INTRODUCTION. FUNDUMENTALS OF THE STRUCTURE AND REACTIVITY OF ORGANIC COMPOUNDS

1. Introduction. The object of bio-organic chemistry. The competences of students.
2. Fundamentals of stereochemistry. Configuration and conformation of organic compounds.
3. Classification, mechanisms and reagents of organic reactions.

Guided independent work **([1] -p.34,44,47,52-54. [2] Test 1*:***

4. Three-dimensional line-dash-wedge representation of configuration, Fischer projection formulas, Newman projection formulas; the rules of drawing.
5. R,S-system of a stereochemical designation. ***Educational resources:***

[1] BIOORGANIC CHEMISTRY lecture course for foreign students of the 1-st year. Assembled by L.G.Hidranovich. Vitebsk: VSMU Press, 2004.

[2] https://do2.vsmu.by/mod/quiz/view.php?id=216616

During studying discipline “bioorganic chemistry” you will receive and form systematized scientific **knowledge** about relationship between structures and chemical properties of biologically important organic compounds as bases for understanding the essence of a metabolism and its regulation at a molecular level and using low-molecular organic compounds for polymerization in dental restorations.

Basic Professional Competence:

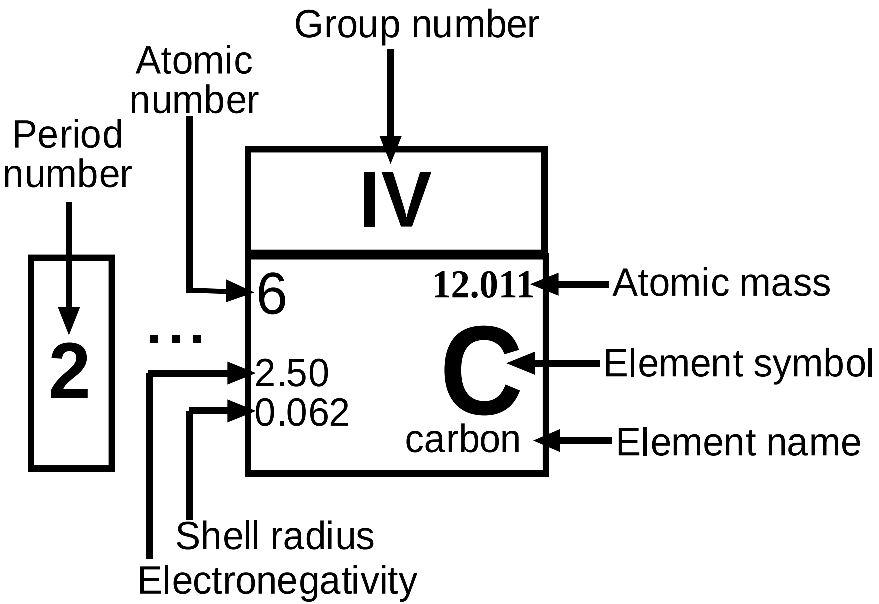
BPC-1. The student must evaluate the properties of natural, synthetic organic compounds, potentially dangerous substances for the human body, predict their activity in biological environments.

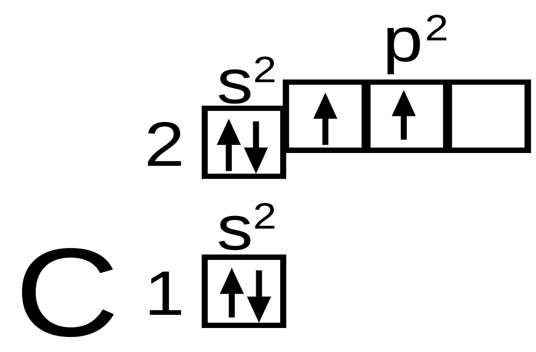
- The knowledge and skills gained in the study of the academic discipline «**Bioorganic chemistry**» are necessary for the successful study of following academic disciplines:
  - «**Biological Chemistry»,**
  - **«Medical Biology and General Genetics»,**
  - **«Normal Physiology», «Pharmacology»,**
  - **«General Hygiene»,**
  - **«Microbiology, Virology, Immunology»**
  - **«Radiation and Environmental Medicine»**

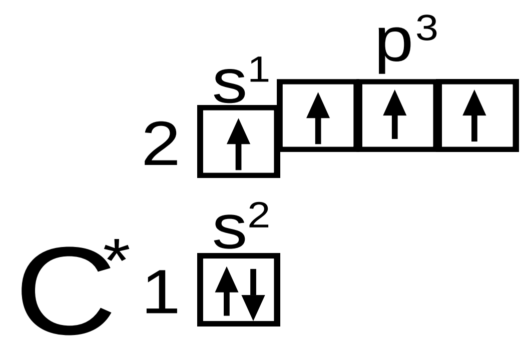
INTRODUCTION

All matter, organic compounds included, are composed of **atoms**. Carbon is the most important atom in bioorganic chemistry.

The outer shell of carbon atom exists in two forms: the ground state and the excited state. In organic compounds carbon is presented in excited state. In this state there are four valence electrons distributed on one 2s orbital and three 2p orbitals.







