

New Transition Metal Complexes with a Multidentate Schiff-base: Synthesis , Characterize and Biological studies

معقدات العناصر الانتقالية الجديدة

مع قاعدة شف متعددة الاسنان تحضير , تشخيص و دراسة الفعالية البايولوجية

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Abstract : The new polydentate Schiff-base ligand E,1'E)-(1,4-phenylene1)-'5,5, bis(methan-1-yl-1-ylidene))bis(azan-1-yl-1-ylidene)bis(1,3,4-thiadiazole-2-thiol) H₂L and its binuclear metal complexes with Co(II) , Ni(II) and Cd(II) are reported. The reaction of thiosemicarbazide with anhydrous sodium carbonate in mole ratios of 1:1 gave the precursor 2-amino-5-mercapto-1,3,4-thiadiazole. Condensation reaction of precursor with Benzen1,4-dicarboxaldehyde in mole ratios of 2:1 gave the new N₂S₄ Schiff-base ligand H₂L. The complexes were prepared from the reaction of the corresponding metal chloride with the ligand .The ligand and its metal complexes were characterised by spectroscopic methods (FTIR, UV-Vis, ¹H.NMR, A.A), chloride content, conductance and melting point measurements. These studies revealed tetrahedral geometries for Co(II) and Cd(II) complexes of general formulae [M₂(L₂)] and square planar for Ni(II) complex. Biological activity of the ligand and its metal complexes against gram positive bacterial strain *Bacillus* (G+) and gram negative bacteria *Ecoli* (G-) The effects of prepared compounds depend on the type of tested bacteria. It is clear that, the ligand and its metal complexes have a potential effect on the gram negative (G-) of the tested bacteria.

Keywords : Schiff-base ligand (E,1'E)-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis(azan-1-yl-1-ylidene) bis (1,3,4-thiadiazole-2-thiol) ; Binuclear complexes; structural and biological studies.

الخلاصة

تضمن البحث تحضير الليكاند الجديد قاعدة شف

(E,1'E)-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis(azan-1-yl-1-ylidene) bis (1,3,4- thiadiazole-2-thiol) [H₂L

المشتق من

2-amino-5-mercapto-1,3,4-thiadiazole و Benzen1,4-dicarboxaldehyde ثم مفاعلة مع بعض العناصر الفلزية باستخدام الميثانول وسطا للتفاعل وبنسبة (2 : 2) حيث تكونت معقدات جديدة ذات الصيغ العامة:

[M₂ (L₂)]

حيث:

M=Co^{II} ,Ni^{II} and Cd^{II}

شخصت جميع المركبات بالطرق الطيفية التالية (الأشعة تحت الحمراء والأشعة فوق البنفسجية – المرئية ومطيافية الامتصاص الذري للعناصر, ¹H NMR, ومحتوى الكلور ودرجات الانصهار) , مع قياس التوصيلية المولارية الكهربائية والفعالية البايولوجية. من النتائج أعلاه كان الشكل الفراغي المقترح لمعقدات الكوبالت والكادميوم رباعي السطوح بينما النيكل يتخذ شكل المربع المستوي.

Introduction:

