

New Metal Complexes of Thiosemicarbazone Mannich base Ligand; Synthesis, Structural Characterisation and Biological Activity

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ABSTRACT

The synthesis of a new tridentate Schiff-base thiosemicarbazone ligand (HL) that derived from the reaction of ((R)-2-((4-(dimethylamino)phenyl)((2-nitrophenyl)amino)methyl)-5,5-di methyl- cyclohexane-1,3-dione with thiosemicarbazide is reported. The reaction of the title ligand(E)-2-((R)-2-((R)-4-(dimethylamino)phenyl)((2-nitrophenyl)amino)methyl)-5,5-dimethyl-3-oxocyclohexylidene)hydrazine-1-carbothioamide with selected metal ions of Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) gave the title monomeric complexes. Analytical and spectroscopic techniques were used, as required, to characterise the prepared compounds. These include; elemental microanalysis, ¹H, ¹³C-NMR and mass spectra, FT-IR and electronic spectra, magnetic susceptibility and conductance. These analyses revealed the formation of monomeric complexes of octahedral arrangement about Co(II); Cu(II) and square planar and tetrahedral geometry with the Ni(II) and Zn(II); Cd(II) ions, respectively. Thermal stability (TGA-DSC) of HL and selected complexes were also explored. The antimicrobial activity of the title compounds (ligand and complexes) towards several microorganism (bacteria and fungi species) were examined. The collected data revealed the antimicrobial activity of the ligand was enhanced upon complex formation.

Keywords: Thiosemicarbazone ligand, Metal complexes, Structural investigation, Thermal stability, Antimicrobial activity.

INTRODUCTION

The multicomponent reaction (MCRs) represents an interesting approach in synthetic green chemistry, in which the Mannich reaction is an example of this approach [1]. The fabrication of a wide range of interesting compounds derived from Mannich bases is reported [2-4]. These materials include the synthesis of a range of pharmaceuticals and natural products [5]. The preparation of the Mannich compound is derived from the mixing of three components, which involve a ketone (with one acidic-hydrogen atom), an aldehyde and an amine (bar from tertiary amine) [6]. One of the fundamental approaches in green chemistry is based on the development of a synthetic procedure that is dependent on multicomponent Mannich reactions. This approach is intended to achieve a cleaner and environmentally friendly reaction by reducing the number of synthetic steps [7]. Further, a variety of Mannich compounds have been used as precursors to fabricate interesting ligands and their metal complexes [1]. These compounds (ligands and complexes) indicated several applications including their role in medicine [8] as pharmaceutical components and as antimicrobial agents [5]. More, the biological activities of Mannich based complexes are enhanced, compared with the free ligands [1,5]. Schiff bases that are derived from the Mannich compound are interesting species that are used constantly as complexation agents [9,10]. This is related to their tendency to give stable complexes with metal ions that have several applications. These include their role in medicine, as a bioactive molecules, in catalysis, in analytical and environmental chemistry and as a scavenger for the removal of heavy metal ions [11]. The biological activities of these species make them potential agents that have been used as antiviral, antibacterial, anti-inflammatory and antiapoptotic agents [12]. Thiosemicarbazones are important Schiff base compounds that incorporate a hard (the nitrogen) and the soft (sulfur) chelating site for complexation [13,14]. Thiosemicarbazone Schiff base compounds have the ability to bind with DNA, to be used as antibacterial, antifungal, anticancer, anti-inflammatory, antioxidant, antiviral, analgesic, and anticonvulsant [15]. In the current work, we report formation and structural characterisation of a new thiosemicarbazone ligand and its monomeric complexes. Further, this work includes studying the antibacterial and antifungal influence of the prepared compounds.

METHODS

Materials and Methods: The consumed reagents were purchased from commercial companies and used as received. The NMR spectra (¹H- and ¹³C-NMR) for the ligand and diamagnetic complexes were acquired in DMSO-d₆ on a Bruker 300 MHz instrument (300 MHz for ¹H- and 75 MHz for ¹³C-NMR) with a

