

Syntheses, Characterization and biological Activity of 4-[[*(Z)*-(2-methoxyphenyl) methylidene] amino]-5-phenyl-4*H*-1, 2, 4-triazole-3-thiol with some transition metal complexes

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ABSTRACT: A new series of transition metal (*Cr(III)*, *Fe(III)*, *Co(III)*, *Ni(II)* and *Cu(II)*) complexes of ligand 4-[[*(Z)*-(2-methoxyphenyl) methylidene] amino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol were synthesized. All the synthesized complexes were characterized by analytical techniques, magnetic susceptibility measurements, elemental analyses, and conductance, IR, ¹H NMR and mass spectra. The electrolytic behavior was confirmed from their conductance data. It may be concluded that the ligand coordinate through nitrogen and sulfur atoms. For all complexes. The ligand acts as a didentate ligand coordinating through the sulfur [*S*⁶] and the nitrogen atom of Schiff base [*N*⁵]. This view is further supported by the appearance of a band corresponding to the metal–nitrogen stretching vibration at (560–570) *cm*⁻¹ in the complexes. From results it was suggested tetrahedral geometry for *Ni(II)* and *Cu(II)* complexes, while *Cr(III)*, *Fe(III)* and *Co(III)* complexes were assigned octahedral geometries. All complexes and their parent organic moiety have been screened for antibacterial activity by using spread method and inhibition zone measurement by using (DMSO). This study showed positive inhibition zone results, for both ligand and complexes with *E. coli* and *staph aureus*.

KEYWORDS: -Triazole, Transitions metal complexes, Antibacterial.

INTRODUCTION

Heterocyclic compound containing nitrogen, oxygen and silver atoms has Gained considerable attention In the last ten years because of their Use in various pharmaceutical Industry. 1,2,4-triazole derivatives are Showed a wide spectrum of biological activities such as antimicrobial [Godhani;2013-Gaikwad;2012], analgesic, anti-inflammatory, anticancer [Sahin;2012-Gadhav;2010]. transition metal complexes are still found to be of major attention in inorganic chemistry, although this subject has been studied extensively [Williams; 1972-Sun; 1992]. transition Metal complexes are proposed as a possible form of drugs, since the action of many drugs is based on the ability of the ions in the complex compound to penetrate cell membranes, While ligands almost lack this ability. Metal chelate differ in their mode of action and activity in biological systems depends on their structural [Singh; 2008]. A complexes of 1, 2, 4-triazoles is being developed for potential use in applications such as magnetic materials and photo chemically driven molecular devices. In the present work, the synthesis novel ligand 4-[[*(Z)*-(2-methoxy) methylidene] amino]-5-phenyl-4*H*-1,2,4-triazole-3-

thiol were synthesized with its complexes and their applications as anti-bacterial activity was also explored.

EXPERIMENTAL

Preparation of the ligand (L)

New ligand 4-[(Z)-(2-methoxyphenyl) methylidene] amino}-5-phenyl-4H-1,2,4-triazole-3-thiol (Scheme 1) was prepared as follows:-

A mixture of (13.6 g, 0.1mol) of methyl benzoate and (6.4ml, 0.2mol) of hydrazine was dissolved in (70ml) ethanol. The resulting mixture was heated under reflux for (4 hours). The resultant mixture was concentrated, the crude product was filtered and washed with ethanol to give the desired product benzohydrazide (A) as white needles, yield (96.32%), m.p. (138-140)°C [Khiati; 2007-Vogl; 1978]. A mixture (A) (13g, 0.1mol) and (5.6g, 0.1mol) of potassium hydroxide dissolved in absolute ethanol (100ml) to this solution (6 ml, 0.1mol) of carbon disulfide was added. The resulting mixture was heated under reflux for (22 hours). The resultant mixture was concentrated, and carefully acidified with hydrochloric acid HCl (5%) to give pale white precipitate. The crude product was filtered and washed with cold water and ethanol to give the desired product (5-phenyl-1,2,3-oxadiazole-2-thiol) (B), as white solid, yield (94.61%), m.p. (220-222)°C [Khiati; 2007-Vogl; 1978]. A mixture (B) (0.056mol, 10gm) and hydrazine (0.1mol, 4ml) dissolved in pyridine (20ml) was refluxed on a water bath for (5) hrs. The resultant mixture was concentrated, and carefully acidified with hydrochloric acid HCl (5%) to give pale light brown precipitate. The crude product was filtered and washed with cold water, recrystallized from ethanol to give the desired product (4-amino-5-phenyl-4H-1,2,4-triazole-3-thiol) (C) as brown solid, yield (90%), m.p. (189-191)°C.