A useful preparative method for 2-amino-5-mercapto-1,3,4-thiadiazole was developed by Guha [1], by treating thiosemicarbazide with carbon disulphide and potassium hydroxide. Heterocyclic amines [2,3], have been widely used for the synthesis of new Schiff's bases. Azoles, thiadiazole and their derivatives continue to draw the attention of synthetic organic and inorganic chemists due to the large group of compounds possessing a wide spectrum of uses. Heterocyclic compounds possessing the 1,3,4-thiadiazole ring system has shown antifungal, bacteriostatic as well as antihelmintic effects [4,5]. Compounds containing the mentioned ring also exhibit anti-inflammatory, antimicrobial properties [6], in addition to the depression effect on the central nervous system [7]. All the tested thiadiazole compounds are less active than oxacillin, which is currently used as clinical antibiotic [8]. Schiff-base compounds have a great importance in coordination chemistry, due to their ability to form a range of stable complexes which have applications in different fields [9]. Schiff-base metal complexes also have application in biomedical [10], biomimetic [11] and catalytic system [12] and in supporting liquid crystalline phase including crystal engineering of coordination polymers, and in the fabrication of potentiometric membrane sensors [13, 14]. Schiff-base compounds are reported to show a variety of biological activities including antibacterial, antifungal, anticancer and herbicidal activities [15-17]. Metal complex of Schiff-bases have also been used in oxidation reactions [18], and for binding metal ions via the nitrogen atom lone pair, especially when used in combination with one or more donor atoms to form polydentate chelating ligands or macrocycles [19,20]. Recently, reported the New Monomeric (Co^{II} , Ni^{II} , Cu^{II} and Zn^{II}) Metal Complexes of a Bidentate Schiff-base Ligand; Synthesis, Characterisation and Biological Studies [21]. In this paper, the synthesis and spectral characterisation of some transition metal complexes with Schiff-base ligand (E,1'E)-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis(azan-1-yl-1-ylidene) bis (1,3,4-thiadiazole-2-thiol) H_2L 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 $4000\text{--}400\text{ cm}^{-1}$. Electronic spectra of the prepared compounds were measured in the region $250\text{--}1100\text{ nm}$ 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 , NMR, spectrum was acquired in DMSO-d_6 solution using a Bruker AMX300 MHz spectrometer with tetramethylsilane (TMS) as an internal standard for ^1H , NMR at Ahl- 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- 665 Dosimat-Metrohm Swiss). Conductivity measurements were made with DMSO solutions using a PW 9526 digital conductivity meter.

Synthesis

Preparation of the precursor (2-amino-5-mercapto-1,3,4-thiadiazole):

A mixture of (2.0g, 20mmol.) of thiosemicarbazide and (2.33g, 20mmol.) of anhydrous sodium carbonate was dissolved in 25ml of absolute ethanol 99.9%. To this solution (3.2g, 40mmol.) of carbon disulphide was added. The resulting mixture was heated under reflux for 7hrs., and the reaction mixture was then allowed to cool down to room temperature. Most of solvent was removed under reduced pressure and the residue was dissolved in distilled water 20ml, after which it was carefully acidified with cold concentrated hydrochloric acid to give a pale yellow precipitate.

The crude product was filtered and washed with cold water, recrystallized from ethanol to give the desired product as yellow needles, with a yield of (1.6g, 67%) and a m.p. of (229-230)^oC [22]. IR data (cm⁻¹): 3398,3278 (N-H₂), 3093(C-H)arom, 2563(S-H) and 879,1357 (w) (C-S).

Preparation of the H₂L :

Preparation of the (E,1'E)-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis(azan-1-yl-1-ylidene) bis (1,3,4-thiadiazole-2-thiol) .A solution of 2-amino-5-mercapto-1,3,4-thiadiazole (0.5g, 3.7 mmole) in methanol(5ml) was added to Benzen1,4-dicarboxaldehyde (0.25g, 1.8 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 (0.71 g , %48), m.p =160^oC .IR data (cm⁻¹): 2544(S-H), 3062 (C-H)arom, 1614(C=N). The ¹H NMR spectrum of the ligand in DMSO-d₆ showed peaks at; δH(300 MHz, DMSO-d₆): 7.01-7.66 (Ar-H); 8.06 (H-C-N), 3.39 (S-H).

General synthesis of the complexes:

A one mmol of metal (II) salts are hydrated chloride; MCl₂.XH₂O was dissolved in methanolic solution (10 mL); where: M= Co ,Ni : X=6 and Cd X= 2 respectively. was stirred into methanolic solution of the Schiff-base ligand (2 mmol) in methanol (15 mL) with (2 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), ether (10 mL) and dried at room temperature. Elemental analysis data, colours, and yields for the complexes are given in (Table 1).

