

Synthesis, Structures and Biological studies of some metal ions with a Schiff base ligand

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Abstract:

The new complexes of Fe(II), Co(II) and Cu(II) with a multidentate Schiff-base ligand [HL] derived from the condensation reaction of (2,6-diformyl-4-methyl-phenol) with (4-phenylthiosemicarbazide) in mole ratios of 1:2. The complexes were synthesized in direct reaction of the corresponding metal chloride with the ligand. (FTIR, UV-Vis, ^1H , ^{13}C NMR, A.A), chloride content, conductance and melting point measurements The data of these measurements suggest octahedral geometry around Fe(II), Co(II) and Cu(II) ions. Biological activity of the ligand and its metal complexes against gram positive bacterial strain *Bacillus* (G+) and gram negative bacteria *Pseudomonase* (G-) revealed that the metal complexes become less resistive to the microbial activities as compared to the free ligand.

Keywords:

Schiff-base ligand (2,6-bis-[(3-phenyl thiourea-imino)-methyl]-phenol); transition metals; structural and biological studies.

Introduction :

In principle thiosemicarbazide reacts with wide variety of aldehydes and ketones to form thiosemicarbazones, which may be used as a ligand. Compounds formed in this way are structurally interesting since both sulfur and nitrogen atoms may be involved in coordination, and many transition metal complexes of thiosemicarbazones have been reported [1]. Thiosemicarbazone moiety without substitute attached to the thion sulfur coordinates as either neutral or anionic (N,S) bidentate ligand depending on the method of complex preparation [2]. When an additional coordinating functionality is presented in the proximity of the donating centers, the ligands bind in a tridentate manner NNS, ONS. This occurs with either the neutral molecule or the mono basic anion upon loss of a hydrogen from N(2) [3]. Schiff-base metal complexes also have applications in biomedical [4, 5], biomimetic and catalytic systems [6, 7] and in supporting liquid crystalline phases [8]. Furthermore, metal complexes of

Synthesis, Structures and Biological studies of some metal ions with a Schiff base ligandLecturer .Enaam I. Yousif

chromium, manganese, nickel, copper, zinc and ruthenium with a wide variety of Schiff-bases have been used as catalysts for carbonylation, hydrogenation, hydroformylation and epoxidation reactions [9,10]. Recently, we reported the Metal-assisted assembly of dinuclear metal (II) dithiocarbamate Schiff-base macrocyclic complexes: Synthesis and biological studies potassium 2,2'-(1*E*,1'*E*)-(1,2-diphenylethane-1,2-diylidene)bis(azan-1-yl-1-ylidene) bis(2,1phenylene)dicarbamodithioate [11]. In this paper, the synthesis and spectral characterisation of some transition metal complexes with (2,6-bis-[(3-phenyl thiourea-imino)-methyl]-phenol) HL are reported .

Experimental

Materials:

All reagents were commercially available and used without further purification. Solvents were distilled from appropriate drying agents immediately prior to use.

Physical measurements:

Melting points were obtained on a Buchi SMP-20 capillary melting point apparatus and are uncorrected. IR spectra were recorded as (KBr) disc using a Shimadzu 8400 FTIR spectrophotometer in the range 4000-400 cm^{-1} . Electronic spectra of the prepared compounds were measured in the region 250-1100 nm for 10^{-3}M solutions in DMSO at 25°C using a Shimadzu 160 spectrophotometer with $1.000\pm 0.001 \text{ cm}^{-1}$ matched quartz cell. ^1H , ^{13}C NMR, spectrum was acquired in DMSO- d_6 solution using a Bruker AMX300 MHz spectrometer with tetramethylsilane (TMS) as an internal standard for ^1H , ^{13}C NMR at AL-al-Bayt University, Jordan. Metals were determined using a Shimadzu (A.A) 680 G atomic absorption spectrophotometer. Chloride was determined using potentiometer titration method on a (686-Titro processor-665Dosimat-Metrohm Swiss). Conductivity measurements were made with DMSO solutions using a PW 9526 digital conductivity meter.