A mixture (C) (0.02mol, 3.8gm) and was refluxed (3hrs), the solution is evaporated to half and filtered, the crystallized using absolute ethanol to give crystals of earth color product [ligand]. Yield: (83.3), m.p. (207-209) °C. (scheme 1)

Preparation of complexes

The Cr(III), Co(III), Fe(III), Ni(II) and Cu(II) complexes were prepared by refluxing the respective hydrated metal chloride (1 mmol) in 15 ml ethanol with 50 ml of an ethanolic solution of the ligand (1mmol, 0.3 gm) for 4 hrs. The separated solids were filtered, washed with ethanol and dried in air.

Measurements

Elemental C, H and N analysis were carried out on a Thermofinigan flash analyzer (Model: 5500; Carloerba Co.), the FTIR spectra in the range (200-4000) cm⁻¹ were recorded as CsI discs using a Shimadzu FTIR spectrophotometer (Model: IR-affinity-1; Shimadzu). Molar conductance measurements were made in anhydrous DMSO at 25 °C using (Inolabcond 720) (Model: cond720:WTWCO.). The ¹H NMR spectra were recorded on a Bruker DRX System AL500 (500MHz) spectrometer (FT-NMR Ultrashield 500 MHz; Bruker, relative to the internal standard tetramethylsilane (TMS), DMSO-d₆ used as solvent. Melting points were determined in open capillary tubes using an electro thermal melting point /SMP3 apparatus.

Mass spectra were recorded in the range (0-800) m/e on 5973 network mass selective detector (Model: 5973; Agilent).

RESULTS & DISCUSSION

The purity of the ligand and its complexes were checked by TLC using silica gel-G as adsorbent and iodine vapour for visualization. Elemental analysis tabulated in Table (1), Melting point, physical properties and molar conductance of all the compounds studied are tabulated in Table (2). The calculated values were in a good accordance with the experimental values.

Infra-Red Spectroscopy

The FTIR spectrum for L shows a characteristic stretching absorption bands at 3078cm^{-1} , 2750cm^{-1} , 1543cm^{-1} , 2939cm^{-1} and 1404cm^{-1} assigned to $\nu(\text{C-H.Ar.})$ [Szikszai; 2001], $\nu(\text{S-H})$ [Daoud; 2002], $\nu(\text{C=N})$, $\nu(\text{C-H})$, and symmetrical C-N-C stretching respectively [Nakamoto; 1997]. The C=N and S-H stretching are important to predict the bonding mode of the ligand, these bands shifted to a lower wavelength in the spectra of complexes compared with ligand, ensuring of complexation. The IR data of the ligand and complexes are shown in Table (3) and figure(6),(7) and (8) [Amir; 2007]. The Table lists the stretching

Frequency (ν) for some of the characteristics groups exhibited by the ligand and complexes.

Nuclear Magnetic Resonance

The data of proton NMR of the ligand 4-[(Z)-(2-methoxyphenyl)methylidene]amino-5-phenyl-4H-1,2,4-triazole-3-thiol displayed good solubility in DMSO. The spectra exhibit a singlet $-\text{CH}_3$ peaks at (2.5)ppm due to methyl group, another singlet peaks exhibit at (3.745)ppm due to $-\text{SH}$ [George; 2008], (8.96)ppm due to, ($-\text{N}=\text{C-H}$) and (7.58-8.56)ppm due to (C-H.Ar) respectively. The proton NMR of the ligand shown in figure(9).

