

Preparation, Identification and Biological Activity of a New Ligand (N, N'-bis (4-Acetamidobenzalidene)1,3-diaminopropane) with Some Transition Metal Complexes

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Abstract

The Schiff base (N, N'-bis (4- Acetamidobenzalidene) 1, 3-diaminopropane) was prepared from 4-acetaminobenzaldehyde and 1, 3-diaminopropane by refluxing the two components in methanolic solution. The metal complexes of Fe (III), Cr (III) Co (II) and Ni (II), were prepared by mixing and refluxing ethanolic solutions of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ and $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ with (N,N'-bis (4-Acetamidobenzalidene)1,3 diaminopropane). The ligand(L) characterized by Elemental Micro Analysis (CHN) and Nuclear Magnetic Resonance Spectroscopy ($^1\text{H-NMR}$). The ligand(L) and its metal complexes were prepared and characterized by different techniques, such as infrared (IR) (using KBr disc to ligand and CsBr disc to complexes), Mass spectra, and (UV-vis) spectra. The complexes for ligand have shown octahedral configuration, the ligand coordinates with metal through Oxygen and Nitrogen atoms for all complexes and with ratio (1:1). All the synthesized compounds were tested for their antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* bacteria.

Keywords: Schiff base, 4-acetamidobenzaldehyde, antibacterial, complex

1. Introduction

Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Schiff [1] in 1864. The common structural feature of these compounds is the azomethine group with a general formula $\text{RHC}=\text{N}-\text{R}_1$, where R and R_1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines. Several studies [2,3] showed that the presence of a lone pair of electrons in an sp^2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance. Because of the relative easiness of preparation, synthetic flexibility, and the special property of $\text{C}=\text{N}$ group, Schiff bases are generally excellent chelating agents, [4,5] especially when a functional group like $-\text{OH}$ or $-\text{SH}$ is present close to the azomethine group so as to form a five or six membered ring with the metal ion. Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable.

Schiff bases form an important group of compounds in chemistry due to their useful physical and chemical properties and they undergo a large number of reactions. They have wide use in industry due to their interesting pharmacological activity [6,7]. A number of reviews on the Schiff bases have been published [6,7]. Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of

applications in many fields, e.g., biological, inorganic and analytical chemistry [8-10]. They are also used in optical and electrochemical sensors, as well as in various chromatographic methods, to enable detection due to enhanced selectivity and sensitivity [11]. Many Schiff base complexes show excellent catalytic activity in various reactions at high temperature ($>100\text{ }^{\circ}\text{C}$) and in the presence of moisture. Over past few years, there have been many reports on their applications in homogeneous and heterogeneous catalysis [12]. In aprotic solvents, at atmospheric pressure and room temperature, cobalt chelated with Schiff bases, catalyzes the oxygenation of indols, phenols, flavones, nitroalkanes, hydrazones, olefins, etc [13]. Polyentate Schiff bases, assisted by metal ions, provide highly organized supramolecular metal complexes. Such complexes possess binding sites and cavities for various cations, anions and organic molecules [14].

2. Experimental

2.1 Chemical and Instrumentals

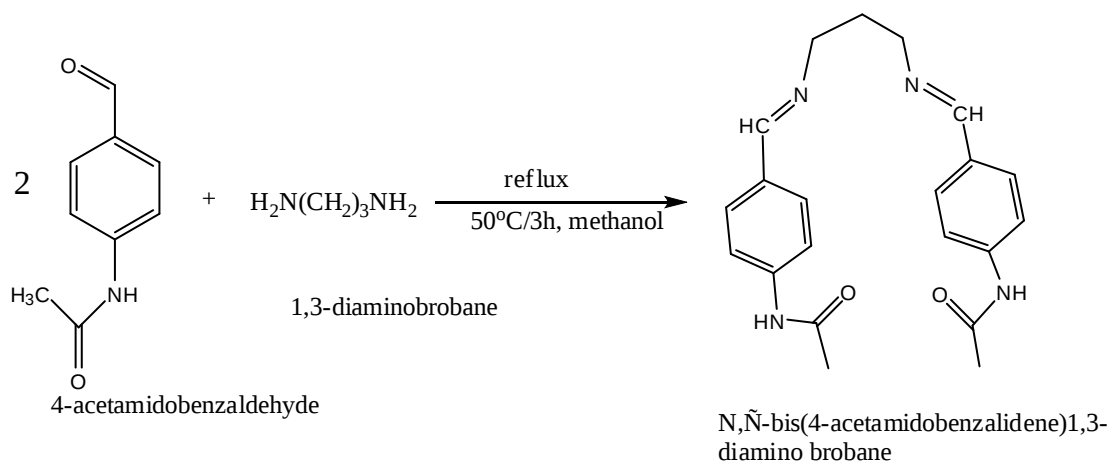
a- Chemical: 4-acetamidobenzaldehyde and 1,3-Diamino brobane, from (Aldrich) , Iron(III) Chlorid hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), Chromium(III) Chloride hexahydrate ($\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$) , Cobalt(II) Chloride hexahydrate ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$), Dimethyl sulfoxide (DMSO) and Glicial acetic acid, from (B.D.H) Methanol and Ethanol from (G.C.C) were used as received.

