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Cobalt and Nickel Complexes of Oxazole Thiosemicarbazone, Synthesis, Structural and Antimicrobial Activity

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ABSTRACT

The ligand, 2-methyl-1,3-oxazole-4-carbaldehyde thiosemicarbazone (HL) was synthesized by reacting equimolar amounts of thiosemicarbazide with the corresponding aldehyde. The synthesized ligand was reacted with Ni(II) and Co(II) chlorides in the 2:1 mole ratio of ligand: metal. These led to the isolation of two new complexes, namely $[Ni(HL)_2]Cl_2$ (1), $[Co(L)_2].1.3Cl$ (2), the ligand and its metal(II) complexes were characterized by elemental analysis, IR, ^1H NMR, ^{13}C NMR spectroscopic methods, UV-Vis spectrophotometry and X-ray diffraction. The X-ray structural studies of the ligand and their corresponding metal complexes 1, 2 revealed that: The free ligand exist in the thione form and remain as neutral tridentate with NNS donor atoms in the complex (1) but in the complex (2) the HL acted as uninegative tridentate ligand, beside Presence of uncoordinated chloride ions in the cavities of the crystal lattice of the complex (2). One of these chlorides is hydrogen bonded to a proton of the amine of the ligand. The coordination environment of Ni(II) and Co(II) metal complexes 1, 2, has a distorted octahedral structure. The oxazole N and S atoms in the two complexes are *cis* to each other whereas the azomethine N atoms are *trans* coordinated. The ligand and its metal complexes were tested for their *in vitro* biological activity against seven standard microorganisms: two Gram positive namely *Bacillus subtilis* and *Micrococcus luteus*, and one Gram negative bacteria *Escherichia coli* and four fungi: *Saccharomyces cerevisiae* (Baker's yeast), *Candida maltosa*, *Mucor spec*., and *Aspergillus niger*, at a concentration 100µg/ml. The results showed that the ligand HL and its Ni(II) Co(II) complexes appear inhibition activity for *Mucor spec*. only.

1. Introduction

Thiosemicarbazones ($R^1R^2C{=}N{-}NH{-}C(=S){-}NR^3R^4$) are regarded as "privileged ligands" [1] because they as a group constitute an important class of NS donor ligands. They are highly reactive compounds that form chelate complexes with metal ions [2] Besides their interesting coordination chemistry, thiosemicarbazones have attracted considerable interest because of their potentially beneficial biological activities such as antitumor [3], antifungal [4, 5] antibacterial [5, 6], and antiviral agents [7].

The chemistry of transition metal complexes of thiosemicarbazones has been receiving considerable attention due to the pharmacological properties of both ligands and complexes [8–10]. Nickel is an essential trace element for bacteria, plants, animals and humans. However, its concentration in human tissue is relatively low (1 µg/L) compared with zinc, iron and copper (100 µg/L) [11]. In recent years, a number of researchers have shown some interest in the biological, medicinal and the structural properties of nickel thiosemicarbazone complexes. Some of these complexes have shown a variety of biological activities like antibacterial [12,13], and antifungal [14,15] activities.

Since the first reported studies on the biological activity of cobalt complexes in 1952[16], various complexes have already been found active not only against leukemia and lymphoma cell lines [17], but also against some bacterial strains [18], and also possesses antifungal activity [19]. Various cobalt(II) thiosemicarbazone complexes have been that have antimicrobial activities. [20].

This work expands upon that type research by introducing an unknown heterocyclic thiosemicarbazones ligands based on a 2-methyl-1, 3-oxazole-4-carbaldehyde thiosemicarbazoneand (HL) and its Ni(II) and Co(II) complexes, and shows the antimicrobial activity toward some organisms.

2. Experimental

2.1 Materials and measurement

All chemicals and solvents were of reagent grade and were purchased from Sigma- Aldrich Chemical Co. they were used without further purification. The materials used in this study were 2-methyl-1,3-oxazole-4-carbaldehyde (97%), thiosemicarbazide (99.0%), nickel(II) chloride hexahydrate (98%), cobalt(II) chloride hexahydrate (98%), absolute ethyl alcohol and dimethyl sulfoxide -d_6 (99.9%).

2.2. Instrumentation

The Partial elemental microanalyses of synthesized ligand and complexes for C, N, H, S contents were performed on Euro EA Elemental Analyzer. HL ligand and its metal

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complexes were mounted on a glass capillary and data collections carried out on a Bruker APEX-II CCD diffractometer. The HL and complexes 1& 2 crystals were kept at 200 and 170 K respectively during data collection. Using Olex2 [21], the structures were solved with the SIR2004 [22] 1, and ShelXT [23] structure solution program using Direct Methods, and refined with the XH (1), ShelXL [24] (2), refinement package using CGLS minimization and Gauss-Newton minimization. IR spectra were recorded as KBr pellets by using a Perkin-Elmer Spectrum RX-1Spectrophotometer in the wave- number ranging between 200 to 3700 cm^{-1}. Spectra of ^{1}H NMR and ^{13}C NMR data were recorded at ambient temperature (about 23 ^{0}C) on Bruker AV-II 300 Spectrometer, operating at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C, with deuterated DMSO. The chemical shifts (δ) are given in ppm relative to TMS and coupling constant (J) are given in Hertz. The solvent signals were used as reference (^{1}H: δ_H 2.500 ppm residual DMSO-d5 in DMSO-d6, ^{13}C: δ_c 39.56 ppm).The UV-visible studies of all compounds in the solid state were performed by using barium chloride as a blank on a Cary 4000 UV-Vis spectrophotometer, in the range (200-900) nm.