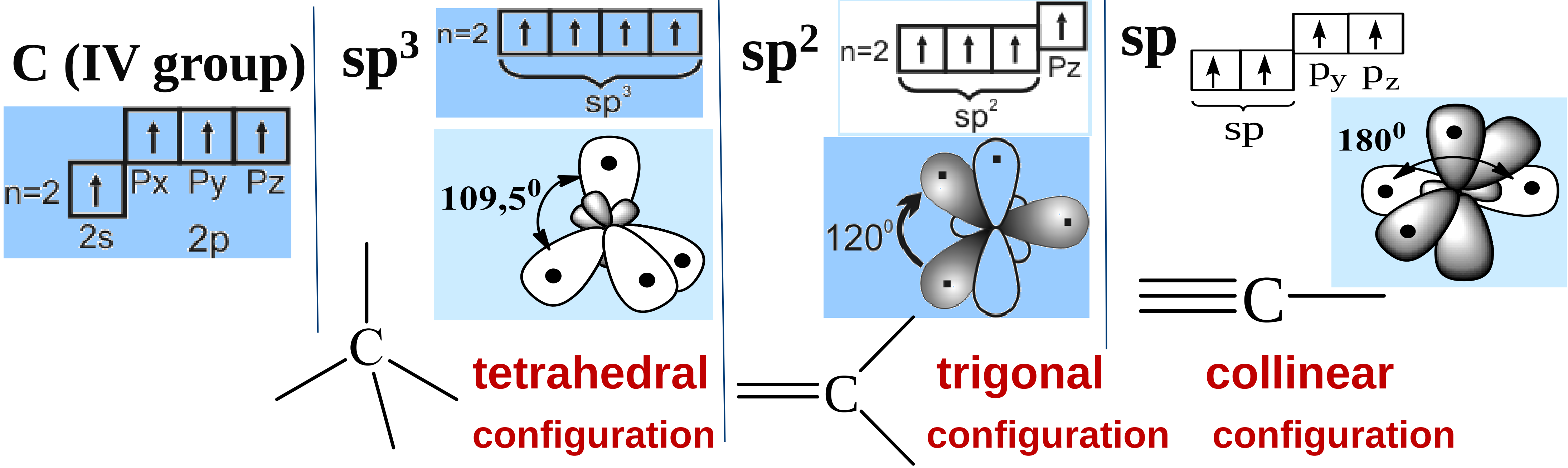
Ground state

$1s^22s^22p_x^12p_y^12p_z^0$

Excited state

$1s^22s^12p_x^12p_y^12p_z^1$

THE ELECTRON CONFIGURATION OF CARBON ATOM



tetrahedral configuration

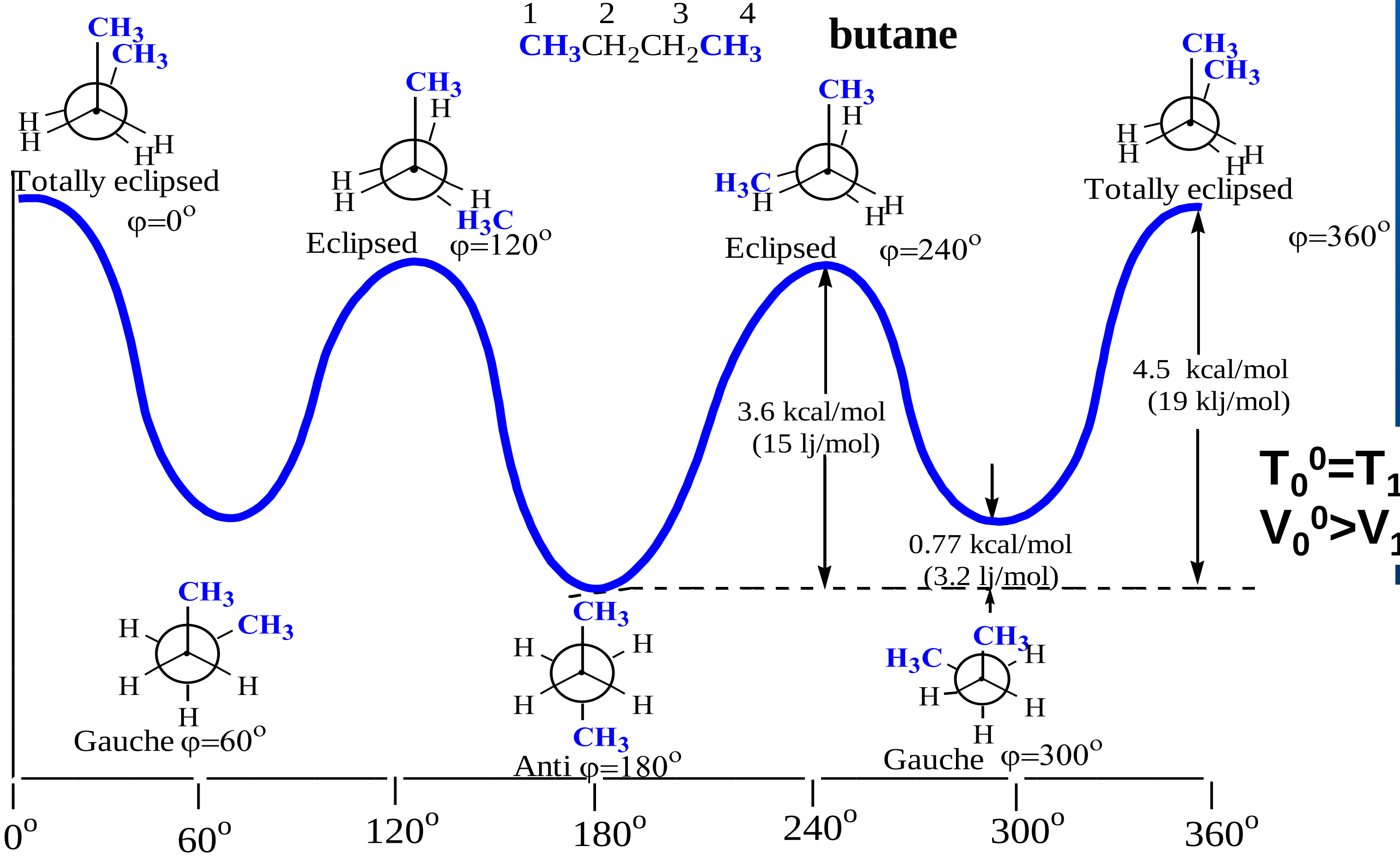
trigonal configuration

collinear configuration

The concept of hybridization is the mathematical combination of atomic orbital wave functions to give a new set of hybrid atomic orbitals containing the same number of atomic orbitals as the starting set. Hybrid atomic orbitals are degenerate, and each has a large front lobe and a smaller back lobe. All hybrid atomic orbitals are cylindrically symmetrical.

STEREOCHEMISTRY. CONFORMATIONS.

Atoms in molecules are constantly in motion relative to each other. The temporary molecular shapes that result from rotations of groups about single bonds are called **conformations** of the molecule. **Staggered conformation** is the most stable conformation due to maximum possible separation of the electron pairs of the six single bonds and it has the lowest energy.



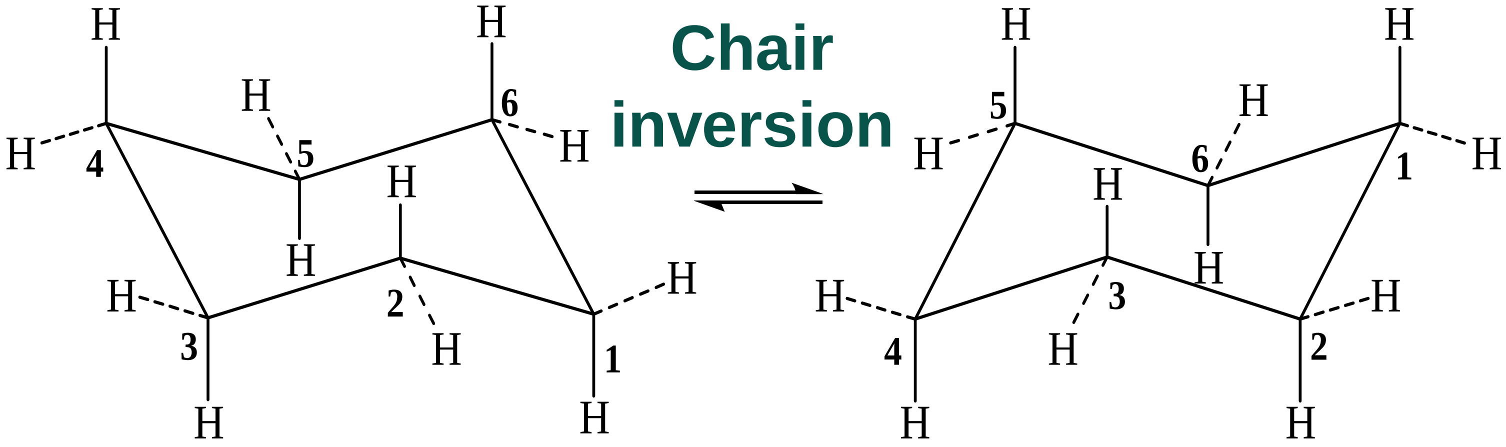
The least stable conformation is the **eclipsed conformation**: the atoms attached to each carbon atom in direct opposition to each other require the maximum repulsive interaction between the **electrons** of the six **s-bonds orbitals**. This kind of molecule destabilization is called **torsion strain.**

$$T_0^0=T_{120}^0=T_{240}^0=\max \quad T_{60}^0=T_{180}^0=T_{300}^0=\min$$

$$V_0^0>V_{120}^0=V_{240}^0=\max \quad V_{180}^0<V_{60}^0=V_{300}^0=\min$$

Van der Waals strain is result of repulsion between the electron clouds of atomic groups, if great groups becomes closed. The greater groups of atoms the more Van der Waals strain

CONFORMATIONS OF CYCLOHEXANE.



Chair inversion

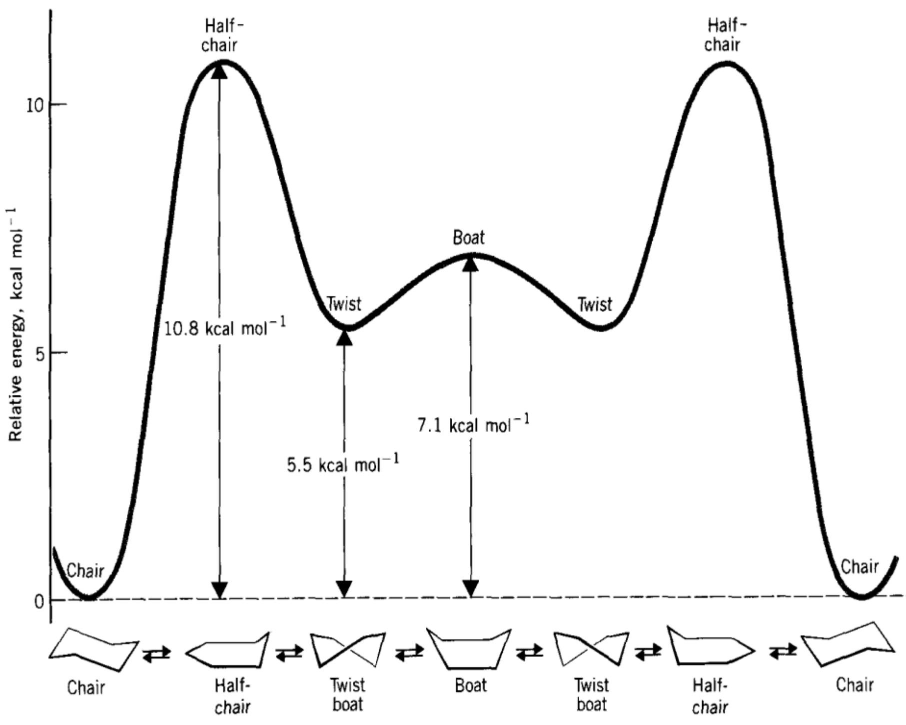
$^4C_1$

$_4C^1$

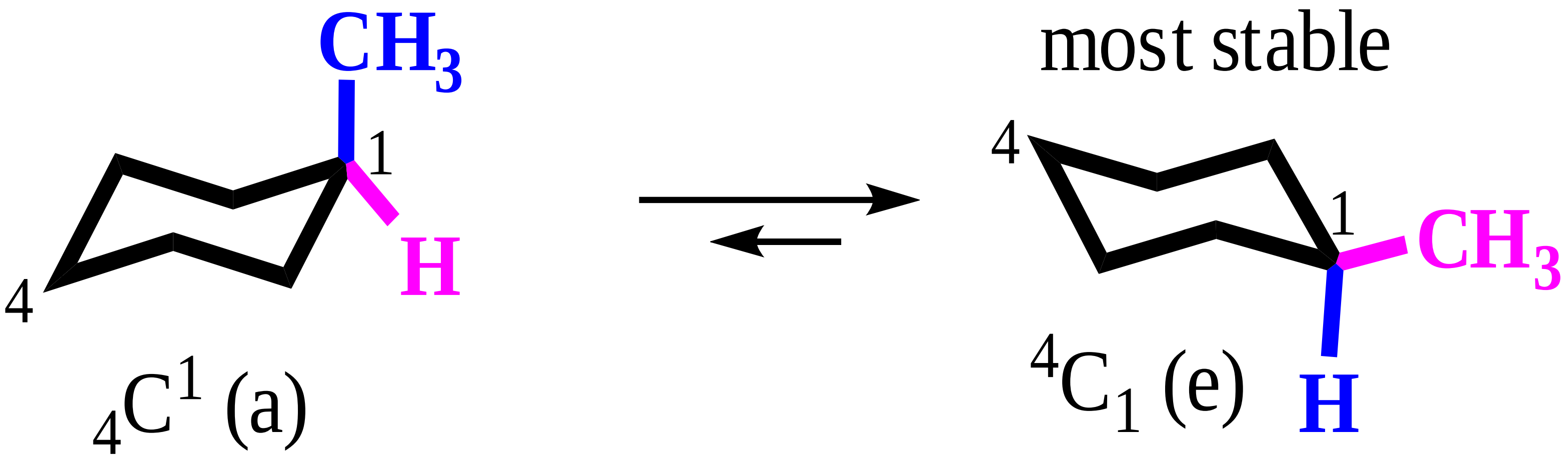
$\mathbf{E}(^4C_1) = \mathbf{E}(_4C^1)$

—— *Axial bonds*

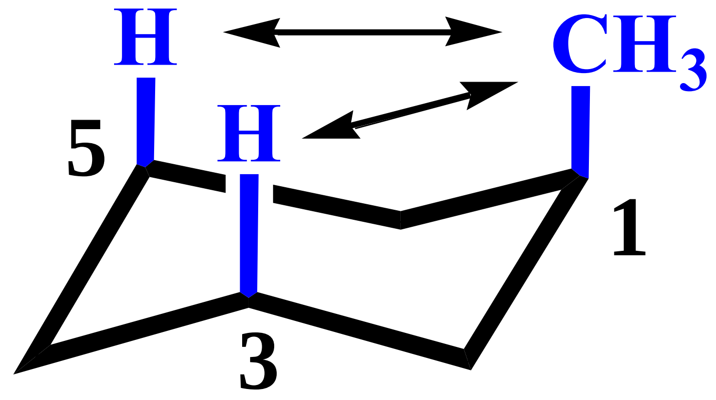
- - - - *Equatorial bonds*



CONFORMATIONS OF METHYLCYCLOHEXANE.



