Foundations of Biochemistry

September 6, 2016

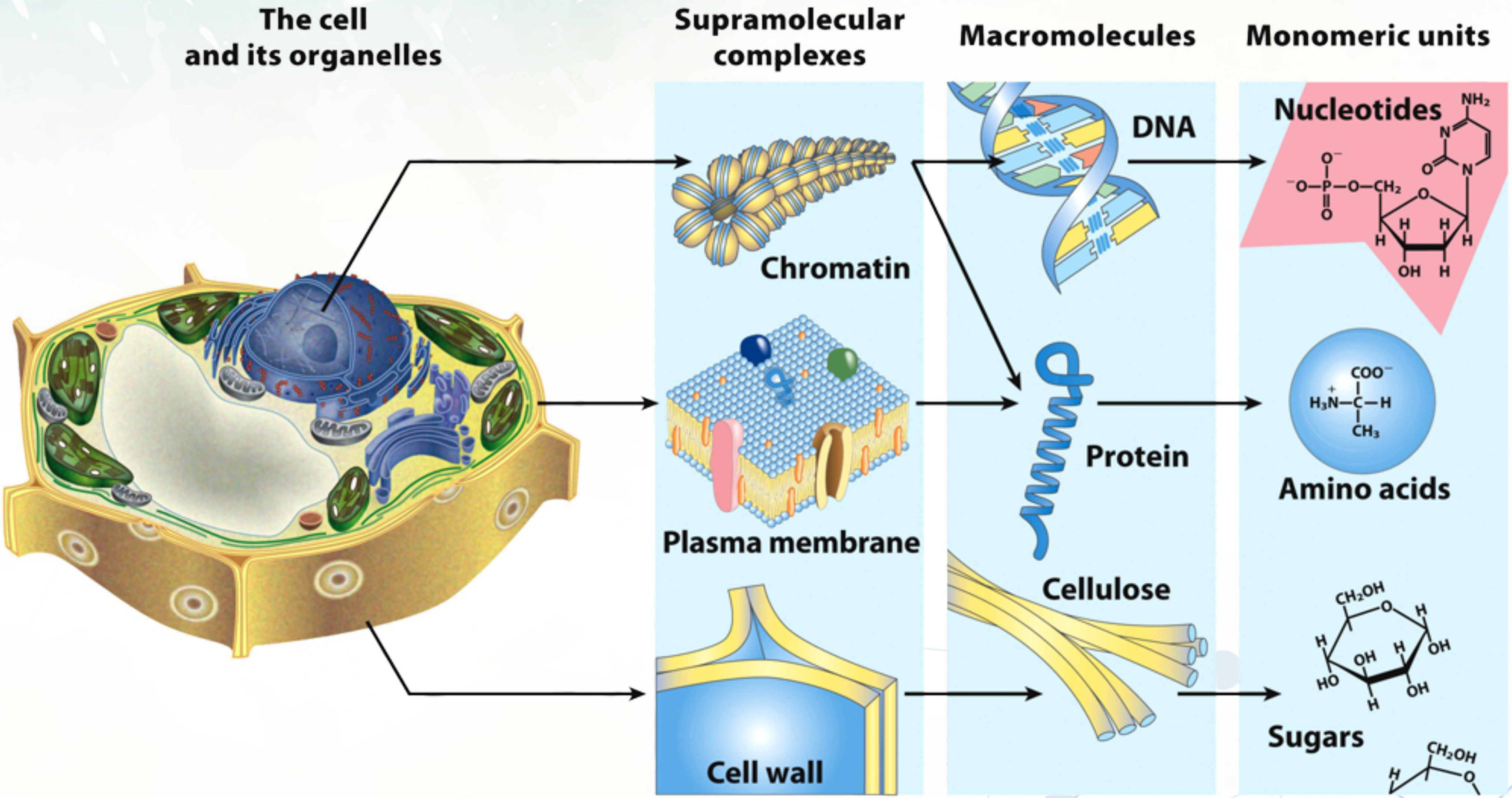
Primary Objectives

1. Understand the central dogma of molecular biology.
2. Comprehend chirality and isomerism.
3. Decipher the functional groups from one another.
4. Work the mechanism for each of the common reactions in biological systems.
5. Comprehend Gibbs free-energy.

