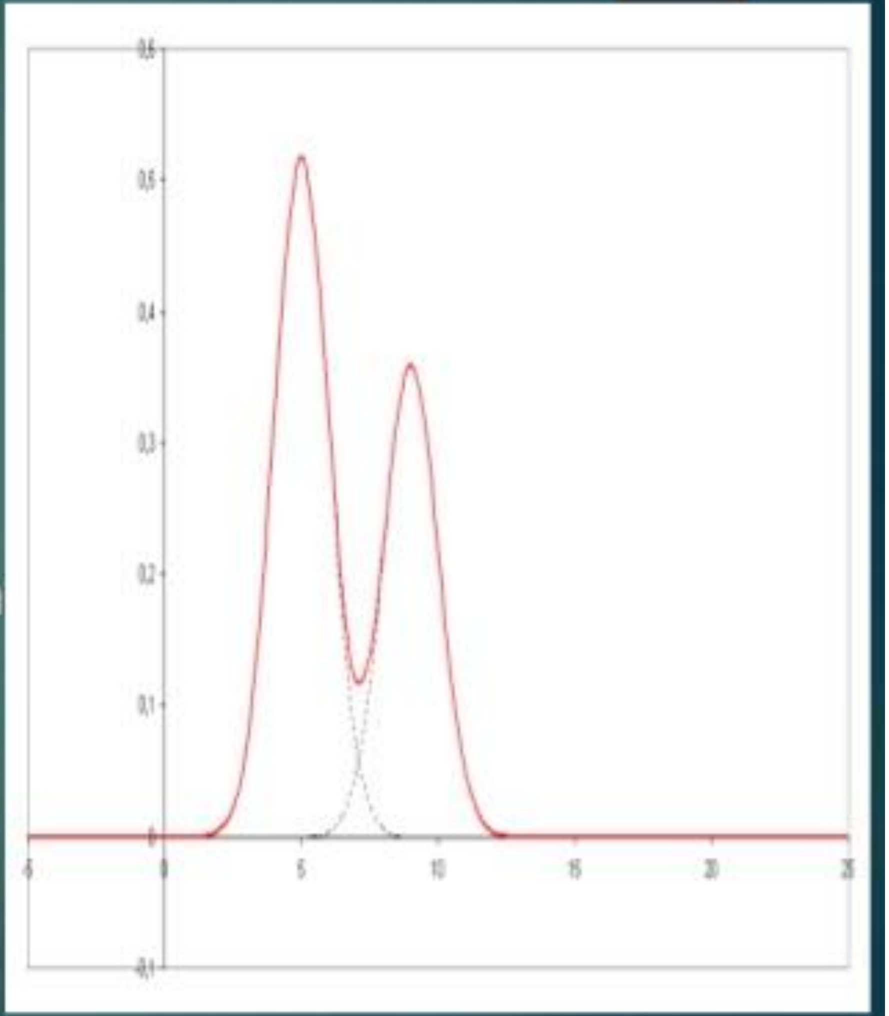
- A graphical presentation of detector response, concentration of analyte in the effluent, or other quantity used as a measure of effluent concentration.


Chromatogram - Detector signal vs. retention time or volume

- The retention time or volume is when a solute exits the injector and passes through the column and the detector .
- Data represented by the chromatogram are used to help identify and quantify the solute(s).

- Because eluting solutes are displayed graphically as a series of peaks, they are frequently referred to as chromatographic peaks.

