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A study of mononuclear 3d transition metal bis-Schiff base complexes: Synthesis, characterization, and evaluation of their antibacterial activity

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Abstract: In this study, we have outlined a conventional and user-friendly procedure for the production of (*E*)-1-((((5-ethyl-1,3,4-thiadiazol-2-yl)imino)methyl)naphthalen-2-ol (HL-1) and (*E*)-1-(((thiazol-2-ylimino)methyl)naphthalen-2-ol (HL-2) by the reaction of heterocyclic amine, aldehyde in the presence of ethanol as a solvent and acid as the catalyst. The synthesis of new HL-1 and HL-2 may be accomplished with ease using this approach, which is also very efficient. In the presence of dipositive Co, Ni, and Cu metal complexation, HL-1 and HL-2 were carried out in the presence of metal: ligand (1:2). HL-1, HL-2, and metal complexes are characterized with the assistance of UV/visible, FT-IR, Mass, and ¹H NMR spectroscopy respectively. Furthermore, the ligands mentioned above (HL-1 and HL-2) and their metal complexes were tested for the antimicrobial study and showed an excellent inhibitory zone. These investigations indicated that HL1–Co (II), HL-1Cu (II), complexes and ligands HL-2Co (II), and HL-1Ni(II) had positive effects on *Escherichia coli* causing severe stomach cramps (Gramnegative-MTCC 1610) and positive impact on *Staphylococcus aureus* (Gram-positive MTCC–96) due to skin infections.

Keywords: Antibacterial activity; Thiadiazol; Naphthalen-2-ol; well diffusion method; Metal complex; Schiff base.

1. Introduction

The Discovery of Schiff bases in the 18th century has attracted attention in coordination chemistry ¹. Schiff bases containing an azomethine group (-HC=N) are formed by a nucleophilic condensation reaction of carbonyl compounds with primary amines, which are often synthesized using acid/base catalysts or heating conditions². Firstly Hugo Schiff invented Schiff base compounds in 1864³. Schiff base functions as a ligand and bind metals through its imine nitrogen and other donating groups derived from the aldehyde group 4,5 . The Sulphur, nitrogen, and oxygen-containing heterocyclic molecules are considered variable ligands in Schiff base formation ⁶. Transition metal complexes have a significant role in several fields of synthetic chemistry 7,8, such as industrial and agricultural chemistry 7. Schiff bases might be utilized as a catalyst in a range of synthetic organic processes, such as the production of physiologically active chemicals, dyes, plant growth regulators, and others ⁹. Multiple metal complexes of Schiff base ligands have excellent catalytic activity in a range of elevated temperatures (>100°C) in an aqueous medium, making them environment-friendly ¹⁰. Due to the vast array of possible configurations as ligands, which depends on the structures of aldehydes and amines¹¹,

**Corresponding author: Mithun Kori Email address: <u>mithunkori587@gmail.com</u>* DOI: http://dx.doi.org/10.13171/mjc02304231686kori research into the formation of these Schiff base metal complexes is a fast-expanding field of study ¹². The structural changes in the reactants may drastically alter the intended reaction and force it to adopt an entirely different course of action ¹³. Differences in the structures of aldehyde and amine may significantly affect the reaction and lead to vastly different reactivity ¹⁴. Schiff base ligands and their complexes are exploited as intermediates in several enzymatic reactions due to their interactions with amino moieties and enzymes ¹⁵. Several Schiff bases and associated metal complexes were researched in the preceding decade due to their critical biological roles ^{16,17}. A fascinating scientific endeavor is discovering new heterocycles with potent biological effects ^{18,19}. Among the many applications of Schiff bases and their complexes are in chemistry, pharmaceutical biochemistry, chemistry, and medicine They show various biological applications, including antibacterial 20,21 antifungal²², antihelminthic²³, antiadhesive²⁴, anticancer²⁵, antioxidant ^{26,27}, antiproliferative ²⁸, antiinflammatory ²⁹, antiviral ³⁰, antitumor ³¹, antiparasitic ³², antitubercular ³³, analgesic ³⁴, antiapoptotic ³⁵, antiparkinson ³⁶, herbicidal ³⁷, antidiabetic ³⁸ and treatment for cytotoxic cancerous

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¹HL-2, as well as their metal complexes. This research also discusses the antibacterial activity of these complexes. Nowadays, heterocyclic compounds having more useful in drug resistance pharmaceutical compounds and biological activities ^{40,41}. When taken as an amine, Thiadiazol shows antibacterial, antiviral, and antifungal properties ². The ligands and complexes of divalent 3d metal ions such as Co^{II}, Ni^{II,} and Cu^{II} were studied using spectroscopic and physical techniques to evaluate their photophysical and biological studies ^{42,43}.