$E(a) > E(e)$

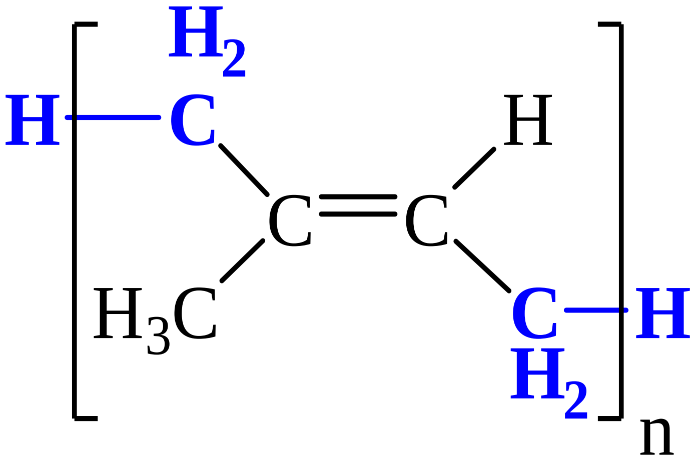


The distance between hydrogen atom and methyl group is less than the sum of the van der Waals radius for two hydrogens (2.4Å), so the axial conformation of methylcyclohexane is destabilized by the strain of the Van der Waals repulsive forces. **The Van der Waals repulsive forces** arise when the electron clouds surrounding the atoms get close enough to repel one another.

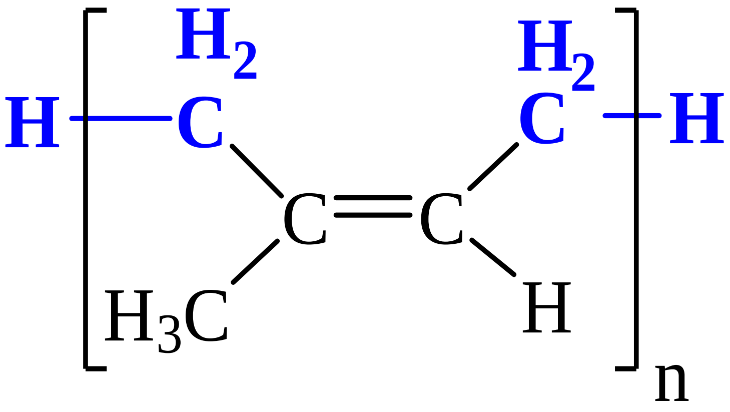
CONFIGURATION. DIASTEREOMERS

Configuration is the three-dimensional arrangement of substituents around a **stereocenter.**

Stereoisomers are compounds having the same structure and different only in arrangement of their atoms in space. Stereoisomers can be subdivided into two general categories: **enantiomers** and **diastereomers.**



Gutta percha:
E(*trans*)-1,4-polyisoprene



Natural rubber:
Z(*cis*)-1,4-polyisoprene

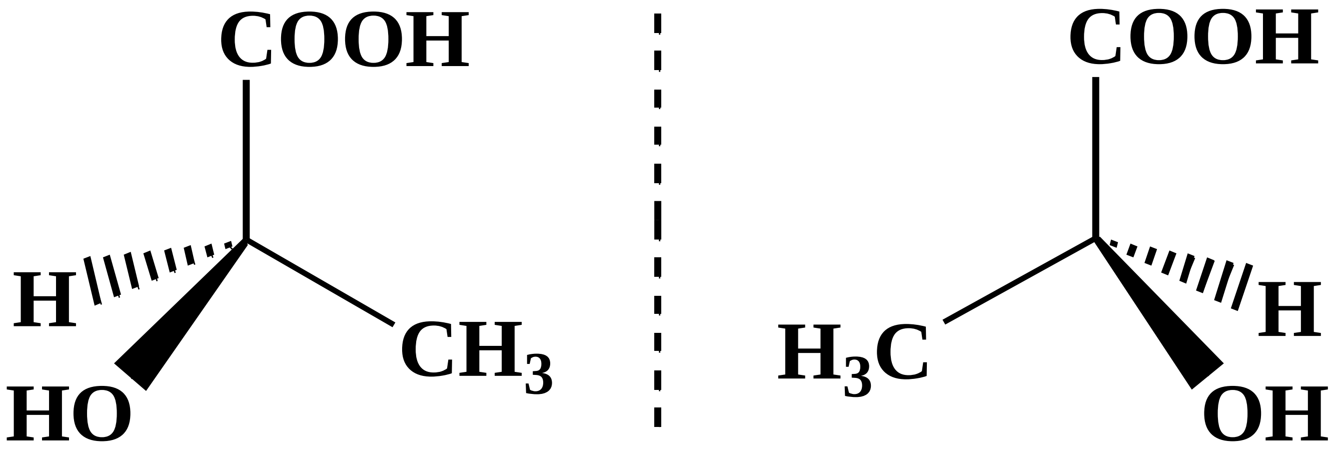
π-diastereomers

Diastereomers are stereoisomers whose molecules are not mirror images of each other. There are **σ-** and **π-diastereomers**. π-Diastereomers are achiral, they are the same as their mirror image.

CONFIGURATION. ENANTIOMERS

Enantiomers are stereoisomers whose molecules are mirror images of each other. Enantiomers occur only for chiral molecules.

A chiral molecule is not identical with its mirror image.



Enantiomers of lactic asid - chiral molecules.

The molecule is **chiral** if it have the following:

1) tetrahedral (sp^3-hybrid) carbon atom with four different groups attached to it. A carbon atom bonded to four different groups atoms are called a **stereocenter**.

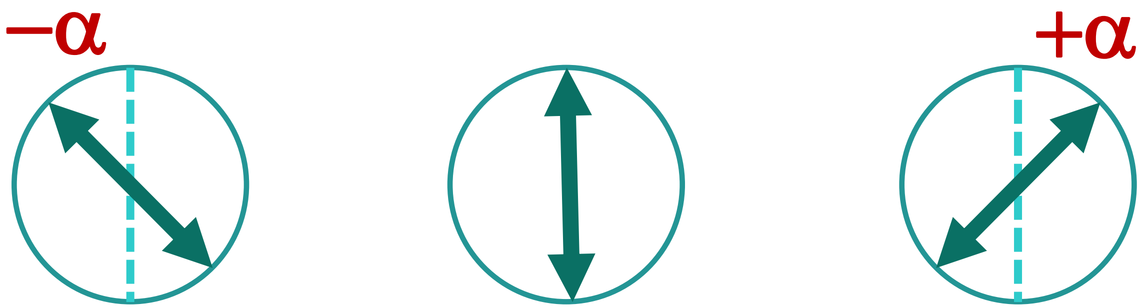
2) no elements of symmetry. A plane of the symmetry is an imaginary plane that cuts a molecule into equal halves that are mirror images of each other.

PROPERTIES OF ENANTIOMERS. OPTICAL ACTIVITY

The properties of enantiomers:

- identical physical scalar properties (melting and boiling points)
- the same reactivity with achiral molecules
- the different reactivity for chiral molecules (enzymes, receptors)
- the same angle and the opposite sign of their optical activity

Optical activity is a property of chiral molecules to rotate the plane of polarized light when it is passed through the solution containing the chiral substance.



levorotatory (-) enantiomer
rotate to the left
(counterclockwise)

plane of polarized light

dextrorotatory (+) enantiomer
rotate to the right
(clockwise)

RACEMATE, RACEMIC MIXTURES

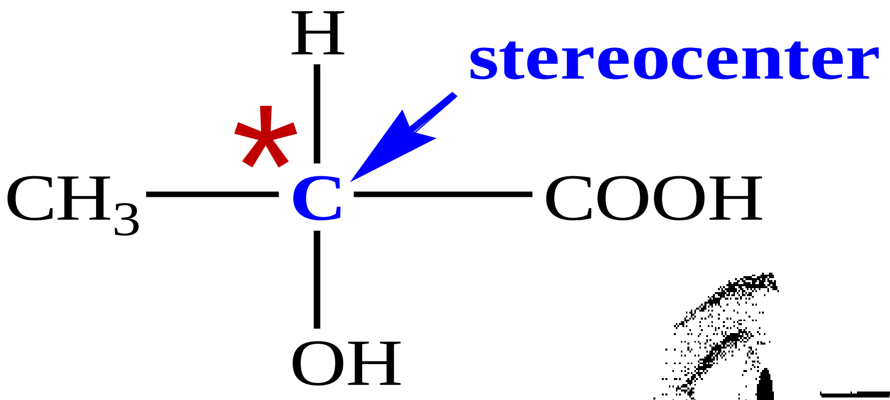
A racemic mixture (racemate) *is an equimolar mixture of enantiomers*

Racemic mixtures do not show optical activity. It is formed generally in chemical syntheses in special conditions of achiral surrounding.