- These Peaks are described in terms of peak (1) width, (2)height, (3)area



CLASSIFICATION

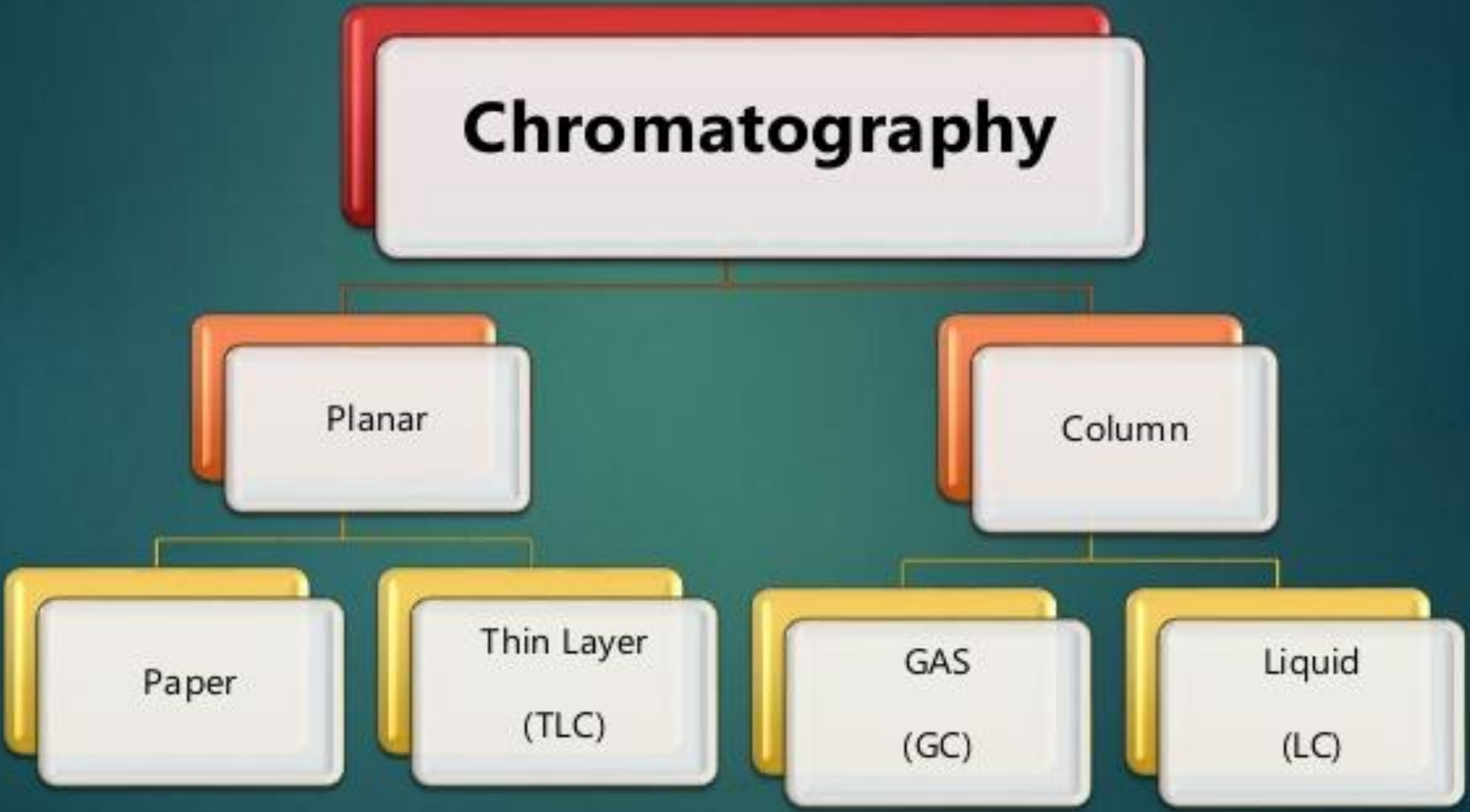
Chromatographic methods can be classified in three different ways :-

a) Based on shape of chromatographic beds .e.g.- Planar and column Chromatography

b) Based on the physical state of mobile and stationary phase. e.g- Gas and liquid chromatography

c) Based on mechanism of separation. e.g.-Ion-exchange chromatography, partition , affinity and adsorption chromatography

Based on shape of chromatographic beds



- Chromatography
  - Planar
    - Paper
    - Thin Layer (TLC)
  - Column
    - GAS (GC)
    - Liquid (LC)

Planar Chromatography

- In Planar Chromatography stationary phase is present on a plane.