This work encouraged to develop of novel Schiff base ligands HL-1 and HL-2 by combining 5-ethyl-1,3,4thiazole-2-amine, 2-amino thiazole, and 2-hydroxy-1naphthaledehyde (1:1) in ethanol. We also developed compounds of other 3d series metals with the ligands HL-1 and HL-2 and characterized them by IR, NMR, Mass spectrometry, and UV/visible. The antibacterial activity of the Schiff base and 3d dipositive metal ion complexes was studied.

2. Experimental section

All chemicals and reactants are purchased from Loba-Chemie, and Sigma Aldrich (Merck, USA). TLC and UV chamber were used to identify the reaction. Solvents were analytically evaluated as received, purified, and dried by standard technique. The compound's melting points were obtained using open capillary thermal melting point equipment in a capillary tube. FT-IR spectra of KBr pellets were obtained using an FT-IR (Bruker Alpha-II) spectroscopy. A JEOL Delta-550 spectrometer was used to produce the ¹HNMR spectra in DMSO-d₆. Between 200 and 800 nm, UV/vis spectra in Dimethyl sulfoxide solvent were determined using a Lab-India (UV3092) UV/vis Spectrometer. The electron-spray ionization mass spectrum (ESI-MS) was obtained using the XEVO G2S QPOF mass spectrometry.

2.1. Synthesis of ligands HL-1 and HL-2

The HL-1 ligand was prepared in an ethanolic mixture (15 mL) of 2-hydroxy-1-naphthaledehyde (0.172 g, 1 mmol) and 5-ethyl-1,3,4-thiadiazole (0.129 g, 1 mmol), whereas the HL-2 ligand was prepared in an ethanolic mixture (15 mL) of 2-hydroxy-1-naphthaledehyde (0.172 g, 1 mmol) by adding thiazole-2-amine (0.100 g, 1 mmol). In a round bottom flask fitted with a heated magnetic stirrer, The amine solution was added dropwise at 75-80°C and heated gently for 5-6 hours. A yellow precipitate was synthesized and allowed to settle at room temperature before being filtered and dried, then recrystallized from ethyl alcohol. The reaction's progress was observed using a TLC sheet in a UV-Vis chamber (Scheme 1).



Scheme 1. Synthesis of ligands HL-1 and HL-2

2.2. General synthetic procedure for [M(HL-1)₂] and [M(HL-2)₂]

Using metal(II) nitrates to a stirring methanolic solution of **HL-1**/ **HL-2** (1.0 mmol, 0.283g/0.254g) and KOH (1.0 mmol, 0.056g), a methanolic solution of metal (II) nitrates (1.0 mmol) were added dropwise at room temperature, and the resulting reaction mixture was further stirred for 20 minutes for the synthesis of complexes of (E)-1-(((5-ethyl-1,3,4-

thiadiazol-2-yl)imino)methyl)naphthalen-2-ol and (E)-1-((thiazol-2-ylimino)methyl)naphthalen-2-ol. The reaction mixture was refluxed at 70–80°C for hours while TLC was used to track the progress of the reaction. The reaction product was cooled, after which a precipitate was produced. This precipitate was filtered, washed with methanol (5 mL), followed by diethyl ether (5–7 mL), and dried under a vacuum.