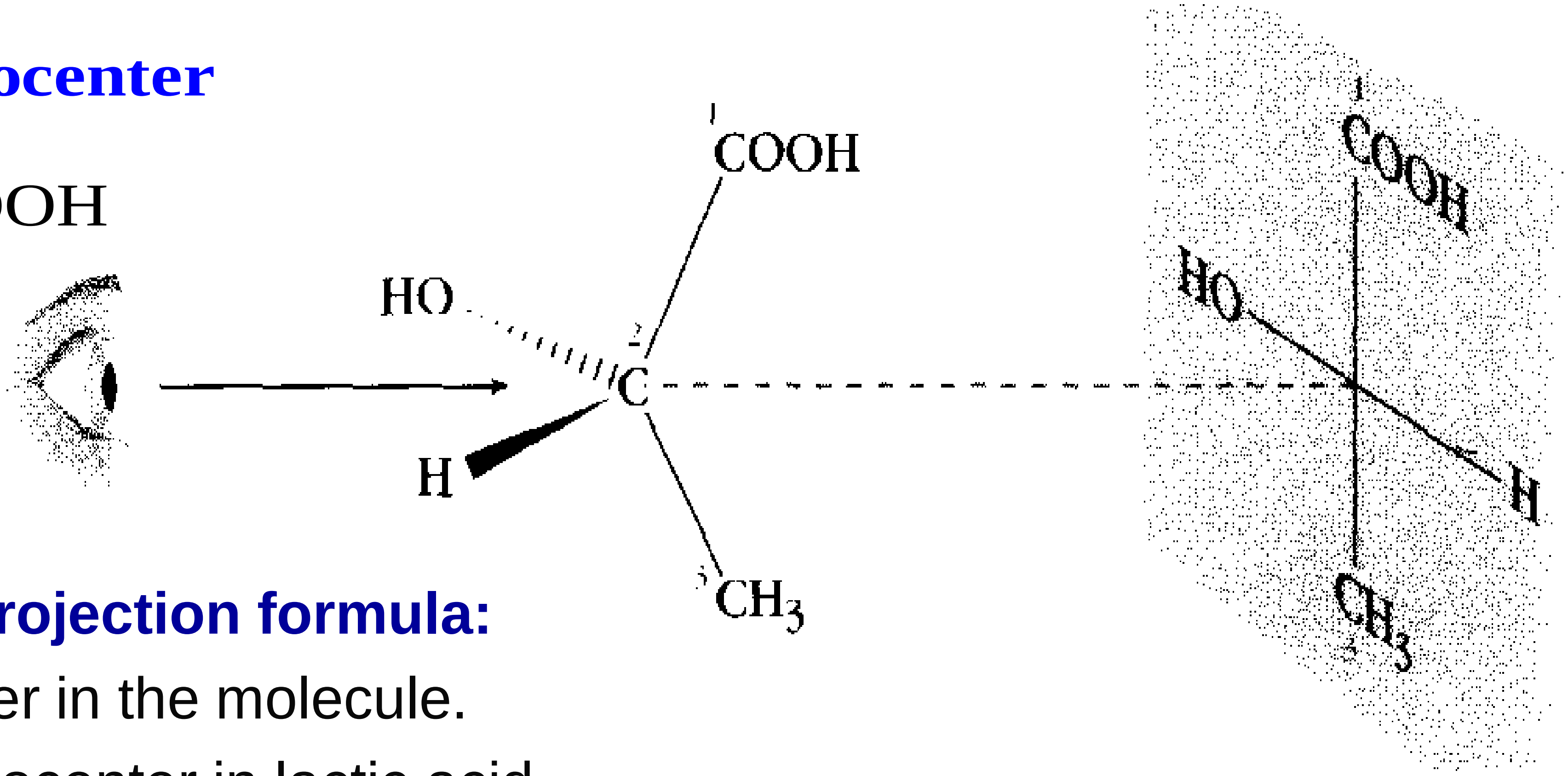
Racemic mixtures separation methods:

- Mechanical separation of crystals with mirror images shapes
- Microbiological method
- Chemical conversion to diastereomers with different melting points and solubility
- Affinity chromatography with a chiral sorbent.

FISCHER PROJECTION FORMULA



Lactic acid



To write the Fisher projection formula:

1. Find the stereocenter in the molecule.

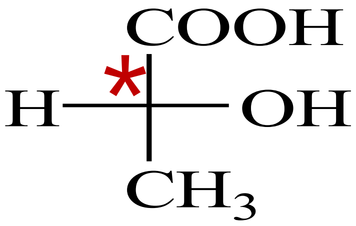
2. Represent the stereocenter in lactic acid

by two crossed lines. By convention, the horizontal lines represent bonds that extend above the plane of the page, while vertical lines represent bonds that extend below the plane.

D, L DESIGNATIONS FOR ENANTIOMERS

1. We must find the stereocenter in the molecule.

2. In Fisher projection formula stereocenter is represented by two crossed lines, at the top of vertical line must be located the most oxidized group (-COOH) and in the lower part of vertical line any carbon-containing groups must be located. On the horizontal line we locate other groups and atoms.



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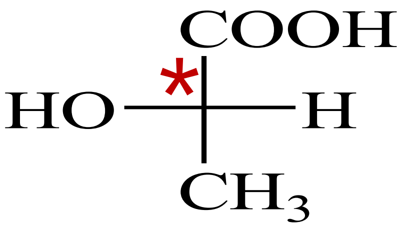
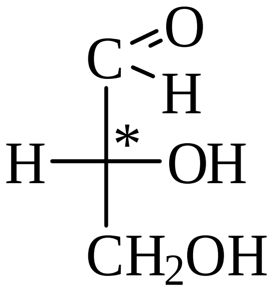
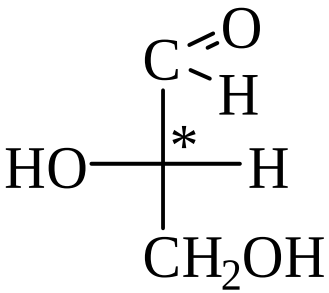


II



D-glyceraldehyde

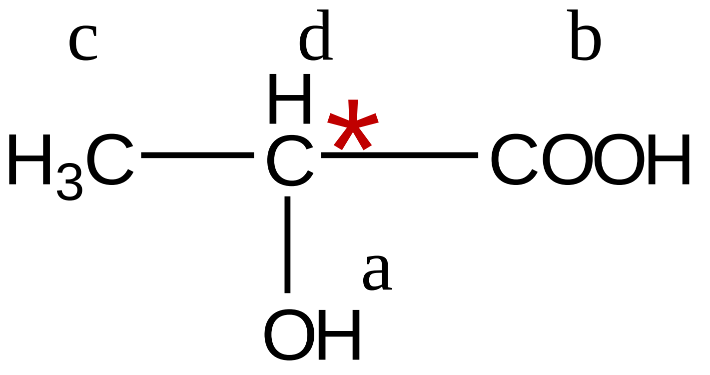


L-glyceraldehyde

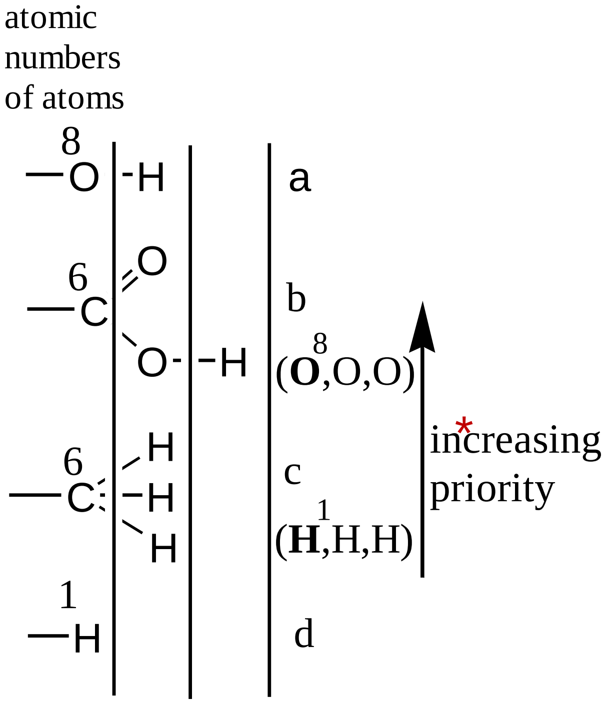
3. Now let’s designate which of these two structures is L-lactic acid and which is D-lactic acid. For this purpose we use glyceraldehyde as a standard:

- **D-lactic acid** (I) has the same configuration as **D-glyceraldehyde.**
- **L-lactic acid** (II) has the same configuration as **L-glyceraldehyde.**

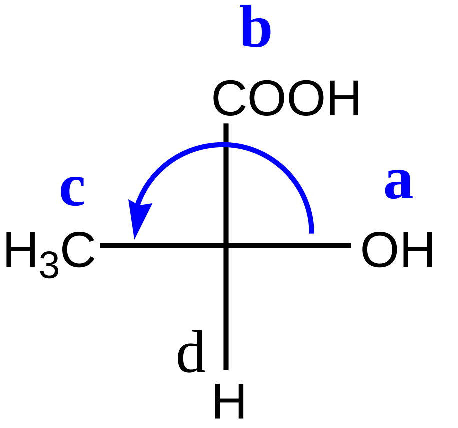
ABSOLUTE CONFIGURATION, (R-S) SYSTEM



lactic acid

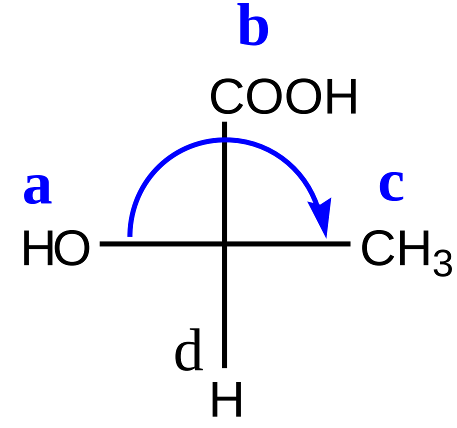


Each of the four groups attached to the stereo-center is assigned a **priority** or **preference** *a, b, c,* or d. Priority is first assigned on the basis of the **atomic number** of the atom that is directly attached to the stereocenter.