- The Plane can be a paper impregnated by a substance acting as a stationary phase- **Paper Chromatography** OR a Thin layer of a substance acting as a stationary phase spread on a glass, metal or plastic plate- **Thin Layer Chromatography.**

- Planar chromatography is also termed as **Open Bed Chromatography.**

Paper Chromatography

- Paper chromatography is a liquid partition chromatography.

- In paper chromatography, the end of the paper is dipped in solvent mixture consisting of aqueous and organic components.

- The solvent soaks in paper by capillary action because of fibrous nature of paper.

- The aqueous component of the solvent binds to the cellulose paper and thereby forms stationary phase with it .

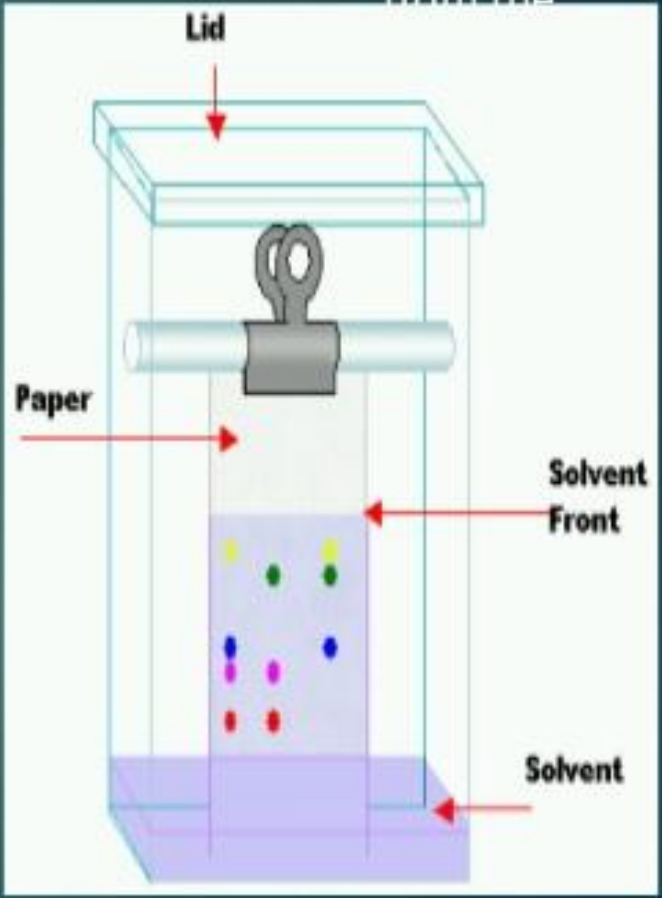
- The organic component of the solvent binds continues migrating, thus forming the mobile phase.

Mechanism of Separation

- Mobile Phase rises up by capillary action.
- Testing sample is concentrated as a minute spot at the bottom of the filter paper.
- Sample mixture gradually rises up with the mobile phase which is liquid.
- Compounds in the mixture will be separated according to their ability of solubility.
- More Polar substances will move slower and less polar substances will travel faster.

Procedure

- A small spot of sample is applied to a strip of chromatography paper about two centimeters away from the base of the plate.
- This sample is absorbed onto the paper and may form interactions with it.
- The paper is then dipped into a solvent, such as ethanol or water, taking care that the spot is above the surface of solvent , and placed in a sealed



- The solvent moves up the paper by capillary action and dissolves the sample mixture, which will then travel up the paper with the solvent solute sample.

- Different compounds in the sample mixture travel at different rates .

- It takes several minutes to several hours.

- **Analysis-** Spots corresponding to different compounds may be located by their color, UV light, Ninhydrin or by treatment with iodine vapors.

Ascending and Descending Paper chromatography

Ascending Chromatography- In this method, the solvent is in pool at the bottom of the vessel in which the paper is supported.

It rises up the paper by capillary action against the force of gravity.