Scheme 2. Synthesis of metal complexes $[M(HL-1)_2]$ and $[M(HL-2)_2]$



Figure 1. Structures of the Metal complexes 1-6 of ligand HL-1 and HL-2

Synthesis of (*E*)-1-(((5-ethyl-1,3,4-thiadiazol-2yl)imino)methyl)naphthalen-2-ol (HL-1): $C_{15}H_{13}N_3OS$; Yellow Colored solid; M.P. 180°C; yield 82%; Chemical formula; [$C_{15}H_{13}CoN_3O_2S$], (Molecular Weight 283);

FT-IR (cm⁻¹): 3420, 1619, 1567, 1250, 1164, 752; Elemental Analysis (in percentage): C, 63.58; H, 4.62; N, 14.83; O, 5.65; S, 11.31 Found C, 63.60; H, 4.65; N, 14.80; O, 5.67; S, 11.35;

¹HNMR (DMSO- d_6 , δ , ppm); 11.13(s, 1H), 8.85(s, 1H) 7.68 (d, 1H), 7.48 (dd, 1H), 7.47 (dd, 1H), 7.27(dd, 1H), 7.25 (dd, 1H), 3.16 (q, 2H), 1.23 (t, 3H);

UV Absorption 369 (λ_{max}) Exact Mass: 283; m/z:283.07 (100.0%), 284.09 (16.2%), 285.07 (1.2%), 284.07 (1.1%).

FT-IR (cm⁻¹): 3385, 1629, 1462, 729; Elemental Analysis(in percentage): C, 66.12; H, 3.96; N, 11.02; O,6.29; S,12.61 Found C, 66.14; H, 3.90; N, 11.00; O,6.35; S,12.65;

¹HNMR (DMSO- d₆, δ, ppm); 10.98(s, 1H), 8.99 (s, 1H) 7.67 (d, 1H), 7.63 (d, 1H), 7.40 (d, 1H), 7.30(d, 1H), 7.17 (dd, 1H), 7.16 (m, 1H), 7. 12 (dd, 1H), 6.95 (dd, 1H);

UV Absorption 297 (λ_{max}) Exact Mass: 254.05; m/z:254.05 (100.0%), 255.06 (15.1%), 256.04 (4.5%), 256.08 (1.1%).

Bis((1-((E)-((5-ethyl-1,3,4-thiadiazol-2yl)amino)methyl)naphthalen-2-yl)oxy)cobalt

[Co(HL-1)₂] (1): Light blue solid, yield 69% MP-240°C, Chemical formula; [C₃₀H₂₄CoN₆O₂S₂], (Molecular Weight 623);

IR (selected vibrations; cm⁻¹); 2969, 1659, 1169, 753; Elemental Analysis(in percentage): C, 57.78; H, 3.88; N, 9.01; Co.9.45; O,5.12; S,10.28 Found C, 57.86; H, 3.90; N, 9.50; Co, 9.44; O,5.14; S,10.33.

UV/vis (λ_{max}); 296 nm;

Mass spectroscopy (ESI-MS): 623.07 $[M]^+$ anal for $[C_{30}H_{24}CoN_6O_2S_2]$.

Bis((1-((E)-((5-ethyl-1,3,4-thiadiazol-

2yl) amino) methyl) naphthalen - 2 - yl) oxy) nickel

[Ni(HL-1)₂] (2): Greenish yellow solid, yield: 81%, MP- 250°C, Chemical formula; [C₃₀H₂₄N₄NiO₂S₂], (Molecular Weight 623);

IR (selected vibrations; cm⁻¹);2969, 1749, 1346, 1169, 753, 680.

Elemental Analysis(in percentage): C, 57.99; H, 2.92; N, 9.02; Ni, 9.45; O, 10.30; S, 10.32; Found; C, 57.89; H, 2.85; N, 9.12; Ni, 9.40; O, 10.33; S, 10.12;

UV/vis (λ_{max}); 347 nm,

Mass spectroscopy (ESI -MS): 622.4 $[M]^{\scriptscriptstyle +}$ anal for $[C_{30}H_{24}NiN_6O_2S_2].$

Bis((1-((E)-((5-ethyl-1,3,4-thiadiazol-2yl)amino)methyl)naphthalen-2-yl)oxy)copper [Cu(HL-1)₂] (3): Dark green solid, yield: 78%,

MP-260°C. Chemical Formula: $[C_{30}H_{24}CuN_6O_2S_2]$, (Molecular Weight 628);

Elemental Analysis(in percentage): C, 57.36; H, 3.85; Cu, 10.12; N, 13.38; O, 5.09; S, 10.21; Found; C, 57.39; H, 3.90; Cu, 10.09; N, 13.40; O, 5.12; S, 10.21, IR (selected vibrations; cm⁻¹); 2920, 1694, 1487, 1131, 741, 523;

UV/vis (λ_{max}); 287 nm,

Mass spectroscopy (ESI -MS): 627.07 $[M]^+$ anal for $[C_{30}H_{24}CuN_6O_2S_2]$.