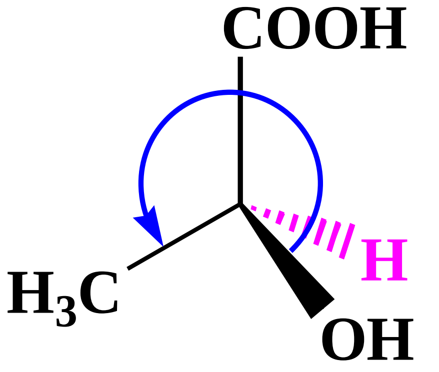
dicreasing of priority from right to left -

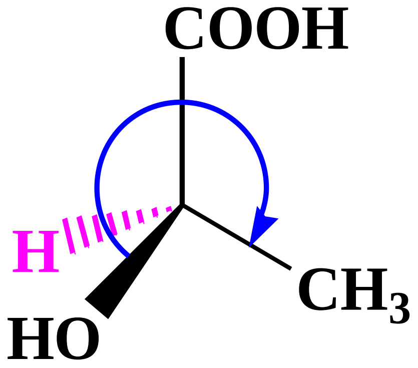
S-isomer



dicreasing of priority from left to right –

R-isomer



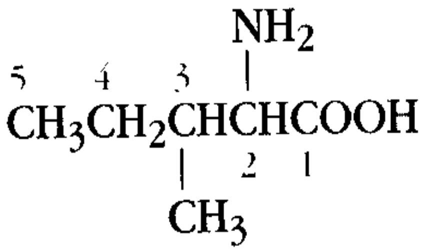


MOLECULES WITH MORE THAN ONE STEREOCENTER

A *molecule with n stereocenters has* a maximum *of* 2^n *stereoisomers.*

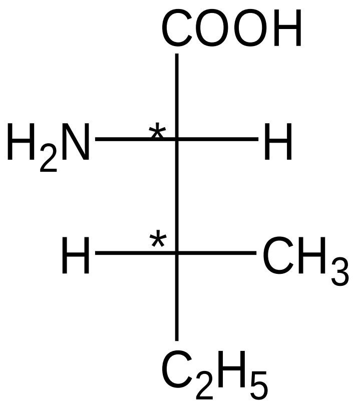
The amino acid 2-amino-3-methylpentanoic acid, which is better known as isoleucine, has two stereocenters.

- **$N=2^n$ $N=2^2=4$**



$\overset{5}{C}H_3\overset{4}{C}H_2\underset{CH_3}{\overset{3}{C}H}\underset{2}{\overset{NH_2}{C}H}\underset{1}{C}OOH$

Isoleucine
(2-Amino-3-methylpentanoic acid)



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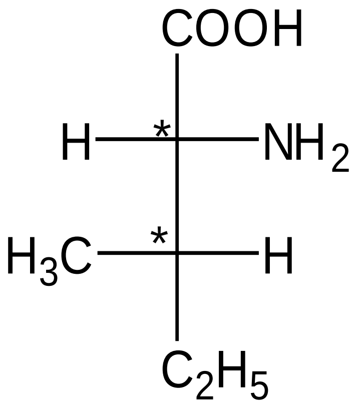

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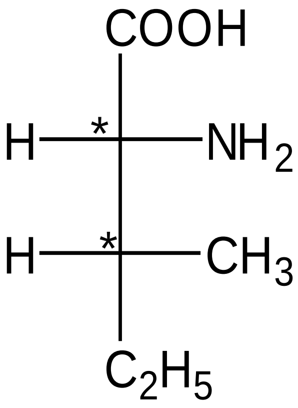
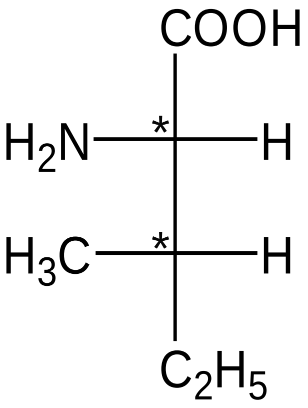


III



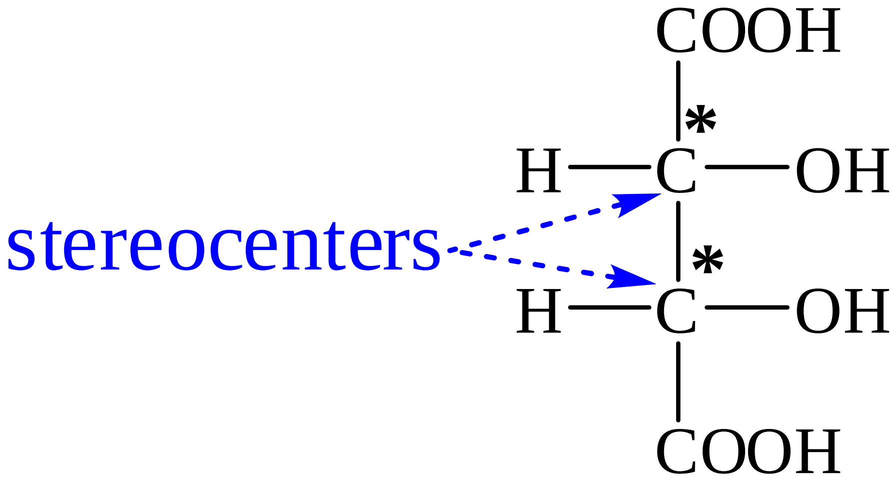
IV

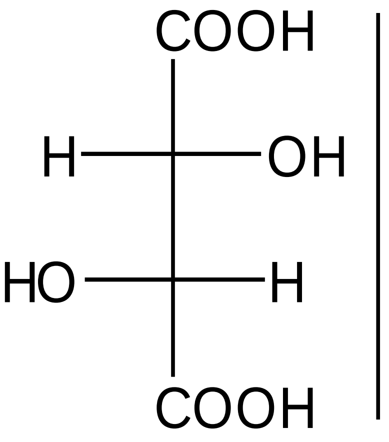
Stereoisomers I and II, III and IV are mirror images of each other – enantiomers.

Stereoisomers I and III, I and IV, II and III, II and IV are not mirror images of each other – σ-diastereomers.

MESO COMPOUNDS.

Tartaric acid, like isoleucine, has two stereocenters and 4 stereoisomers.





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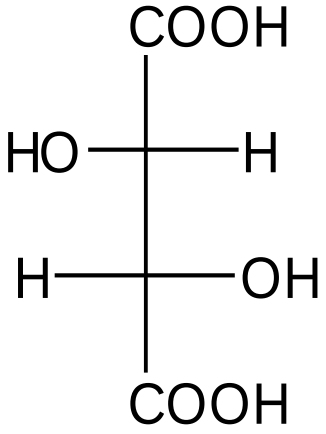

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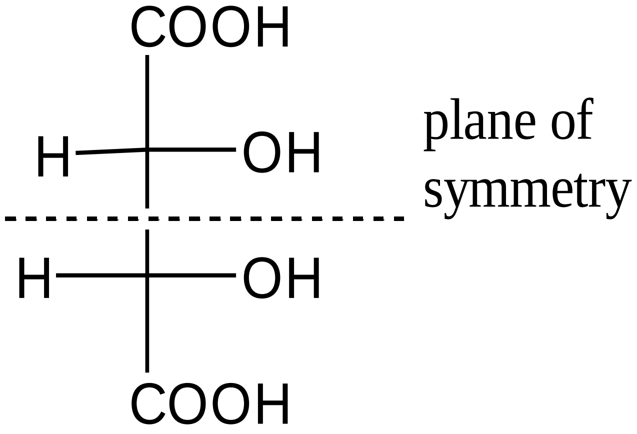


III *Meso compound*

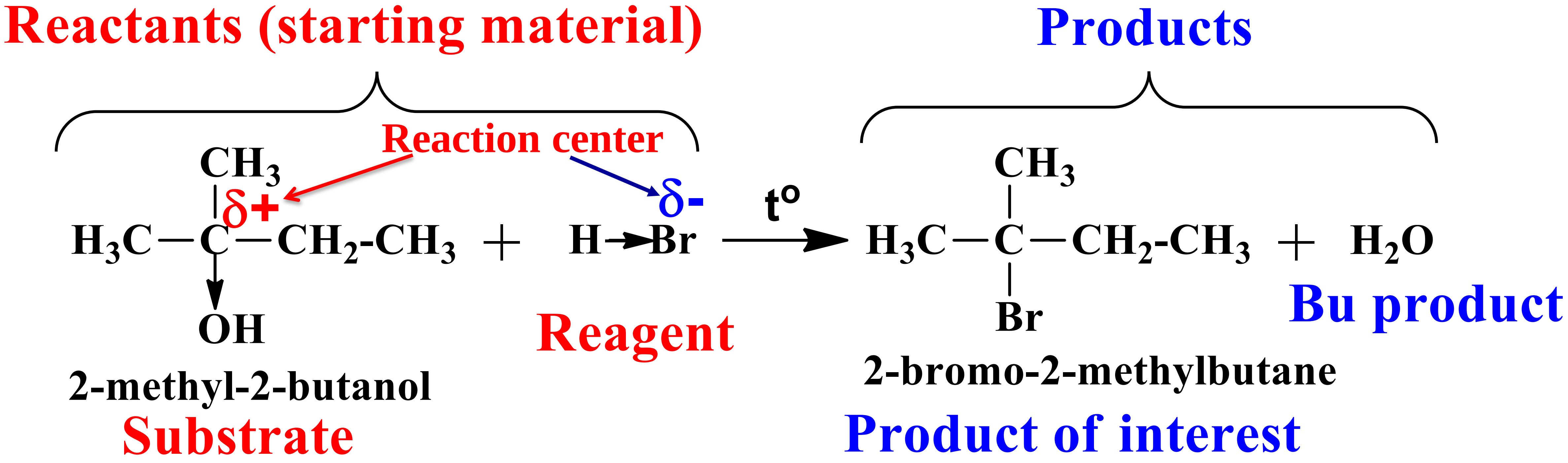
1 and 2 are enantiomers. Stereoisomers 1 and 3, 2 and 3 are diastereomers.