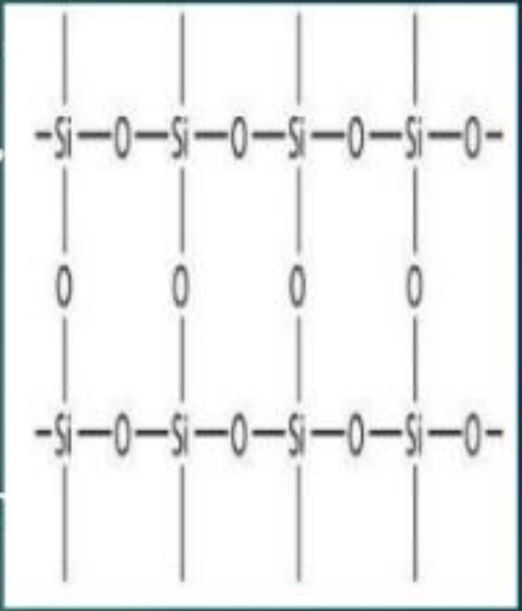
Descending Chromatography- In this method , the solvent is kept in a trough at the top of the chamber and is allowed to flow down the paper .

The liquid moves down by capillary action as well as by the gravitational force.

Significance of Paper Chromatography

- It is very easy, simple , rapid and highly efficient method of separation.
- Can be applied in even in micrograms quantities of the sample.
- Can also be used for the separation of a wide variety of material like amino acids , oligosaccharides, glycosides, purines and pyrimidines, steroids, vitamins and alkaloids like penicillin , tetracyclin and streptomycin.

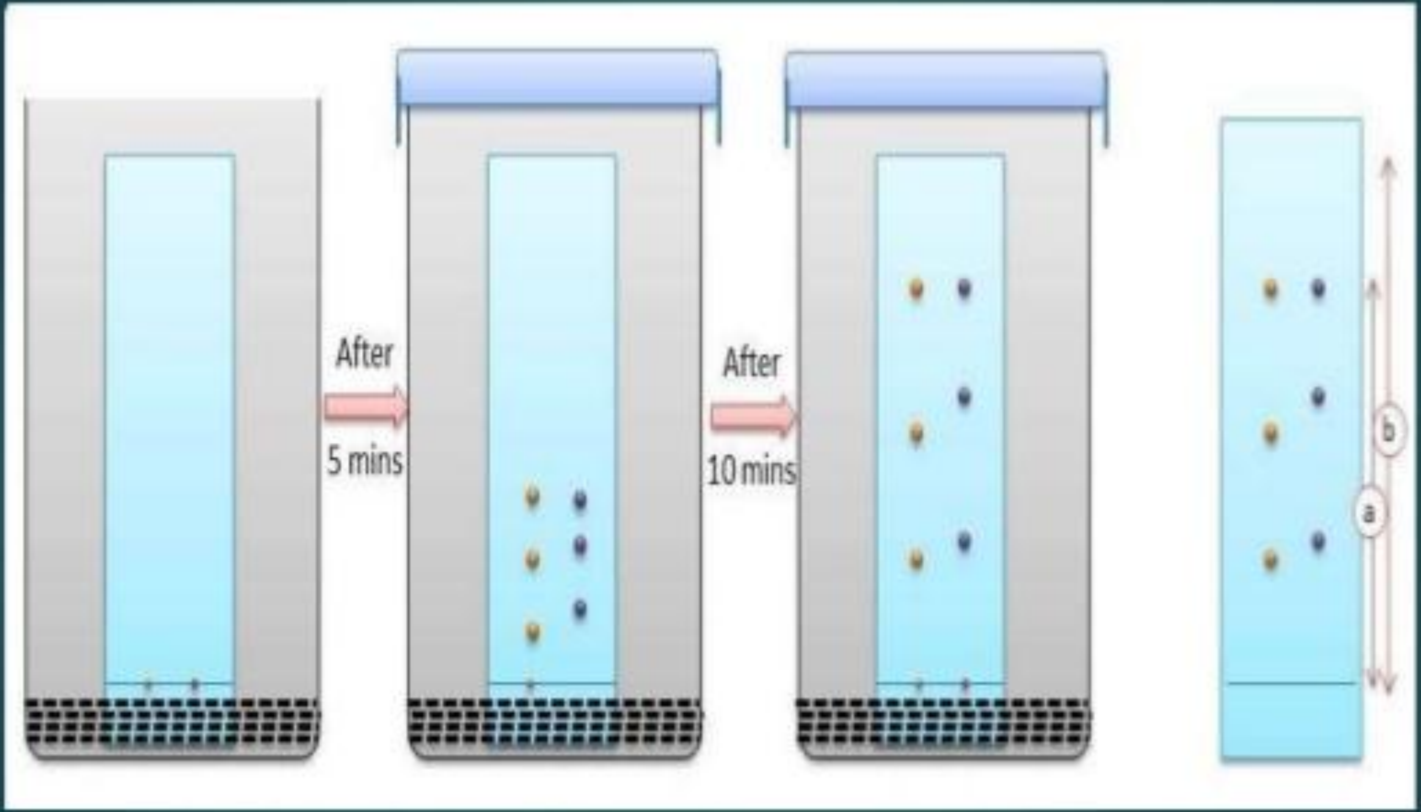
Thin Layer Chromatography (TLC)