tetramethylsilane (TMS) as an internal reference. The FTIR spectra of compounds were recorded using KBr and CsI discs from 4000–250 cm⁻¹ on a Shimadzu Fourier Transform Infrared Spectrometer (FTIR-600). Electro spray (+) mass spectrophotometer was recorded using a Sciex Esi mass analysis. Melting points were determined on an electrothermal Stuart apparatus, model SMP40. The electronic spectra were acquired on a Shimadzu UV-160 in the range 1000-200 nm with a concentration of 10⁻³-10⁻⁵ mol L⁻¹ of samples in DMSO solutions. The molar conductivity measurements of the complexes were recorded at room temperature for 10⁻³ M solutions of the samples in DMSO using a Eutech Instruments Cyber scan con. 510 digital conductivity meter. Elements analysis (C.H.N.S) and metal content were carried out on an Eager 300 for EA1112 analyzer and Shimadzu (A A- 680G) atomic absorption spectrophotometer, respectively. The chloride content for complexes was determined using the potentiometric titration method on 686–Titro Processor-665 Dosim A-Metrohm/Swiss. Thermogravimetric analysis (TGA and DSC) was carried out on STA PT-1000 Linseis Company/Germany. Magnetic moments at 306 K were measured with a magnetic susceptibility balance on Johnson Matthey. The biological evaluation of the ligand and its metal complexes against four bacterial species (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus subtilis*) and two types of fungi (*Candida albicans* and *Trichomonas vaginalis*) were performed using agar-well diffusion approach. In this method, the wells were dug in the media with the help of a sterile metallic borer with centres of at least 6 mm. Recommended concentration (100 μL) of the test sample of 1 mg/mL in DMSO was introduced in the respective wells. The plates were incubated immediately at 37 °C for 24 h. The activity was evaluated by measuring the diameter of inhibition zones (mm).

Preparation of precursor: The preparation of ((R)-2-((4-(dimethylamino)phenyl)((2nitrophenyl)amino)methyl)-5,5-dimethyl-cyclohexane-1,3-dione) was implemented with a metod reported in [16,17].

Synthesis of Schiff-base ligand (HL): To a mixture of ((R)-2-((4-(dimethylamino)phenyl)((2nitrophenyl)amino)methyl)-5,5-dimethylcyclohexane-1,3-dione) (0.5g, 1.22mmol) in 15ml of hot EtOH, was added with stirring a solution of thiosemicarbazide (0.11g, 1.22mmol) in 15ml of EtOH with 3 drops of glacial acetic acid. The reaction mixture was allowed to reflux for 6h, during wich time a pale-yellow powder was formed that collected by filtration and washed with cold ethanol (5ml) and then air dried, Figure 1. Yield: 0.4g (68%), mp = 181-183°C. FT-IR (KBr, cm⁻¹), 3442 ν(N-H) _{hydrazinic}, 3371 ν(NH) _{secondary amine}, 3263, 3174 ν(NH₂) _{asy, sy}, 1664 ν(C=O) _{ket.}, 1622 ν(C=N), 1198 ν(C=S) and 1460 ν(NO₂). The ¹H-

NMR spectrum (300MHz, DMSO-d₆, ppm) showed peaks at δ H: 0.85-1.04 (6H, s, C₁, 1'-H), 2.08-2.28 (4H, s, CH₂; C₃, 3'-H), 2.36 - 2.51 (6H, s, N(CH₃)₂; C₁₀, 10'-H), 2.56-2.59 (1H, d, C₄-H, J_{HH}= 9 Hz), 4.78-4.80 (H, t, CH; C₅-H, J_{HH}= 8 Hz), 5.59 (H, d, NH), 7.09 (2H, d, CH; C₈, 8'-H), 7.22-7.23 (H, t, CH; C₁₃-H, J_{HH}= 4 Hz), 7.24-7.25 (2H, d, CH; C₇, 7'-H, J_{HH}= 4 Hz), 7.26-7.27 (H, d, J_{HH}= 6Hz; C₁₁-H, J_{HH}= 4 Hz), 7.31 (H, t, J_{HH}= 6 Hz; C₁₂-H), 8.01 (1H, d, J_{HH}=6Hz; C₁₄-H), 10.23-10.03 (2H, s, NH₂), 11.08 (1H, s, NH) (Figure 2A). The ¹³C-NMR spectrum of H₂L(75MHz, DMSO-d₆, ppm) exhibits signals at δ C: 149.33(C₉), 144.72 (C₁₆), 131.71 (C₁₂), 131.28 (C₆), 129.59 (C₁₅), 127.07 (C_{7,7'}), 128.49 (C₁₄), 128.70 (C₁₃), 113.70 (C₁₁), 100.53(C_{8,8'}), 53.82 (C₄), 53.73 (C₃), 53.13 (C₅), 49.52 - 45.00(C_{10,10'}), 28.38-26.07(C₂), 31.99-30.00 (C₁), 169.00 C=N, 186.75 C=S. C=O 195.55 (Figure 3B). The positive (ES) mass spectrum of HL showed the parent ion peak at m/z= 483 amu (M+H)⁺ and the following fragments; Peaks detected at m/z= 455.55, 395.46, 347.44, 305.43, 291.37, 221.28 [(M+H-(C₂₂H₂₇N₆O₃S))⁺, [(M+H-(C₂₁H₂₅N₅O₃))⁺, [(M+H)-(C₂₁H₂₃N₄O)]⁺, [(M+H) (C₂₀H₂₁N₂O)]⁺, [(M+H)-(C₂₀H₂₁N₂O)]⁺, [(M+H)-(C₁₅H₁₃N)]⁺ (Figure 4).

