MODERN MEDICINE AND PRACTICE
https://inovatus.es/index.php/ejmmp
EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 5 No. 12 (Dec - 2025) EJMMP ISSN: 2795-921X

DERIVATIVES OF KETO ACIDS WITH HYDRAZINE AND THEIR METAL COMPLEXES

Amrilloyev Akbar Azamat O'g'li
Lecturer, Asia International University

Abstract: This article provides a detailed overview of the chemistry of keto acids and their reactions with hydrazine to form hydrazones. The structural features, physicochemical properties, and coordination behavior of hydrazone derivatives toward metal ions are discussed. Examples of synthesis, spectral characterization, and complex formation mechanisms are presented, highlighting their analytical, biological, and coordination chemistry applications.

Introduction Keto acids (α-keto acids) are organic compounds that contain both a ketone group (–CO–) and a carboxylic acid group (–COOH) within the same molecule. These compounds play essential roles in metabolic pathways (e.g., pyruvate, α-ketoglutarate). Their reactivity toward nucleophiles, especially hydrazine ($NH_2–NH_2$) and its derivatives, results in the formation of hydrazones, which are important ligands in coordination chemistry.

Hydrazone derivatives of keto acids serve as bidentate ligands, producing highly stable chelate complexes with transition metal ions. This property makes them valuable in analytical chemistry, bioinorganic chemistry, and catalyst design.

2. Reaction of Keto Acids with Hydrazine

2.1. Reaction Mechanism

The reaction between a keto acid and hydrazine proceeds via:

Step 1: Nucleophilic attack

The $–NH_2$ group of hydrazine attacks the electrophilic carbonyl carbon of the keto group:

R–CO–COOH+NH2NH2→R–C(OH)(NHNH2)–COOHR–CO–COOH + NH2NH2 R–C(OH)(NHNH2)–COOHR–CO–COOH+NH2NH2→R–C(OH)(NHNH2)–COOH

Step 2: Dehydration

The intermediate loses water to form the hydrazone:

R–C(OH)(NHNH2)–COOH→R–C=NNH2–COOH+H2OR–C(OH)(NHNH2)–COOH R–C=NNH2–COOH + H2OR–C(OH)(NHNH2)–COOH→R–C=NNH2–COOH+H2O

General equation:

R–CO–COOH+NH2–NH2→R–C=NNH2–COOH+H2OR–CO–COOH + NH2–NH2 R–C=NNH_2 –COOH + H_2OR–CO–COOH+NH2–NH2→R–C=NNH2–COOH+H2O

2.2. Examples of Keto Acids and Their Hydrazone Derivatives

Example 1: Pyruvic acid ($CH_3–CO–COOH$) + hydrazine

$CH3–CO–COOH+NH2NH2→CH3–C=NNH2–COOH+H2OCH3–CO–COOH + NH2NH2 CH3–C=NNH2–COOH + H2OCH3–CO–COOH+NH2NH2→CH3–C=NNH2–COOH+H2O$

Product: Pyruvic acid hydrazone

Example 2: α-Ketoglutaric acid + hydrazine

$HOOC–CH2–CH2–CO–COOH+NH2NH2→HOOC–CH2–CH2–C=NNH2–COOH+H2OHOOC–CH2–CH2–CO–COOH + NH_2NH2$

$HOOC–CH_2–CH_2–C=NNH_2–COOH + H_2OHOOC–CH2–CH2–CO–COOH+NH2NH2→HOOC–CH2–CH2–C=NNH2–COOH+H2O$

Product: α-Ketoglutaric acid monohydrazone

Example 3: Phenylhydrazine reaction

Phenylhydrazine forms more stable, colored hydrazones:

$R–CO–COOH+C6H5NHNH2→R–C=NNHC6H5–COOH+H2OR–CO–COOH + C6H5NHNH2 R–C=NNHC6H5–COOH + H2O$

$R–CO–COOH+C6H5NHNH2→R–C=NNHC6H5–COOH+H2O$

These derivatives are important in identification reactions (Brady's test).

3. Structural Properties of Keto Acid Hydrazones

3.1. Structural Features

Hydrazones contain the characteristic $C=N–NH_2$ (or C=N–NHR) azomethine group.

Key features:

- Bidentate donor atoms:
  - Azomethine nitrogen (–C=N–)
  - Carboxylate oxygen ($–COO^-$)
- Possible tautomerism:
  - Keto–enol
  - Amide–imine
- Intramolecular hydrogen bonding, increasing stability.

3.2. Spectroscopic Characteristics

IR spectroscopy:

- C=N stretch: 1600–1640 cm^{-1}
- Carboxylate stretch: 1300–1400 cm^{-1}

UV-Vis spectroscopy:

- $n→π^*$ transitions of azomethine
- d–d transitions in metal complexes

^{1}H NMR:

- –NH hydrogens around 4–6 ppm

4. Metal Complexes of Keto Acid Hydrazones

Because hydrazones contain an azomethine nitrogen and a carboxylate oxygen, they act as bidentate chelating ligands, forming stable complexes with many transition metals.