- Stationary Phase consists of a thin layer of adsorbent material, usually silica gel , aluminium oxide, or cellulose immobilized onto a flat carrier sheet.

- A Liqiud Phase consisting of the solution to be separated which is dissolved in an appropriate solvent and is drawn up the plate via capillary action , separating the solution based on the polarity of the compound.

Steps of TLC



Significance

Its wide range uses include -

- Determination of the pigments a plant contains.
- Detection of pesticides or insecticides in food .
- Identifying compounds present in a given substance.
- Monitoring organic reaction.

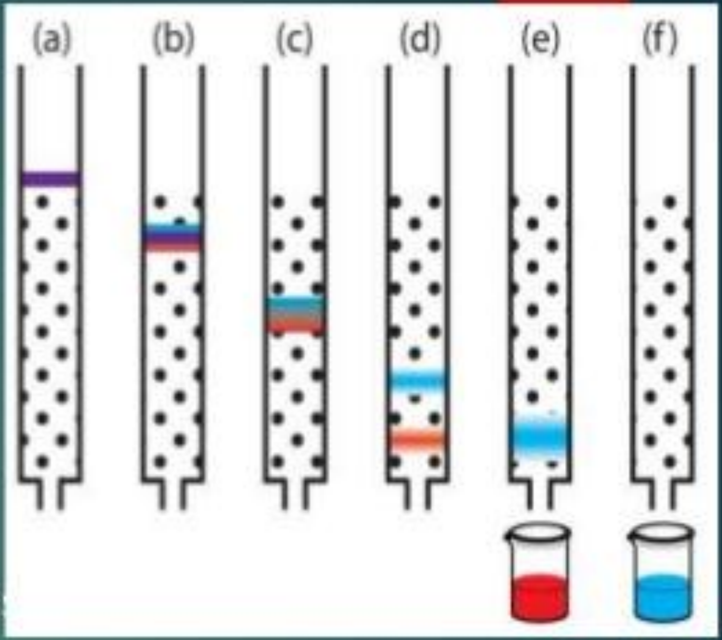
Advantages Of TLC over Paper Chromatography

- In case of Paper Chromatography, it takes 14- 16 hrs for the separation of the components, but in TLC , it takes only 3-4 hrs.
- TLC has the advantage that the corrosive reagents like sulphuric acid can also be used which pose a limitation for the paper chromatography.
- It is easier to separate and visualise the components by this method.
- It has capacity to analyse multiple samples in a single run.
- It is relatively a low cost.