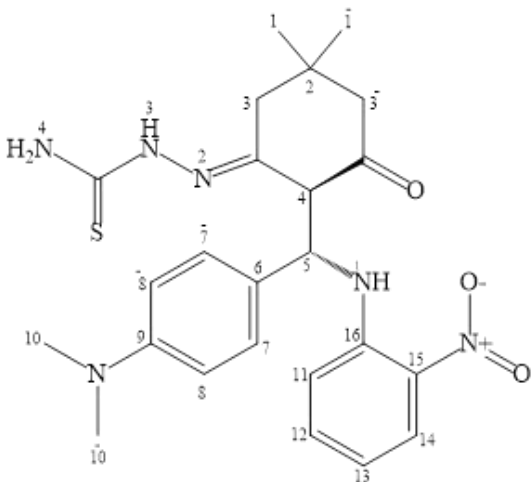


Figure 1: Chemical structure of thiosemicarbazone ligand (HL).

General procedure for the synthesis of complexes: To a solution of the thiosemicarbazone ligand (0.5mmol) in 10ml of EtOH was added with stirring an ethanolic solution of KOH to adjust the pH to ca. 9. A mixture of metal chloride salt in 10ml of DMF was added slowly with stirring to the above solution. The reaction mixture was allowed to stir for 4h, during which time a coloured precipitate was formed. The obtained solid was filtered off, washed with cold absolute ethanol (5ml) and air-dried, Scheme (1). Metal salts quantities, yields colours, and melting points of the complexes are given in (Table 1).

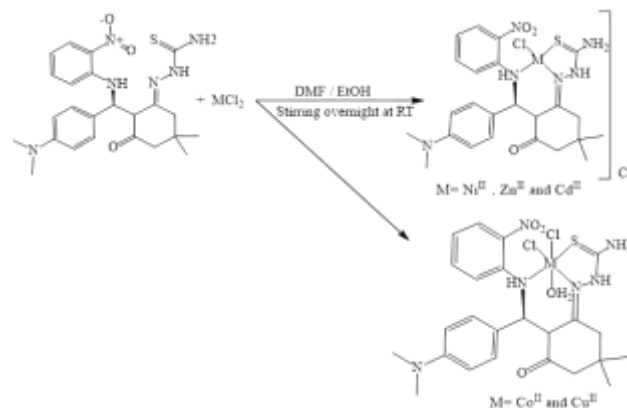
NMR Data: The ¹H-NMR spectrum of [Zn(HL)Cl]Cl in DMSO-d₆ solvent, Figure 2A, showed the following peaks at δ H: 0.93-1.10 (6H, s, C₁, 1'-H), 2.06-2.26 (4H, s, CH₂, C₃, 3'-H), 2.53 (6H, s, N(Me)₂, C₁₀, 10'-H), 2.57 (H, d, CH, C₄-H), 4.26-4.43 (H, t, CH, C₅-H),

5.73 (1H, d, N-H), 6.56 (2H, d, CH, C₈, 8'-H), 6.57 (H, t, CH, C₁₃-H), 6.97 (2H, d, CH, C₇, 7'-H), 7.09 (H, d, C₁₁-H), 7.22 (H, t, C₁₂-H), 7.96 (H, d, C₁₄-H), 8.52 N-H₂ (H, s, NH₂), 12.95 N-H (H, s, NH). The ¹³C-NMR spectrum of [Zn(HL)Cl]Cl in DMSO-d₆ solvent showed peaks at δ C: 148.29 (C₉), 144.00(C₁₆), 131.66(C₁₂), 129.34 (C₆), 128.88 (C₁₅), 128.82(C_{7,7'}), 127.22 (C₁₄), 119.22(C₁₃), 113.45(C₁₁), 113.33(C_{8,8'}), 56.66(C₄), 52.38(C₃), 49.80(C₅), 49.62N-(C_{10,10'}), 31.28-29.41 (C₂), 28.17-26.00 (C₁), 161.00 C=N, 181.68 C=S, 198.72C=O. (Figure 3 A).

Table 1: Metal salts quantities, yields colours, melting points of complexes of HL.

complex	Weight of metal salt(g)	Weight of complex(g)	Yield (%)	Colour	m.p. °C
[Co(HL)Cl ₂ H ₂ O]	0.098	0.253	67	Dark green	360*
[Ni(HL)Cl]Cl	0.098	0.253	68	Pale grey	223
[Cu(HL)Cl ₂ H ₂ O]	0.07	0.25	50	Red	233
[Zn(HL)Cl]Cl	0.056	0.25	47	White	360*
[Cd(HL)Cl]Cl	0.094	0.27	46	Pale yellow	265

*= Decomposed



Scheme 1: Synthesis route of HL complexes.