2.3. Synthesis of the ligand (HL)

2-methyl-1,3-oxazole-4-carbaldehydethiosemicarbazone ligand, HL was prepared by using the following procedure [25]. Equimolar quantities 1:1 of 2-methyl-1,3-oxazole-4-carbaldehyde and thiosemicarbazide were reacted. Thiosemicarbazide (5.0 mmol, 0.4557 g), was dissolved in (aprox. 60mL of 60% ethanol-water) by refluxing at 50°C in 250 mL Round bottom flask (Rbf). In the refluxing solution, the aldehyde (5.0 mmol, 0.5555g) solution in ethanol (aprox. 30mL) was added dropwise. The reaction mixture was refluxed for 6-8 h at 60 ^{o}C on steam-bath. A clear solution of the reaction mixture filtered and the filtrate was allowed to cool slowly at room temperature. A colorless crystalline product suitable for X-ray of HL obtained (scheme 1) were separated, washed with hot water then with cold ethanol, dried on air, weight 0.6542 g. Color: colorless, yield: 64.6%, FT-IR (KBr, ν,cm-1): 3413(s) (NH_2), 3284(s) (NH), 1604(s) (C=N) (azomethine), 1353(s) (C-N) (oxazole ring), 1582(s) (C=N) (oxazole ring). 1H NMR (300 MHz, 300 MHz for ^{1}H and 75.5 MHz for ^{13}C, DMSO DMSO-d6, δ, ppm): 2.90 (s, 3H,CH3), 8.25 (t, 1H, oxazole-H), 11.45 (m,1H, HN2CS), 7.65&7.90 (2H, $CSNH_2$), 8.39 (1H, HC=N, azomethine), 136.37 (C2, imine), 178.19 (thione), 134.28, 139.31, 162.13 (C3, C4, C5, ring) respectively, 13.60 (C6) (methyl). Anal. calcd. for $C_6H_8N_4OS$: C, 39.12; H, 4.38; N, 30.41, S, 17.41. Found: C, 39.17, H, 4.22 ; N, 30.74, S, 18.85 %. (Molar mass g/mol).

2.4. Synthesis of complexes

2.4.1. Synthesis of $[Ni(HL)_2]Cl_2$ (1)

The $[Ni(HL)_2]Cl_2$ (**1**), (scheme 2) was synthesized according to the published procedure [26]. A hot solution of $NiCl_2.6H_2O$ (0.50 mmol, 0.12 g) in 5 mL of hot distilled water was added to a boiling solution of the ligand (HL) (1.00 mmol, 0.184 g) in ethanol. The reaction mixture was refluxed on a water bath for 4 h then allowed to cool overnight at room temperature. The dark green crystals suitable for X-ray were filtered, washed with ethanol and dried in air. color: dark green, yield: 68, FT-IR (KBr, ν,cm-1): 3280 (s) (NH_2), 3140 (s) (NH), 1576 (s) (C=N) (azomethine), 1604 (s) (C=N) (oxazole ring), 525 (Ni-N), 626 (Ni-N Oxazole ring), 660 (Ni-S). UV-visible ($BaCl_2$, range (200-900) nm: 369, 416, 564, 737. Anal. calcd. for $C_{12}H_{16}Cl_2N_8NiO_{3.12}S_2$: C, 28.04; H, 3.14; N, 21.80, S, 12.48. Found: C, 28.00, H, 3.374; N, 21.80, S, 12.30 %. (Molar mass g/mol).

2.4.2. Synthesis of $[Co(L)_2]1.3Cl$ (2)

$[Co(L)_2]Cl_2$ (**2**), (scheme 2) was prepared according to the published procedure [27]. $CoCl_2.6H_2O$ (0.064 g; 0.25 mmol, 10 cm^3) was added to the (HL) ethanolic solution (0.09211 g, 0.5 mmol, 20 cm^3) under refluxing conditions. The reflux was maintained for 24 h. The resulting solution was concentrated and a dark brown precipitate was filtered off. Recrystallization from water-ethanol mixture gave dark brown crystals suitable for X-ray analysis. Yield%: 50, FT-IR (KBr, ν,cm-1): 3310 (s) (NH_2), 3138 (s) (NH), 1590 (s) (C=N) (azomethine), 1477 (s) (C=N) (oxazole ring), 437 (Co-N), 484 (Co-N Oxazole ring), .620 (Co-S). UV-visible ($BaCl_2$, range (200-900) nm: 365, 414, 574, 730. Anal. calcd. for $C_{12}H_{14}Cl_2CoN_8O_2S_2$: C, 29.04; H, 2.84; N, 22.58, S, 12.92. Found: C, 29.949, H, 3.374; N, 23.257, S, 13.46%. (Molar mass g/mol).