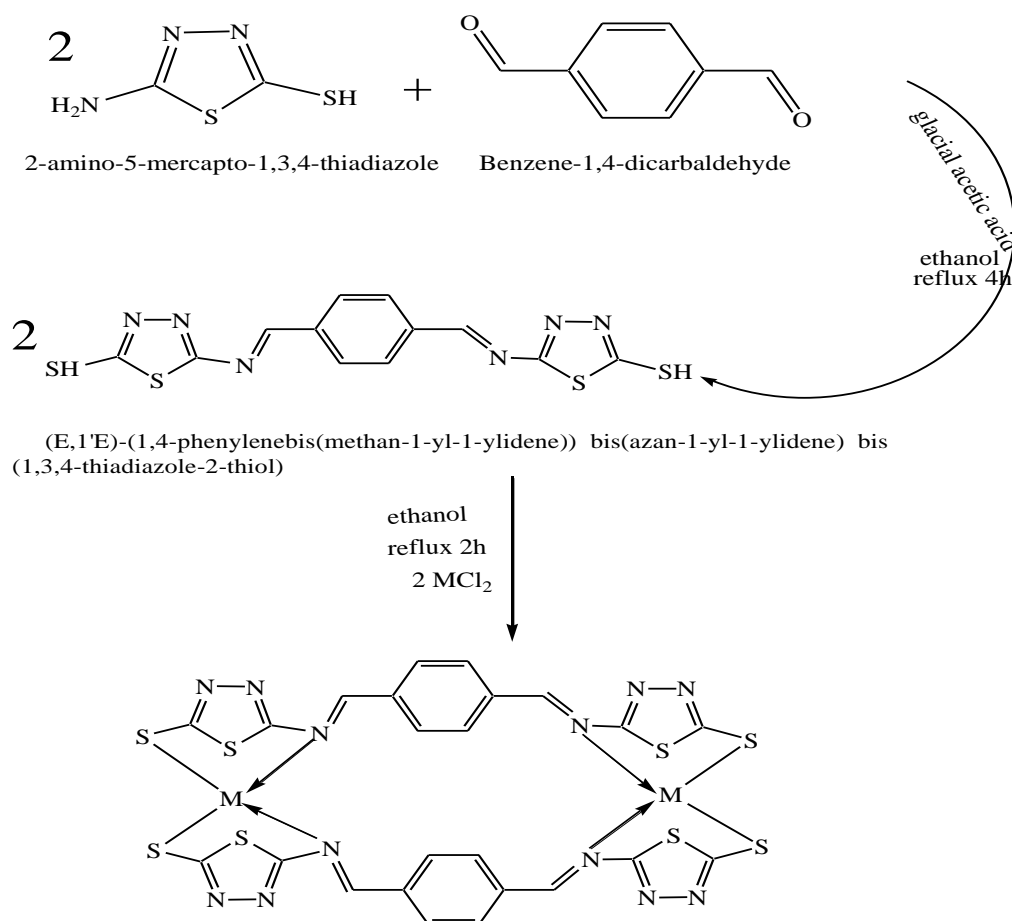
Determination of Bacteriological Activity :

Bioactivities were investigated using agar-well diffusion method [23]. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm. Recommended concentration (100 μL) of the test sample 1 mg/mL in DMSO was introduced in the respective wells. The plates were incubated immediately at 37^oC 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

Chemistry:

The condensation reaction of 2-amino-5-mercapto-1,3,4-thiadiazole with Benzen1,4-dicarboxaldehyde in mole ratios of 1:2 gave the Ligand (E,1'E)-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis(azan-1-yl-1-ylidene) bis (1,3,4-thiadiazole-2-thiol) H₂L in good yield. The Schiff-base ligand was characterised by elemental analysis (Table 1), IR (Table 2), UV-Vis (Table 3) spectroscopy and ¹H. NMR spectrum. The complexes are air-stable solids, soluble in EtOH, DMSO and DMF. The complexes are sparingly soluble in MeOH and not soluble in other common organic solvents. The coordination geometries of the complexes were deduced from their spectra. The analytical data (Table 1) agree well with the suggested formulae. Conductivity measurements of the complexes in DMSO solutions lie in the (19.2-8.33) cm²Ω⁻¹mol⁻¹ range, indicating their non-electrolytes behavior (Table 1) [24].