RESULTS AND DISCUSSION

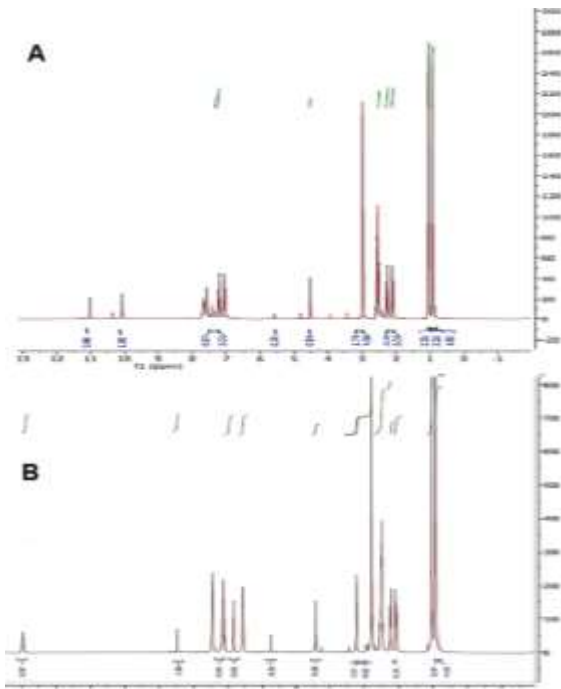
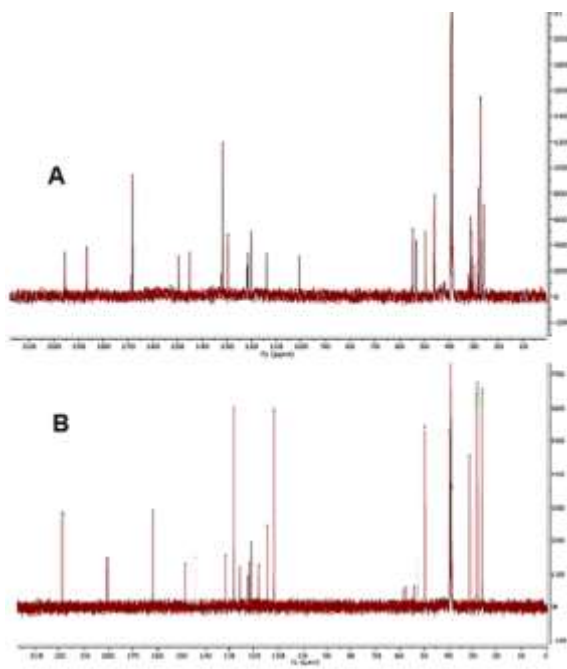
The ligand HL was prepared from the reaction of (R)-2-((4-(dimethylamino)phenyl)((2-nitrophenyl)amino)methyl)-5,5-dimethylcyclohexane-1,3-dione with thiosemicarbazide in a 1:1 molar ratio at reflux, Scheme (1). The reaction of the ligand with metal chloride salts of Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) in a 1:1 (L:M) mole ratio resulted in the formation of six and four coordinate monomeric complexes (Scheme (2)). The obtained monomeric complexes are air-stable solids and dissolve in DMSO and DMF. The complexation behaviour and coordination geometries of complexes were assumed from their physicochemical data. These data (Table 2) agree well with the suggested formula. Conductance measurements of the complexes in DMSO solutions indicated complexes are neutral [18].

Table 2: Microanalysis and physical properties of HL its complexes.

Complex	Molecular formula	M.Wt	Microanalysis calculated; found (%)					
			C	H	N	S	Cl	M
[Co(HL)Cl ₂ H ₂ O]	C ₂₄ H ₃₂ CoN ₆ O ₄ .2Cl	630.45	(45.52) 45.72	(5.1) 5.126	(13.3) 13.33	(5.06) 5.09	(11.23) 11.25	(9.13) 9.35
[Ni(HL)Cl]Cl	C ₂₄ H ₃₀ NiN ₆ O ₃ .2Cl	612.228	(47.00) 47.08	(4.81) 4.95	(13.50) 13.72	(5.00) 5.23	(11.50) 11.58	(9.22) 9.58
[Cu(HL)Cl ₂ H ₂ O]	C ₂₄ H ₃₂ CuN ₆ O ₄ .2Cl	635.06	(45.00) 45.39	(5.04) 5.08	(13.12) 13.23	(4.96) 5.05	(11.00) 11.16	(9.92) 10.01
[Zn(HL)Cl]Cl	C ₂₄ H ₃₀ ZnN ₆ O ₃ .2Cl	618.94	(46.12) 46.57	(4.56) 4.89	(13.23) 13.57	(5.00) 5.18	(11.23) 11.45	(10.21) 10.56
[Cd(HL)Cl]Cl	C ₂₄ H ₃₀ CdN ₆ O ₃ .2Cl	665.94	(43.10) 43.28	(4.26) 4.54	(12.33) 12.61	(4.67) 4.81	(10.58) 10.64	(16.76) 16.87

Table 3: The FT-IR spectral data of HL and its complexes (cm⁻¹).