b- Instrumentals: The melting points were determined in SMP31 melting point. (C, H, N) analyses of ligand was carried on a Thermofinigan flash. Infrared spectra of the solid compounds were recorded on a FTIR affinity Spectormeter (Shimadzu) in the range $4000\text{--}200\text{ cm}^{-1}$ used KBr discs for the ligands and CsI discs for the complexes. ^1H - NMR spectra were recorded on a Bruker 500 MHZ, using DMSO as a solvent and TMS as the internal standard. The Conductivity Measurement was performed using Hanna hi2300 in DMSO having 10^{-3} M at room temp. The UV-Vis spectra of the ligand and complexes were recorded on PG (T60UV) spectrometer. Mass spectra were recorded with Agilent Technologies 5975 mass spectrometer.

2.2. Preparation of Schiff base ligand

2.2.1 Preparation of (L)

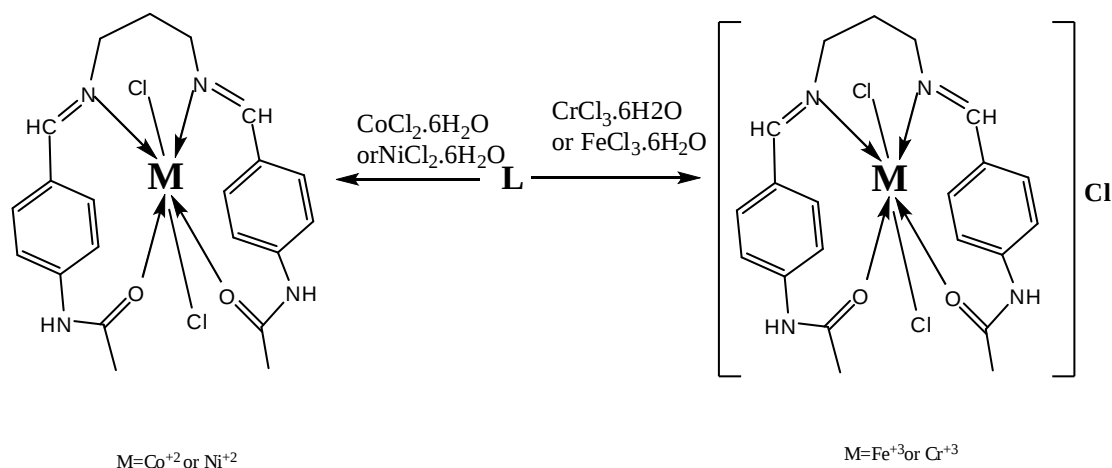
Schiff base ligand [L] was prepared by the following general method Mixture (0.02 mol, 3.26g) from 4-acetamidobenzaldehyde dissolved in (20 ml) methanol with added few drops (2-3) of glicial acetic acid and added (0.01mol, 0.833 ml, 0.74g) from 1,3-Diamino brobane to ratio (2:1) the mixture added in a round bottom flask under reflux for(3hrs) at $50\text{ }^{\circ}\text{C}$. The precipitated ligand was filtered off, recrystallized from ethanol [15] (**Scheme 1**).