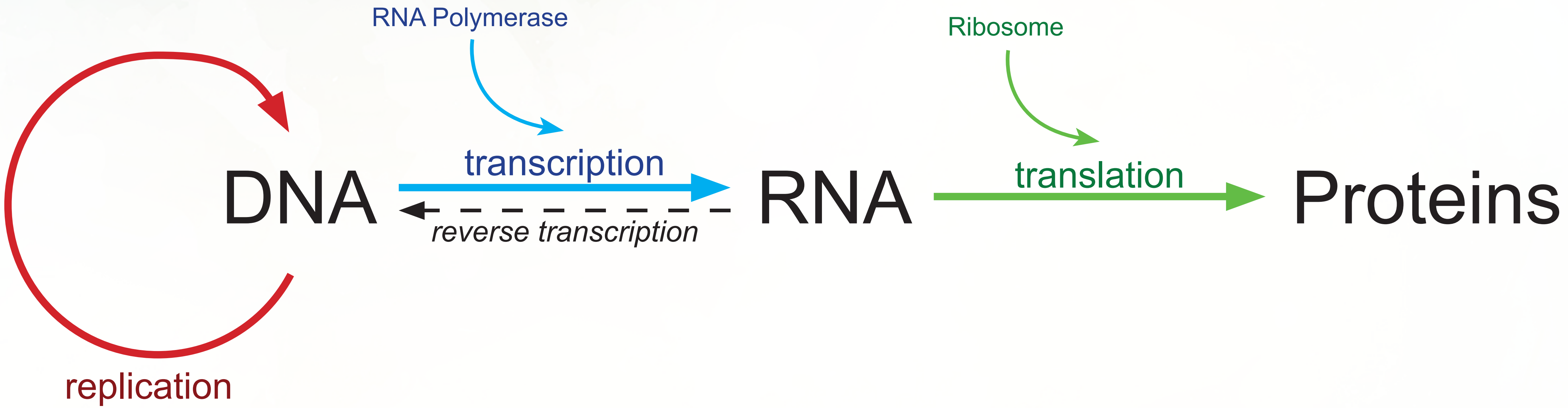
Section 1

Life

Basic Biomolecules Are Building Blocks for Macromolecule Structures



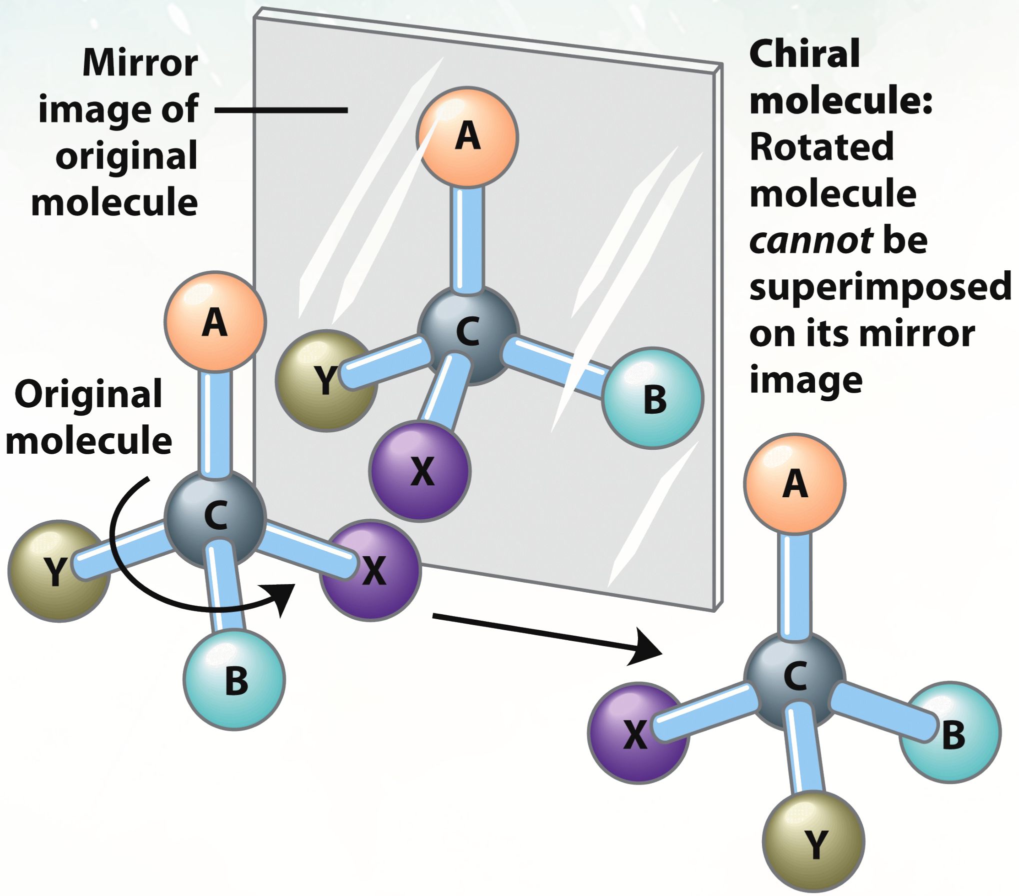
The Central Dogma of Molecular Biology Is Universal