R_F value -

- The rate of migration of the various substances being separated are governed by their relative solubilities in the polar stationary phase and non polar mobile phase.
- The migration rate of a substances usually expressed as R_f (relative front).
- $R_f = \dfrac{\text{Distance travelled by the substance}}{\text{Distance travelled by the solvent front}}$

Column Chromatography



- The Stationary bed is within the tube.
- In column Chromatography the stationary Phase may be pure silica or polymer, or may be coated onto , chemically bonded to, support particles.
- Depending on whether mobile phase is a ga
Chromatography or liquid Chromatography.
- When the Stationary phase in LC consists of small-diameter particles, the technique is High Performance Liquid Chromatography (HPLC).

Gas Chromatography

- Gas mobile phase is used to pass a mixture of volatile solutes through a column containing the stationary phase.

- The mobile phase often referred to as the carrier gas , is typically an inert gas such as nitrogen, helium ,or argon.

- Solute separation is based on the relative differences in the solutes vapor pressures and interactions with the stationary phase.

- Thus more volatile solute elutes from the column

- A solute that selectively interacts with the stationary phase elutes from the column after with lesser degree of interaction.

- The column effluent carries separated solutes to the detector in order of their elution.

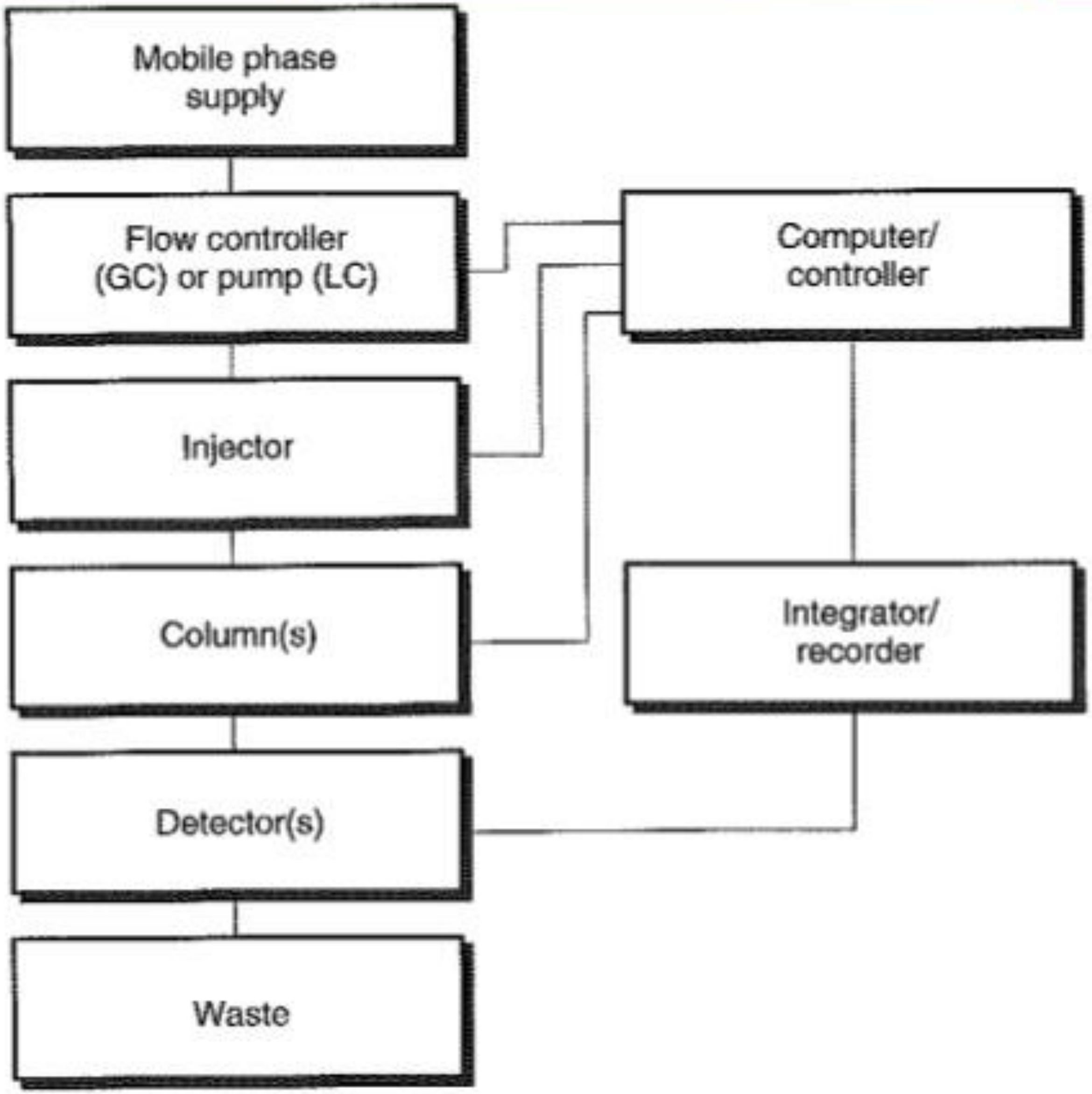
- Solutes are identified qualitatively by their retention times.