Scheme 1: Synthesis of L

2.3. Preparation of Schiff base transition metal complexes:

The complexes were prepared easily and a good yield from an equimolar ratio of the ligand and the metal chloride. So, by the addition of (0.001 mmol) of ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ and $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$) dissolved in 10ml ethanol, to a magnetically stirred warmed (50°C) solution of the ligand (0.001 mmol) in hot ethanol (25ml). The color of the mixture changed instantly. The mixtures were refluxed for (2-3 h). The complexes were precipitated which, upon cooling, were filtered, washed several times with cold methanol and recrystallized from hot ethanol [16] **Scheme 2.**



Scheme2: Synthesis of metal complexes

2.4. Biological Studies:

2.4.1 Bacterial strains:

The metal complexes and ligand were individually tested against a panel of microorganisms (Gram negative and Gram positive), namely *Staphylococcus aureus* and *Escherichia coli*. The organisms were obtained from the department of Biology

2.4.2 Disc diffusion assay:

Antibacterial activity of the ligand and metal complexes were carried out using the disc diffusion method described by Bauer *et al* [17]. Bacteria were maintained on

Mueller–Hinton nutrient agar at 4°C. Molten Mueller-Hinton agar was inoculated with a broth culture of the respective bacterial strains and poured over previously washed and sterilized 90 mm Petri dishes. Metal complexes, and ligands were dissolved in DMSO to a final concentration of 1000 ppm. The plates were incubated at 37°C for 24 hours during which activity was evidenced by the presence of a zone of inhibition surrounding the well and antibacterial activity was expressed as mean of diameter of inhibition zones (mm) produced by the synthesised compound.

3. Results and Discussion

3.1 Characterization of Schiff base and metal complexes:

The ligand and complexes were characterized by using, FT-IR, UV-Vis spectroscopy and conductance measurements. Elemental analysis and $^1\text{H-NMR}$ for Schiff base only. Physical properties of the prepared ligand and their complexes in Table (1) which show different melting points and the complexes are colored.

3.2 Molar Conductance (Λ_m):

The observed molar conductance values (Table 1) measured in DMSO in 10^{-3}M solution lie in the $(13-38) \text{ s.cm}^2.\text{mol}^{-1}$ range, indicated that the some complexes are electrolytes and another non electrolytes (1:1) nature.

Table (1): Physical properties and Molar Conductance of ligand and its Co (II), Ni(II), Fe (III) and Cr (III) complexes and elemental analysis for Schiff base only

Compound	Molecular Formula	Molecular Weight	Melting Point ($^{\circ}\text{C}$)	Colour	Molar Conductance (Λ_m)($\text{S.cm}^2.\text{mol}^{-1}$)	elemental analysis		
						C% Fou (cal)	H% Fou (cal)	N% Fou (cal)
L	$\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_2$	364	208-210	Pale Yellow	-----	69.28 (69.25)	6.63 (6.59)	15.41 (15.40)
$[\text{Co}(\text{L})\text{Cl}_2]$	$[\text{Co}(\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_2)\text{Cl}_2]$	493	160d*	Dark Green	14			
$[\text{Cr}(\text{L})\text{Cl}_2]\text{Cl}$	$[\text{Cr}(\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_2)\text{Cl}_2]\text{Cl}$	522	218-220	Yellow	38			
$[\text{Fe}(\text{L})\text{Cl}_2]\text{Cl}$	$[\text{Fe}(\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_2)\text{Cl}_2]\text{Cl}$	526	220-223	Brown	37			
$[\text{Ni}(\text{L})\text{Cl}_2]$	$[\text{Ni}(\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_2)\text{Cl}_2]$	493	277-280	Pale Green	13			

d* = decomposition

3.3. Fourier transforms infrared spectra:

Infrared spectral data have been reported by research groups working on the synthesis of Schiff base and metal complexes. The characteristic bands in Schiff base are used to determine the binding modes found in the system are $\nu(\text{C}=\text{N})$, $\nu(\text{O}-\text{H})$, $\nu(\text{M}-\text{O})$, $\nu(\text{M}-\text{N})$, $\nu(\text{M}-\text{Cl})$.

A summary of characteristics IR bands is shown in Table 2 (Figure.2-4). Generally, the band that in the 1640 cm^{-1} is assigned to the existence of $\nu(\text{HC}=\text{N}-)$ group of the azomethine. for ligand and complexes are in the range of $1597-1632 \text{ cm}^{-1}$

¹. This band gets shifted to lower frequency in the complexes, indicating the coordination through azomethine nitrogen to metal atom [18]. ν (C=O) in the 1666 cm^{-1} is assigned to ligand and $1650\text{--}1685\text{ cm}^{-1}$ are assigned to complexes. The complexes show band at $(585\text{--}550)$, $(466\text{--}563)$, $(301\text{--}398)\text{ cm}^{-1}$ rang, due to the ν (M-O), ν (M-N), (M-Cl) vibrations respectively [19,20].