Mass spectra

The mass spectrum of the ligand exhibits a molecular ion peak [M0] at m/z 310, the ligand spectra shows fragment the spectra peaks at m/z (207, 192, 177, 144, 135 and 108) due to $[(\text{C}_9\text{H}_9\text{N}_3\text{SO})^+]$, $(\text{C}_8\text{H}_8\text{N}_4\text{S})^+$, $(\text{C}_8\text{H}_7\text{N}_3\text{S})^+$, $(\text{C}_8\text{H}_6\text{N}_3)^+$, $(\text{C}_8\text{H}_9\text{NO})^+$, $(\text{C}_7\text{H}_8\text{O})^+$ respectively as shown in Figure(10). The mass spectrum of the complex $[\text{Cr}(\text{L})_2\text{Cl}_2]\text{Cl}$ shows a molecular ion peak at m/z [M0] (777) which is equivalent to molecular mass of the complex. This complex shows another a fragmentation peak with loss of chlorine atom at m/z (742). The complex spectrum shows fragment ion peak with loss two chlorine atom at m/z (707, 672) due to $[\text{Cr}(\text{L})_2\text{Cl}]^+$ and $[\text{Cr}(\text{L})_2]^+$ respectively. The mass spectrum of the complex $[\text{Fe}(\text{L})_2\text{Cl}_2]\text{Cl}$ shows a molecular ion peak at m/z [M0] (781) 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 (746). The complex spectrum shows fragment ion peak with loss two chlorine atom at m/z (711, 676) due to $[\text{Fe}(\text{L})_2\text{Cl}]^+$ and $[\text{Fe}(\text{L})_2]^+$ respectively. The mass spectrum of the complex $[\text{Co}(\text{L})_2\text{Cl}_2]\text{Cl}$ shows a molecular ion peak at m/z [M0] (784) which is equivalent to molecular mass of the complex. This complex shows another a fragment ion peak with loss of chlorine

atom at $m/z(749)$. the complex spectrum shows fragment ion peak with loss two chlorine atom at $m/z (714, 679)$ due to $[Co(L)_2Cl]^+$ and $[Co(L)_2]^+$ respectively. The mass spectrum of the complex $[NiLCl_2]$ shows a molecular ion peak at $m/z [M0](438)$, This complex shows another a fragment ion peak with loss of chlorine atom at $m/z (403)$ and (368) .

The mass spectrum of the complex $[CuLCl_2]$ shows a molecular ion peak at $m/z [M0] (443)$, This complex shows another a fragment ion peak with loss of chlorine atom at $m/z (408)$ and (373) . the mass spectra of the complexes shown in figure(11), (12), (13)(14)(15).

Analytical and spectral data (1H NMR, IR, mass spectra) of all synthesized compounds were in full agreement with the proposed structure. figure(1,2,3). figure(1) shows mix chelation sites (N,S) atoms, their electronic density profiles are represented in figure(2). figure(3) shows the octahedral (a) coordination as represented by iron (b). while figure(4) shows the tetrahedral(a) coordination as by nical(b).

Molar Electrical Conductivity

molar conductivity of the solid solutions of complexes was measured for (Cr(III), Fe(III), Co(III), Ni(II), Cu(II)) with ligand. Results are shown in table (4), indicating that the conductivity values of some complexes behave as neutral compounds (non- Electrolyte) and others behave as ionic compounds (Electrolyte).

Biological Activity

The antibacterial activity of all the synthesized complexes was evaluated by using agar well diffusion method. All the microbial cultures were adjusted to 0.5mm McFarland standard, which is visually comparable to a microbial suspension of approximately 1.5×10^8 cfu/mL. 20mL of Mueller Hinton agar medium was poured into each Petri plate and plates were swabbed with 100 μ L inocula of the test microorganisms and kept for 15 min for adsorption. Using sterile cork borer of 8mm diameter, wells were bored into the seeded agar plates, and these were loaded with a 100 μ L volume with concentration of 4.0mg/mL of each compound reconstituted in the dimethyl sulphoxide (DMSO). All the plates were incubated at 37°C for 24 hrs. Antibacterial activity of each compound was evaluated by measuring the zone of growth inhibition against the test organisms with zone reader (Hi Antibiotic zone scale). DMSO was used as a negative control whereas Ciprofloxacin was used as positive control. This procedure was performed in three replicate plates for each organism [Ahmad; 2001-Andrews; 2001] the antibacterial activity in table (5) and figure (5).