Synthesis

Preparation of the precursor (2,6-diformyl-4-methyl-phenol):

To a solution of p-cresol (10.8 g, 10 mmol) in (50 ml) glacial acetic acid, hexamethylenetetramine (28.2g,20mmol) and (30g,100mmol) of paraformaldehyde were added. The mixture was allowed to stirred continuously until the deep orange viscous solution was obtained then heated to (70-90°C).for two hrs. The solution was cooled to room temperature and concentration H_2SO_4 (10 ml) carefully added. The resulting solution was refluxed for half-hr, and then on treatment with distilled water (400 ml) a light yellow precipitate was formed, which was stored over night at (4°C).The yellow product was isolated by filtration and washed in small amount of cold methanol.More pure product was obtained by means of recrystallisation from toluene, Yield (%35),(5.6 g), m.p

Synthesis, Structures and Biological studies of some metal ions with a Schiff base ligandLecturer .Enaam I. Yousif

(134-132⁰C). IR data (cm⁻¹): 3349(O-H), 2970(C-H)arom, 2924 and 2791 (C-H) aldehydic, 1665 (C=O), 1240 (C-O).

Preparation of the HL :

Preparation of the (2,6-bis-[(3-phenyl thiourea-imino)-methyl]-phenol) .A solution of 2,6-diformyl-4-methyl-phenol (0.5g, 3.0488 mmole) in methanol(5ml) was added to 4-phenylthiosemicarbazide (1.01g, 6.0976 mmole) dissolving in methanol (5ml),and then(2-4) drops of glacial acetic acid was added slowly to the reaction mixture. The mixture was refluxed for 4 hrs, and allowed to dry at room temperature for (24) hrs. pale yellow solid metal was obtained. Yield (1.11 g , %78), m.p =87-89⁰C .IR data (cm⁻¹): 3342(O-H), 3062 (C-H)arom, 2868(C-H) iminic, 1606 (C=N). The ¹H NMR spectrum of the ligand in DMSO-d₆ showed peaks at; δ H(300 MHz, DMSO-d₆): 7.34-7.56 (Ar-H); 2.78, 2.87 (N-H-2) and (N-H-4), 4.85(O-H).

General synthesis of the complexes:

A methanolic solution (10 mL) of the metal salt (metal (II) salts are hydrated chloride; MCl₂.XH₂O; where: M= Fe^{II} : X=4 , Co^{II} : X= 6 and Cu X= 2 respectively, was stirred into methanolic solution of the Schiff-base ligand (1 mmol) in methanol (15 mL) with (1 mmol) in methanol (15 mL) KOH. The reaction mixture was then refluxed for 2 h on a water bath until a coloured precipitate formed which was collected by filtration, washed with cold ethanol (5 mL) and dried at room temperature. Elemental analysis data, colours, and yields for the complexes are given in(Table 1).

Determination of Bacteriological Activity :

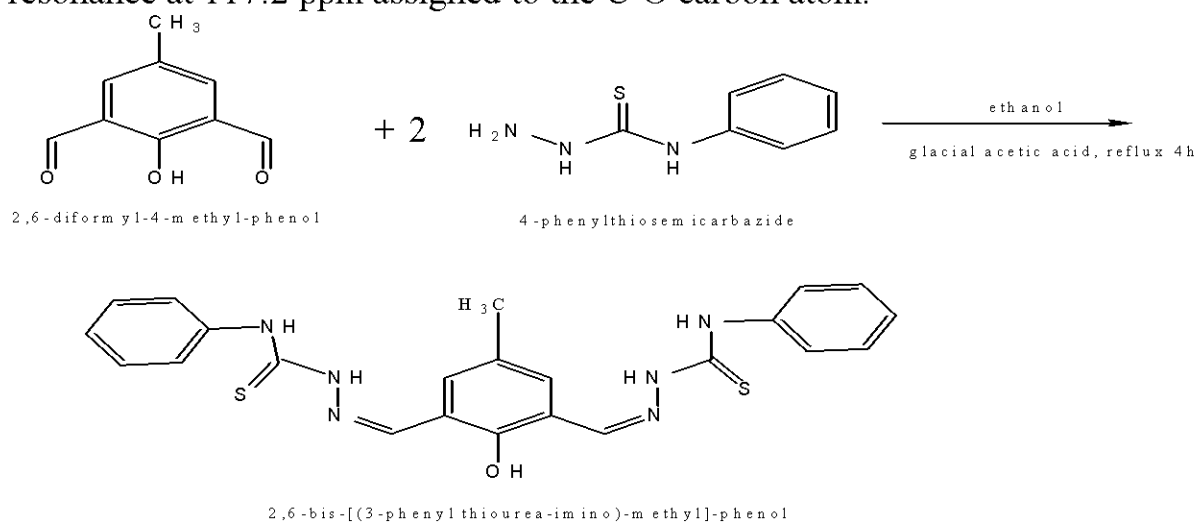
Bioactivities were investigated using agar-well diffusion method [12]. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm. Recommended concentration (100 μ L) of the test sample 1 mg/mL in DMSO was introduced in the respective wells. The plates were incubated immediately at 37⁰C for 20 hours. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). In order to clarify the role of DMSO in the biological screening, separate studies were carried out with the solutions alone of DMSO and they showed no activity against any bacterial strains. Ligand found to be potentially active against these bacterial strains compared with its complexes.