One part of the molecule of stereoisomer 3 is the mirror image of it's other part. The structure 3 is achiral.

An achiral molecule with stereocenters is called a meso compound or a meso form.

ORGANIC REACTION TERMINOLOGY

Reaction of organic compounds is a process involved the making of new and breaking of previous covalent bonds.



$$H_3C-\overset{CH_3}{\underset{OH}{\overset{\delta+}{C}}}-CH_2\text{-}CH_3 + H\rightarrow\overset{\delta-}{Br} \xrightarrow{t^o} H_3C-\overset{CH_3}{\underset{Br}{C}}-CH_2\text{-}CH_3 + H_2O$$

Reactants (starting material)

Products

Reaction center

2-methyl-2-butanol

Substrate

Reagent

2-bromo-2-methylbutane

Product of interest

Bu product

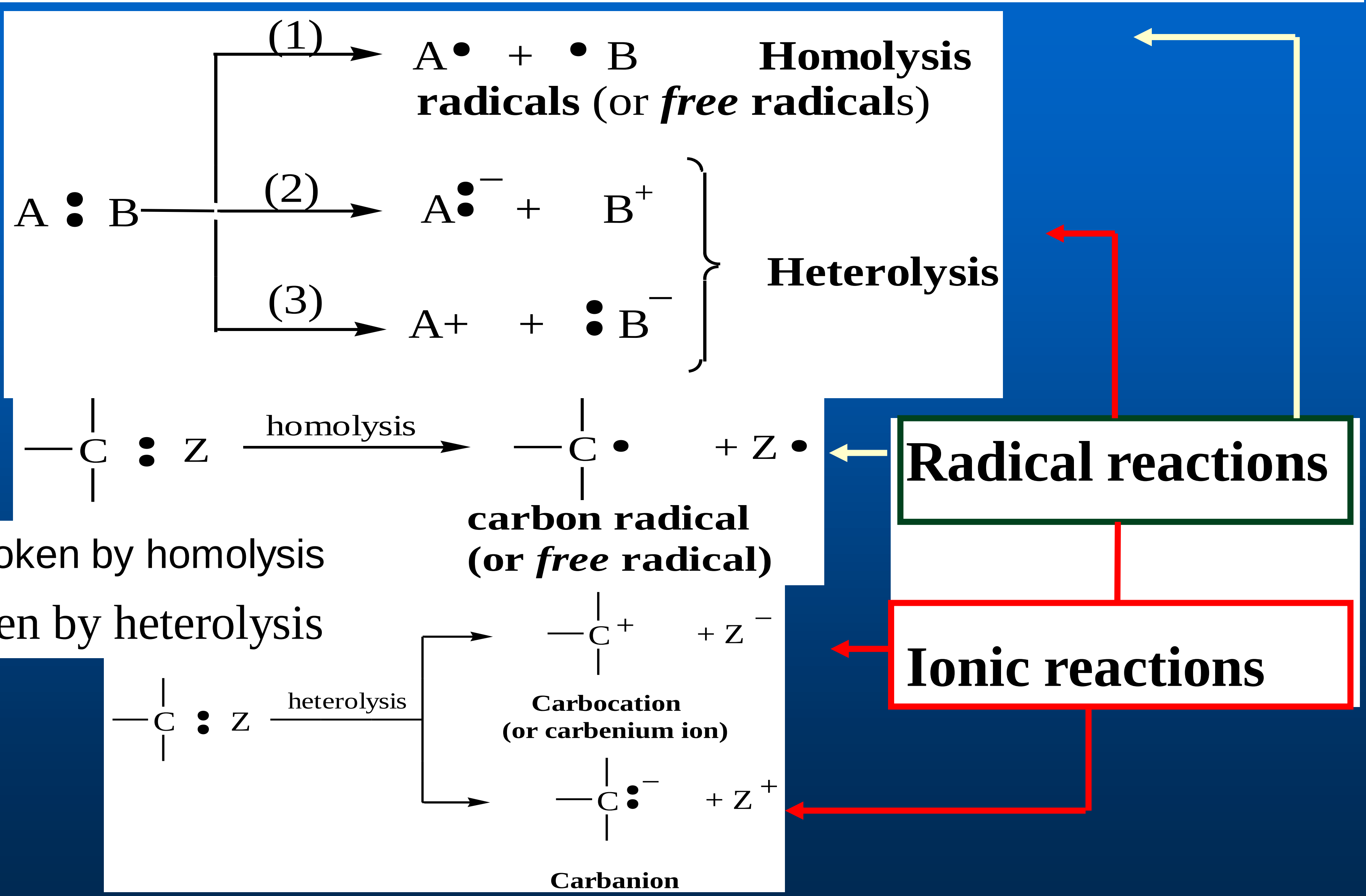
Reaction center is an atom or a group of atoms, where reaction occurs.

THE MECHANISM OF COVALENT BONDS CLEAVAGE

- Reactive intermediates in organic chemistry:
  - ○ **Free radicals**
  - ○ **Carbonations**
  - ○ **carbanions**

Nonpolar bonds are broken by homolysis

Polar bonds are broken by heterolysis



$$A{:}B \xrightarrow{(1)} A\bullet + \bullet B$$

Homolysis

radicals (or ***free*** **radicals**)

$$A{:}B \xrightarrow{(2)} A{:}^{-} + B^{+}$$

$$A{:}B \xrightarrow{(3)} A^{+} + {:}B^{-}$$

Heterolysis

$$-\overset{|}{\underset{|}{C}}{:}Z \xrightarrow{\text{homolysis}} -\overset{|}{\underset{|}{C}}\bullet + Z\bullet$$

carbon radical
(or *free* radical)

$$-\overset{|}{\underset{|}{C}}{:}Z \xrightarrow{\text{heterolysis}} -\overset{|}{\underset{|}{C}}^{+} + Z^{-}$$

Carbocation
(or carbenium ion)

$$-\overset{|}{\underset{|}{C}}{:}^{-} + Z^{+}$$

Carbanion

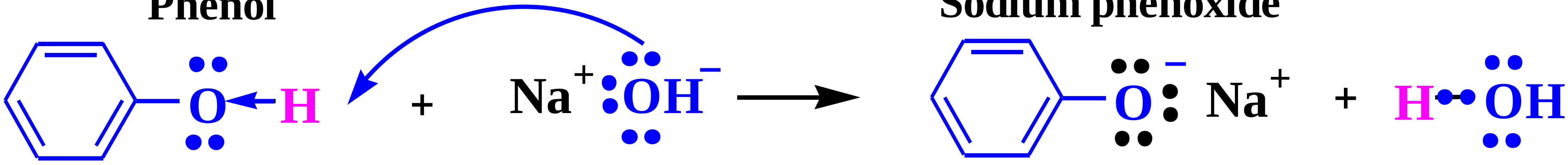
Radical reactions

Ionic reactions

THE BRONSTED-LOWRY DEFINITION OF ACIDS AND BASES

We can categorize most organic reactions as acid-base reactions.

According to the **Bronsted — Lowry theory**, an **acid** is a substance that can donate a proton, and a **base** is a substance that can accept a proton.



Phenol

Sodium phenoxide

Acid (proton donor)

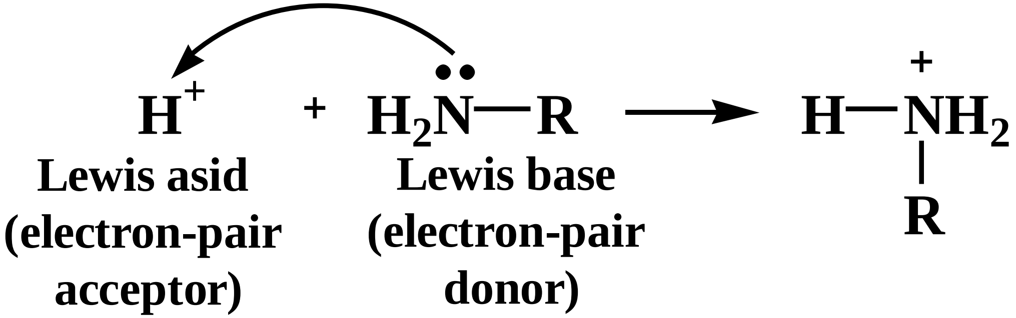
Base (proton acceptor)