Scheme (1): Synthesis diagram of the Schiff-base Ligand H₂L and its complexes.

IR and NMR Spectra:

The important infrared bands for the ligand and its metal complexes together with their assignments are listed in Table 2. The IR spectra of the ligand shows characteristic bands at 2544, (879, 1357(w)) and 1614 cm⁻¹ due to the $\nu(\text{S-H})$, $\nu(\text{C-S})$ and $\nu(\text{C=N})$ imine functional groups, respectively [25,26]. The IR spectra of the complexes exhibited ligand bands with the appropriate shifts due to complex formation (Table 2). The $\nu(\text{C=N})$ imine at 1616 cm⁻¹ in the free Schiff-base ligand is shifted to lower frequency and observed in the range 1594-1605 cm⁻¹ for the complexes. The bands are assigned to a $\nu(\text{C=N})$ stretch of reduced bond order. This can be attributed to delocalisation of metal electron density (t_{2g}) to the π -system of the ligand [27, 28], indicating coordination of nitrogen of the C=N moieties to the metal atoms [29]. Figure (1) represents the IR of the ligand and its Ni-complex. At lower frequency the complexes exhibited bands around 646–677 and 540-585 cm⁻¹ which could be assigned to $\nu(\text{M-N})$ and $\nu(\text{M-S})$ vibration mode [27]. 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 H₂L are collected in the experimental section “preparation of H₂L and presented in Figure (5). The resonance peaks associated with the aromatic groups are observed in the range 7.01-7.66 ppm.. The spectrum involves two chemical shifts at 8.07 ppm and 3.39 assigned to S-H and H-C-N groups [30].

Electronic spectra :

The electronic spectra data of the ligand and its complexes are summarised in (Table 3). The UV-Vis spectrum of H₂L exhibits a high intense absorption peaks at 228 and 384 nm, assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$, transition [31]. respectively. The electronic spectra of the complexes Co (II)

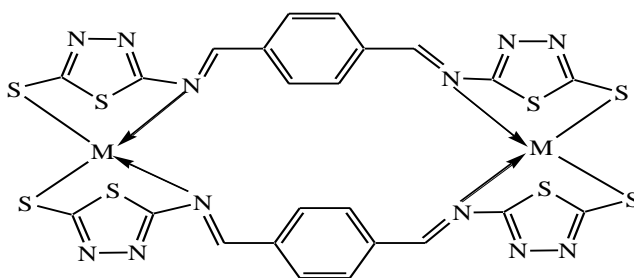
and Ni (II) exhibit a high intensity peak around 268-270 nm related to the intra-ligand field transition. Bands exhibit around 336-414 nm assigned to the charge transfer (CT) [32]. The spectrum of the Co (II) complex exhibited peak at 607 which can be attributed to ${}^4T_{1g}^{(F)} \rightarrow {}^4T_{1g}^{(P)}$ transition, corresponding to tetrahedral Co (II) complexes [33-36]. The electronic spectrum of the Ni (II) complex shows peaks at 439 and 462 which can be attributed to ${}^1A_{1g} \rightarrow {}^1B_{2g}$ transition, corresponding to square planar [33, 37]. The spectrum of the Cd(II) complex exhibited peaks assigned to ligand $\pi \rightarrow \pi^*$ and L \rightarrow M charge transfer [33, 38]. The metal normally prefers tetrahedral coordination.