Results & Discussion

The ligand [HL] was prepared in step according to the general method of preparation of Schiff base ligand (13) shown in Scheme (2). The infrared spectrum of the ligand HL Fig.(1),was recorded within the 4000-400cm⁻¹ range and compared with those of the new complexes (Table 1). The IR spectra of the ligand shows characteristic bands at 3342, 3219 and 1614 cm⁻¹ due to the ν (O-H), ν (N-H), and ν (C=N)imine functional groups, respectively [14,15]. The IR

Synthesis, Structures and Biological studies of some metal ions with a Schiff base ligandLecturer .Enaam I. Yousif

spectra of the complexes exhibited ligand bands with the appropriate shifts due to complex formation (Table 2). The $\nu(\text{C}=\text{N})$ imine at 1614 cm^{-1} in the free Schiff-base ligand is shifted to lower frequency and observed in the range $1597\text{--}1600\text{ cm}^{-1}$ for the complexes. The bands are assigned to a $\nu(\text{C}=\text{N})$ stretch of reduced bond order. This can be attributed to delocalisation of metal electron density (t_{2g}) to the π -system of the ligand [16, 17], indicating coordination of nitrogen of the $\text{C}=\text{N}$ moieties to the metal atoms [18]. Figure (1) represents the IR of the ligand. Upon complex formation, The $\nu(\text{N-H})$ bands at $3342, 3219\text{ cm}^{-1}$ in the free ligand is shifted to higher wave number for the complexes [18]. At lower frequency the complexes exhibited bands around $690\text{--}617, 565\text{--}574$ and $445\text{--}468\text{ cm}^{-1}$ which could be assigned to $\nu(\text{M-O})$ $\nu(\text{M-N})$ and $\nu(\text{M-S})$ vibration mode [16] (Table3). These bands indicated that the imine nitrogens and the thione sulphur of the ligand is involved in coordination with metal ion. The main peaks of ^1H NMR of HL are collected in the experimental section “preparation of HL and presented in Figure (3). The resonance peaks associated with the aromatic groups are observed in the range $7.34\text{--}7.56$ ppm.. A resonance around 4.85 ppm equivalent to one proton assigned to the hydroxyl group. While the chemical shift at $2.78, 2.87$ ppm may assigned to the secondary amine groups (N-H-4) and (N-H-2), the shift to high field may be caused by intra molecular hydrogen bonding ($\text{N-H}\dots\text{N}$), ($\text{N-H}\dots\text{S}$). The ^{13}C NMR spectrum of the ligand HL is shown in Figure (4). The spectrum reveals two sharp resonance at 180 and 155 ppm refer to the thioamide and imino carbons respectively. The sharp resonance at 22 ppm is corresponding to the methyl carbon. The shifts at the range $132.4\text{--}121.3$ ppm refer to the aromatic carbon atoms. The two shifts centered at $139.4, 134.7$ ppm refers to the C-N carbon atoms, finally the resonance at 117.2 ppm assigned to the C-O carbon atom.



Scheme (1): Synthesis diagram of the Schiff-base Ligand HL and it's complexes.