2.5. Biological activity

Experiments were done at Institute of Microbiology, General Microbiology-TU-Dresden-Germany.

The ligand HL and its metal complexes were tested for *in vitro* biological activity by using a modified agar diffusion method [28]. All The tested substances were dissolved in DMSO in concentration (100 mg mL^{-1}), and all the tested microorganisms were obtained from a prepared cell suspension of fresh overnight culture of each strain. Cell suspension of 100 µL of each strain was plated on an agar plates, and a sterile cork borer was used to stamp out two holes on each agar plate, 100 µL of each chemical substance (100 mg mL^{-1}) was added into the agar plate holes.

2.5.1. Antibacterial screening

The antibacterial activity of the ligand and its metal complexes were performed against *Bacillus subtilis*-ATCC, *Micrococcus luteus*-ATCC as (Gram positive) and *Escherichia coli- ATCC as* (Gram negative). The Agar plate was incubated at 37^{o}C, zone of inhibition (radius "r" in mm, Figure 1) was determined after 20, 24 and 48 h of incubation.

2.5.2. Antifungal screening

Antifungal activity of the synthesized ligand and its corresponding metal complexes in term of their inhibition were tested against three fungai; *Saccharomyces cerevisiae* (Baker's yeast), *Mucor spec* and *Aspergillus niger*. The agar plate were incubated at 28 °C for *Saccharomyces cerevisiae* and at room temperature for *Mucor spec* and *Aspergillus niger*. The zone of inhibition (radius "r" in mm) was determined after 20, 24 and 48 h of incubation.

3. Results and Discussion

The synthesized ligand 2-methyl-1, 3-oxazole-4-carbaldehyde thiosemicarbazone and its complexes were characterized by using partial elemental analysis, IR, UV-Visible, ^{1}H NMR and ^{13}C NMR spectroscopy and single x-ray diffraction.

3.1. Physical Properties and elemental analysis

The ligand HL and its Co(II) and Ni(II) complexes (**1**,**2**) are stable at under ambient conditions; they are soluble in dimethyl sulfoxide (DMSO), hot methanol and ethanol, complex (2) soluble in water.The analytical data for compounds the ligand and complex (1&2) are in close agreement with the theoretical values obtained, Table 1.

3.2. IR Spectra

Some of the IR spectra of the ligand HL and its complexes 1& 2 are listed in table 2.The IR spectra of the complex $Ni(HL)_2Cl_2$ (1) showed bands at 3280 and 3140 cm^{-1} which are assigned to $\nu(N^1\text{-}H_2)$ and $\nu(\text{-}N^2\ H)$ respectively[29],

these data suggested that the HL ligand is coordinating to the metal center in the neutral form[30]. The ν(C=N) $_{azomethine}$ is shifted to lower frequency from 1604 to 1576 cm^{-1}, indicating the coordination of the azomethine nitrogen [31]. As well as the ν(C=S) which appeared at 845 cm^{-1} in the free ligand is shifted to lower frequency at 832 cm^{-1} this attributed to the coordinated to the metal center [32]. This result confirmed by crystal structure. On the other hand, the bands at 1582 cm^{-1} which attributed to the $\nu(C=N)_{oxazole\ ring}$ in the free ligand [33], undergo higher shift to 1604 cm^{-1}, which is an indication of the involvement of the nitrogen of the oxazole ring in complexation. New bands appeared at 525,626 and 660 cm^{-1} are assigned to $\nu(M\text{-}N)_{azomethine}$, $\nu(M\text{-}N)_{oxazole\ nitrogen}$ and $\nu(C=S)_{thioamide}$ respectively are consider more evidence for formation of complex.

The IR spectra of the complex $[Co(L)_2]$ 1.3Cl appearing the $\nu(NH_2)$ stretching band at 3310 cm^{-1} this band shifted to lower frequency from that in the free ligand. The band at 1461 cm^{-1} due to the ν(C=S) stretching is absence from the spectrum this indicated that the complex existing in the thiol form [34]. This result was confirmed by absence of δ(NHCS) at 11.45 ppm in ^{1}H NMR spectrum, X-ray crystallography and by appearance of band at 1642 cm^{-1} corresponding to the newly formed N=C bond. The lower shift of ν(C=N) stretching frequency from 1604 cm^{-1} in the free ligand to 1590 cm^{-1} is assigned to the coordination of the thiosemicarbazone through the azomethine nitrogen [35]. On the other hand, the bands at 1582 cm^{-1} which attributed to the $\nu(C=N)_{oxazole\ ring}$ in the free ligand undergo lower shift to 1477 cm^{-1}, which is an indication of the involvement of the nitrogen of the oxazole ring in complexation[33]. The new bands at 437, 484 and 620 cm^{-1} are assigned to $\nu(M\text{-}N)_{a_{zomethine}}$, $\nu(M\text{-}N)_{oxazole\ nitrogen}$ and $\nu(C=S)_{thioamide}$ respectively.

3.3. Crystal structure of the ligand HL

The molecular structure and atom numbering schemes are shown in Figure 1. Crystal structure data and structure refinement parameters for the ligands are given in Table3. The selected bond distances and torsion angles are listed in (Table 4).