CONCLUSION

The ligand 4-[(Z)-(2-methoxyphenyl)methylidene]amino}-5-phenyl-4H-1,2,4- triazole -3-thiol. was successfully synthesized. The elemental analysis, IR, 1H NMR and mass spectral observations suggest the octahedral geometry for the Cr(III), Co(III), Fe(III). Tetrahedral geometry was proposed for Ni (II), Cu(II). Both ligand and complexes exhibited positive bacterial inhibition.

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Table 1. Elemental analysis for the ligand

Experimental			Theoretical		
C%	H%	N%	C%	H%	N%
61.99	4.59	18.05	61.92	4.55	18.05

Table 2. Conductance, physical properties data of the ligand and its complexes

No	Compound	Molecular formula	Color	Λ Scm ² . mol ⁻¹	Melting Point °C
1	Ligand	C ₁₆ H ₁₄ N ₄ SO	Earthy	-----	207-209
2	[Cr(L) ₂ Cl ₂]Cl	Cr(C ₁₆ H ₁₄ N ₄ SO) ₂ Cl ₃	Light brown	37	218-220
3	[Fe(L) ₂ Cl ₂]Cl	Fe(C ₁₆ H ₁₄ N ₄ SO) ₂ Cl ₃	Light yellow	39.2	245d*
4	[Co(L) ₂ Cl ₂]Cl	Co(C ₁₆ H ₁₄ N ₄ SO) ₂ Cl ₃	Dark yellow	39	225-227
5	[Ni(L)Cl ₂]	Ni(C ₁₆ H ₁₄ N ₄ SO)Cl ₂	Light yellow	17.5	215-217
6	[Cu(L)Cl ₂]	Cu(C ₁₆ H ₁₄ N ₄ SO)Cl ₂	Green	18.1	222-224

d*=decomposition

Table 3: Characteristic absorption bands of ligand and its complexes

N O	ν C-H	ν C-H.Ar	ν SH	ν C=N	ν C-N-C	Skeletal Movement	ν M-N	ν M-S	ν M-Cl
L	2939	3078	2750	1543	1404	1018	—	—	—
1	2935	3032	2769	1543	1404	1018	560	397	250
2	2993	3035	2774	1546	1408	1022	570	385	297
3	2935	3032	2769	1546	1404	1018	560	397	293

No of Complex	Complexes	Λ_m (S .cm ² .mole ⁻¹)	Electrolyte Type
1	[Fe(L ₃) ₂ Cl ₂]Cl	39	1:1
2	[Co(L ₃) ₂ Cl ₂]Cl	36	1:1
3	[Cr(L ₃) ₂ Cl ₂]Cl	38.4	1:1
4	[Cu(L ₃) Cl ₂]	16	non Electrolyte
5	[Ni(L ₃)Cl ₂]	17	non Electrolyte

Table 4: Molar Electrical Conductivity for the complexes

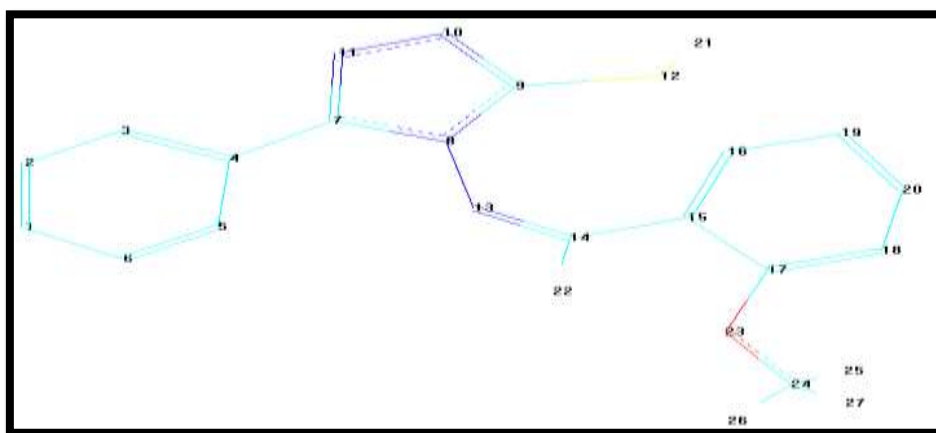


Figure 1: The stereochemistry of the Ligand (C₁₆H₁₄N₄SO)