IR (selected vibrations; cm⁻¹); 3385, 2920, 1629, 1462, 753, 620;

Elemental Analysis (in percentage): C, 59.54; H, 3.21; Co, 10.42; N, 9.91; O, 5.66; S, 11.34; Found; C, 59.47; H, 3.18; Co, 10.44; N, 9.90; O, 5.68; S, 11.40, UV/vis (λ_{max}); 287 nm,

Mass spectroscopy (ESI -MS): 565 $[M]^+$ anal for $[C_{28}H_{18}CoN_4O_2S_2]$.

Bis((1-)-(thiazol-2-ylimino) methyl)napthalen-2yl)oxy)nickel [Ni(HL-2)2] (5): Dark green solid, yield: 80%, MP -258°C. Chemical Formula: [C₂₈H₁₈N₄NiO₂S₂], (Molecular Weight 565.29);

IR (selected vibrations; cm⁻¹); 3414, 2983, 1635, 1576, 1395, 737, 533;

Elemental Analysis (in percentage): C, 59.49; H, 3.21; Ni, 10.38; N, 9.91; O, 5.66; S, 11.34; Found; C, 59.47; H, 3.20; Ni, 10.40; N, 9.93; O, 5.60; S, 11.32; UV/vis (λ_{max}); 287 nm,

Mass spectroscopy (ESI -MS): 564 $[M]^+$ anal for $[C_{28}H_{18}N_4NiO_2S_2]$.

Bis((1-((E)-(thiazol-2-ylimino) methyl) napthalen-2yl) oxy) copper [Cu(HL-2)_2] (6): Dark green solid, yield: 79% MP-190°C. Chemical Formula: [$C_{28}H_{18}CuN_4O_2S_2$], (Molecular Weight 570);

IR (selected vibrations; cm⁻¹); 3344, 2352, 1631, 1552, 1407, 730, 557;

Elemental Analysis (in percentage): C, 58.99; H, 3.18; Cu, 11.15; N, 9.83; O, 5.61; S, 11.25, Found; C, 59.10; H, 3.20; Cu, 11.18; N, 9.93; O, 5.58; S, 11.32,; UV/vis (λ_{max}); 287 nm, Mass spectroscopy (ESI-MS): 669 [M]⁺ anal for [C₂₈H₁₈N₄CuO₂S₂].

3. Results and Discussion

Tri-dentate Schiff ligands HL-1 and HL-2 were produced by reacting ethyl-1,3,4-thiadiazole, thiazole-2-amine, and 2-hydroxy-1-naphthaledehyde in an alcoholic solution at a 1:1 molar ratio (Scheme 1) these compounds were characterized by elemental analyses, IR, UV/vis, ¹H NMR, and mass spectroscopy. The presence of resonances at 8.85 and 8.99 ppm in ¹H NMR spectra ascribed to the azomethine -HC=N group highly indicates the formation of Schiff bases HL-1 and HL-2, respectively. In addition, IR spectrum vibrations due to the stretching frequency of -C=N (1619 cm⁻¹) and the 1600 group imply the formation of Schiff bases. Functional group stretching frequencies of -OH (3420 cm⁻¹) and -C=N (1619 cm⁻¹) are reflected in the corresponding vibrational modes ^{44–46}.