HL crystallized with two molecules per asymmetric unit into triclinic crystal system with a space group of P-1. The structural analysis reveals that the ligand exists in the thione form [36]. the atoms S1 and N3 are found trans to each other with respect to the N2—C1 bond or in E-configuration (Figure 1) .This is confirmed by the torsion angle of -172.55(7) of the S1—C1—N2—N3 moiety, which is close to reported value for salicylaldehyde thiosemicarbazone [37], thus, the N1 atom lies cis to N3. The thione form in the solid state is strongly confirmed by the C1—S1 and C1—N2 observed bond lengths of [1.693(1) Å] and [1.352(1) Å] respectively. The C1—S1 distance of 1.692(10) Å is closer to the C=S bond length [1.62 Å] than to the C—S bond length [1.81 Å], and the C1—N2 distance of 1.352(12) Å is in the range of 1.349(6)—1.386(4) Å for other thiosemicarbazones having the C—N single bond reported earlier [38, 39]. Also, the (N_2C-H) vibration band at 3284(m) cm^{-1} in the IR spectral consider further confirmed of the thione form. In the crystal structure, the two crystallographically independent molecules are linked through intermolecular N—H... N hydrogen bonds, between N1 (molecule 1) and N6 (molecule 2) as donor of N7(molecule 2) and N4 of oxazole ring (molecule 1) as acceptor atoms, and this lead to stabilize the crystal structure.

3.4. Crystal structure of the complex $[Ni(HL)_2]Cl_2$ (1)

Complex (1) crystallized into a triclinic crystal system with two molecules in the unit cell. The molecular structure of the complex along with the atomic numbering scheme is given in Figure 2. Crystal data and structure refinement parameters for the complex presented in Table 3, and selected bond lengths and bond angles summarized in Table 4.

The X-ray crystal structure showed that the nickel (II) atom in this complex is coordinated to two ligands of HL. The ligand consists of two units; an oxazole ring and a thiosemicarbazonic chain. The ligand is coordinated as a neutral tridentate ligand *via* the azomethine nitrogen, the thione sulfur and the oxazole nitrogen. Therefore, the coordination number for Ni(II) is six and the complex has an octahedral geometry as shown in Figure 2. In addition, the structure showed the presence of two uncoordinated chlorides and three disordered water molecules. In the crystal unit cell. The two azomethine nitrogen atoms N3 and N7 are *trans* to each other, while the oxazole nitrogen atoms N4 and N8 and the thione sulfur atoms S1 and S2 are in the *cis* position. This structure is identical to the published structure of Ni(II) [40] where the two coordinating azomethine nitrogen atoms are *trans* to each other and the other two sets of identical donor atoms are *cis* to each other.

The E configuration of the thiosemicarbazone ligand chain about C1-N2 bond changed to Z (*cis*) configuration to facilitate the coordination of thione sulfur and imine nitrogen to Ni atom in complex. This reveals that rotation has occurred about the azomethine bond for coordination. This is confirmed by the torsion angle of -172.55(7)^o of the S1—C1—N2—N3 moiety of the ligand which become 3.7 (4)^o in the complex [26]. As observed, the N3 and N7 atoms with bonds lengths 2.017 Å in (Ni1-N3) and 2.029 Å of (Ni1-N7) act as axial ligands and S1, S2, N4, N8 atoms are considered to form a square plane exhibiting considerable distortion from octahedral symmetry. This is indicated by the bond angles of N3–Ni1–N7 (173.56) ^{o} and N7–Ni1–S2 (82.62) ^{o}, that slightly deviated from the ideal octahedral angles. The bond angles N3–Ni1–S1 (81.85)^o, N7–Ni1–S2 (82.62)^o, S1–Ni1–S2 (94.16)^o, N4–Ni1–N8 (88.25)^o, N3-Ni1-N4 (78.72)^o and N8-Ni1-N7 (78.73)^o, showed considerable distortion in the octahedral geometry of the complex.

Coordination shortens the thiosemicarbazone bond lengths. Thus, the C1–S1 bond length is shortened from 1.6927 to 1.691 Å indicating the coordination as thione form [40]. Figure 2 shows the intermolecular H-bonding interactions in the molecule. Moreover, this molecular conformation is stabilized by the intramolecular interactions between the chloride ion(Cl1) and the two hydrogen atoms, one of the (H-N2) and the other from second molecule (N9-H) as well as the hydrogen bonding between (O6….H-N1) (8.72)^o and N8-Ni1-N7 (78.73)^o, showed considerable distortion in the octahedral geometry of the complex.

3.5. Crystal structure of the complex $[Co(HL)_2]1.3Cl$ (2)

The main crystal data and structure refinement parameters are reported in Table 3 Selected bond distances and bond angles are summarized in Table 4. The complex (2) crystallized into a monoclinic crystal system with one molecule in the unit cell. The molecular structure together with the atom numbering scheme is shown in Figure 3.

