Lecture 11
Discipline: Bioorganic Chemistry
Lecturer: Associate Professor, Dr. Gulnaz Seitimova

Title: Hydroxy and oxoacids. Classification, distribution, application, physiological role of hydroxy and oxoacids, their preparation and chemical properties. Keto-enol tautomerism of oxoacids.

Objective: The aim of this lecture is to introduce the structural, chemical, and biological characteristics of hydroxy acids and oxoacids, explore their classification, describe their physiological significance in humans and other organisms, and examine the phenomenon of keto–enol tautomerism in oxoacids.

Main Questions: Classification and general characteristics of hydroxy acids and oxoacids. Distribution in nature. Methods of preparation. Chemical properties. Biological and physiological roles. Application in medicine, biochemistry, and industry. Keto-enol tautomerism in oxoacids.

Key Notes and Theses

Introduction

Hydroxy acids and oxoacids are organic acids containing functional groups such as hydroxyl (–OH) or carbonyl (>C=O) in addition to the carboxyl group. The presence of additional functional groups significantly affects their reactivity, stability, acidity, and biological roles. Many of these compounds play essential functions in metabolic pathways, energy production, biosynthesis, and regulation of physiological processes.

Classification of Hydroxy Acids

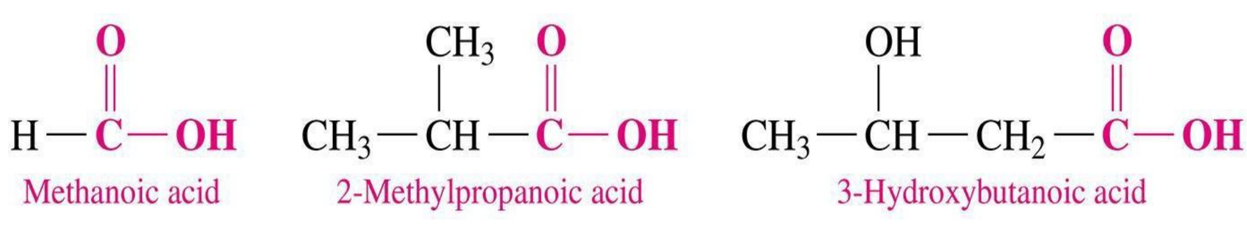
Hydroxy acids contain one or more hydroxyl (–OH) groups attached to the carbon chain of a carboxylic acid.

Types of Hydroxy Acids:

1. *α*-Hydroxy acids (α-HAs): –OH on the carbon adjacent to –COOH
   - Examples: *lactic acid, glycolic acid, mandelic acid*
2. *β*-Hydroxy acids (β-HAs): –OH on the second carbon from –COOH
   - Examples: *β-hydroxybutyric acid*
3. γ- and δ-Hydroxy acids: longer distances from –COOH
   - Examples: *γ-hydroxybutyric acid (GHB), δ-hydroxyvaleric acid*

General Properties

- Exhibit both acidic (–COOH) and alcoholic (–OH) properties
- Can undergo internal esterification (lactonization)
- Form hydrogen bonds, increasing boiling points and solubility



Classification of Oxoacids

Oxoacids contain an oxo group (>C=O) located in the structure of the carboxylic acid.

Types of Oxoacids:

1. Aldo-oxoacids: carbonyl group as an aldehyde
   - Example: *pyruvic acid* (CH_3*–CO–COOH)*
2. Ketoacids: ketone functional group alongside –COOH
   - Examples:
     - *acetoacetic acid* (β-ketoacid)
     - *oxaloacetic acid*
     - *α-ketoglutaric acid*

General Properties

- Highly reactive due to the electrophilic carbonyl carbon
- Can undergo decarboxylation, reduction, and condensation reactions
- Exhibit keto–enol tautomerism

Distribution in Nature

Hydroxy and oxoacids are widely distributed in biological systems:

Hydroxy Acids:

- Lactic acid: product of anaerobic glycolysis
- Glycolic & citric acids: found in plants, fruits
- Malic acid: key intermediate in the TCA cycle
- Mandelic acid: found in bitter almonds

Oxoacids:

- Pyruvic acid: central metabolic intermediate
- Oxaloacetic acid: TCA cycle intermediate
- α-Ketoglutaric acid: important in amino acid metabolism
- Acetoacetic acid: ketone body produced during fasting

Preparation of Hydroxy Acids

1. Oxidation of polyhydric alcohols:
   - Ethylene glycol → glycolic acid
2. Hydrolysis of cyanohydrins:
   - R–CH(OH)–CN → R–CH(OH)–COOH
3. Aldol reaction followed by oxidation
4. Fermentation processes:
   - Lactic acid via *Lactobacillus* species

Preparation of Oxoacids

1. Controlled oxidation of α-hydroxy acids
   - Lactic acid → pyruvic acid
2. Oxidation of ketones or aldehydes
3. Biochemical pathways:
   - Transamination reactions produce α-ketoacids
4. Decarboxylation of β-ketoacids:
   - Produces enolate intermediates