Electronic spectra measurement :

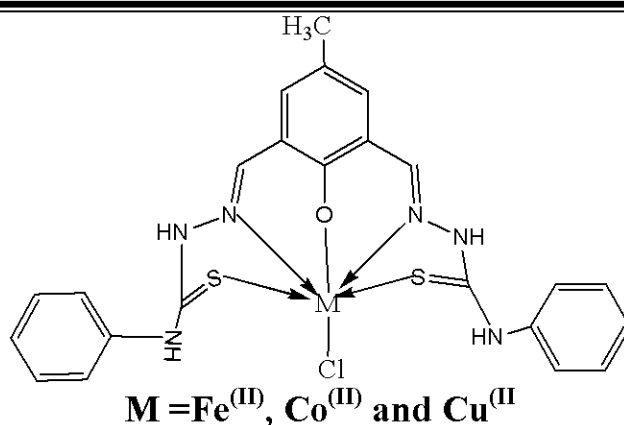
The UV-Vis spectrum of HL exhibits a high intense absorption peaks at 282 and 302 nm, assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$. The electronic spectra of the complexes Fe (II) , Co (II) and Cu (II) exhibit a high intensity peak around 277-290 nm related to the intra-ligand field transition. Bands exhibit around 320-334 nm assigned to the charge transfer (CT).transition respectively transition .spectrum of the Fe (II) complex exhibited two bands characteristic of octahedral Fe (II) complex[19-22]. The electronic spectrum of the Co (II) complex shows two bands Bands exhibit around which can be attributed to ${}^4T_{1g}^{(F)} \rightarrow {}^4A_{2g}^{(F)}$ transition, corresponding to octahedral geometry [19, 23], while the electronic spectrum of the Cu (II) complex shows band which can be attributed to ${}^2B_{1g} \rightarrow {}^2B_{2g}$ transition[19, 24]. The molar conductance values determined in (DMSO) solution (10^{-3} M) were found in the range (8.9-16.5) $\Lambda m (\Omega^1.cm^2.Mole^{-1})$ (Table -3) which indicates that the complexes are non-electrolytes (Table 1) [25].The atomic absorption analysis and the chloride content results of the complexes are in a good agreement with suggested formula[M (L)]Cl] .

Antimicrobial activity:

The free Schiff-base ligand and its metal complexes were screened against *Bacillus* (G+) and *Pseudomonase* (G-) to assess their potential as an antimicrobial agent by disc diffusion method. The measured zone of inhibition against the growth of various microorganisms is listed in Table 4. It is found that the ligand has higher antimicrobial activity than its metal complexes. This can be explained as follows: The biological activity of the Schiff-base ligand is related to the imine moiety, which plays a key role in the inhibition of the tested bacteria. The lower antimicrobial activity of the metal complexes compared with that in the ligand may be due to the strong interaction between the imine moieties and the metal ions. Such interaction will reduce the activity of the imine moiety in the inhibition.

Conclusion:

In this paper, the synthesis and coordination chemistry of some monomeric metal complexes derived from the Schiff base HL are investigated. The complexes were prepared by mixing at reflux 1 mmole of the Schiff-base ligand with 2 mmole of the appropriate metal chloride. Complexes of the general formula[M (L)]Cl] ,(where M = Fe^{II} (II) ,Co (II) , and Cu (II) was obtained. Physico-chemical analysis indicated the formation of four coordinate dicationic metal complexes. Biological activities revealed that the ligand has higher antimicrobial activity than its metal complexes.



Scheme(2): Proposed structures of complexes

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Synthesis, Structures and Biological studies of some metal ions with a Schiff base ligandLecturer .Enaam I. Yousif

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Table (1) : some physical properties of the complexes and their reactants quantities .