In this complex the Co(II) ion adopts a distorted octahedral environment with the thiosemicarbazone ligand (L) behaves as mononegative tridentate ligand and coordinated to the metal ion through deprotonated thiolate sulfur atoms S1 and S2, the azomethine nitrogen atoms N3

and N7 and oxazole nitrogen atoms N4 and N8. Since the two molecules of ligands L are coordinated to cobalt(II) as mononegative tridentate ligands the complex is a neutral[41]. The crystal structure, however, showed the presence of disordered non-coordinated chloride anions (see Figure 3). These chloride anions, it seems, lie in the cavities in the crystals. This has been observed in the crystal structure of a nickel (II) thiosemicarbazone complex [14]. The chloride anions may control the packing of the complex by forming a hydrogen bond between the methyl group of the ligand with one chloride anion.

The thiol form of the complex $[Co(L)_2]1.3$ Cl is confirmed by the C1-S1 bond distance (1.7359 Å) which appears to be closer to C-S single bond (1.81 Å) than C-S double bond (1.62 Å) [42,43]. Furthermore, the shortening of (SC1-N1) bond distance from (1.3523Å) to (1.322Å) indicates that this bond has changed to a double bond (C=N). Additional evidence is provided by the IR spectrum of the cobalt(II) complex.

The E configuration of the thiosemicarbazone ligand seem to change about C1-N2 bond into a Z configuration after coordination to the metal to facilitate the coordination of the thiol sulfur and imine nitrogen to the Co(II) in complex. This is confirmed by the torsion angle -172.55(7)^o of the S1—C1—N2—N3 moiety of the ligand which become 0.7(2)^o in the complex. The two azomethine nitrogen atoms N3 and N7 are *trans* to each other whereas the oxazole nitrogen atoms N4 and N8 and the thiolate Sulfur S1 and S2 are in the *cis* position.

3.6. ^{1}H &^{13}C NMR spectra of the ligand HL

The ^{1}HNMR spectral data of the ligand HL shows absorption at δ 11.45 ppm due to the hydrogen atom of N^2-H [44]. The amino group (- N^1H_2) of the thiosemicarbazone showed two bands at δ 7.65 and δ 7.90 ppm. This is due to the restricted rotation of this group about C^1- N^1 bond axis caused by the delocalization of the lone pair of electrons on the N^1H_2 nitrogen [45]. The spectrum exhibits absorption at δ 8.39 ppm which is assigned to (C2H=N3). The oxazole ring protons (C4-H) were observed at δ 8.25 ppm. The peak at δ 2.90 ppm is for methyl group hydrogen -2-substituted of the oxazole ring. Besides this, a medium singlet peak appeared at δ 7.22 ppm which is attributed to intramolecular hydrogen bonding between the nitrogen of the oxazole ring (N4) and the hydrogen of the hydrazinic nitrogen (H-NC) of the second molecule (see Figure 1).

The ^{13}C NMR spectral data of the ligand HL showed a sharp singlet appearing at δ 178.19 ppm due to carbon of the thione (C1–S). The peak for the azomethine (–CH=N) carbon (C2) appeared at δ 136.37 ppm [45]. The oxazole ring carbon atoms showed signals starting from (C3) at δ 134.28 ppm, (C4) at δ 139.31 ppm and (C5) at δ 162.13 ppm (see Figure 26). The signal at δ 13.60 (C6) is attributed to the methyl group.

The ^{1}H NMR spectra of the nickel complex of the ligand HL was not appeared any signal, therefore, no ^{13}C NMR recorded.

As for Co(II) complex of the ligand L the ^{1}H NMR spectral data was recorded using D_2O. The singlet that appeared at δ11.45 ppm in the free ligand and assigned to the N(6)HCS group, is absent in the spectrum of the complex (Figure 3) indicating that the ligand coordinates as thiolate ion upon deprotonation at N(6)[46]. The spectrum showed a signal at δ 8.22 ppm which is assigned to azomethine proton –CH=N. The lower shift of the frequency of this band from that of the free ligand at δ 8.39 ppm indicated coordination of the thiosemicarbazone through the imine nitrogen. The signal that appeared at δ 2.25 ppm is assigned to the methyl group (-CH_3) [47]. In the spectrum of the complex the NH_2 signal appears as singlet at δ 8.18 ppm with respect to the free ligand, this may be due to the free rotation of $N5H_2$ group caused by the reduction of the double bond character of C(S) N5 bond after deprotonation of N(6)H[48].

The ^{13}C NMR spectrum provides direct information about the carbon skeleton of compounds. The ^{13}C NMR spectra of the Co(II) complex of the ligand HL^1 showed a sharp singlet peak appearing at δ 181.7 ppm due to C1–S carbon. The peak for the azomethine (–C2H=N) carbon exhibited at δ 140.0 ppm. The peaks observed at δ 134.28, 139.31 and 162.13 ppm have been assigned to oxazole ring carbon atoms. The signal shown at δ 13.42 ppm is assigned to the methyl group (-CH_3).