Compounds	v(NH)	v(NH) _{am}	v(NH ₂) _{sy,asy}	v(C=O)	v(C=N)	v(C=C)	v(NO ₂)	v(M-O)	v(M-N)	v(M-S)	v(M-Cl)
[Co(H ₂ L)Cl ₂ H ₂ O]	3431	3309	3282, 3194	1660	1612	1516	1466	565	476,405	372	262, 246
[Ni(H ₂ L)Cl]Cl	3479	3315	3257, 3151	1658	1612	1516	1466	-	476,440	370	273
[Cu(H ₂ L)Cl ₂ H ₂ O]	3431	3386	3276, 3176	1658	1616	1516	1468	536	498,444	395	275, 256
[Zn(H ₂ L)Cl]Cl	3433	3309	3251, 3190	1666	1618	1581	1468	-	497,430	378	271
[Cd(H ₂ L)Cl]Cl	3436	3390	3211, 3163	1660	1614	1518	1465	-	478,406	374	270

Figure 2: ¹H-NMR spectra in DMSO-d₆ solutions for: a) H₂L; b) [Zn(HL)Cl]Cl.Figure 3: ¹³C-NMR spectra in DMSO-d₆ solutions for: a) H₂L; b) [Zn(HL)Cl]Cl.

FT-IR Spectra: The FT-IR spectrum of the free thiosemicarbazone

ligand (HL) shows characteristic bands at 3442, 3371, 3263;3174, 1664, 1622, 1510 and 1198 cm⁻¹ that are attributed to v(NH), v(NH)_{am}, v(NH₂)_{sy,asy}, v(C=O)_{ket}, v(C=N)imine, v(C=C) aromatic and v(C=S), respectively [19,20]. The FT-IR spectrum shows no peak around ca. 2600 cm⁻¹ may assign to v(S-H). The collected infrared data of complexes and their assignments are listed in (Table 3). The FT-IR spectra of complexes exhibited ligand bands with the appropriate shifts due to complex formation. The imine band that appeared at 1622 cm⁻¹ in the free ligand (HL) suffered shifting to a lower frequency and appeared around 1612-1618 cm⁻¹ in the complexes [21]. This shift confirmed the involvement of the nitrogen atom of the imine group of the ligand in the coordination with the metal centre [22,23]. The shift that occurred in the v(C-S) group in the spectra of complexes, compared with that in the free ligand, may indicate the coordination of the ligand through the S atom to the metal ions. The FT-IR spectra of the complexes show new bands in the ranges 405-498 and 370-395 cm⁻¹ assigned to v(M-N) and v(M-S), respectively [23,24]. Further, bands recorded in the range 246-271 cm⁻¹ related to v(M-Cl) [24].

NMR Spectra: The ¹H-NMR spectrum of the thiosemicarbazone ligand (HL) in DMSO-d₆ solvent showed a peak at δH= 5.59 ppm, equivalent to one proton, assigned to (N₁-H) group. This peak was detected at ~ 5.73 ppm in the spectrum of the Zn(II) complex. The up-field shift of this peak may attribute to the coordination of the nitrogen atom to the metal centre. In the spectrum of the ligand, the peak that attributed to the (N₃-H) was detected at δH= 11.08 ppm (1H, s) correlated to (N₃-H) group (see Figure 2A). This peak disappeared in the spectrum of the Zn(II)-complex conforming of the deprotonation of the ligand upon complex formation (Figure 2B). Peak detected at δH= 10.23ppm in the spectrum of HL, equivalent to two protons, attributed to (N₄-H) group. The appearance of this peak at a low field is due to the inter and/or intra- hydrogen bonding that occurred between the (N₄-H) group and the NMR solvent or with the other heteroatoms within the ligand. This signal has detected around ~8.52 ppm in the spectrum of the Zn(II) complex. The ¹³C-NMR spectrum of the Zn(II)-complex in DMSO-d₆ solvent exhibited a signal at ~ 161 ppm assigned to the C=N group. This signal was detected downfield, compared with that in the free ligand at 169ppm. Chemical shift at ~ 181 ppm due to the C-S group appeared up-field in the spectrum of the complex, compared with that in the free ligand at 186ppm (Figure 3A and B).