Table (2): IR spectral data of the ligand and Co (II), Fe (III), Cr (III), Ni(II) complexes

Compound	ν (NH)	ν (C-H) _{Ar}	ν (C=N)	ν (C=O)	ν (M-O)	ν (M-N)	ν (M-Cl)
L	3302	3032	1643	1666	-----	-----	-----
[Co(L)Cl ₂]	3304	3062	1597	1639	420	542	254
[Cr(L)Cl ₂]Cl	3310	3082	1639	1645	428	550	331
[Fe(L)Cl ₂]Cl	3306	3066	1632	1650	457	555	289
[Ni(L)Cl ₂]	3302	3024	1597	1639	444	513	231

3.4 Electronic spectra (UV-vis spectra):

The UV-vis spectrum of the ligand (L) (Figure 5) show two peaks at (349) nm, (243) nm assigned to $(n - \pi^*)$, $(\pi^* - \pi^*)$ electronic transitions respectively [20]. In the complex show peaks at (454) nm (Figure 6).

3.5 ¹H- NMR Spectra of ligand:

¹H- NMR spectral data gave additional support for the composition of the ligand. The spectra also exhibit peak at (2.21-2.79) ppm due to (CH₃,CH₂) groups, another peaks exhibit at (4.78)ppm due to -NH[21]. The aromatic ring [22] exhibit peaks at (7.13-8.01)ppm and peaks exhibit at (8.65)ppm due to singlet-proton isomethine ¹H-NMR of the ligand shown in figure (1).

3.6 Mass Spectra

The mass spectrum of the ligand exhibits a molecular ion peak [M⁺] at m/z (364), the ligand spectra show fragment peaks at m/z (203, 161, 134, 77) due to [C₁₂H₁₅N₂O]⁺; [C₉H₉N₂O]⁺; [C₁₀H₇O]⁺; [C₆H₅]⁺; respectively as shown in figure (7).

The mass spectrum of the complex [Cr (L) Cl₂] Cl show a molecular ion peak at m/z 522 which is equivalent to molecular mass of the complex. This complex shows another a fragment ion peak with loss of chlorine atom at m/z 486. The complex [Cr (L) Cl₂] Cl spectra show fragment ion peak with loss two chlorine atom at m/z (451, 415) due to [Cr (L) Cl]⁺ [Cr (L)] respectively figure (8).

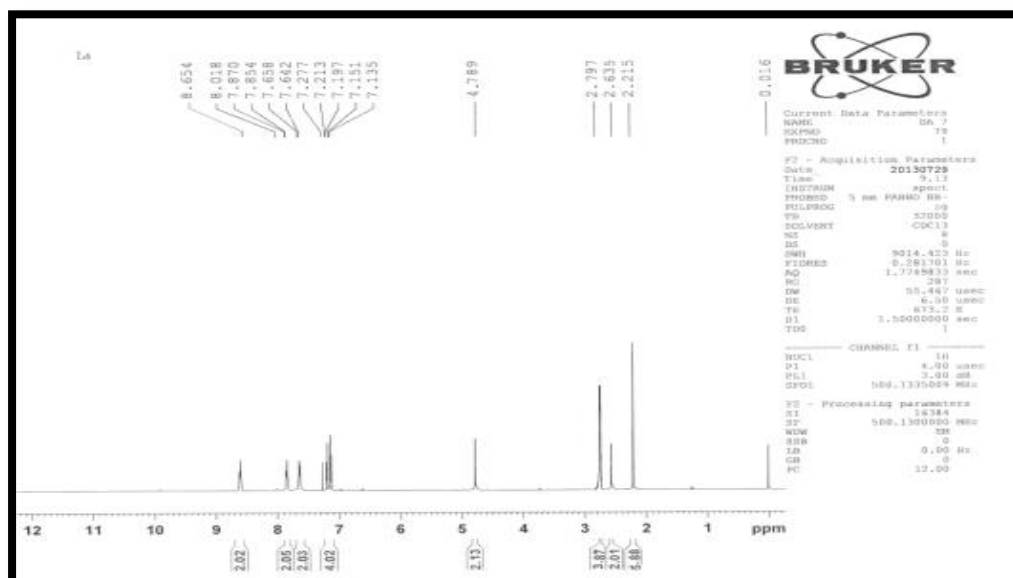
The mass spectrum of the complex [(L)NiCl₂] show a molecular ion peak at m/z (493), this complex show another fragment ion peak with loss two chlorine atom at m/z (458, 422). The mass spectra of the ligand shown in figure (9).