3.7. UV-Vis spectra

The UV-Vis spectrum showed the intraligand absorption at 369 and 365 nm for complexes (1 & 2) of the ligand HL attributed to the π-π* transition these bands shifted to higher energy in complexes. This shift on complexation indicates coordination via thioamide bands C–S (2) and C=S (1&3). The intraligand bands corresponding to n-π* transition of the complexes (1&2) shifted to higher this change due to the involvement of thioamide, azomethine nitrogen and oxazole nitrogen atom in coordination [49]

3.8. Biological Activity

The new Ni(II), Co(II) complexes of heterocyclic thiosemicarbazone ligands HL were tested for their in vitro biological activity against seven of standard microorganisms: two Gram positive namely *Bacillus subtilis* and *Micrococcus luteus,* and Gram negative bacteria *Escherichia coli* and four fungi that is *Saccharomyces cerevisiae* (Baker's yeast), *Candida maltosa, Mucor spec*. and *Aspergillus niger.*

All compounds were tested at concentration 100 µg/mL and the Zone of inhibition has been measured in mm after 20, 24 and 48 hours of incubation. The results showed that the ligand HL and their Ni(II) Co(II) complexes appear inhibition activity for Mucor spec. only.

4. Conclusion

The new ligand, 2-methyl-1,3-oxazole-4-carbaldehyde thiosemicarbazone (HL) and their Ni(II) and Co(II) complexes were synthesized and characterized by elemental analysis, IR, (^{1}H&^{13}C) NMR (ligand) and UV-Vis spectroscopy. The crystal structure of the free ligand and complexes has been determined by single crystal X-ray diffraction technique. It is examined that in these complexes the ligand has NNS donor tridentate nature, bind to the center metal through the azomethine nitrogen, oxazole nitrogen and thione/thiolate sulfur atom. As well as, the results of the above studies exhibited considerable distortion from octahedral symmetry. The antimicrobial activity results of the ligand HL and their Ni(II) Co(II) complexes appear inhibition activity for *Mucor spec*. only.

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Disclosure statement

Conflict of interests: The authors declare that they have no conflict of interest.

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Sample availability: Samples of the compounds are available from the author.

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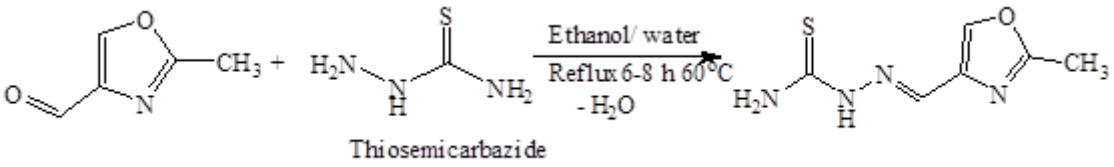
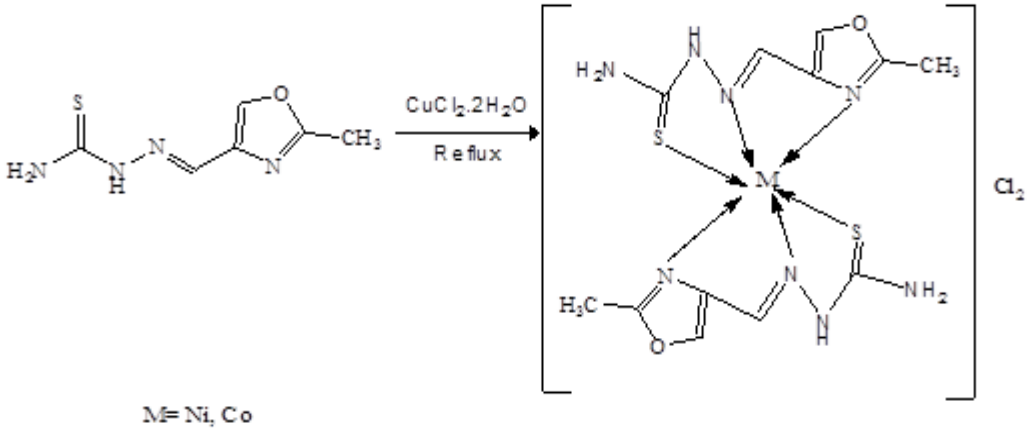


Scheme 1. Synthesis of the ligand (HL).



Scheme 2. Synthesis of the complex 1.

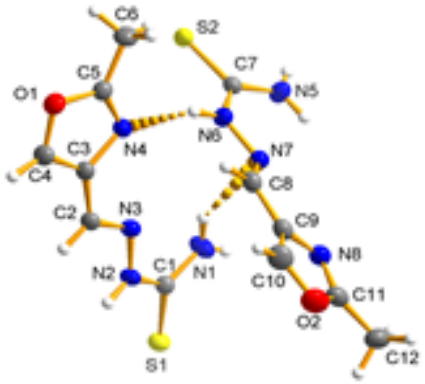


Figure 1. Molecular structure and numbering sequence of [HL]