Mass Spectroscopy: The positive (ES) mass spectrum of HL showed the parent ion peak at m/z = 483amu (M+H)⁺. The following fragments at m/z=455.55, 395.46, 347.44, 305.43, 291.37, 221.28 attributed to [M+H-(C₂₂H₂₇N₆O₃S)]⁺, [M+H-(C₂₁H₂₅N₅O₃)]⁺, [(M+H)-(C₂₁H₂₃N₄O)]⁺, [(M+H)-(C₂₀H₂₁N₂O)]⁺, [(M+H)-(C₂₀H₂₁N₂O)]⁺ and [(M+H)-(C₁₅H₁₃N₂)]⁺, respectively (Figure 4). The assignment of the fragmentation species and their relative abundance is shown in Scheme 2.

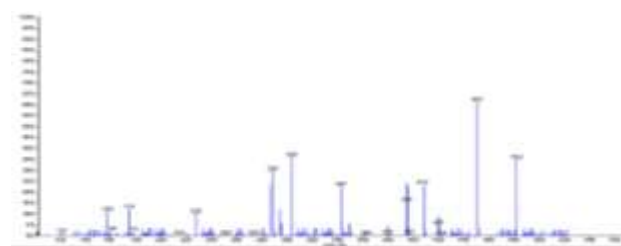
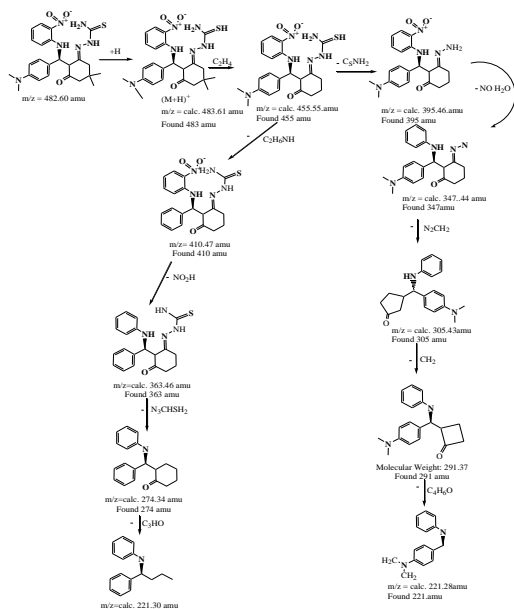


Figure 4: The electrospray (+) mass spectrum of HL.



Scheme 2: The fragmentation pattern and relative abundance of HL fragments.

Electronic Spectra and Magnetic Moment Measurements: The UV-Vis spectrum of HL exhibits an intense absorption peak at 275nm; $\epsilon_{\max} = 1132 \text{ molar}^{-1}\text{cm}^{-1}$ and 313nm; $\epsilon_{\max} = 932 \text{ molar}^{-1}\text{cm}^{-1}$, which are assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, respectively [25]. The electronic spectra and magnetic moments data of the ligand HL and its complexes are collected in (Table 3). The electronic spectra of the complexes display various peaks around 267-289 and 301-388 nm attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$, respectively [25]. The electronic spectrum of the Co(II) complex displays peaks in the d-d region at 526 and 614 nm related to ${}^4T_{1g}(F) \rightarrow {}^4A_{1g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ transitions [26]. The electronic spectrum of the Co(II) complex and its magnetic moment value is consistent with the formation of distorted octahedral structure [26]. The electronic spectrum of the Ni(II) complex exhibited a peak in the d-d region at 618 correlated to ${}^1A_{1g} \rightarrow {}^1A_{2g}$, indicating a square planar geometry about the Ni atom [26]. The Cu(II) complex recorded a broad peak with two hubs in the d-d region attributed to ${}^2B_{1g} \rightarrow {}^2B_{2g}$ transition, confirming a distorted octahedral arrangement for the Cu atom [27]. This spectrum and the μ_{eff} value are in agreement with the suggested geometry. The spectrum of the Zn(II) and Cd(II) complexes exhibited bands assigned to ligand field $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions [28]. The tetrahedral geometry structure is suggested for the Zn(II) and Cd(II) centres [29].

Table 3: Electronic spectra data in DMSO solutions and magnetic moment of HL complexes.