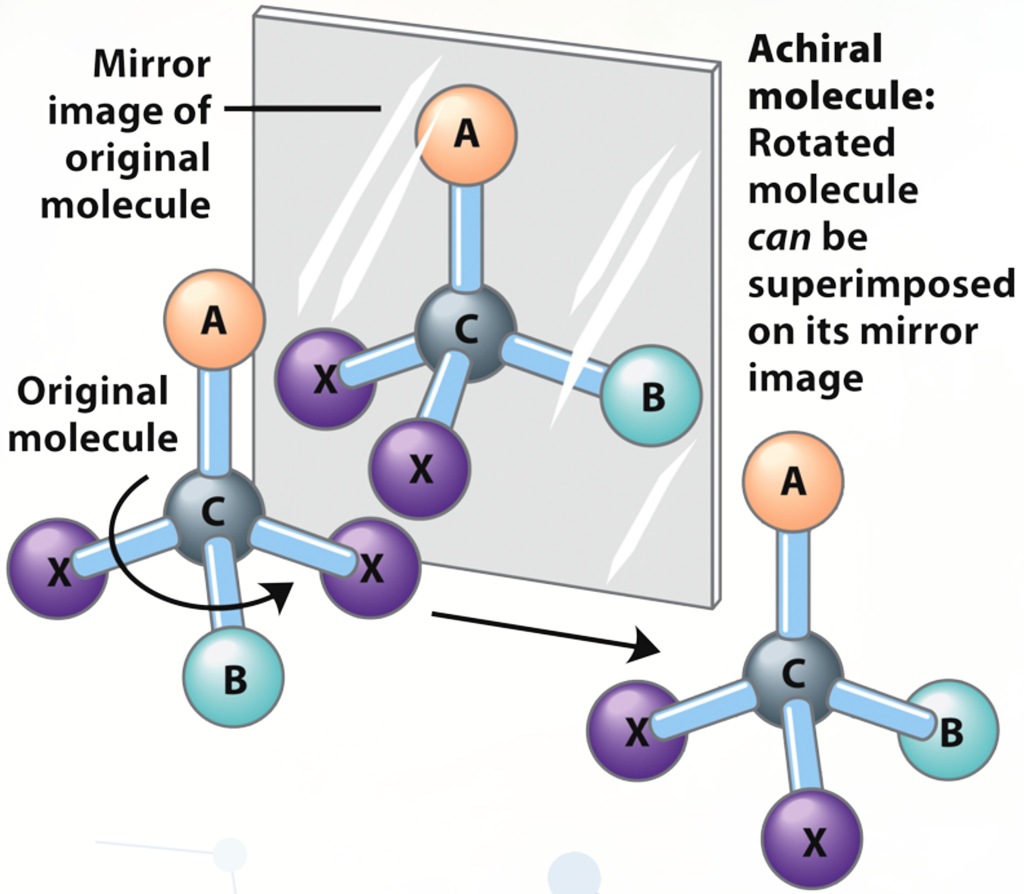


Section 2

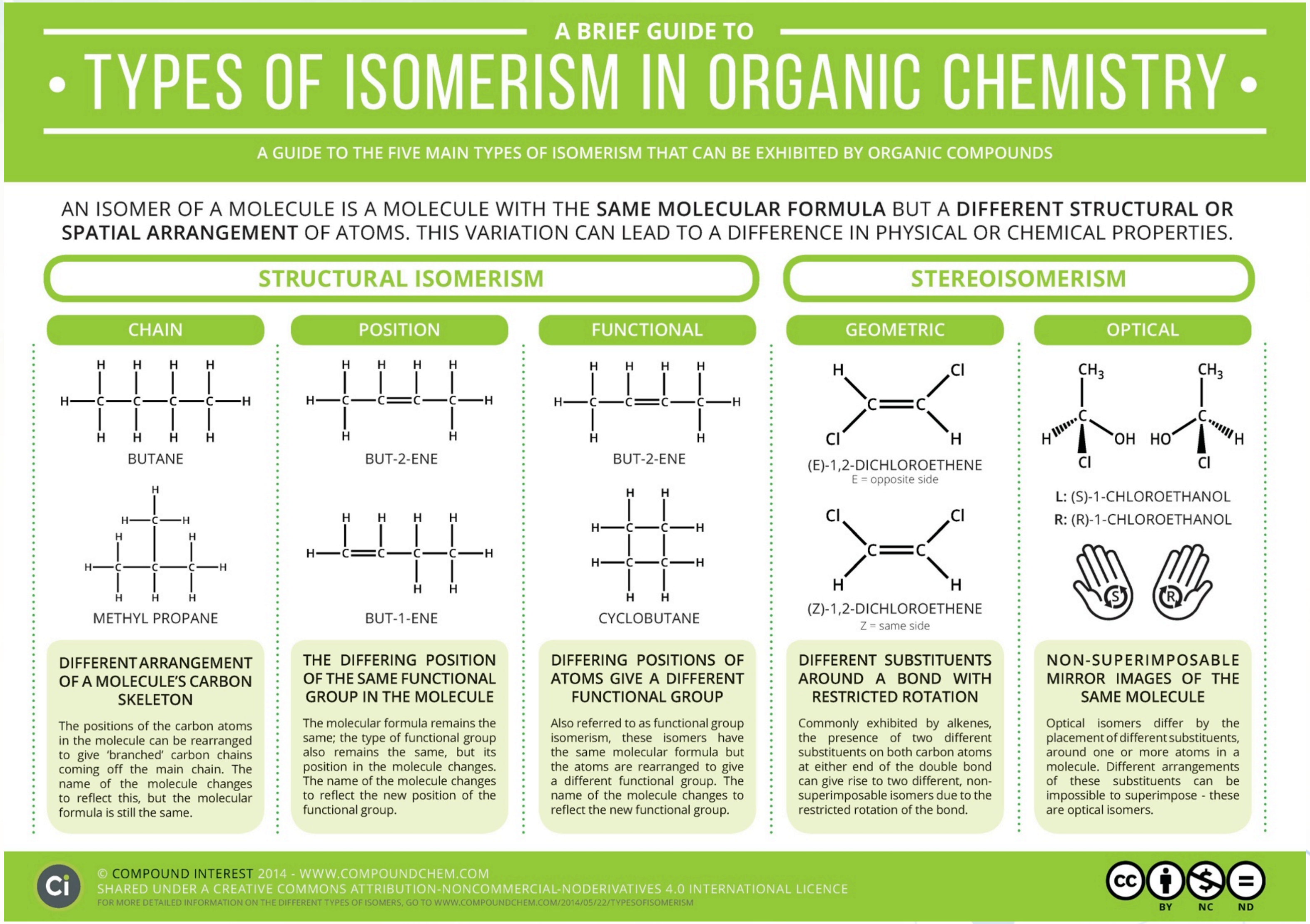
The Properties Of Molecules

Chirality Changes the Chemical Properties of Molecules





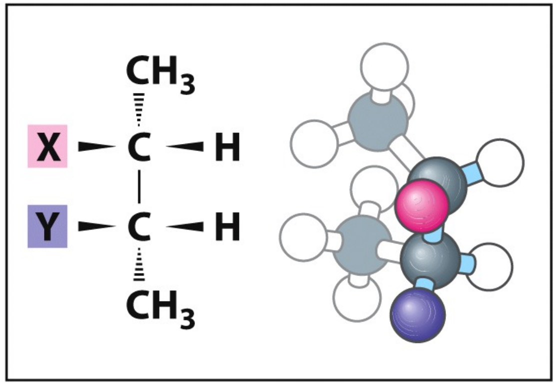
Types of Isomerism in Organic Chemistry



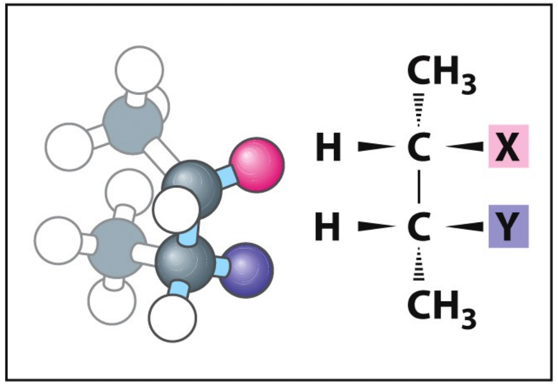
Isomeric Relationships Are Hierarchical

- Isomers
  - Constitutional Isomers
  - Stereoisomers
    - Configurational Isomers
      - Diastereomers
        - *cis/trans* isomers
        - Epimers
      - Enantiomers
    - Conformational Isomers