3.7 Biological activity

The result of antimicrobial study was shown in Table 3 and the plates were shown in figure (10).

Table (3): Antibacterial screening data of the ligand and its metal complexes

Compound		Staphylococcus Aureus Inhibition zone(mm)	Escherichia coli Inhibition zone(mm)
L_1 [$C_{21}H_{24}N_4O_2$]		15++	10+
$[Cr(L_1)Cl_2]Cl$		5	17++
$[Co(L_1)Cl_2]$		26++++	37+++++
$[Fe(L_1)Cl_2]Cl$		16++	16++
$[Ni(L_1)Cl_2]$		22+++	25++++
DMSO		-----	-----
Cipro.	30++++	28++++	



+=weak inhibition, ++=Medium inhibition, +++=good inhibition

Figure (1): 1H NMR spectrum of the ligand

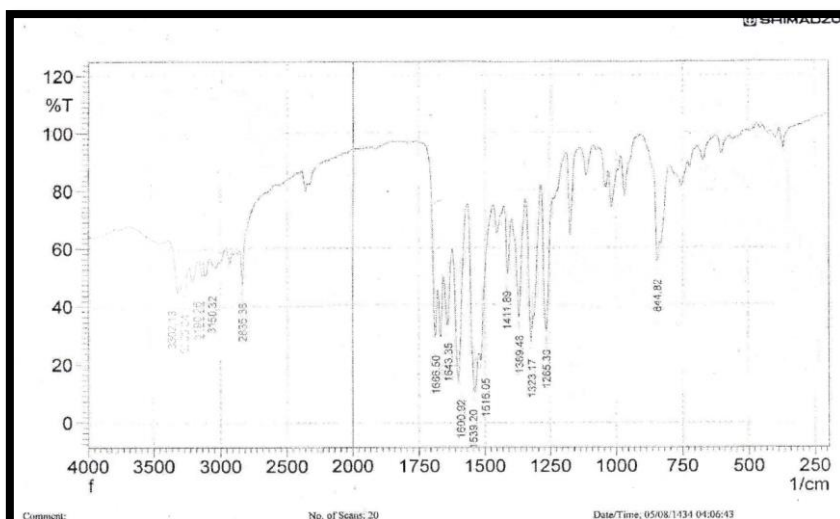


Figure (2): IR spectrum of ligand L [C₂₁H₂₄N₄O₂]

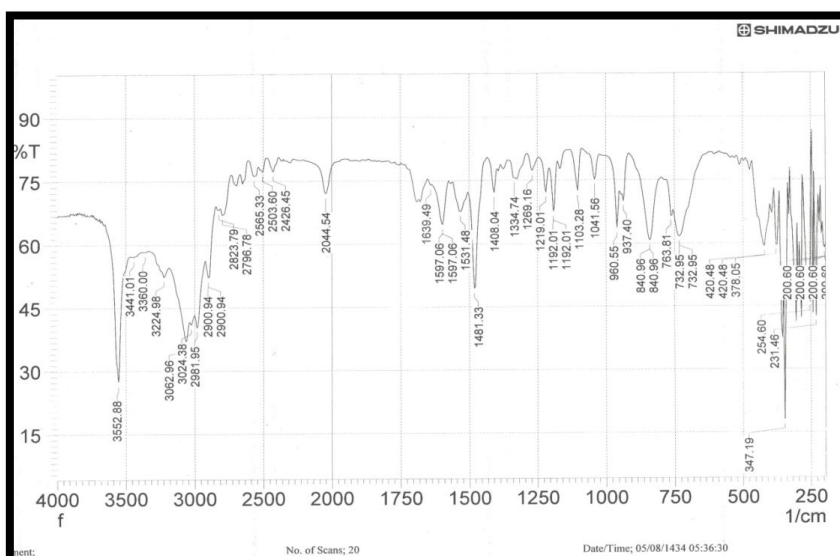


Figure (3): IR spectrum of [Co (L) Cl₂]