3.1. Spectral analysis of UV/Vis

HL-1 and HL-2 have absorption bands at 351 and 223 nm, 297 and 242 nm, respectively, corresponding to the $n-\pi^*$ and $\pi-\pi^*$ transitions. Metal complexes formed when HL-1 and HL-2 ligands reacted with Co(II), Ni(II), and Cu(II) nitrates in methanol under primary conditions shown in Figure 2. These compounds are persistent at room temperature, non-hygroscopic solids, soluble in a variety of common organic solvents such methyl alcohol, ethyl alcohol, methane carbonitrile, DMF, and DMSO, but insoluble in hexane, chloroform, dichloromethane, petroleum ether, and diethyl ether. The complexes were examined using elements, IR, UV/vis, and mass

spectroscopy. The uni-negatively charged ligands HL-1 and HL-2 react with metal ions in a 1:2 stoichiometric manners, producing six coordination sites that permit the core metal ion to take on an octahedral form, according to FT-IR, 1H NMR, and mass spectrum investigations. The suggested six coordination number from two ligand units (HL-1/ HL-2) is achieved by negatively charged and lone pair on oxygen, azomethine (thiadiazol) nitrogen, and (thiazole) nitrogen, respectively (Scheme 2). However, developing a coordination connection between the nitrogen of 5-ethyl-1,3,4-thiadiazole and a metal center may be unstable due to the production of a four-membered ring. However, (thiadiazol) nitrogen and (thiazole) nitrogen may exhibit pseudocoordination to the metal centers, forming an octahedral environment around the metal ion. An arrow shows pseudo-coordination bonds. Similar compounds based on 2-hydroxy-1-naphthaledehyde provided further support for the structures of 1 through 6 complexes ^{47–49}. Literature suggests that such ligands attach to metal centers in a ratio of 2:1 (ligand: metal).



Figure 2. UV-Visible spectra of metal complexes Co(II), Ni(II) and Cu(II) with Schiff base ligands HL-1 and HL-2 in MeOH solution (1.0 x10⁻⁶ M) at room temperature

3.2. Infrared spectral studies

The typical infrared data of Schiff base ligands and the metal complexes of those ligands are shown in Table 1.

Because of the –OH symmetric stretching vibrations, the infrared spectra of HL–1 can be seen to have two vibrations at 3420 cm⁻¹. The vibration at 1619 cm⁻¹ corresponds to the frequency of –C=N stretching. On the creation of a compound with Co(II), a wide band centered at 3500 cm1 may be ascribed to the existence of a lattice of the water molecule (s). The vibrations of the –OH, –CH (aromatic), and –C=N functional groups in complex 1 moved to lower frequencies (1525 cm⁻¹). Similarly, HL–1 complex (2-5) demonstrates relative changes toward lower

frequency between 1700 and 500 cm⁻¹. However, the total number of vibrations varies in the range of 2100 to 3200 cm⁻¹, which the existence of lattice water molecules may explain in differing numbers. In addition, the IR spectra of HL-2 display a band at 3385 cm⁻¹ owing to the vibrational stretching of the -OH group. At 1629 and 1462 cm⁻¹, the asymmetric and symmetric stretching vibrations of emerge, respectively. In addition, the band developed at 1629 cm⁻¹ due to the -C=N stretching vibration in HL-2. Co (II)-complex 6 has an expansive band center at 3344 cm⁻¹. Other vibrations related to the -OH and -C=N functional groups change in frequency (1525 cm⁻¹) in complexes 4-6. IR spectral analyses provide significant evidence for forming complexes 1–6, including HL-1 and HL-2 ligands ⁵⁰.

Compound	v(OH)	v _{azo.} (C=N)	v _{aro.} (C=C)	(C-S)	v(M-O)
HL-1	3420	1619	1567	752	-
[Co(HL-1)2]	-	1626	-	753	540
[Ni(HL-1) ₂]	-	1601	1595	785	533
[Cu(HL-1)2]	-	1632	1487	741	523
HL-2	3385	1600	1462	729	-
[Co(HL-2)2]	-	1610	1531	740	555
[Ni(HL-2)2]	-	1630	1576	737	562
[Cu(HL-2)2]	-	1623	1552	730	557

Table 1. Schiff base ligands and their complexes in FT-IR (cm⁻¹).

3.3. Spectra of the ¹H NMR

¹H NMR spectral data of the HL-1 and HL-2 free ligands, dissolved in DMSO-d₆, exhibited hydroxy peaks at 11.13 ppm and 10.98 ppm, respectively. The multiplets at the 7.68–6.98 ppm region are assigned to the protons of 2-hydroxy-1-naphthaldehyde ring groups (commonly present in HL-1 & HL-2). The strong singlet at 8.85 ppm and 8.99 ppm is assigned for the azomethine proton ⁴⁵. The HL-1 -CH₂ (methylene), -CH₃ (methyl) signals were detected at 3.3 ppm and 1.23 ppm, respectively.