Compound	Metal chloride	M.p ^o C	Color	Weight of metal chloride		Weight of product (g)	Yield %	Metal content Prac (Theo.)	chloride content Prac (Theo.)
				g	mmole				
[HL]	-	87-89	pale Yellow	-	-	1.11	78	-	-
[Fe ^{II} (L) Cl]	Fe Cl ₂ .4H ₂ O	186	Deep brown	0.08	0.4	0.013	54	905 (10.10)	5.75 (6.41)
[Co ^{II} (L) Cl]	Co Cl ₂ .6H ₂ O	313	brown	0.1	0.42	0.14	58	9.12 (10.60)	5.74 (6.38)
[Cu ^{II} (L) Cl]	CuCl ₂ . 2H ₂ O	243	Red brown	0.07	0.41	0.12	49	10.23 (11.34)	5.96 (6.32)

Table (2): I.R frequencies(cm⁻¹) of the complexes

Compound	v(N-H)	v(C=N) _{imin}	v(-N-C-S)	v(C=S)	v(N- N)	v(M- O)	v(M- N)	v(M-S)
[HL]	3342,3219	1614	1446	867,1342 (w)	1029	-	-	-
[Fe ^{II} (L) Cl]	3396,3366	1600	1475	848,1398 (w)	1035	619	574	468
[Co ^{II} (L) Cl]	3295,3138	1598	1490	827,1355 (w)	1078	617	569	464
[Cu ^{II} (L) Cl]	3300,3134	1597	1496	831,1357(w)	1080	690	565	445

Table (3) : Electronic spectral data and conductance measurement for the complexes

Compound	λ nm	Wave number Cm^{-1}	ϵ_{max} Molar Cm^{-1}	Assignment	Δ_{m} ($\Omega^1 \cdot \text{cm}^2 \cdot \text{Mole}^{-1}$)	Propose structure
[HL]	282		3915	$\pi \rightarrow \pi^*$	-	-
	302		3804	$n \rightarrow \pi^*$		
[Fe ^{II} (L) Cl]	277		993	Ligand field	11.4	octahedral
	334		573	charge transfer		
	495		136	${}^5A_{2g} \rightarrow T_{2g}$		
	648		136	${}^5T_{2g} \rightarrow {}^5E_g$		
[Co ^{II} (L) Cl]	290		630	Ligand field	8.9	octahedral
	366		543	charge transfer		
	610		122	${}^4T_{1g}^{(F)} \rightarrow {}^4A_{2g}^{(F)}$		
	685		97	${}^4T_{1g}^{(F)} \rightarrow {}^4A_{2g}^{(F)}$		
[Cu ^{II} (L) Cl]	281		321	Ligand field	16.5	octahedral
	320		242	charge transfe		
	635		144	${}^2B_{1g} \rightarrow {}^2B_{2g}$		

Table (4) : Antibacterial activities of the synthesised Schiff-base and metal complexes.

Compounds	<i>Bacillus (G+)</i>	<i>Pseudomonase (G-)</i>
[HL]	2.5	3.8
[Fe ^{II} (L) Cl]	1.7	2.1
[Co ^{II} (L) Cl]	0.5	3.2
[Cu ^{II} (L) Cl]	1.1	0.5

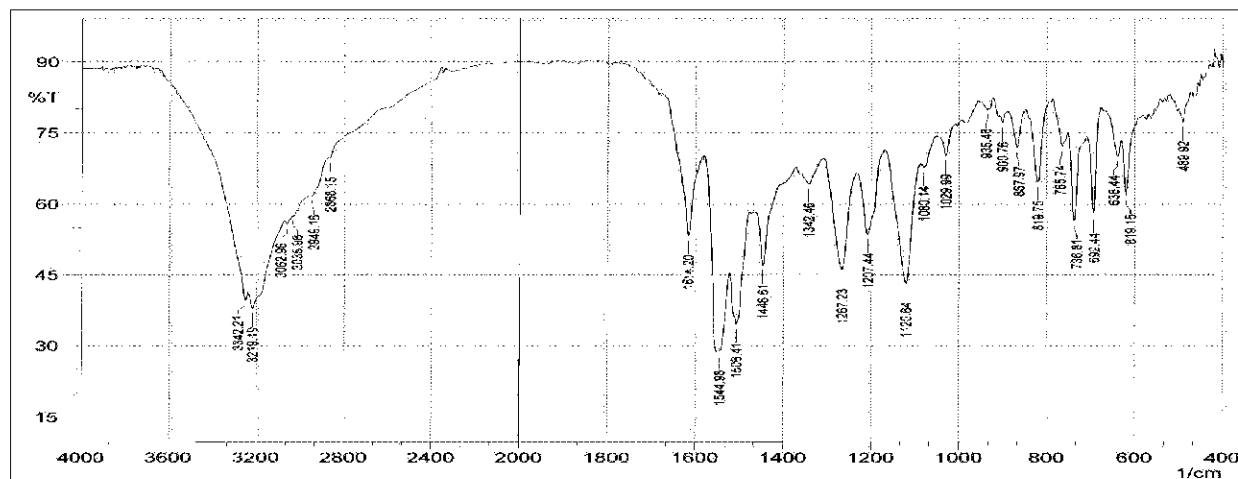


Figure 1: The I.R. Spectrum of the ligand [HL]

