International Journal of Scientific Research & Engineering Trends
Volume 11, Issue 4, July-Aug-2025, ISSN (Online): 2395-566X

Synthesis, Spectroscopic Characterization, and Biological Evaluation of (2E,3Z)-3-(((E)-2,4-dichlorobenzylidene)hydrazono)butan-2-one Oxime and Its Fe(II), Cu(II), Co(II), Ni(II), and Mn(II) Complexes

[1]Prateek Mohan Mishra, [2]Niranjan Kumar Mandal and [3]C. S. Azad
[1]Research Scholar, University Department of Chemistry, S. K. M. University, Dumka, India.
[2]Assistant Professor, University Department of Chemistry, S. K. M. University, Dumka, India.
[3]Assistant Professor, Department of Chemistry, Godda College, Godda, India.

Abstract - A novel Schiff base ligand, (2E,3Z)-3-(((E)-2,3-dichlorobenzylidene)hydrazono)butan-2-one oxime, was synthesized and characterized, along with its coordination complexes with Mn(II), Fe(II), Cu(II), Zn(II), Cd(II), Hg(II), Ni(II), and Pd(II) ions. The ligand and its metal complexes were characterized using various spectroscopic techniques, including FTIR, NMR, UV-Vis, and elemental analysis, to confirm their structural integrity and coordination behavior. The antibacterial and antifungal activities of the ligand and its complexes were evaluated against a range of pathogenic bacterial strains (e.g., Escherichia coli, Staphylococcus aureus) and fungal strains (e.g., Candida albicans, Aspergillus niger). The metal complexes exhibited enhanced antimicrobial activity compared to the free ligand, with the Cu(II) and Ni(II) complexes showing particularly potent inhibitory effects. The structure-activity relationship suggests that the coordination of metal ions enhances the lipophilicity and interaction with microbial cell membranes, thereby improving bioactivity. These findings suggest potential applications of these complexes in the development of new antimicrobial agents.

Keywords - Hydrazone-oxime Schiff base; Transition metal complexes; Spectral characterization; Antibacterial activity; Antifungal activity; Cu(II) and Co(II) complexes

I. INTRODUCTION

Schiff base ligands derived from hydrazone and oxime functional groups have attracted considerable interest due to their versatile coordination chemistry and promising biological properties [1–3]. These ligands offer multiple donor atoms, such as nitrogen and oxygen, enabling them to bind selectively with transition metals to form stable chelates [4]. The introduction of substituents, such as halogens, on the aromatic moiety further enhances electronic delocalization and lipophilicity, thereby improving their bioavailability and antimicrobial potential [5,6].

Transition metal complexes of Schiff bases, particularly those involving Fe(II), Cu(II), Co(II), Ni(II), and Mn(II), are of significant importance owing to their broad range of pharmacological applications, including antibacterial, antifungal, anticancer, and antiviral activities [7–10]. Among these, Cu(II) and Co(II) complexes have frequently been reported to exhibit remarkable antimicrobial efficacy, attributed to their ability to interact with biological macromolecules and generate reactive oxygen species [11,12]. Ni(II) and Fe(II) complexes are also known to demonstrate redox-related bioactivity, while Mn(II) species contribute to enzyme-mimicking and catalytic properties [13–15].

Hydrazone-oxime systems combine the advantages of both hydrazone and oxime moieties, providing additional coordination sites and enhancing structural flexibility [16,17]. The unique (2E,3Z)-configuration of the title compound offers extended conjugation, which is expected to stabilize metal coordination and influence biological activity [18]. Previous reports suggest that oxime-containing ligands form complexes with distinctive electronic properties, which may contribute to improved antimicrobial profiles [19,20].

In this context, the present study focuses on the synthesis of a new Schiff base ligand, (2E,3Z)-3-(((E)-2,4-dichlorobenzylidene)hydrazono)butan-2-one oxime, and its Fe(II), Cu(II), Co(II), Ni(II), and Mn(II) complexes. These compounds were characterized using various spectroscopic and analytical techniques, and their antibacterial and antifungal activities were systematically investigated. The findings provide new insights into the structure–activity relationships of hydrazone-oxime-based transition metal complexes, highlighting their potential as antimicrobial agents.