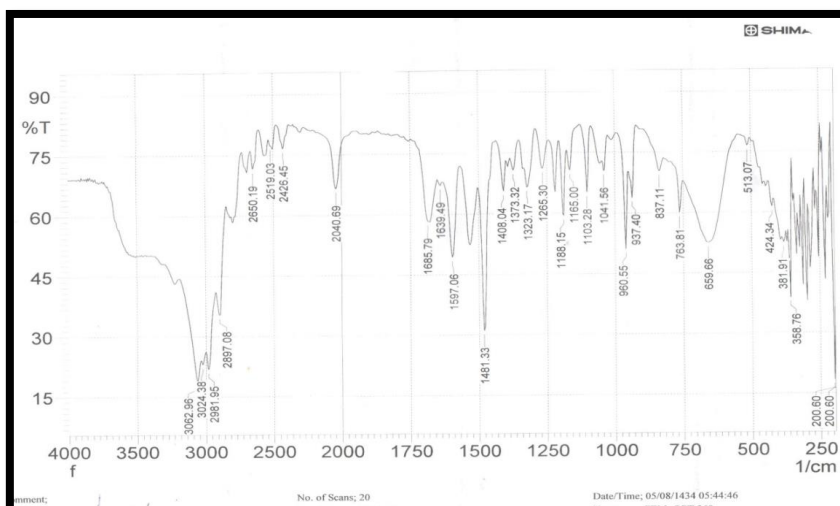


Figure (4): IR spectrum of [Ni (L) Cl₂]