Complex	μ_{eff} (BM)	λ_{nm}	$\Sigma \epsilon_{\text{max}}$ ($\text{dm}^3\text{mol}^{-1}\text{cm}^{-1}$)	Assignment	Suggested geometry
[Co(HL)Cl ₂ ·H ₂ O]	2.6	268 375 442 526 614	1621 1830 2500 72 102	L.F C.T C.T ${}^4T_{1g}(F) \rightarrow {}^4A_{1g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$	Distorted octahedral
[Ni(HL)Cl] ₂	Diamagnetic	267 301 618	1467 1431 19	L.F C.T ${}^1A_{1g} \rightarrow {}^1A_{2g}$	Square planer
[Cu(HL)Cl ₂ ·H ₂ O]	2.0	270 388 615 675	1356 1341 108 80	L.F C.T ${}^2B_{1g} \rightarrow {}^2B_{2g}$ ${}^2B_{1g} \rightarrow {}^2B_{2g}$	Distorted octahedral
[Zn(HL)Cl] ₂	Diamagnetic	289 385	2236 1114	L.F C.T	Tetrahedral
[Cd(HL)Cl] ₂	Diamagnetic	278 325	1157 2011	L.F C.F	Tetrahedral

Thermal Analysis: The thermal analysis data (TGA and DSC) for the ligand (HL), Figure 5, and some metal complexes. The TG and DSC thermograms of HL and its complexes were determined from ambient temperature to 1000°C in a nitrogen atmosphere. The analysis of the thermal data showed that the ligand (HL) is stable up to 181°C. The DSC analysis recorded peaks at 181, 210, 441, 459, 509 and 542°C. The TGA step between 181-315°C attributed to the loss of (CO + NO + NH₂ + NH₃ + H₂S + H₂CO + CH₄) segments (obs. = 0.8497mg, 35.05%; calc. = 0.8480mg, 35.02). The second process between 320-660°C indicated the loss of (4NH₂ + C₄H₂ + C₇H₂ + C₈H₃) fragment (obs. = 1.347mg, 55.55%; calc. = 1.340mg, 55.30%). The third step recorded at 665-1000°C indicated the loss of (NH₃+H₂) molecule, (obs. = 0.112mg, 4.61%; calc. = 0.0955mg, 3.94%). The final residue of the compound is related to (C₂H) (calc. = 25.01mg, 5.18%). The thermogram of [Ni(HL)Cl]₂ is depicted in Figure 6. The first exothermic peak detected at 223-500°C may attribute to the loss of a molecule of the (2NO + H₂S + Cl₂ + CHCO) segment; (obs. = 3.145mg, 66.53%; calc. = 3.13mg, 66.30%). The second step occurred at 510-1000°C indicated the loss of (2NH₃ + C₆H₉) fragment; (obs. = 0.8918mg, 18.87%; calc. = 0.888mg, 18.80%). The final residue of the (C₂H₇ + NiO) calc. = 89.7634mg, 14.662%. The DTGA indicated several peaks at 210, 221, 441, 459, 509 and 542°C. In the DSC analysis, peaks pointed at 223°C correlated to

the exothermic decompositions process. However, the peaks at 231 and 500°C refer to the endothermic decompositions process. The exothermic and endothermic peaks may indicate combustion of the organic ligand in the nitrogen atmosphere. The thermogram of [Cu(HL)Cl₂·H₂O] is depicted in Figure 7. The first exothermic peak detected at 140-320°C may be attributed to the loss of a molecule of the (H₂O + H₂S + CO₂ + CO) segments; (obs. = 0.5178mg, 14.85%; calc. = 0.5164mg, 14.81). The second step occurred at 325-1000°C indicated the loss of C₃H₈+Cl₂ +N₂H₄+C₂H₆) fragment; (obs. = 1.125mg, 32.25%; calc. = 1.120mg, 32.13%). The final residue of the (C₆H₄N₂+ C₆H₃N+C₅H₃N + CuO) calc. = 33.553mg, 52.52%. The DSC indicated several peaks at 233, 280, 320, 769 and 789°C. In the DSC analysis, peaks at 233 and 789°C are correlated to the exothermic decompositions process. However, the peak at 280, 320 and 769°C. refers to the endothermic decompositions process. The exothermic and endothermic peaks may indicate the combustion of the organic ligand in the nitrogen atmosphere.

Biological Activity: Thiosemicarbazone ligand (HL) and its complexes were tested against four types of bacterial species: Gram-negative and Gram-positive species (Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa). Mueller Hinton agar is a method, used to examine compounds [30]. DMSO solvent showed no effect on the tested