3.4. Analysis of mass spectra

The ESI-MS spectrum reveals molecular ion peaks for HL-1, HL-2, and every metal complex (1-6). In Table 1, the complete ESI-MS spectrum data have been compiled. Peaks at m/z 283.00 and 254.05 have been ascribed to the molecular ion peaks $[M+H]^+$ of HL-1 and HL-2, respectively. In addition, compound (1) exhibits a molecular ion peak $[M]^+$ at m/z 623.07 that corresponds to the entity $[Co(HL-1)_2]$ as well as

higher isotopic peaks. Similarly, complexes 2 and 3 have molecular ion peaks comparable to the formulas $[Ni(HL-1)_2]$ and the presence of higher isotopic peaks. The HL-2 complex 4 has a greater isotopic peak at m/z 565 $[M+2]^+$ that corresponds to $[Co(HL-2)_2]$. while complexes 5 and 6 have $[M]_+$ peaks at m/z 564 and 669, respectively, comparable to $[Ni(HL-2)_2]$ and $[Cu(HL-2)_2]$ complex entities, as well as higher isotopic peaks.

3.5. Antimicrobial activity

Following the measurement in the zone of inhibition for the two bacterial strains, a wall diffusion assay on MH Agar was used to assess the antibacterial activity of the HL-1 and HL-2 ligands and metal complexes. The metal complex is stable in pH 7-8 range. The synthetic HL-1 and HL-2 ligands and metal complex's antibacterial activity against the select microorganism at a concentration of 10 micrograms/mL is depicted in graphs **1a** and **1b** as shown in Figure 3.



Figure 3. Antimicrobial activity of metal complexes and their control (Ligands)

As a control substance, DMSO has no zone of inhibition. The thiadiazol derivatives did, however,

exhibit antibacterial activity even at the lesser concentration $(10\mu g)$. Various ligands and metal

complexes were tested against Gram-negative and Gram-positive Escherichia coli and Staphylococcus aureus. Following the information in the bar graphs (1a and 1b), HL-1 does not show any effects, but their metal complexes demonstrated good antimicrobial properties against the tested strains. In contrast, HL-2 Ligand and their respective Co(II) complexes established good antimicrobial properties against the tested strains, outperforming Co(II), Ni(II), and Cu(II) complexes. All of the examined bacterial strains were found to be inhibited by the ligands and complexes, and the overall inhibition order is 4>5>3>1>(HL-

2)>2> (HL-1). Therefore, the change in complex metal polarity may account for greater antibacterial effectiveness and associations with specific bacterial strains' cell membranes shown in Figure 4 ^{44,51}. The bacterial strain may experience cell death because of this interaction, which may increase permeability through the lipid layers of the bacterial cell membrane. The comparable Schiff bases of amino-thiazole and standard Diuron like S. aureus and E. coli52 played a biological function in preventing bacterial growth towards marine biofilm-inducing bacterial strains.



Figure 4. Comparative study of antimicrobial activity of ligands and their metal complexes 1a and 2b

4. Conclusion

We have synthesized and studied two novel Schiff base ligands (HL-1 and HL-2) based on 2-hydroxy-1naphthaledehyde and 2-5-ethyl-1,3,4-thiadiazole, thiazole-2-amine. In addition, FT-IR, 1HNMR (ESI-MS) mass, and UV/vis spectral analyses were used to describe a series of metal complexes (1-6) containing these ligands. The coordination behavior of these ligands has been investigated, and it has been shown that they prefer to bond with metal centers in a ratio of 2:1 (ligand: metal). Remarkably, both the ligands and the transition metal complexes may be antibacterial against harmful bacteria and fungi. HL-1 and HL-2 ligands, together with their Co (II), Ni (II), and Cu (II) complexes, have strong antibacterial capabilities and are effective against harmful bacteria and fungi, according to this research. Ni (II) complexes are much more antibacterial than ligands and complexes of other metals in their respective series.

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