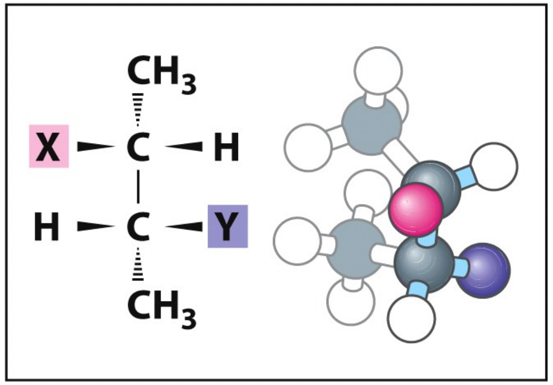
IN-CLASS EXERCISE:



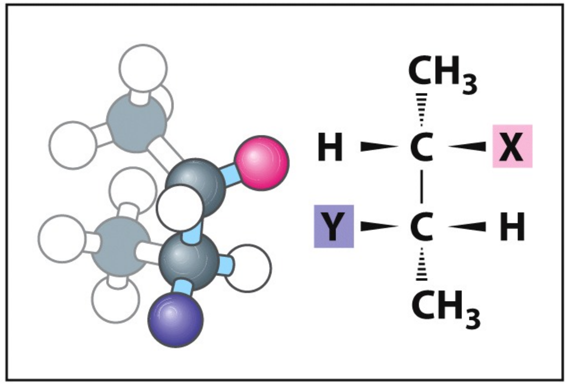
A



B



C



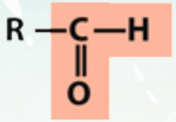
D

Which of the above molecules are enantiomers?

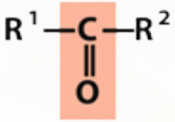
Which of the above molecules are diastereomers?

A Set of Functional Groups Are Common to Biochemical Reactions

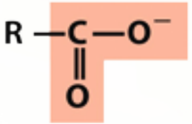
Carbonyl (aldehyde)



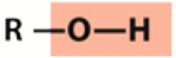
Carbonyl (ketone)



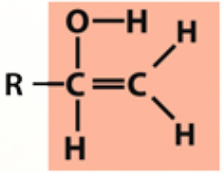
Carboxylate



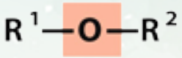
Hydroxyl (alcohol)



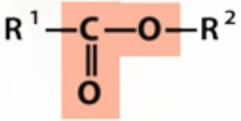
Enol



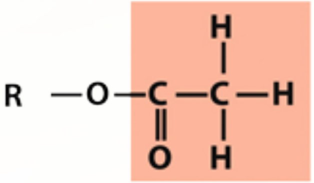
Ether



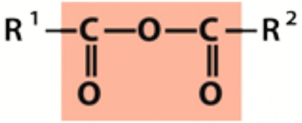
Ester



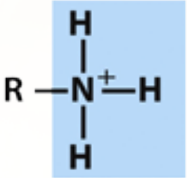
Acetyl



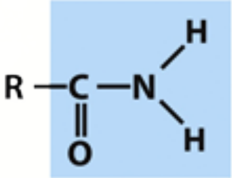
Anhydride (two carboxylic acids)



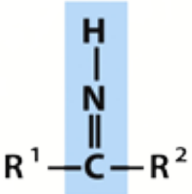
Amino (protonated)



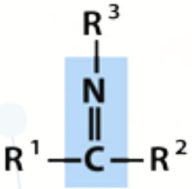
Amido



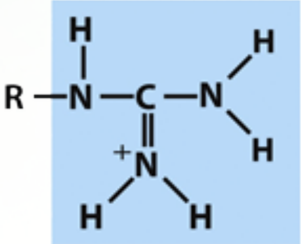
Imine



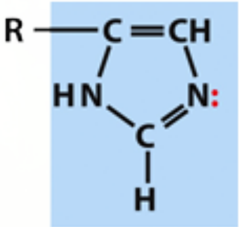
N-Substituted imine (Schiff base)