compounds. The concentration used is 100 ppm in DMSO solvent. According to the results presented in Table (5). The ligand (HL) showed no activity towards all bacterial strains. Complexes of HL have shown more antimicrobial activity against all types of bacteria, compared with the free ligand (HL). The Cd(II)-complex exhibited excellent activity against all bacterial strains compared with free ligand and other complexes. The Ni(II) complex showed no activity against any type of bacterial strains. The Co(II)-complex exhibits antibacterial activity against *Escherichia coli*. The Cu(II)-complex exhibits antibacterial activity against (*Escherichia coli*. and *Bacillus subtilis*). The Zn(II)-complex exhibits antibacterial activity against (*Staphylococcus aureus* and *Bacillus subtilis*). The enhanced activity of the complexes can be discussed based on chelation theory and Overtone's model [31]. The antifungal activities of thiosemicarbazone ligand (HL) and its complexes were studied against two types of fungi species (*Candida albicans* and *Trichomonas vaginalis*), Table (6). The ligand indicated no activity against the two types of fungi. The Cd(II) complex was found to be more active against (*Candida albicans* and *Trichomonas vaginalis*). The Zn(II)-complex indicated a high activity against *Trichomonas vaginalis*. The complex of Co(II) revealed inhibition activity against the *Candida*. The complexes of Ni(II) and Cu(II) ions show no activity against both types of fungi [32,33].

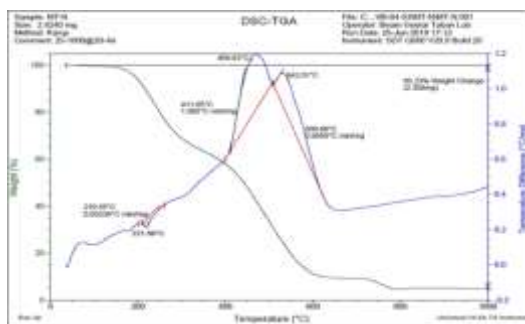


Figure 5: TGA and DSC thermogram of HL in the N₂ atmosphere.

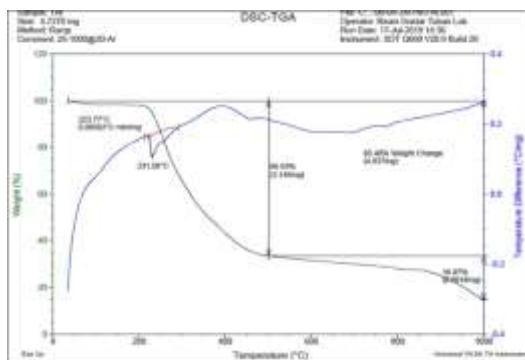


Figure 6: TGA and DSC of [Ni(HL)Cl]Cl in the N₂ atmosphere.

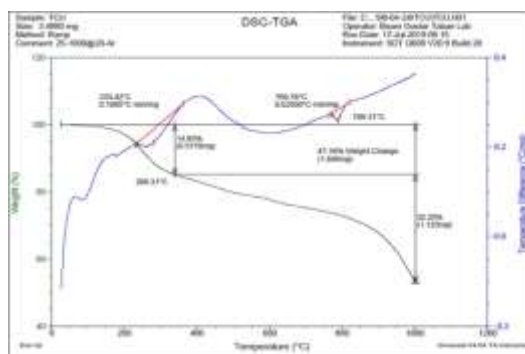


Figure 7: TGA and DSC of [Cu(HL)Cl₂H₂O] in the N₂ atmosphere.

Table 5: The inhibition zones (mm) of anti-bacterial activity for ligand and its complexes.

Compounds	Escherichia coli (G-)	Pseudomonas aeruginosa (G-)	Bacillus subtilis (G+)	Staphylococcus aureus (G+)
HL	-	-	-	-
[Co(HL)Cl ₂ H ₂ O]	16	-	-	-
[Ni(HL)Cl]Cl	-	-	-	-
[Cu(HL)Cl ₂ H ₂ O]	13	-	15	-
[Zn(HL)Cl]Cl	-	-	18	11
[Cd(HL)Cl]Cl	18	24	27	22

Table 6: The inhibition zones (mm) of anti-fungal activity for ligand and its complexes.

Compounds	Candida albicans	Trichomonas vaginalis
HL	-	-
[Co(HL)Cl ₂ H ₂ O]	11	-
[Ni(HL)Cl]Cl	-	-
[Cu(HL)Cl ₂ H ₂ O]	-	-
[Zn(HL)Cl]Cl	-	17
[Cd(HL)Cl]Cl	22	14

CONCLUSIONS

In this paper, a new thiosemicarbazone ligand (HL) and its metal complexes were synthesised and characterised. The reaction of the ligand with Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) metal ions in a 1:1 (L:M) mole ratio resulted in the isolation of monomeric complexes. Physico-chemical and spectroscopic methods were implemented to confirm the mode of bonding and the overall structure of the complexes. These results suggest the isolation of six and four coordinate complexes. More, the thermal stability of the ligand and selected metal complexes were also explored. The biological activity of the ligand and its complexes against bacterial species and fungi pathogens were also tested. Generally, thiosemicarbazone complexes showed more antimicrobial activities, compared with the free ligand.

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