Antimicrobial activity:

The free Schiff-base ligand and its metal complexes were screened against *Bacillus* (G+) and *Ecoli* (G-) to assess their potential as an antimicrobial agent by disc diffusion method. The effects of prepared compounds depend on the type of tested bacteria. It is clear that, the ligand and its metal complexes have a potential effect on the gram negative (G-) of the tested bacteria.

Conclusion:

In this paper, the synthesis and coordination chemistry of some complexes derived from the Schiff-base (E,1'E)-(1,4-phenylenebis(methan-1-yl-1-ylidene)) bis(azan-1-yl-1-ylidene) bis (1,3,4-thiadiazole-2-thiol) are investigated. The complexes were prepared by mixing at reflux 2 mmole of the Schiff-base ligand with 2 mmole of the appropriate metal chloride. Complexes of the general formulae $[M_2(L_2)]$ (where M = Co(II), Ni (II) and Cd(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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Table1 Colours, yields, elemental analyses, and molar conductance values.

Compound $\Lambda_M(\text{cm}^2\Omega^{-1}\text{mol}^{-1})$	Colour	Yield (%)	m.p	Found (Calcd.) (%)	
				M	Cl
H ₂ L	deep yellow	48	160	-	-
[Co ^{II} (L ₂)] 19.2	pale green	52	287	12.24 (13.98)	nill
[Ni ^{II} (L ₂)] 8.33	pale yellow	43	295	11.78 (13.93)	nill
[Cd ^{II} (L ₂)] 14.45	red yellow	51	293	21.04 (22.71)	nill

Table 2. IR frequencies (cm⁻¹) of the compounds.

Compound	$\nu(\text{S-H})$	$\nu(\text{C=N})$	$\nu(-\text{N-C-S})$	$\nu(\text{C-S})$	$\nu(\text{M-N})$	$\nu(\text{M-S})$
H ₂ L	2544	1616	1454	1045	-	-
[Co ^{II} (L ₂)]	-	1605	1418	1026	677	585
[Ni ^{II} (L)]	-	1600	1435	1043	653	540
[Cd ^{II} (L ₂)]	-	1594	1432	1019	646	562

Table 3: U.V-Vis spectral data in DMSO solutions.

Compound	Band position (λ nm)	Extinction coefficient $\epsilon_{max}(\text{dm}^3 \text{mol}^{-1}\text{cm}^{-1})$	Assignments
H ₂ L	228 384	2305 2023	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$
[Co ₂ ^{II} (L ₂)]	268 436 607	967 158 39	$\pi \rightarrow \pi^*$ CT ${}^4T_{1g}^{(F)} \rightarrow {}^4T_{1g}^{(P)}$
[Ni ₂ ^{II} (L ₂)]	270 390 414 439 462	737 154 154 170 174	$\pi \rightarrow \pi^*$ CT CT ${}^1A_{1g} \rightarrow {}^1B_{2g}$ ${}^1A_{1g} \rightarrow {}^1B_{2g}$
[Cd ₂ ^{II} (L ₂)]	269 390 463	797 68 86	$\pi \rightarrow \pi^*$ CT CT

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

Compounds	<i>Bacillus</i> (G+)	<i>Ecoli</i> (G-)
Free ligand	-	+++
[Co ₂ ^{II} (L ₂)]	-	+++
[Ni ₂ ^{II} (L ₂)]	-	++
[Cd ₂ ^{II} (L ₂)]	-	++

(-) = No inhibition = inactive, (+) = (2-4) mm = active, (++) = (5-7) mm = more active, (+++) = (8- 13) mm = highly active