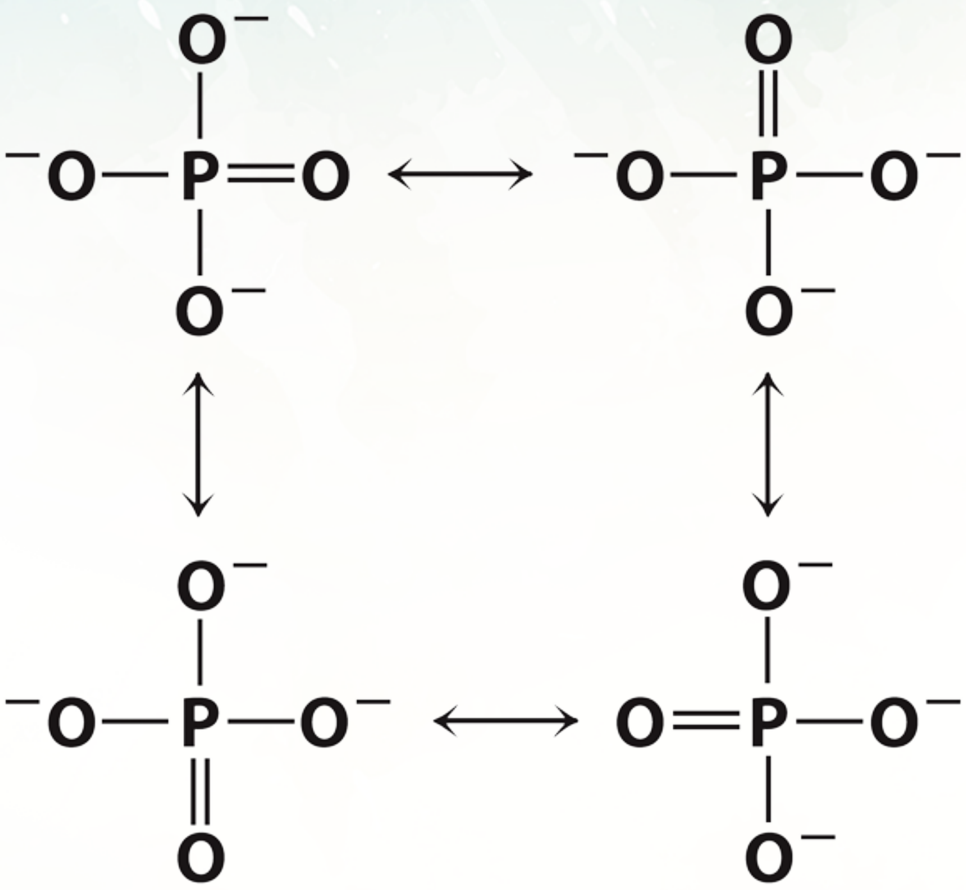
Guanidinium

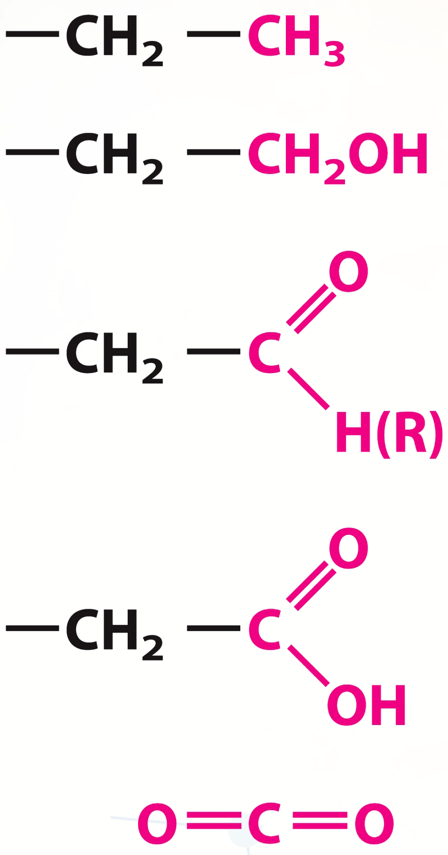


Imidazole



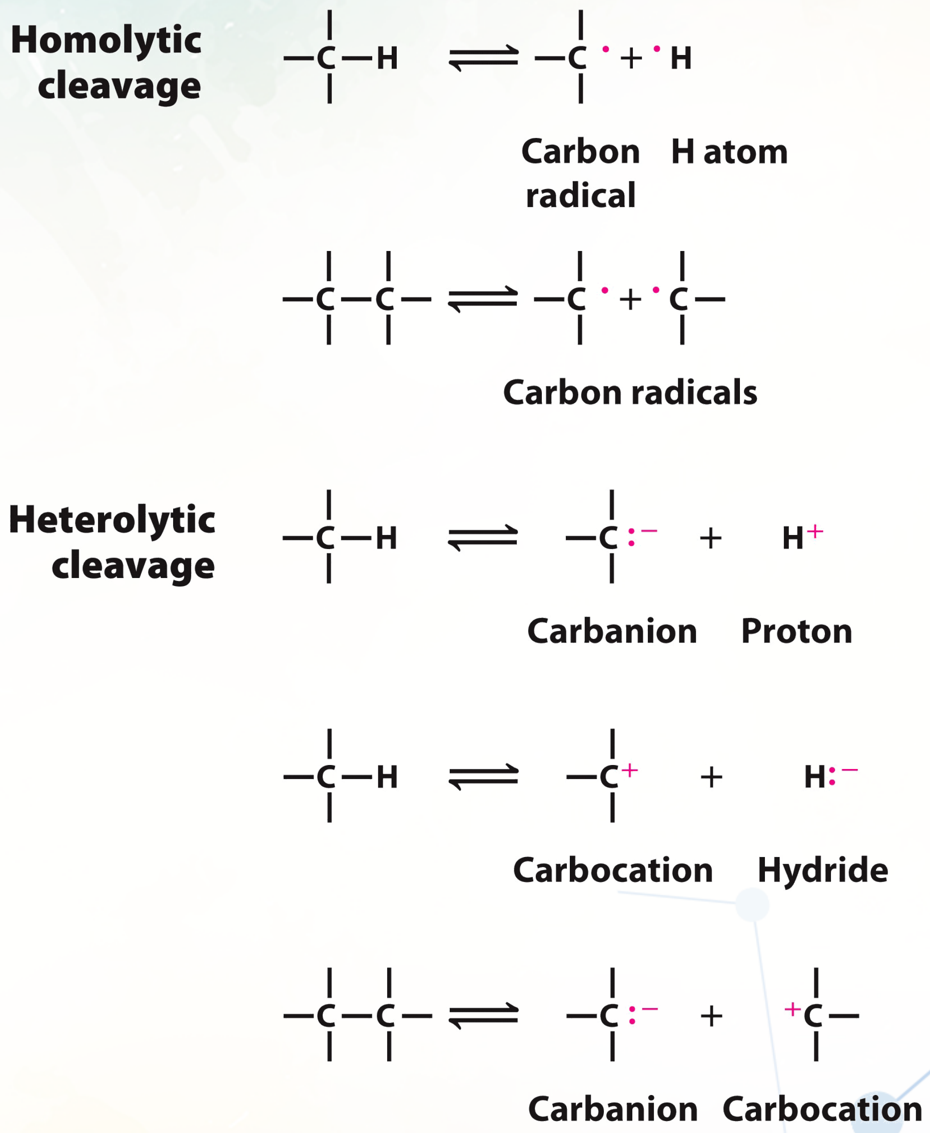
A Set of Functional Groups Are Common to Biochemical Reactions