- Peak size is proportional to the amount of solute detected and is used to quantify it.

Instrumentation

A basic gas Chromatograph consists of the following:-

- A chromatographic column to separate the solutes
- A supply of carrier gas and flow- control apparatus to regulate the flow of carrier gas through the system.
- An injector to introduce an aliquot of sample or derivatized analytes as they elute from the column.
- A computer to control the system and process data.



Mobile phase supply

Flow controller (GC) or pump (LC)

Injector

Column(s)

Detector(s)

Waste

Computer/ controller

Integrator/ recorder

Liquid Chromatography

- Separation by LC is based on the distribution of the solutes between a liquid mobile phase and a stationary phase.
- When particles of small diameter are used as stationary phase support, the technique is HPLC.
- Most widely used form of LC.

Instrumentation

A basic Liquid chromatograph consists of following elements :-

- A solvent reservoir to hold the mobile phase through the system.
- An injector to introduce sample into the column.
- A chromatographic column to separate the solutes.
- Detector to detect the separated analytes as they elute from the column.
- A computer that processes the system and processes data.

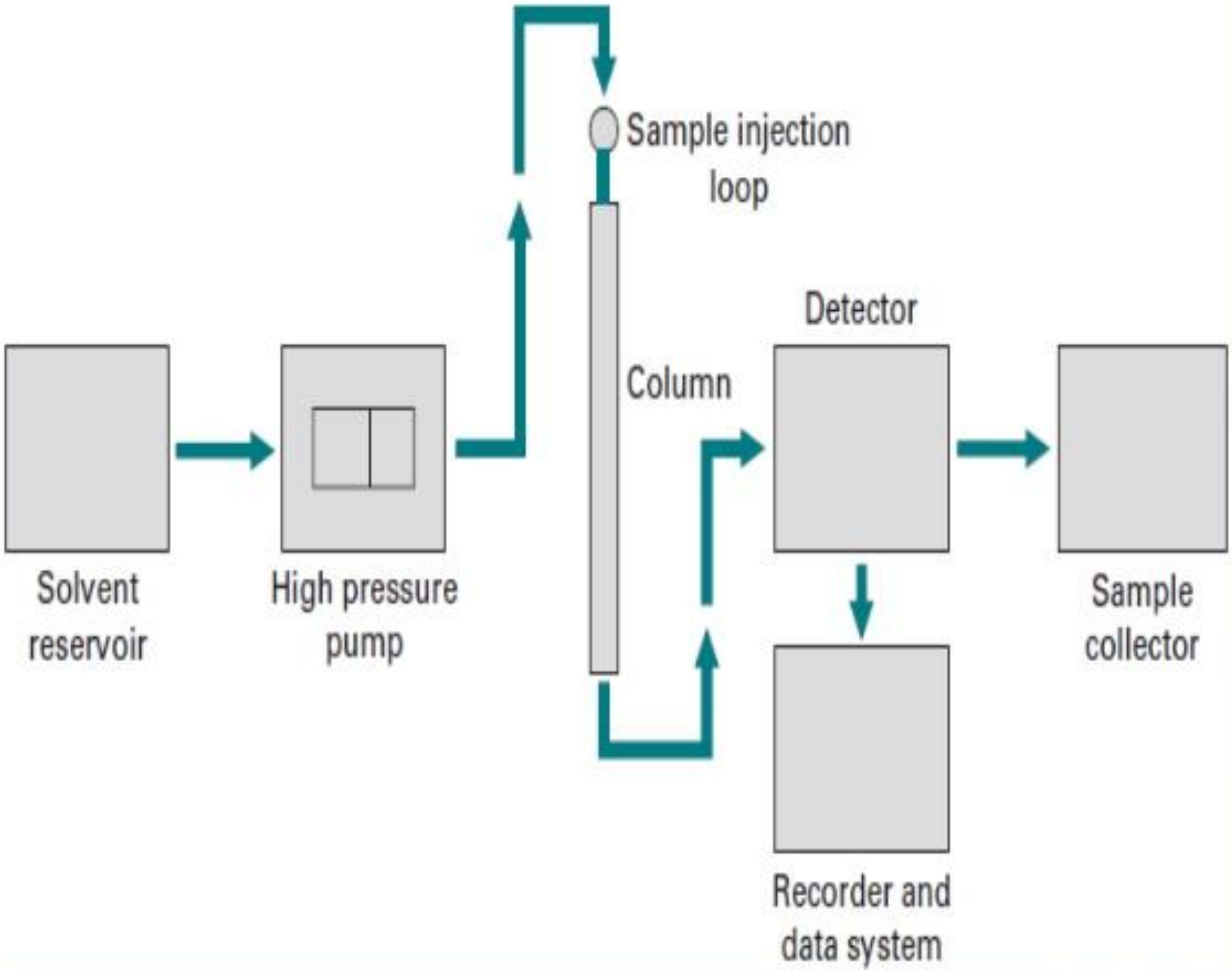
HPLC

- HPLC is basically a highly improved form of Liquid Chromatography.
- Instead of a solvent (mobile phase) being allowed to drip through the column under gravity, it is forced through under high pressure.
- Yeilds high performance and high speed as compared with traditional column chromatography.

- The parameters used to describe a HPLC column refer to the nature, type and size of its packaging material, and the dimensions of the column used.