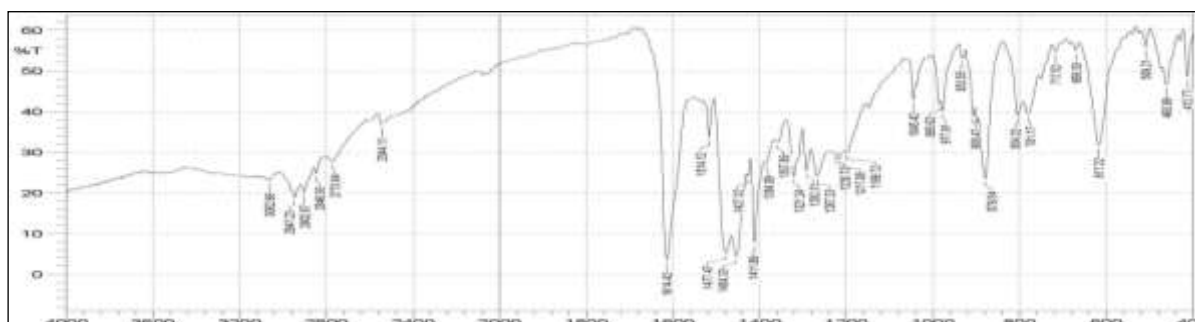


Figure 1: IR spectra for the ligand

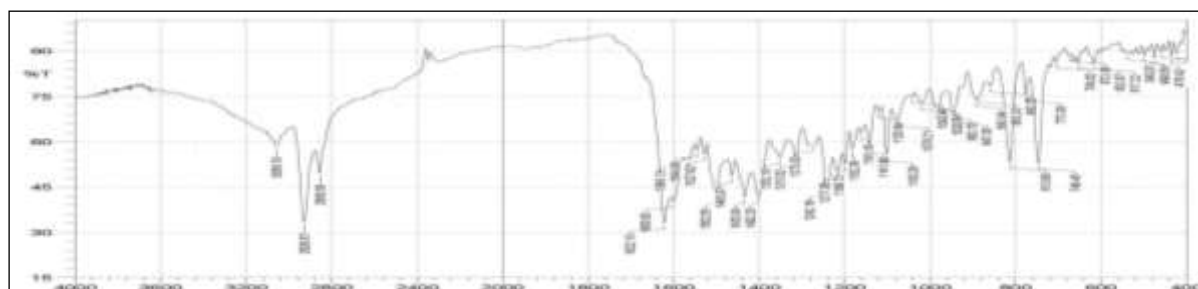


Figure 2: IR spectra for the ligand and Ni-complex

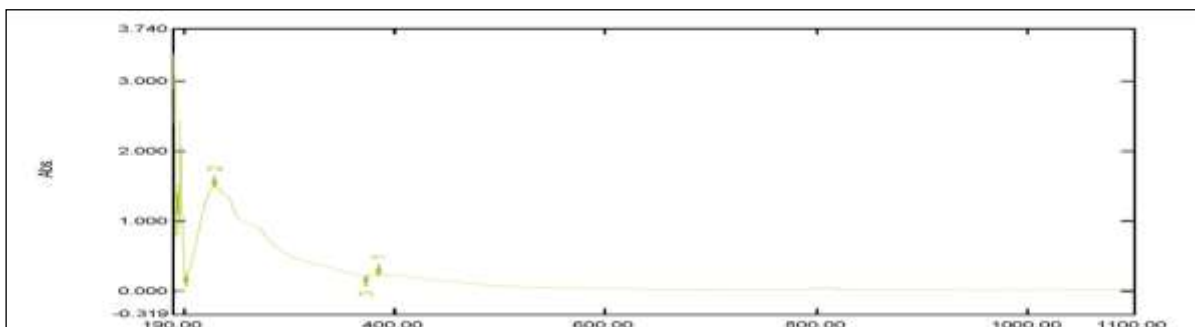