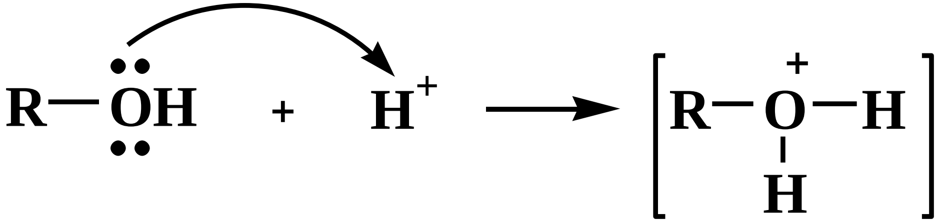
Conjugate base of phenol

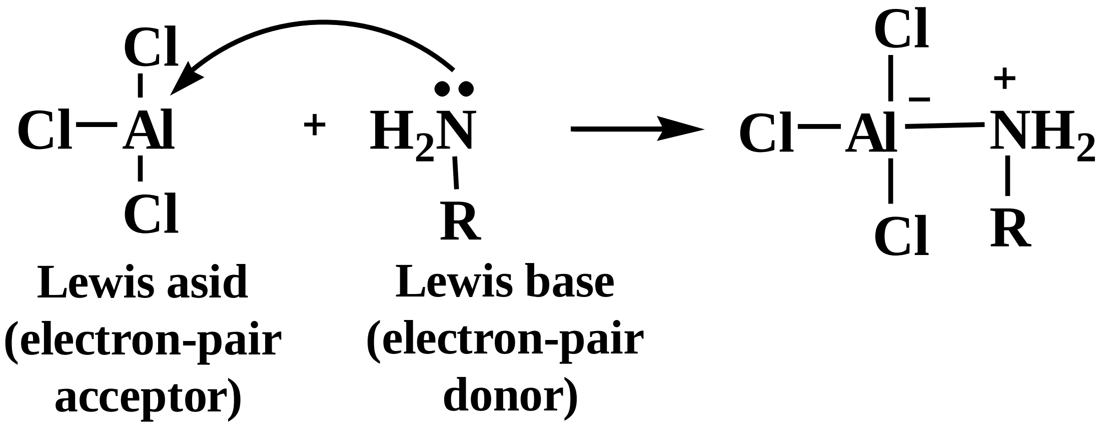
Conjugate acid of OH^-

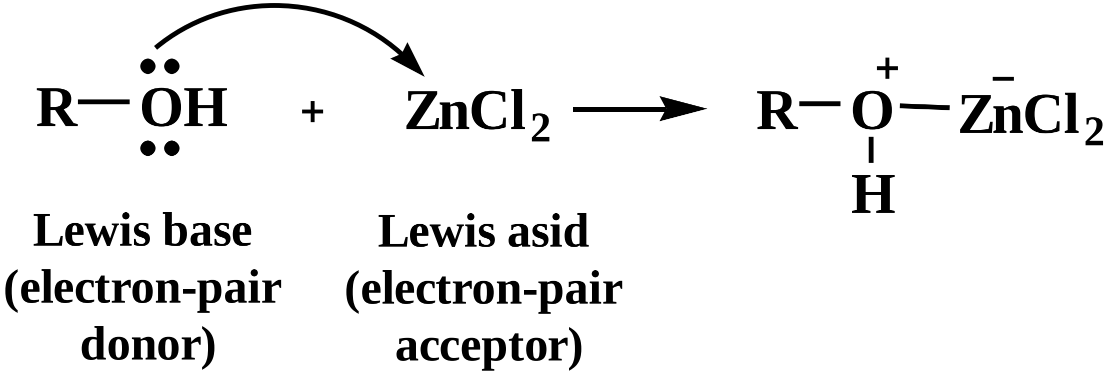
THE LEWIS DEFINITION OF ACIDS AND BASES

Lewis proposed that **acid** be defined as electron-pair acceptor and **base** be defined as electron-pair donor.









CLASSIFICATION OF REAGENTS IN ORGANIC REACTIONS

Chemists classify reagents in organic reactions as either electrophiles or nucleophiles according to the **Lewis theory**.

An ***electrophilic*** reagent is a Lewis acid, it reacts with electron-rich substrates that is a Lewis base.

A ***nucleophilic*** reagent is a Lewis base, it reacts with an electron-poor substrate that is a Lewis acid.

Nucleophiles - Lewis bases

$^{\ominus}OH$, $CH_3O^{\ominus}$, $CH_3CH_2^{\ominus}$,

$^{\ominus}SH$, $CH_3S^{\ominus}$, $CH_3CH_2S^{\ominus}$,

$^{\ominus}CN$, $I^{\ominus}$, $Br^{\ominus}$, NH_3, $^{\ominus}CH_3$,

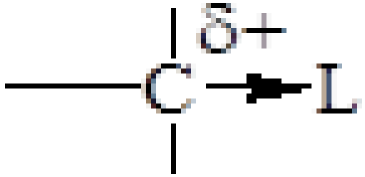
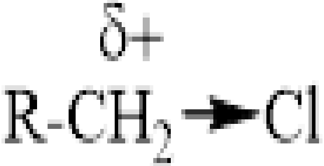
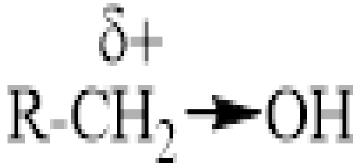
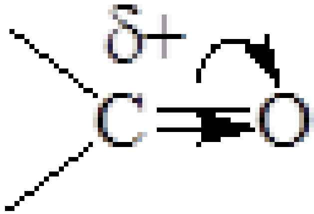
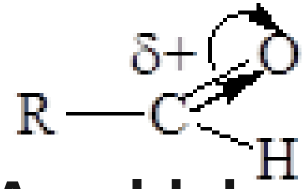
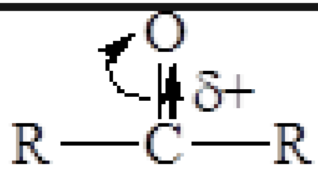
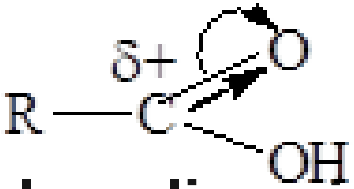
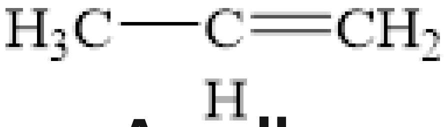
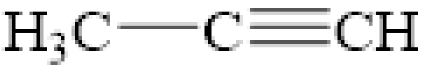
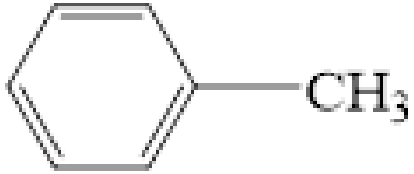
$CH_3\ddot{N}H_2$

Electrophiles - Lewis acids

$H^{\oplus}$, $Cl^{\oplus}$, $Br^{\oplus}$, $^{\oplus}CH_3$, BF_3,

$^{\oplus}NO_2$

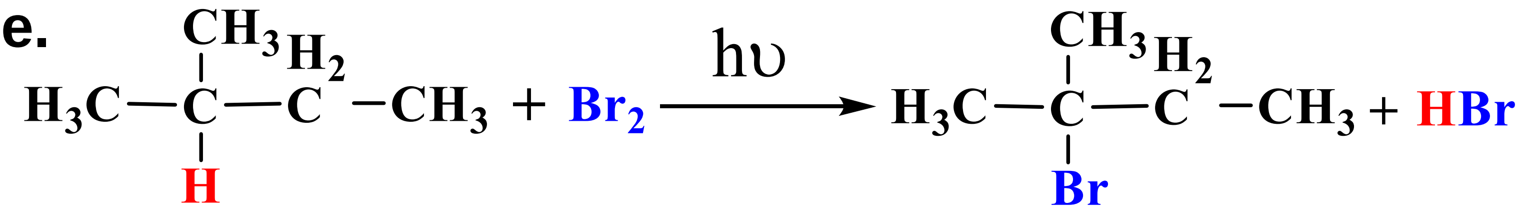
REACTION CENTERS IN SUBSTRATES

The type of reaction center	The sign in the structural formula.	Examples
Electrophilic (a Lewis acid)		 $\overset{\delta+}{R\text{-}CH_2} \rightarrow Cl$ a halocompound  $\overset{\delta+}{R\text{-}CH_2} \rightarrow OH$ an alcohol
		 An aldehyde  a ketone  a carboxylic acid
Nucleophilic (a Lewis base)	>C=C< -C≡C-	 An alkene  an alkyne  an arene

CLASSIFICATION OF ORGANIC REACTIONS:
substitution reactions

A substitution reaction is a type of reaction in which one atom or a group of atoms from the reagent replaces or substitutes itself for one atom or a group of atoms on the substrate.

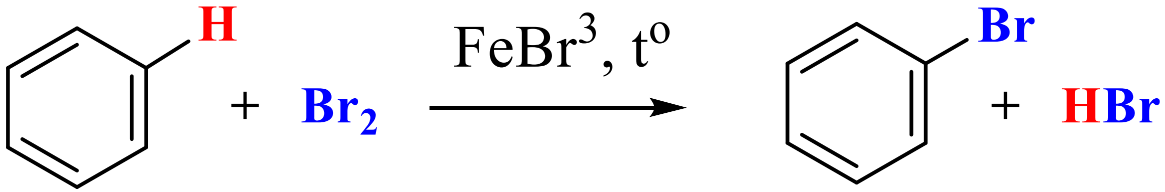
Alkanes



$$H_3C-\overset{CH_3}{\underset{H}{C}}-\overset{H_2}{C}-CH_3 + Br_2 \xrightarrow{h\upsilon} H_3C-\overset{CH_3}{\underset{Br}{C}}-\overset{H_2}{C}-CH_3 + HBr$$

S_R

Arenes
(nucleophilic substrate)



S_E

Alkyl halides
(electrophilic substrates)

$$CH_3\text{-}\overset{\delta+}{CH_2}\rightarrow Cl + Na\bar{O}H \xrightarrow{t^o} CH_3\text{-}CH_2\text{-}OH + NaCl$$

S_N

Alcohols
(electrophilic substrates)

$$CH_3\text{-}\overset{\delta+}{CH_2}\rightarrow OH + H\bar{Br} \xrightarrow{t^o} CH_3\text{-}CH_2\text{-}Br + HOH$$

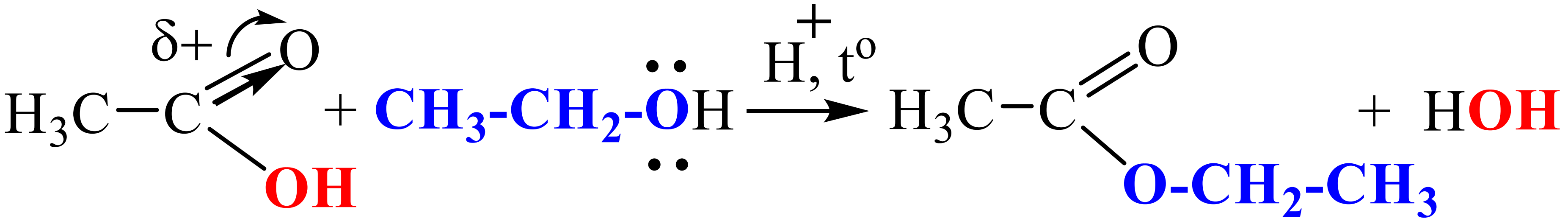
S_N

CLASSIFICATION OF ORGANIC REACTIONS:
substitution reactions

Carboxylic acids

(electrophilic substrates)