4.1. General Complex Formation Mechanism

Step 1: Deprotonation

R–C=NNH2–COOH→R–C=NNH2–COO−+H+R–C=NNH2–COOH

R–C=NNH2–COO^- + H^+R–C=NNH2–COOH→R–C=NNH2–COO−+H+

Step 2: Coordination

Mn++L2−→[M(L)](n−2)+M^{n+} + L^{2-} \rightarrow [M(L)]^{(n-2)+}Mn++L2−→[M(L)](n−2)+

Chelate ring formation

A 5- or 6-membered ring is formed through:

- N (azomethine) → M
- O (carboxylate) → M

This greatly increases stability (chelate effect).

4.2. Examples of Metal Complexes

Example 1: Cu(II) complex

Cu2++HL→[CuL]+H+Cu^{2+} + HL \rightarrow [CuL] + H^+Cu2++HL→[CuL]+H+

Color: yellow-brown or orange

Example 2: Ni(II) complex

Ni2++HL→[NiL]+H+Ni^{2+} + HL \rightarrow [NiL] + H^+Ni2++HL→[NiL]+H+

Color: greenish or light yellow

Example 3: Fe(III) complex

Forms intensely colored complexes, often red-brown:

Fe3++HL→[FeL]++H+Fe^{3+} + HL \rightarrow [FeL]^{+} + H^+Fe3++HL→[FeL]++H+

Example 4: Zn(II) and Cd(II) complexes

These metals form colorless or pale yellow complexes due to d^{10} configuration.

5. Applications of Keto Acid Hydrazones and Their Complexes

5.1. Analytical Chemistry

Hydrazones are widely used as reagents for:

- Colorimetric determination of metals (Cu^{2+}, Ni^{2+}, Co^{2+}, Fe^{3+})
- Precipitation of metal ions
- Indicators in complexometric titrations

Example:

Pyruvic acid hydrazone forms a strong colored complex with Cu^{2+}, useful for spectrophotometric detection.

5.2. Coordination Chemistry

Hydrazone-based ligands are ideal for:

- Design of new chelating ligands
- Stability and geometry studies
- Modeling enzyme active sites

5.3. Medicinal and Biological Chemistry

Some hydrazone complexes show:

- Antitumor activity
- Antimicrobial properties
- Enzyme inhibition (e.g., dehydrogenases)

Example:
Cu(II)–pyruvate hydrazone complexes exhibit significant antibacterial effects.

6. Conclusion

Keto acids react readily with hydrazine to form hydrazones that possess strong chelating abilities due to the presence of an azomethine nitrogen and a carboxylate oxygen. These hydrazones form stable, often colored complexes with a wide range of transition metals. Their structural versatility and coordination behavior make them valuable in analytical chemistry, coordination chemistry, catalysis, and biomedical research.

Referens

1. Amrullaev, A., Boltaeva, S., Rashitova, S., & Ganiev, B. (2024). Synthesis and study sorption properties oligo (poly)-mer sorbents based on urea-formaldehyde and cyanuric acid. In *BIO Web of Conferences* (Vol. 130, p. 06004). EDP Sciences.
2. Amrilloyev, A. (2024). Farmatsevtik Kimyo Fani Laboratoriya MashgUlotlarini Noan'anaviy OTkazish Metodlari. *AMALIY VA FUNDAMENTAL TADQIQOTLAR JURNALI*, *3*(12), 22-25.
3. O'g'li, A. A. A.Building Green Cities and Developing A Green Economy Within Them. International Journal of BiologicalEngineering and Agriculture 2025, 4(4), 38-41
4. Azamat ogli, "The effect of using interactive methods in teaching chemistry to school students on educational efficiency," Central Asian Journal of Medical and Natural Science, vol. 4, no. 5, pp. 771–774, 2023
5. Ganiev, B., Mardonov, U., & Kholikova, G. (2023). Molecular structure, HOMO-LUMO, MEP-–Analysis of triazine compounds using DFT (B3LYP) calculations. *Materials Today: Proceedings*.
6. Норов, Ю. Д., Мардонов, У. М., & Тошев, О. Э. (2005). Изучение влияния водных растворов ПАВ на изменение прочности горного массива. *Горный журнал*, (3), 15-16.
7. Мардонов, У. М., Ганиев, Б. Ш., Сайфуллаев, М. С. У., & Музафаров, Ф. И. (2022). Изучение методами кванто-химического расчета и ЭПР спектроскопии электронно-структурных и координационных свойств различных форм глютамина. *Universum: химия и биология*, (2-1 (92)), 49-54.