Figure 3: Electronic spectrum of the ligand

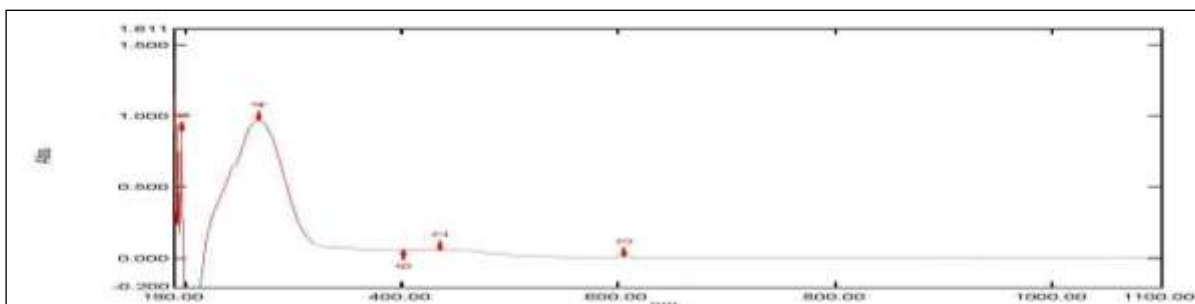


Figure 4: Electronic spectrum of the Co - complex.

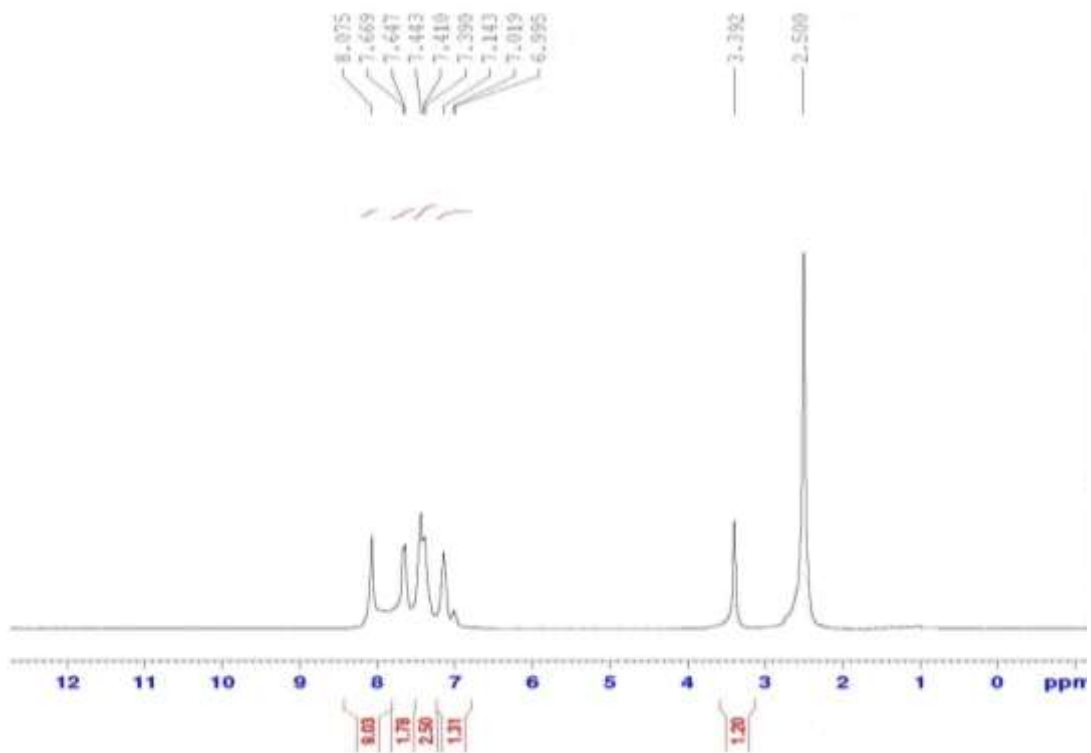


Figure 5: ¹H-NMR spectrum of the ligand H₂L in DMSO-d₆ solution.