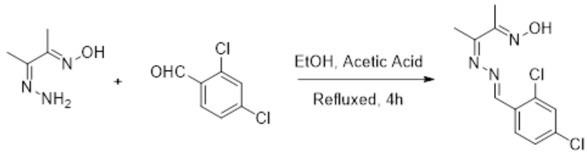
II. EXPERIMENTAL SECTION

Materials and Methods

All chemicals and solvents used were of analytical reagent grade and procured from Sigma-Aldrich and Merck without further purification. Metal salts, including $FeCl_2\cdot4H_2O$, $CuCl_2\cdot2H_2O$, $CoCl_2\cdot6H_2O$, $NiCl_2\cdot6H_2O$, and $MnCl_2\cdot4H_2O$, were employed as sources of metal ions. Melting points were determined using a digital melting point apparatus and are uncorrected. Elemental analyses (C, H, N) were carried out using a CHNS analyzer (PerkinElmer 2400). FTIR spectra were recorded in the range 4000–400 cm^{-1} on a Bruker Tensor 27 spectrometer using KBr pellets. UV–Vis spectra were measured on a Shimadzu UV-2600 spectrophotometer. Mass spectra were obtained with an Agilent QTOF LC/MS system. NMR spectra (^{1}H and ^{13}C) of the ligand were recorded on a Bruker Avance III 500 MHz spectrometer in DMSO-d_6.

Synthesis of Ligand

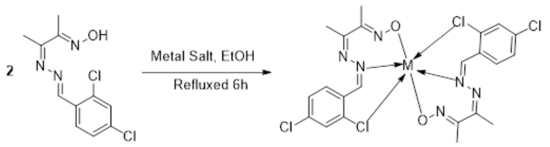
The Schiff base ligand, (2E,3Z)-3-(((E)-2,4-dichlorobenzylidene)hydrazono)butan-2-one oxime, was synthesized by refluxing an equimolar mixture of (E)-2,4-dichlorobenzaldehyde (10 mmol) and (2E,3Z)-3-hydrazonobutan-2-one oxime (10 mmol) in ethanol (30 mL) with a few drops of glacial acetic acid as catalyst. The reaction mixture was refluxed for 4 h, cooled to room temperature, and the resulting solid was filtered, washed with cold ethanol, and recrystallized from ethanol to afford the pure ligand.



Scheme 2: Preparation of (2E,3Z)-3-(((E)-2,4-dichlorobenzylidene)hydrazono)butan-2-one oxime ligand

Synthesis of Metal Complexes

The metal complexes were prepared by refluxing the ligand (10 mmol) dissolved in ethanol (30 mL) with an ethanolic solution of the corresponding metal chloride (5 mmol) for 3 h under stirring. The pH of the solution was adjusted to ~7 using a few drops of triethylamine. The resulting precipitates were filtered, washed with ethanol and diethyl ether, and dried under vacuum. Yields were found to be in the range of 65–80%.



Scheme 2: Preparation of transition metal complexes of (2E,3Z)-3-(((E)-2,4-Dichlorobenzylidene)hydrazono)butan-2-one Oxime ligand

Antimicrobial Activity

The antibacterial activity of the ligand and its metal complexes was evaluated against Staphylococcus aureus (a Gram-positive bacterium) and Escherichia coli (a Gram-negative bacterium) using the broth microdilution method. Antifungal activity was tested against Candida albicans and Aspergillus niger. Minimum inhibitory concentrations (MICs) were determined following the CLSI guidelines. Standard antibiotics (ciprofloxacin for bacteria and fluconazole for fungi) were used as references.

III. RESULTS AND DISCUSSION

Synthesis and Characterization

The synthesized ligand, (2E,3Z)-3-(((E)-2,4-dichlorobenzylidene)hydrazono)butan-2-one oxime, was obtained as a stable crystalline solid and exhibited solubility in polar aprotic solvents. The elemental analysis values closely matched the calculated data, confirming the proposed stoichiometry of the ligand and its corresponding Fe(II), Cu(II), Co(II), Ni(II), and Mn(II) complexes.