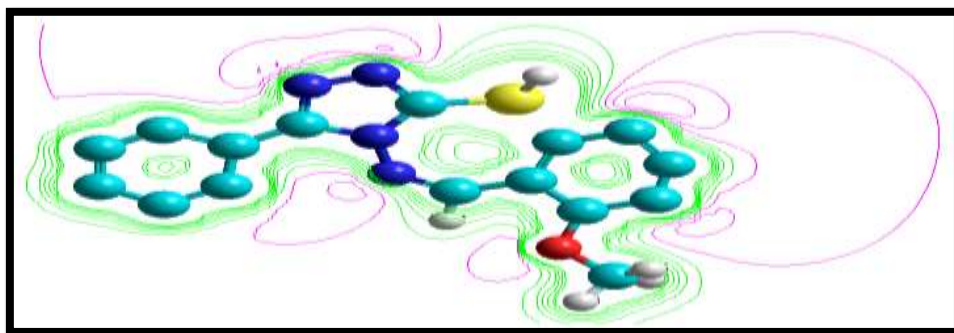


Figure 2: Electrostatic potential 2D for Ligand

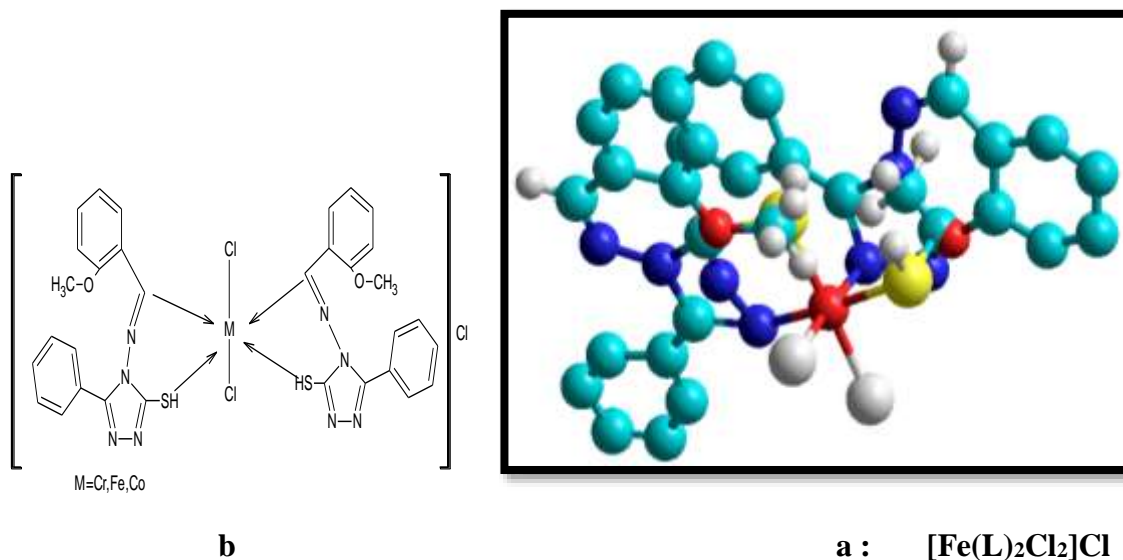


Figure 3

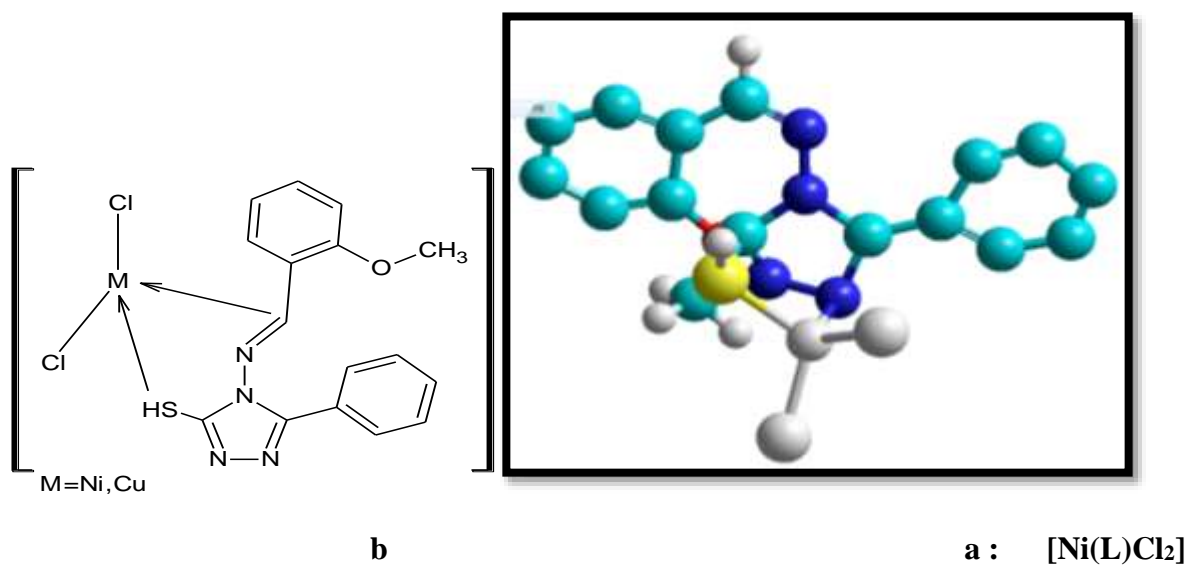
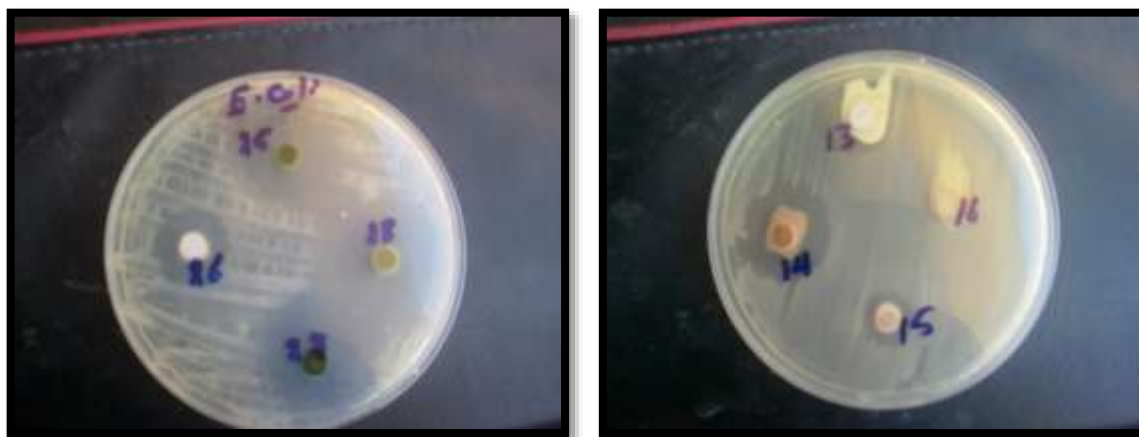


Figure 4

Table 5. Antibacterial screening data of the ligand and its metal complexes

Compound	Escherichia coli Inhibition zone(mm)	Staphylococcus Aureus Inhibition zone(mm)
L= C ₁₆ H ₁₄ N ₄ SO	14+	18++
[Cr(L1) ₂ Cl ₂]Cl A=	19++	12+
B=[Fe(L1) ₂ Cl ₂]Cl	20+++	12+
C = [Co(L1) ₂ Cl ₂]Cl	16++	19++
[Ni(L1)Cl ₂] D=	25++++	23+++
E=[Cu(L1)CL ₂]	28+++++	21+++

**(+ = Weak Inhibition , ++ =Medium Inhibition , +++ = Good Inhibition ,++++ =Very good Inhibition)



A

B

Figure 5: Images of inhibition of Coli (A) and Staphylococcus Auras (B).