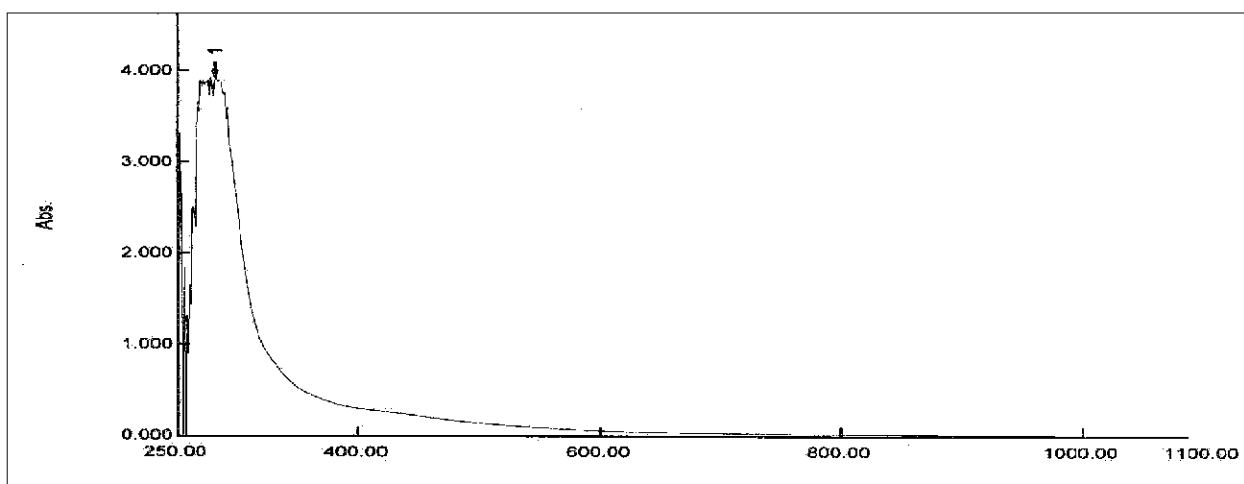


Figure 2: The U.V. Spectrum of the ligand [HL]

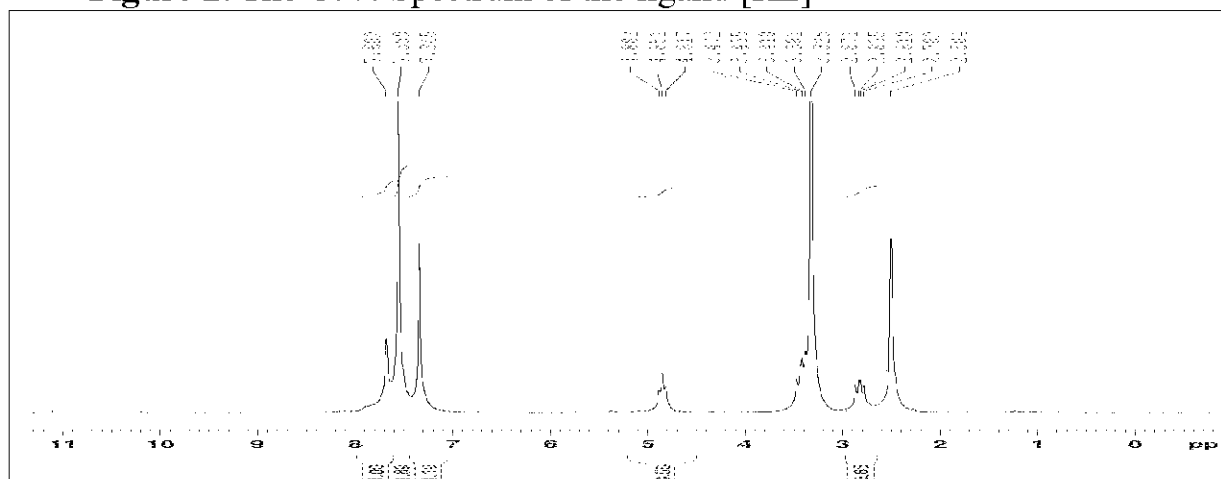


Figure 3: ¹H-NMR spectrum of the ligand HL in DMSO-d₆ solution.