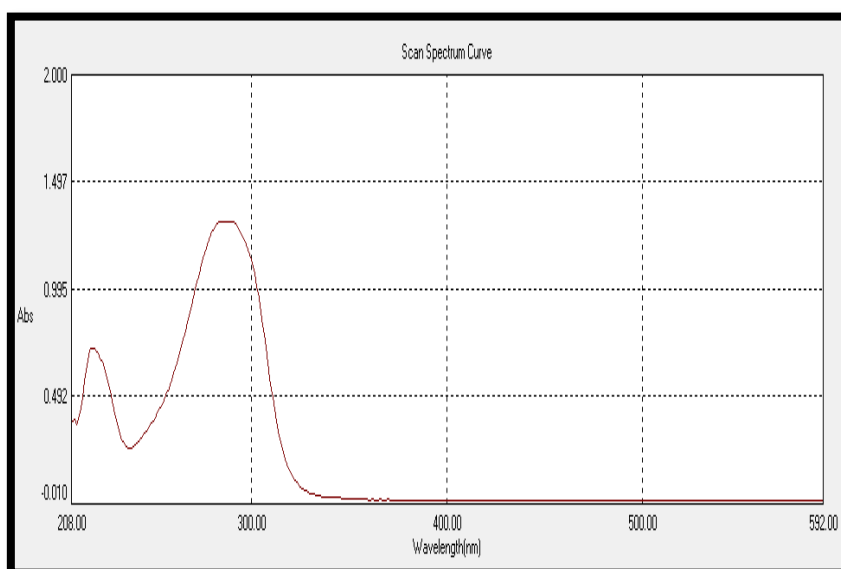


Figure (5): Electronic Spectrum of L

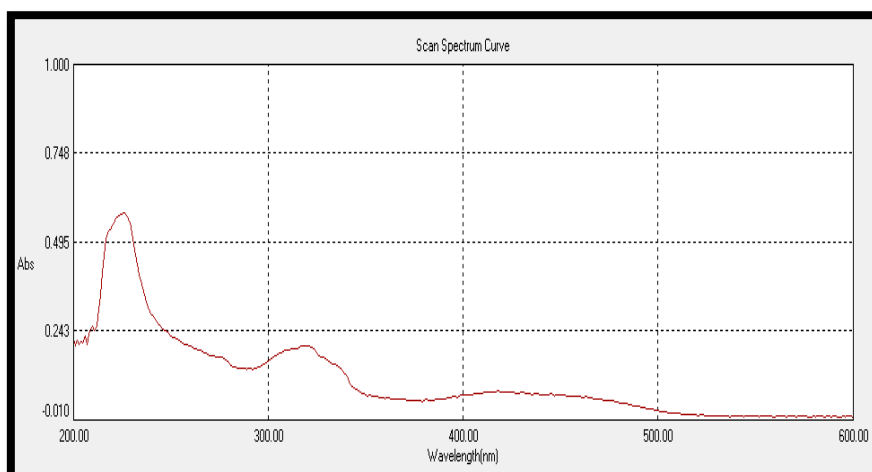


Figure (6): Electronic Spectrum of L-Fe⁺³

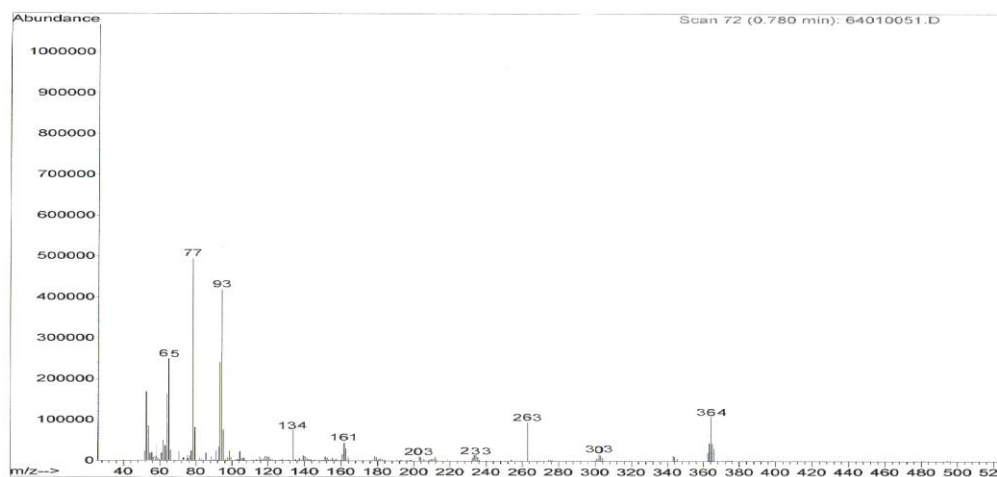


Figure (7): Mass spectrum of L

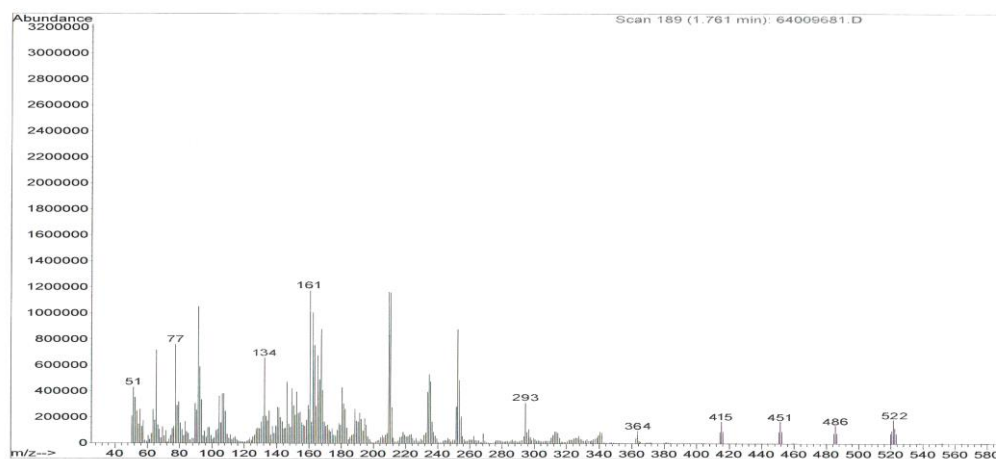


Figure (8): Mass spectrum of [Cr (L) Cl₂]Cl

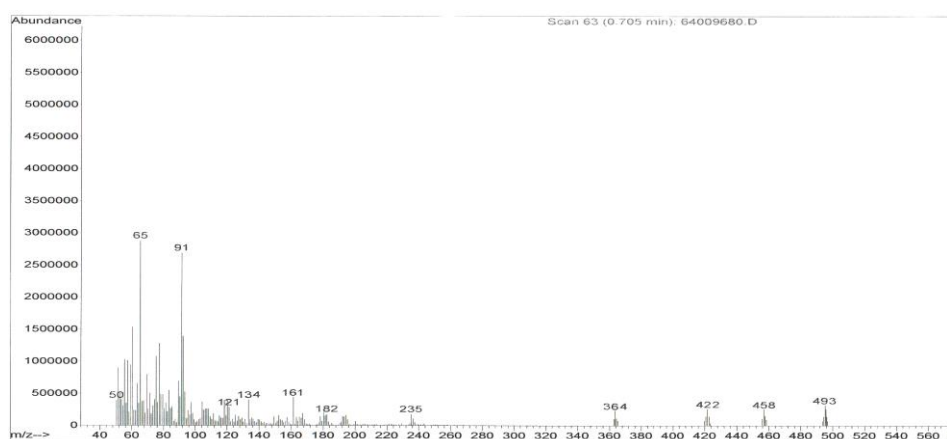


Figure (9): Mass spectrum of [Ni (L) Cl₂]