- Alkane
- Alcohol
- Aldehyde (ketone)
- Carboxylic acid
- Carbon dioxide

Cleavage of C-C and C-H Bonds Can Be Homolytic or Heterolytic

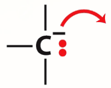


Common Nucleophiles and Electrophiles Are The Centers of Biochemical Reactions

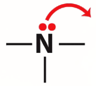
Nucleophiles

Negatively charged oxygen (as in an unprotonated hydroxyl group or an ionized carboxylic acid)

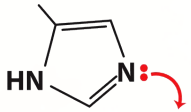
Negatively charged sulfhydryl



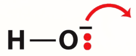
Carbanion



Uncharged amine group

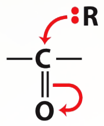


Imidazole

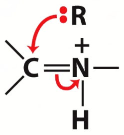


Hydroxide ion

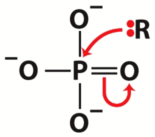
Electrophiles



Carbon atom of a carbonyl group (the more electronegative oxygen of the carbonyl group pulls electrons away from the carbon)



Protonated imine group (activated for nucleophilic attack at the carbon by protonation of the imine)



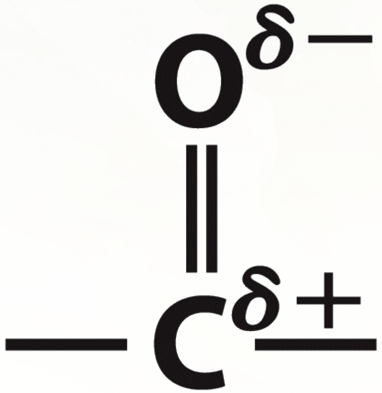
Phosphorus of a phosphate group

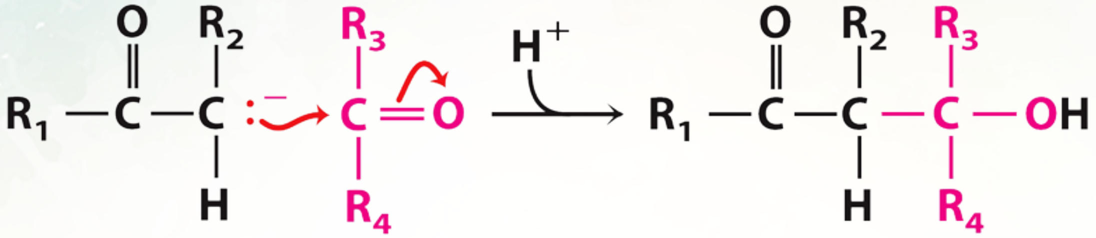
Proton

Section 3

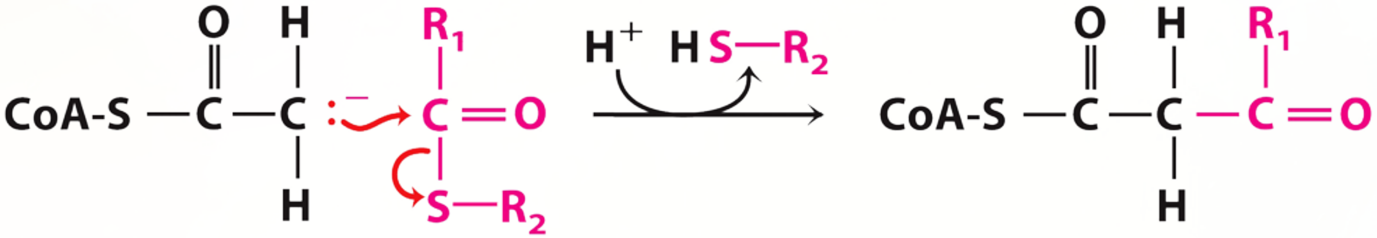
The Properties Of Reactions

There Are Common Reactions of Biological Systems

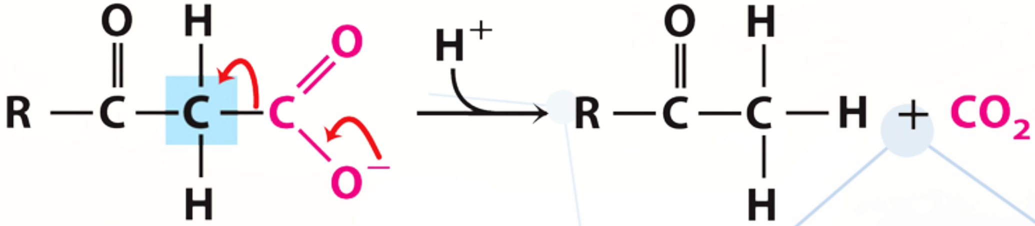




Aldol condensation

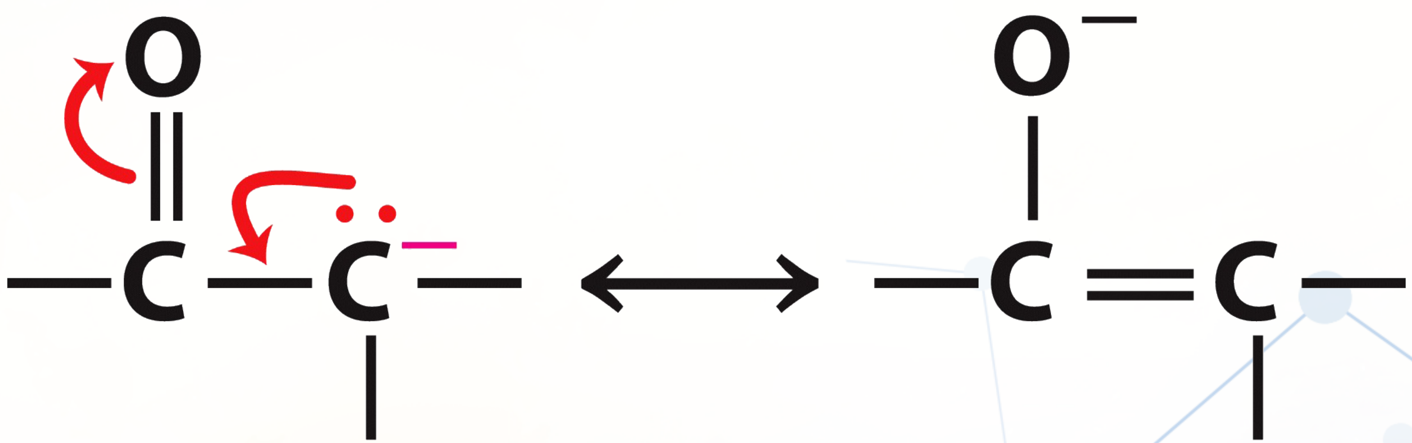


Claisen ester condensation

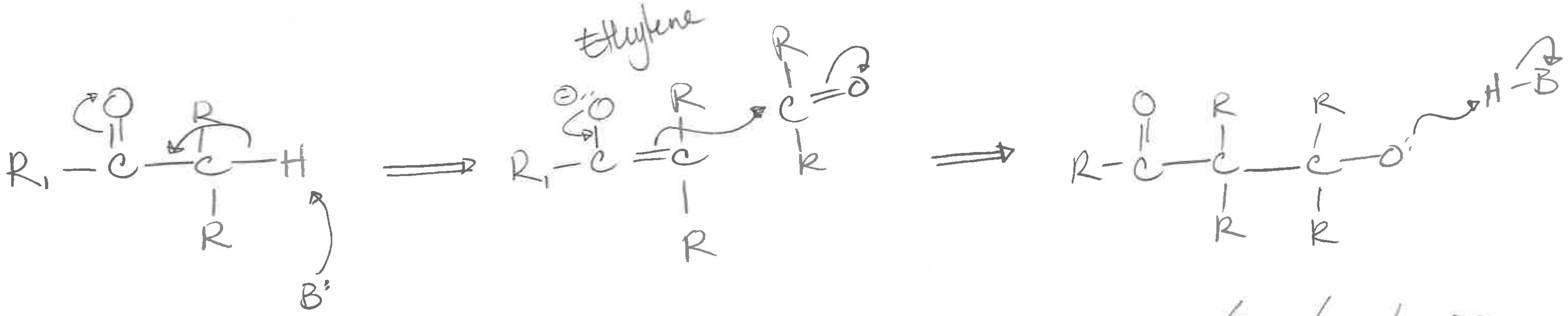


Decarboxylation of a β-keto acid

Delocalization of Electrons Are Stabilized on Nucleophiles

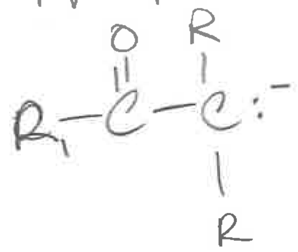


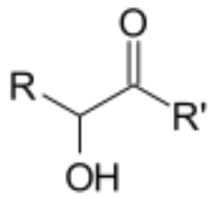
The Aldol Condensation Is One of the Most Common Mechanisms



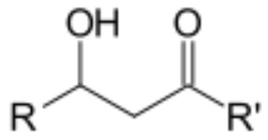
- can also be shown as a concerted mechanism
- the easiest base to use is OH^- and the easiest acid to use is H_2O

Also appropriate:



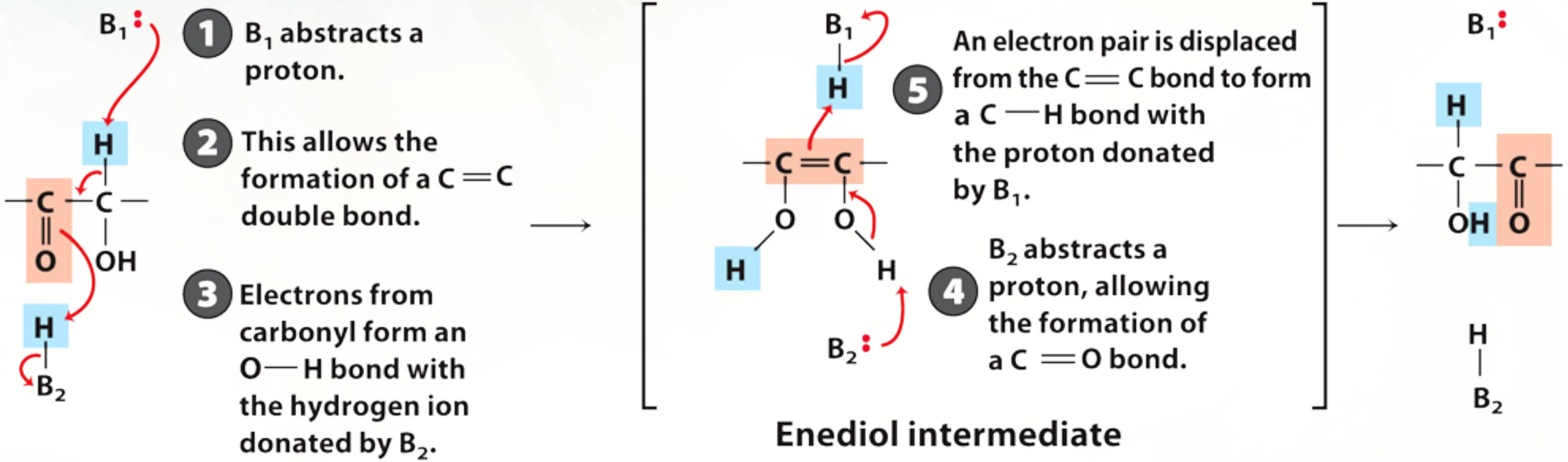


alpha-hydroxy ketone



beta-hydroxy ketone

Isomerizations Utilize a Cascade of Electrons



Section 4

The Properties of Free-energy

Gibbs Free-Energy Can Be Used for Work

- Free-energy (G) is the energy in a closed system that can be used to do work
- Enthalpy (H) reflects the number and kinds of bonds in the system that are being formed or broken
- Temperature (T) is the absolute temperature (in Kelvins)
- Entropy (S) describes the randomness or disorder of the components in a chemical system

$$\Delta G = \Delta H - T\Delta S$$

ΔG : free-energy change

ΔH : change in enthalpy

T : temperature

ΔS : change in entropy

Differences Between Notations Are Important Distinctions

$$\Delta G \neq \Delta G_f \neq \Delta G^{\circ\prime}$$

Enthalpy and Entropy of Formation Is Basic to Elemental Reactions

$$\Delta H_f \text{ and } \Delta S_f$$

IN-CLASS EXERCISE:

$$2K + Cl_2 \rightleftharpoons 2KCl$$

	$\Delta H_f°$ (kJ/mol)	$\Delta S_f°$ (J/mol)	$\Delta G_f°$ (kJ/mol)
KCl	-435.89	82.68	?
K	0	64.68	0
Cl_2	0	222.97	0

Calculate the $\Delta G_f°$ for KCl

Standard Free-Energy Change Is About Chemical Reactions from Molecules

- $\Delta G°'$ is an experimentally determined value
  - Specific for a particular reaction
- Standard states:
  - All reactants and products are at an initial concentration of 1.0M
  - 298.15 K (25.00 °C; 77.00 °F)
  - 1 atm (101.325 kPa; 14.696 psi)

$$\Delta G°' = -RT \ln K_{eq}$$

R : gas constant

T : absolute temperature

Standard state assumption

R, The Gas Constant, is Derived from Avogadro's Number

R is related to the Boltzmann constant, k, by:

R = k • NA

k = 1.3806 x 10-23 J•K-1

NA = 6.022 x 1023•mol-1

$$R = 8.314 \frac{J}{mol \bullet K}$$

Equilibrium & Steady State Are Similar, But Functionally Distinct

- Equilibrium (chemical equilibrium) is defined as the state of the system in which no net changes in [reactants] or [products]
- The Keq DOES NOT tell you anything about the spontaneity of the reaction
  - Keq < 1 : reactants at equilibrium are favored
  - Keq > 1 : products at equilibrium are favored
  - K'q ≈ 1 : both concentrations at equilibrium are similar (neither favored)

Given the reaction:

$$aA + bB \Leftrightarrow cC + dD$$

After the system has reached equilibrium:

$$K_{eq} = \frac{[C]_{eq}^{c}[D]_{eq}^{d}}{[A]_{eq}^{a}[B]_{eq}^{b}}$$

K_{eq} is the equilibrium constant

There Is a Relationship Between K'_{eq} and $\Delta G'^{\circ}$

TABLE 13–3 Relationships among K'_{eq}, $\Delta G'^{\circ}$, and the Direction of Chemical Reactions

When K'_{eq} is . . .	$\Delta G'^{\circ}$ is . . .	Starting with all components at 1 M, the reaction . . .
>1.0	negative	proceeds forward
1.0	zero	is at equilibrium
<1.0	positive	proceeds in reverse

Table 13-3
Lehninger Principles of Biochemistry, Sixth Edition

TABLE 13–2 Relationship between Equilibrium Constants and Standard Free-Energy Changes of Chemical Reactions

	$\Delta G'^{\circ}$	
K'_{eq}	(kJ/mol)	(kcal/mol)*
10^{3}	−17.1	−4.1
10^{2}	−11.4	−2.7
10^{1}	−5.7	−1.4
1	0.0	0.0
10^{-1}	5.7	1.4
10^{-2}	11.4	2.7
10^{-3}	17.1	4.1
10^{-4}	22.8	5.5
10^{-5}	28.5	6.8
10^{-6}	34.2	8.2

*Although joules and kilojoules are the standard units of energy and are used throughout this text, biochemists and nutritionists sometimes express $\Delta G'^{\circ}$ values in kilocalories per mole. We have therefore included values in both kilojoules and kilocalories in this table and in Tables 13–4 and 13–6. To convert kilojoules to kilocalories, divide the number of kilojoules by 4.184.

Table 13-2
Lehninger Principles of Biochemistry, Sixth Edition

TABLE 13–1 Some Physical Constants and Units Used in Thermodynamics

Boltzmann constant,	$\mathbf{k} = 1.381 \times 10^{-23}$ J/K
Avogadro's number,	$N = 6.022 \times 10^{23}$ mol^{-1}
Faraday constant,	$\mathcal{F} = 96{,}480$ J/V·mol
Gas constant,	$R = 8.315$ J/mol·K
	(= 1.987 cal/mol·K)

Units of ΔG and ΔH are J/mol (or cal/mol)

Units of ΔS are J/mol·K (or cal/mol·K)

1 cal = 4.184 J

Units of absolute temperature, T, are Kelvin, K

25 °C = 298 K

At 25 °C, $RT = 2.478$ kJ/mol

(= 0.592 kcal/mol)

Table 13-1
Lehninger Principles of Biochemistry, Sixth Edition