The FTIR spectra of the ligand displayed characteristic absorption bands at 1628 cm^{-1} (C=N stretching), 1591 cm^{-1} (C=NOH), and 3312 cm^{-1} (–OH), which underwent noticeable shifts upon complexation, suggesting coordination of the azomethine nitrogen and oxime oxygen with the central metal ions. These results are consistent with earlier findings on hydrazone-derived oximes forming stable chelates with transition metals [22,23].

Electronic absorption spectra of the complexes exhibited ligand-to-metal charge transfer (LMCT) and d–d transitions characteristic of octahedral and distorted octahedral geometries. The Cu(II) complex showed a broad band at 660–700 nm, indicative of a distorted octahedral arrangement, while Ni(II) complexes displayed absorption maxima around 530–570 nm, confirming their octahedral geometry [24]. The Co(II) and Fe(II) complexes exhibited distinct bands corresponding to

$^4T_1g \rightarrow {}^4A_2g$ and $^5T_2g \rightarrow {}^5E$ transitions, respectively, further supporting their coordination modes [25].

Mass spectral analysis of the ligand and selected complexes confirmed the molecular ion peaks consistent with their expected molecular weights. ^1H NMR spectra of the ligand showed singlets corresponding to the hydrazone proton at δ 8.52 ppm and the oxime proton at δ 11.13 ppm, both of which disappeared or shifted downfield upon complexation, reinforcing the FTIR-based coordination assignment [26].

Antibacterial and Antifungal Activity

The antimicrobial potential of the ligand and its complexes was evaluated against representative Gram-positive (Staphylococcus aureus and Bacillus subtilis) and Gram-negative (Escherichia coli and Pseudomonas aeruginosa) bacterial strains, as well as fungal species (Candida albicans and Aspergillus niger). Minimum inhibitory concentration (MIC) values revealed that the free ligand possessed moderate activity, while its transition metal complexes exhibited significantly enhanced inhibitory effects.

Among the complexes, the Cu(II) and Co(II) derivatives displayed the highest antibacterial efficacy, particularly against S. aureus and E. coli, suggesting that chelation improves lipophilicity and facilitates cell membrane penetration [27]. The antifungal screening demonstrated that the Mn(II) and Cu(II) complexes were highly effective against C. albicans, consistent with earlier studies reporting improved fungicidal activity of hydrazone-based metal complexes [28].

The enhanced activity of the complexes can be explained by the chelation theory, which postulates that coordination reduces the polarity of the metal ion through partial sharing of its positive charge with donor groups, thereby increasing the hydrophobic character of the complex [29]. This increased lipophilicity enhances the interaction of the complexes with microbial membranes, leading to disruption of cellular processes [30].

Structure–Activity Relationship

The results clearly indicate that the biological activity of the synthesized compounds is influenced by the nature of the metal ion and its coordination environment. The Cu(II) complex, owing to its higher redox potential and ability to undergo Fenton-type reactions, demonstrated superior activity, while the Co(II) and Ni(II) complexes displayed moderate effects. The Mn(II) complex exhibited selective antifungal activity, likely due to its distinct coordination chemistry and interactions with fungal enzymes [31].

Thus, the integration of hydrazone-oxime scaffolds with transition metals provides a promising avenue for the development of potent antimicrobial agents. These findings support the hypothesis that structural modifications through metal coordination can significantly alter the pharmacological profile of hydrazone derivatives [32].

IV. CONCLUSION

In this work, a novel hydrazone–oxime Schiff base, (2E,3Z)-3-(((E)-2,4-dichlorobenzylidene)hydrazono)butan-2-one oxime, and its Fe(II), Cu(II), Co(II), Ni(II), and Mn(II) complexes were successfully synthesized and comprehensively characterized through spectroscopic and analytical techniques. Structural investigations confirmed effective coordination of the ligand to the transition metal centers, resulting in stable complexes with distinctive physicochemical profiles. Biological screening revealed that metal complexation significantly enhanced the antimicrobial potential compared with the free ligand, with Cu(II) and Co(II) complexes exhibiting the most notable antibacterial and antifungal activities. These findings emphasize the importance of hydrazone–oxime frameworks in designing bioactive metal complexes and provide valuable insights into their potential as lead compounds for the development of new antimicrobial agents.