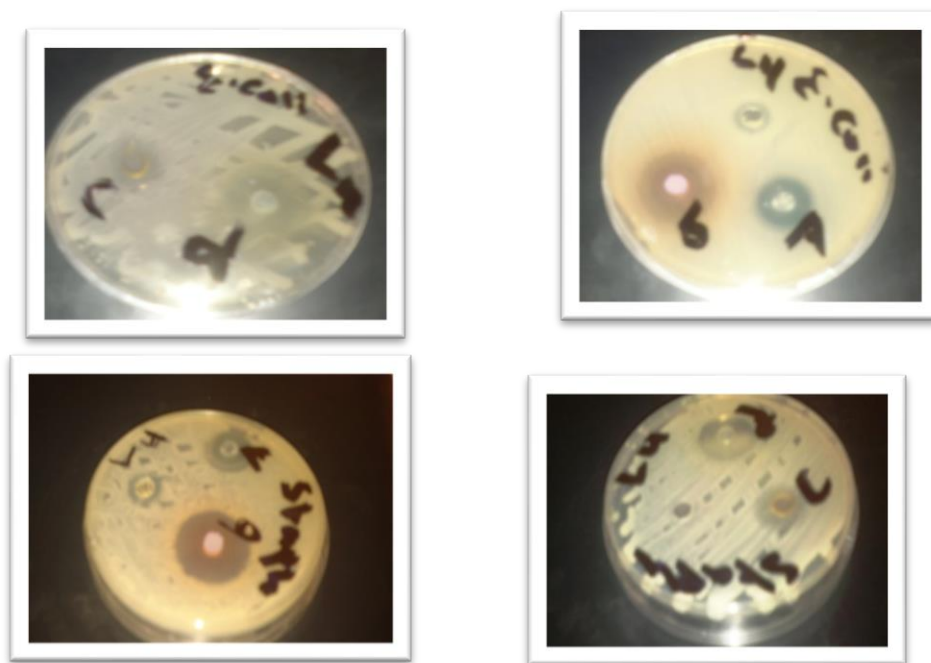


Figure (10): Zone of inhibition against subtilis, S. aureus, and E. coli

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تحضير وتشخيص وفعالية بايولوجية لليكاند جديد [N,N-بس-4-استميدو بنزليدين] 1,3-داي امينو بروبان] ومعقداته مع بعض العناصر الانتقالية

حيدر عباس
قسم الكيمياء, كلية العلوم, جامعة ذي قار

مريم علوان

الخلاصة

قاع شف [N,N-بس-4 - استميدو بنزليدين] 1,3 - داي امينو بروبان] حضرت من تكاثف 4- استميدو بنزليدهايد مع 3,1- داي امينو بروبان بواسطة التقطير الارجاعي باستخدام محلول الميثانول. المعقدات (Cr(III), Fe(III)) مع [N,N-بس 4--استميدو بنزليدين] 1,3 - داي امينو بروبان]. شخص الليكاند باستخدام التحليل الدقيق للعناصر (CHN), وطيف الرنين النووي المغناطيسي للبروتون (¹H-NMR). الليكاند ومعقداته حضر وشخص بتقنيات مختلفة, الاشعة تحت الحمراء (باستخدام بروميد البوتاسيوم لليكاند وقرص يوديد السيزيوم للمعقدات), طيف الكتلة و الاشعة المرئية-فوق البنفسجية ومن نتائج التشخيص تبين ان هذه المعقدات ثماني السطوح ترتبط فيها العناصر مع الليكاند مع ذرتي النايتروجين وذرتي الاوكسجين وكانت نسبة الارتباط بين الفلز والليكاند هي (1:1) وتم اختبار الفعالية البايولوجية ضد بكتريا *Escherichia coli* و *Staphylococcus aureus* bacteria.