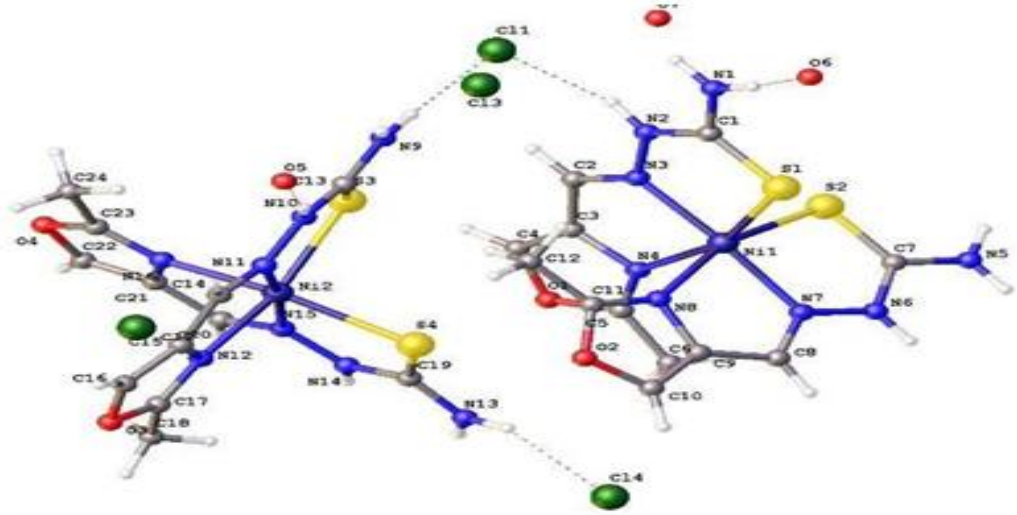


Figure 2. The crystal structure of the $[Ni(HL)_2]Cl_2$ complex

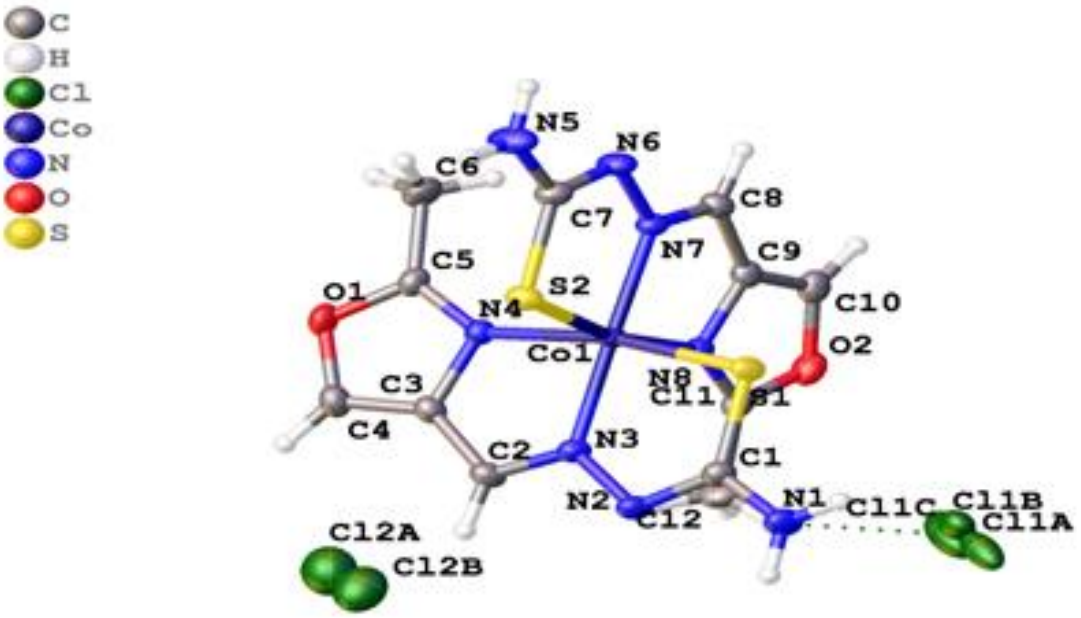


Figure 3. The structure of $[Co(L)_2]1.3Cl$ (2) complex

Table 1.The physicochemical characteristics of the synthesized ligand and its metal complexes.

Complex	Formula	Color	Yield%	Elemental analysis, % found (%calculated)				Molar massg/mol
				C	N	H	S	
HL	$C_6H_8N_4OS$	Colorless	64.6	39.17 (39.12)	30.74 (30.41)	4.22 (4.38)	18.85 (17.41)	184.22 (184.2)
$Ni(HL)_2Cl_2$	$C_{12}H_{16}Cl_2N_8NiO_{3.12}S_2$	Dark Green	68	28.00 (28.04)	21.80 (21.80)	3.374 (3.14)	12.30 (12.48)	516.06
$Co(L)_2$ 1.3Cl	$C_{12}H_{14}Cl_2CoN_8O_2S_2$	Dark brown	50	29.949 (29.04)	23.257 (22.58)	3.034 (2.84)	13.46 (12.92)	496.26

Table 2. IR frequencies (cm^{-1}) of characteristic groups

mode	HL	$Ni(HL)_2Cl_2$	$Co(L)_21.3Cl$	references
$\nu(N^2H)_{imine}$	3284(s)	3140	3138	16
$\nu(N^1H_2)_{amine}$	3413(s)	3280	3310	16
$\nu(C=N)_{oxazole\ ring}$	1582(s)	1604	1477	33
ν(C=S) thione	1461(s)& 845(m)	832	830	29
$\nu(C=N)_{azomethine}$	1604(s)	1576	1590+new 1642	14
$\nu(M\text{-}N)_{azomethine}$	-	525	437	
$\nu(M\text{-}N)_{oxazole\ nitrogen}$	-	626	484	
$\nu(M\text{-}S)_{thioamide}$	-	660	620	