- Increased flow rates are obtained by applying a pressure difference across the column.

- A combination of high pressure and adsorbents of small particle size leads to the high resolving power and short analysis time characteristic of HPLC


Sample injection loop
Column
Detector
Solvent reservoir
High pressure pump
Sample collector
Recorder and data system

The advantages of HPLC are the result of two major advances :-

- The development of stationary supports with very small particle sizes and large surface areas .
- The improvement of elution rates by applying high pressure to the solvent flow.

Applications

Pharmaceutical- Tablet dissolution of pharmaceutical dosages

- Shelf life determination of pharmaceutical products
- Identification of counterfeit drug products
- Pharmaceutical quality control

Forensics- On site identification and quantification of the drug Ecstasy.

- Identification of anabolic steroids in serum, urine, sweat and hair
- Forensic determination of textile dyes.
- Simultaneous quantification of psycotherapeutic drugs in human plasma

Clinical-

- Analysis of antibiotics.
- Detection of endogenous neuropeptides in brain extracellular fluids.

Food and Flavour-

- Ensuring soft drink consistency and quality
- Analysis of vicinal diketones in beer.
- Sugar analysis in fruit juices.

- Trace analysis of military high explosives in agricultural crops.

Based on Separation Mechanisms

- Chromatographic separations are classified by the chemical or physical mechanisms used to separate solutes.

- These include-

1. Ion- exchange
2. Partition
3. Adsorption
4. Size exclusion
5. Affinity mechanisms

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