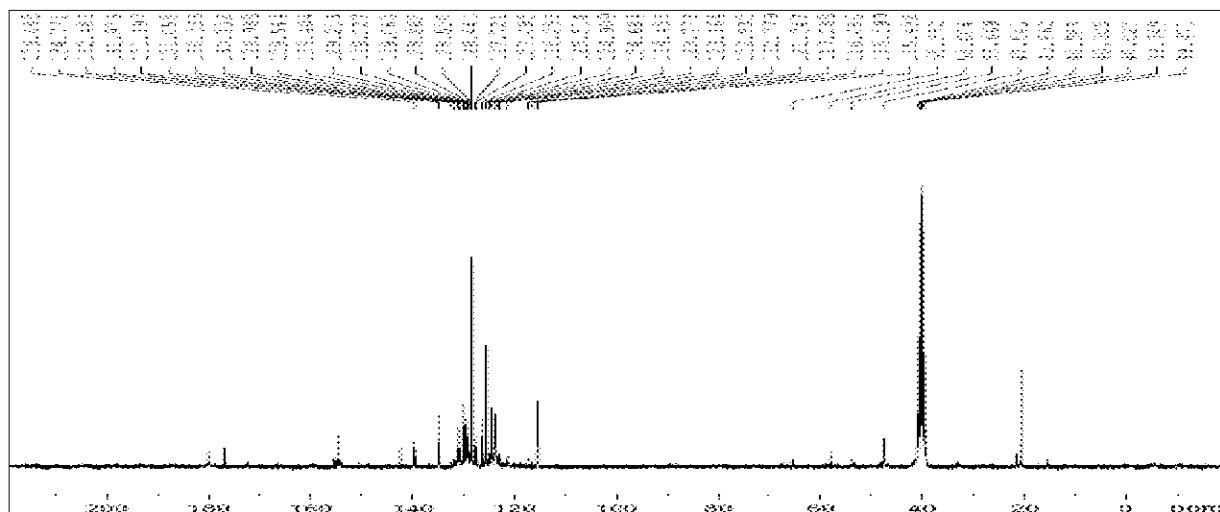


Figure 4: ^{13}C spectrum of the ligand HL in DMSO-d_6 solution

تحضير، تركيب و دراسة الفعالية البايولوجية (قاعدة شف) لبعض ايونات المعادن مع لكاند

م. انعام اسماعيل يوسف

جامعة بغداد

كلية التربية- ابن الهيثم- قسم الكيمياء

الخلاصة

تضمن البحث تحضير الليكاند الجديد قاعدة شف - [2,6-bis-[(3-phenyl thiourea-imino)- methyl]-phenol] (HL) المشتق من 2,6-diformyl- و 4-phenylthiosemicarbazide و 4-methyl-phenol ثم مفاعلة مع بعض العناصر الفلزية باستخدام الميثانول وسطا للتفاعل وبنسبة (1 : 2) حيث تكونت معقدات جديدة ذات الصيغ العامة: $[\text{M}(\text{L})\text{Cl}]$ حيث: $\text{M}=\text{Fe}^{\text{II}}, \text{Co}^{\text{II}}$ and Cu^{II}

شخصت جميع المركبات بالطرق الطيفية (التالية) الأشعة تحت الحمراء والأشعة فوق البنفسجية - المرئية ومطيافية الامتصاص الذري للعناصر، ^1H , ^{13}C NMR، ومحتوى الكلور ودرجات الانصهار) ، مع قياس التوصيلية المولارية الكهربائية والفعالية البايولوجية..، من النتائج أعلاه كان الشكل الفراغي المقترح لمعقدات الحديد، الكوبالت والنحاس ثنائي السطوح.