5. Chemical synthesis via Claisen condensation

Chemical Properties

Hydroxy Acids

- Esterification: alcohol groups can form esters
- Dehydration to lactones (especially with γ- and δ-hydroxy acids)
- Oxidation to oxoacids
- Acid-base reactions: dissociate to form carboxylate ions

Oxoacids

- Keto–enol tautomerism
- Decarboxylation reactions:
  - β-ketoacids easily decarboxylate to form ketones
- Reduction:
  - carbonyl group reduced to hydroxy acids
- Condensation reactions:
  - Aldol and Claisen condensations

Physiological Role

Hydroxy Acids:

- Lactic acid:
  - Regulates muscle metabolism under anaerobic conditions
  - Serves as a gluconeogenic substrate
- Citric and malic acids:
  - Key intermediates of the Krebs cycle
- β-Hydroxybutyric acid:
  - Major ketone body during fasting
- Glycolic and malic acids:
  - Contribute to plant metabolism

Oxoacids:

- Pyruvic acid:
  - Central node linking glycolysis, gluconeogenesis, and TCA cycle
- Oxaloacetic acid:
  - Accepts acetyl-CoA in the TCA cycle
  - Important for amino acid biosynthesis
- α-Ketoglutaric acid:
  - Key substrate for transamination
- Acetoacetic acid:
  - Alternative energy source during fasting or diabetes

Applications

Hydroxy and oxoacids are widely used in:

Medicine:

- α-Hydroxy acids for dermatology (peeling, regeneration)

- Lactic acid in IV solutions to correct acidosis
- Pyruvate as metabolic supplement

Industry:

- Food industry (acidifiers, preservatives)
- Production of biodegradable plastics (polylactic acid)
- Synthesis of pharmaceuticals

Biotechnology:

- Fermentation processes
- Biosensors and metabolic engineering

Keto–Enol Tautomerism of Oxoacids

Definition

Keto–enol tautomerism is a dynamic equilibrium between a carbonyl (keto) form and an enol form containing a C=C double bond and a hydroxyl group.

Example: Pyruvic Acid

- Predominantly keto form
- Enol form stabilized by hydrogen bonding

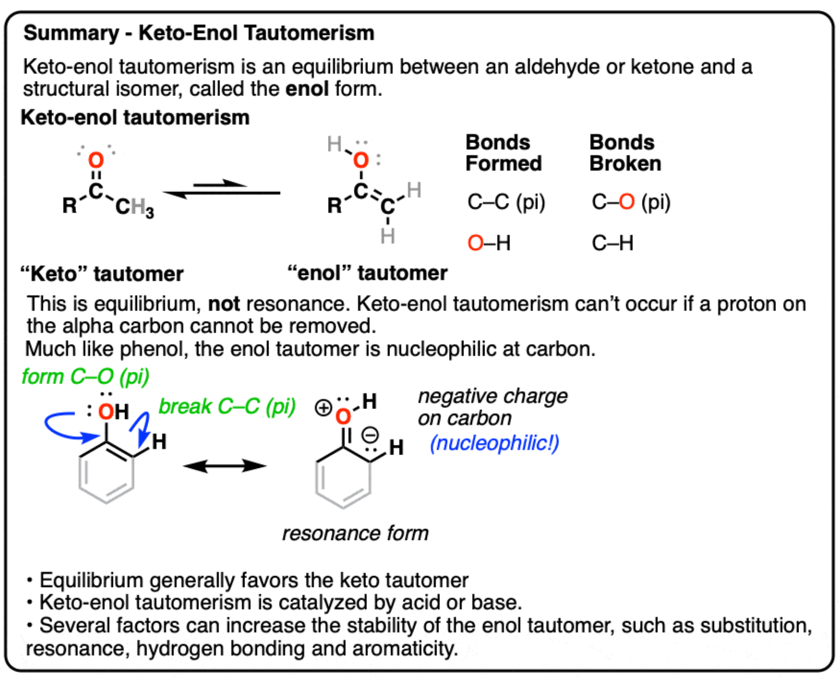
Importance:

- Determines acidity of α-hydrogen
- Responsible for α-ketoacid reactivity
- Plays a key role in:
  - Aldol reactions
  - Enzyme-catalyzed isomerizations
  - Decarboxylation of β-ketoacids

General Scheme:

R–CO–CH_2–COOH ⇌ R–C(OH)=CH–COOH

The enol form contributes to nucleophilicity and reaction specificity in biochemical pathways.



Questions for Knowledge Assessment

1. Define hydroxy acids and oxoacids.
2. How are hydroxy acids classified according to their structure?
3. Provide examples of physiologically important oxoacids.
4. Describe the main chemical reactions of hydroxy acids.
5. Explain the mechanism and significance of keto–enol tautomerism.
6. Why are β-ketoacids prone to decarboxylation?
7. Describe the biological role of pyruvic and α-ketoglutaric acids.

Recommended Literature

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