Note: figures inside Petridish refer to the numbering of samples

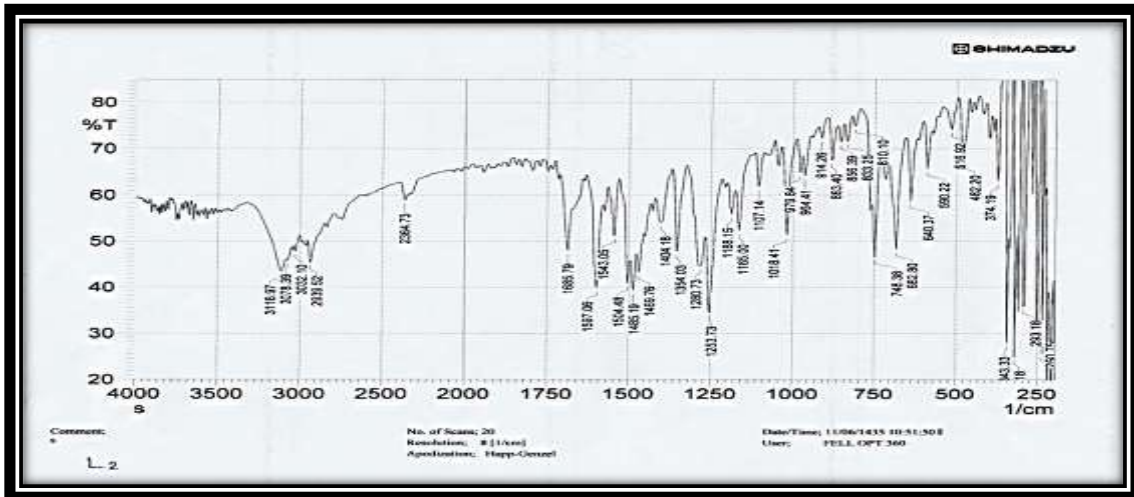


Figure6: IR spectra of Ligand ($C_{16}H_{14}N_4SO$)