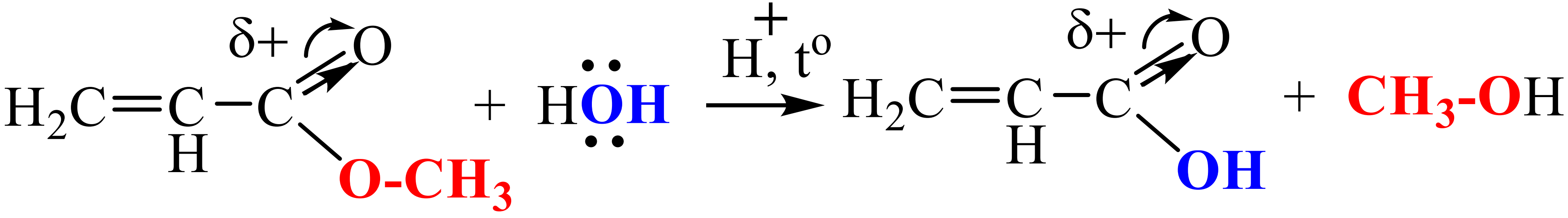
S_N



Esters

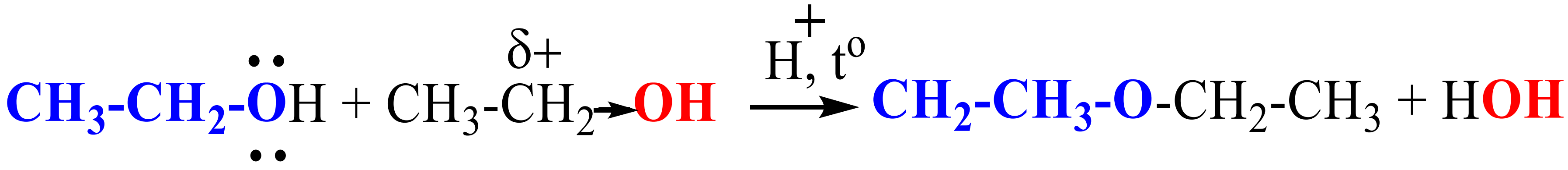
(electrophilic substrates)

S_N



CLASSIFICATION OF ORGANIC REACTIONS:
substitution reactions

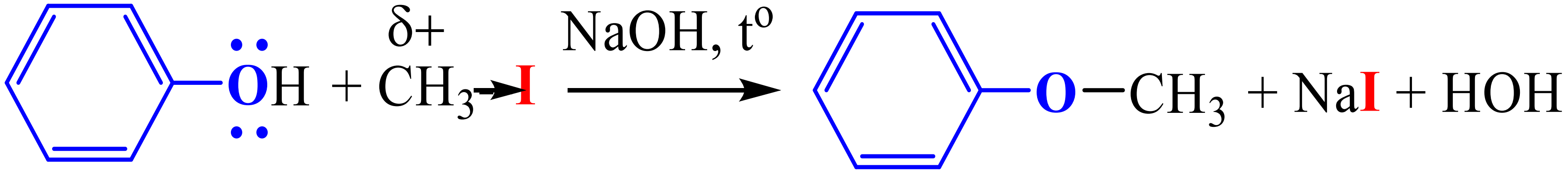
Alcohol
(nucleophilic reagent)



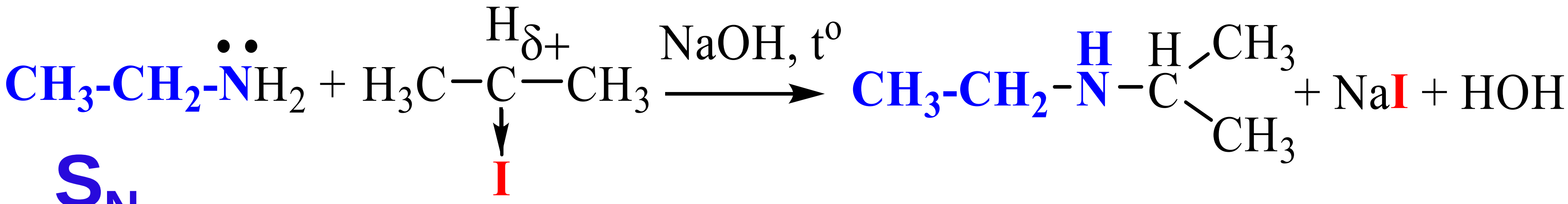
$$CH_3\text{-}CH_2\text{-}\underset{\cdot\cdot}{\ddot{O}}H + \overset{\delta+}{CH_3\text{-}CH_2}\rightarrow OH \xrightarrow{H^+,\ t^o} CH_2\text{-}CH_3\text{-}O\text{-}CH_2\text{-}CH_3 + HOH$$

S_N

Phenol
(nucleophilic reagent)



S_N



Amine
(nucleophilic Reagent)

S_N

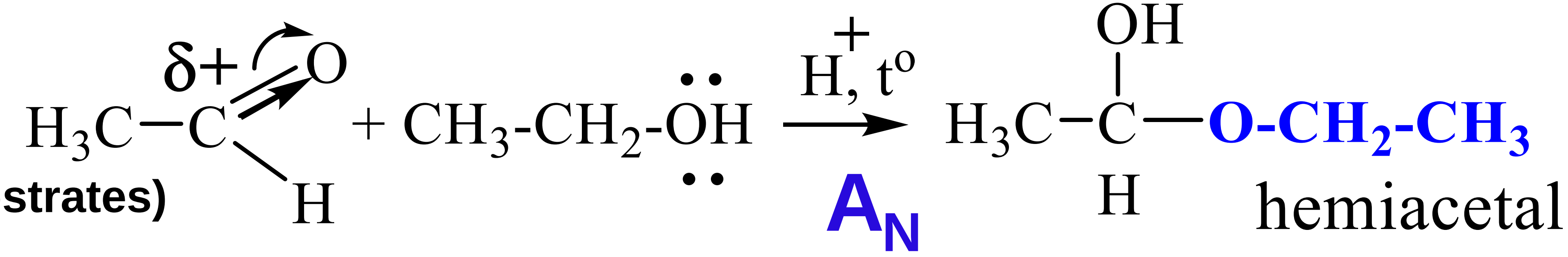
CLASSIFICATION OF ORGANIC REACTIONS:
addition reactions

In an **addition reaction**, atoms or groups of atoms from the reagent bond, or add, to the substrate without losing any atoms from the substrate and the reagent. The substrate for an addition reaction is an unsaturated molecule.

Alkenes
(nucleophilic substrate)

$$CH_3CH=CH_2 + HCl \xrightarrow{A_E} H_3C-\overset{H}{\underset{Cl}{C}}-CH_3$$

Aldehydes
(electrophilic substrates)

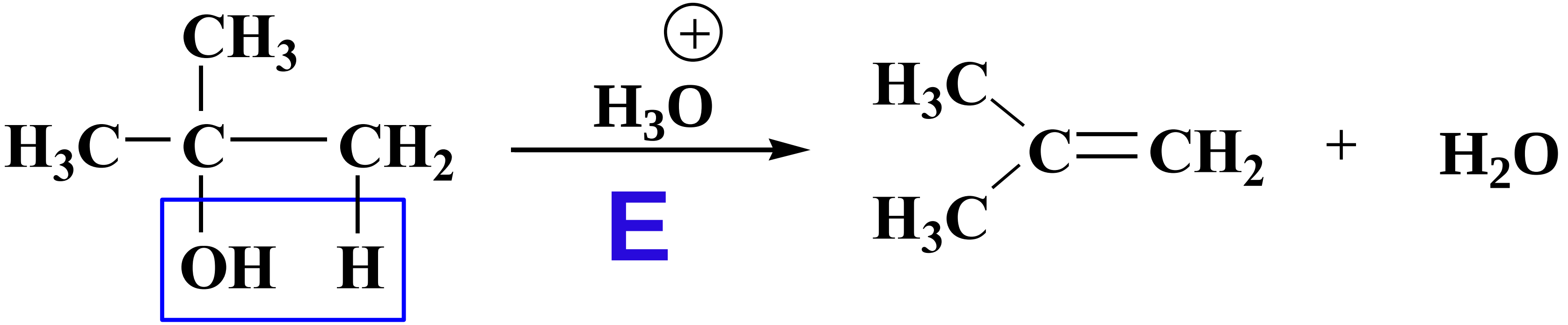


CLASSIFICATION OF ORGANIC REACTIONS

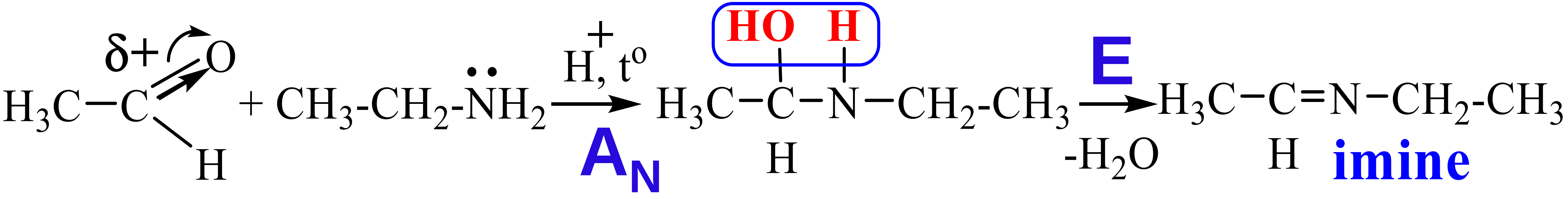
elimination reaction

An **elimination reaction** is the opposite of an addition reaction. An elimination reaction removes two atoms or two groups of atoms from the substrate, giving the product a multiple bond.

Alcohols



Aldehydes



Thank you

for

Your attention