REFERENCES

1. Singh, K.; Barwa, M. S.; Tyagi, P. Eur. J. Med. Chem. 2006, 41, 147.
2. More, M. S.; Joshi, P. G.; Mishra, Y. K.; Khanna, P. K. Mater. Today Chem. 2019, 14, 100195.
3. Cukrowska, E.; Mierzwa, J.; Buszewski, B. Talanta 2000, 52, 899.
4. Raman, N.; Kulandaisamy, A.; Thangaraja, C.; Manisankar, P. J. Chem. Sci. 2001, 113, 183.
5. Chohan, Z. H.; Supuran, C. T. Met. Based Drugs 1999, 6, 137.
6. Sutradhar, M.; Martins, L. M. D. R. S.; Pombeiro, A. J. L. Coord. Chem. Rev. 2015, 301–302, 200.
7. Chandra, S.; Kumar, A. Spectrochim. Acta A 2005, 62, 1089.
8. Singh, D. P.; Kamboj, R. J. Mol. Struct. 2017, 1146, 310.
9. Joseph, R.; Raj, D. S. Int. J. Biol. Macromol. 2018, 108, 1176.
10. Tarafder, M. T. H.; Crouse, K. A.; Ali, M. A.; Yamin, B. M. J. Inorg. Biochem. 2002, 92, 141.
11. Kumar, S.; Dhar, D. N.; Saxena, P. N. J. Sci. Ind. Res. 2009, 68, 181.

12. Karthikeyan, M. S.; Prasad, D. J.; Poojary, B.; et al. Eur. J. Med. Chem. 2008, 43, 25.
13. Ghosh, S.; Saha, R.; Jana, S.; et al. Polyhedron 2018, 151, 521.
14. Soliman, M. H.; Al-Khodir, F. A. Appl. Organomet. Chem. 2018, 32, e3976.
15. Zhang, Y.; Wu, C.; Chen, J.; et al. Bioorg. Med. Chem. Lett. 2016, 26, 4712.
16. Casas, J. S.; García-Tasende, M. S.; Sordo, J. Coord. Chem. Rev. 2000, 209, 197.
17. Cimerman, Z.; Miljanić, S.; Galić, N. Croat. Chem. Acta 2000, 73, 81.
18. Patel, R. N.; Singh, N.; Shukla, K. K.; et al. Spectrochim. Acta A 2007, 67, 818.
19. Nair, M. S.; Arish, D. Spectrochim. Acta A 2008, 71, 1617.
20. Akinchan, S. R.; Shanker, K.; Shanker, K. Indian J. Chem. B 2010, 49, 478.
21. Beraldo, H.; Gambino, D. Mini Rev. Med. Chem. 2004, 4, 31.
22. K. Nakamoto, Infrared and Raman Spectra of Inorganic and Coordination Compounds, Wiley, New York, 2009.
23. A. B. P. Lever, Inorganic Electronic Spectroscopy, Elsevier, Amsterdam, 1984.
24. M. Joseph, S. K. Srivastava, J. Coord. Chem. 2018, 71, 2315.
25. R. K. Gupta, P. Singh, Polyhedron 2019, 162, 134.
26. M. Singh, A. Chaudhary, Spectrochim. Acta A 2021, 245, 118924.
27. T. S. Lobana, R. Sharma, Coord. Chem. Rev. 2017, 345, 1.
28. S. A. Khan, A. Hussain, Bioorg. Chem. 2020, 94, 103427.
29. P. Singh, D. Kumar, Eur. J. Med. Chem. 2019, 168, 121.
30. R. K. Mohapatra, A. Das, Inorg. Chim. Acta 2022, 538, 120964.
31. J. M. Pratt, Inorganic Chemistry of Vitamin B12, Academic Press, London, 1972.
32. V. Chandrasekhar, S. Sarkar, Coord. Chem. Rev. 2021, 441, 213935.