Table 3. Crystal data and structure refinement parameters for HL and complexes (1&2)

Compound	HL	1	2
Formula	$C_6H_8N_4OS$	$C_{12}H_{16}Cl_2N_8NiO_{3.12}S_2$	$C_{12}H_{14}Cl_{1.30}N_8CoO_2S_2$
Formula Weight	184.22	516.06	471.45
Temperature /K	200(2)	170/2	170/2
Colour	Colorless	Dark Green	Dark brown
Crystal System	Triclinic	Triclinic	Monoclinic
Space Group	P-1	P-1	P 21/n
Unit cell dimensions	α°=100.288(3) a = 9.0132(4) Å β°=109.073(3) b =9.2290(4) Å γ°=100.476(3) c =11.8473(5) Å	a=11.7587(5) α°=99.074(2) Å b=14.1180(5)β°=103.783(2) Å c=14.8170(6) γ°=113.153(2) Å	a=8.7423(3) Å α°= 90 b=17.7091(6) β°=109.536(2) c=12.9496(5) Å γ°= 90
Volume/Å3	851.96(6)	2107.69(15)	1889.42(12)
$D_{calc.}$ /g cm^{-3}	1.436	1.626	1.657
μ/mm^{-1}	0.337	1.404	1.339
Z	4	4	4
Wavelength/Å	0.710730	MoKα (λ = 0.71073)	MoKα (λ =0.71073)
2Θ range for data collection/°	1.873 to 28.999	2.95 to 60.336	2.027 to 29.997
F(000)	-	1052.0	956
Reflections collected	4263	29147	5487
Independent reflections	0.0148	12396 [R_{int} = 0.0268, R_{sigma} = 0.0551]	5487[R_{int} = 0.0345 R_{sigma} = 0.0405]
Final R indexes [I>=2σ (I)]	R_1 = 0.0302, $wR_{2=}$ 0.0829	R1= 0.0482, wR_2 = 0.1127	R1= 0.0345, wR_2 = 0.0879
Final R indexes [all data]	R_1 = 0.0302, $wR_{2=}$ 0.0829	R_1 = 0.0782, wR_2 = 0.1253	R1= 0.0405, wR_2 = 0.0910
Goodness-of-fit on F^2	1.044	1.040	1.099

Table 4. Selected bond lengths (Å), bond angles and torsion angle (°) of the ligand HL and complexes (1&2)

Compound	Bond length Å			Bond angle (°)				Torsion angle (°)				
	Atom	atom	length	Atom	atom	atom	angle	Atom	A	A	A	Angle
HL	S1	C1	1.6927(10)					N3	N2	C1	S1	-172.55(7)
	N1	C1	1.3225(13)									
	N2	C1	1.3523(12)									
	Ni1	N3	2.017(2)	N3	Ni1	N7	173.56(10)	N3	N2	C1	S1	3.7(4)
	Ni1	N7	2.029(2)	N7	Ni1	S2	82.62(7)					
	Ni1	N8	2.098(2)	N3	Ni1	S1	81.85(7)					
	Ni1	N4	2.125(2)	S1	Ni1	S2	94.16(3)					
$[Ni(HL)_2]Cl_2$ (1)	Ni1	S2	2.3681(9)	N4	Ni1	N8	88.25(9)					
	Ni1	S1	2.4215(9)	N3	Ni1	N4	78.72(10)					
	S1	C1	1.691(3)	N8	Ni1	N7	78.73(10)					
	Co1	N3	1.9025(15)	N7	Co1	N3	178.02(7)	N3	N2	C1	S1	0.7(2)
	Co1	N7	1.9013(15)	N7	Co1	N8	82.98(6)					
	Co1	N8	1.9819(16)	N3	Co1	N8	97.48(7)					
[Co(L)]1.3Cl	Co1	N4	1.9826(15)	N7	Co1	N4	99.03(6)					
(2)	Co1	S2	2.2078(5)	N3	Co1	N4	82.87(6)					
	Co1	S1	2.2041(5)	N8	Co1	N4	93.97(6)					
	S1	C1	1.7359(19)	N7	Co1	S1	92.55(5)					
				N3	Co1	S1	85.54(5)					
				N8	Co1	S1	88.96(5)					
				N4	Co1	S1	168.32(5)					

Table 5. Antimicrobial* screening data of investigated ligand and their Ni(II) and Co(II) complexes

Compound	Conc.µg/mL	Diameter of inhibition zone in millimeter (mm)					
		Gram +ve: Bacteria		Gram–ve Bacteria	Baker's yeast	Fungus	
		B. subtilis	*M.luteus*	*E. coli*	*S. cerevisiae*	*Mucor spec.*	*A. niger*
HL	*100*	-	-	-	-	50	-
1- $Ni(HL)_2Cl_2$	*100*	-	-	-	-	40	-
2- $Co(L)_2$1.3Cl	*100*	-	-	-	-	40	-

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