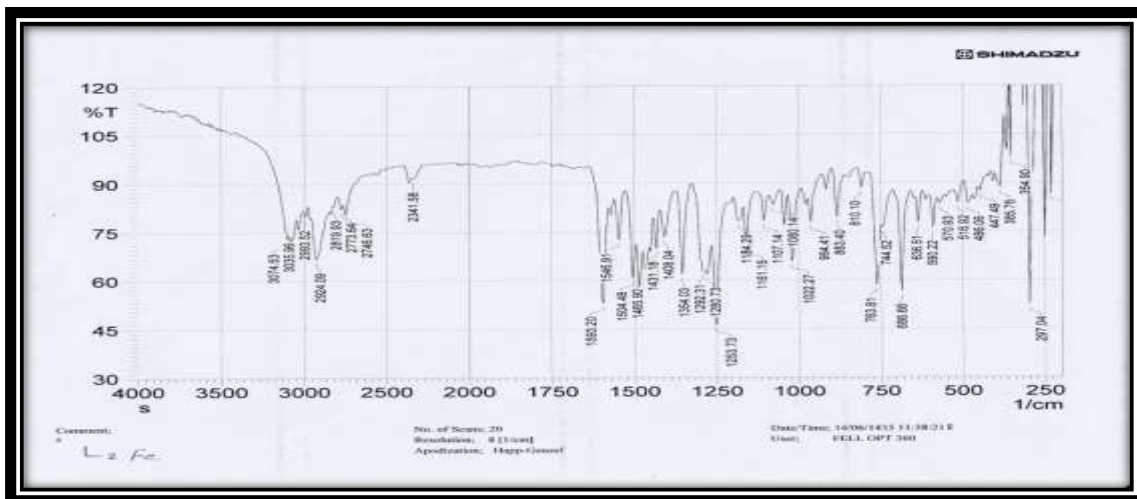


Figure7: IR spectra of $[Fe(L)_2Cl_2]Cl$

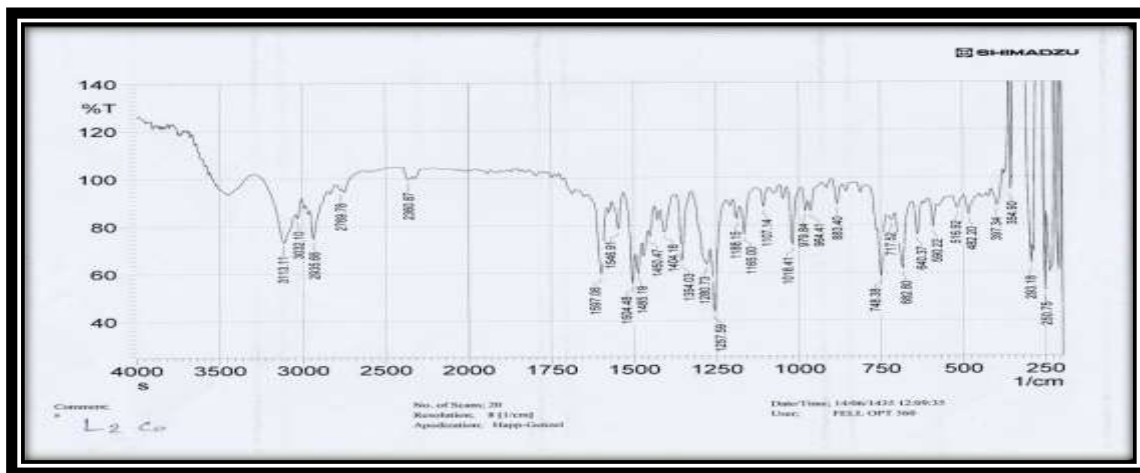


Figure8: IR spectra of $[Co(L)_2Cl_2]$

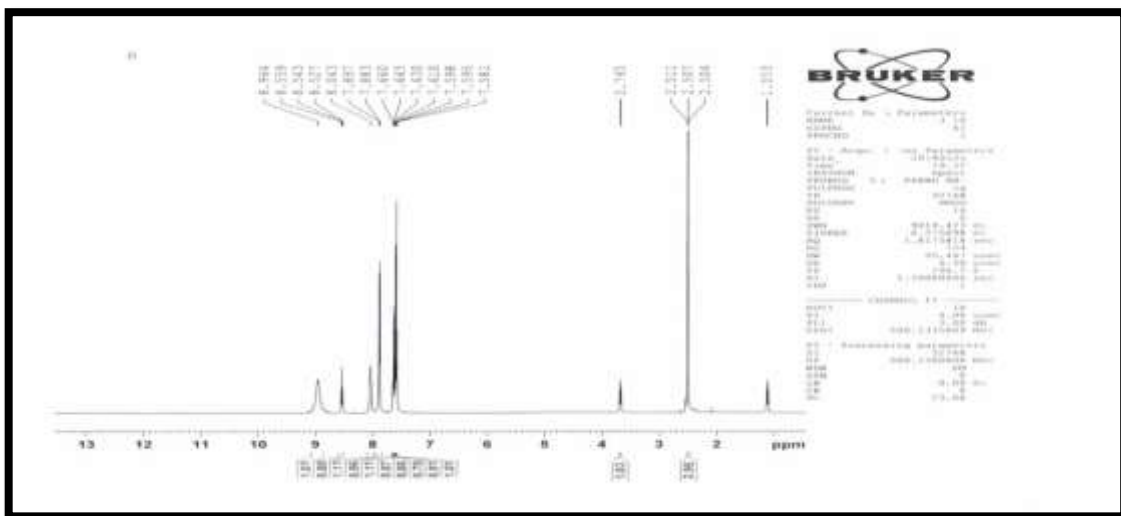


Figure9: NMR spectra of the ligand (C₁₆H₁₄N₄SO)

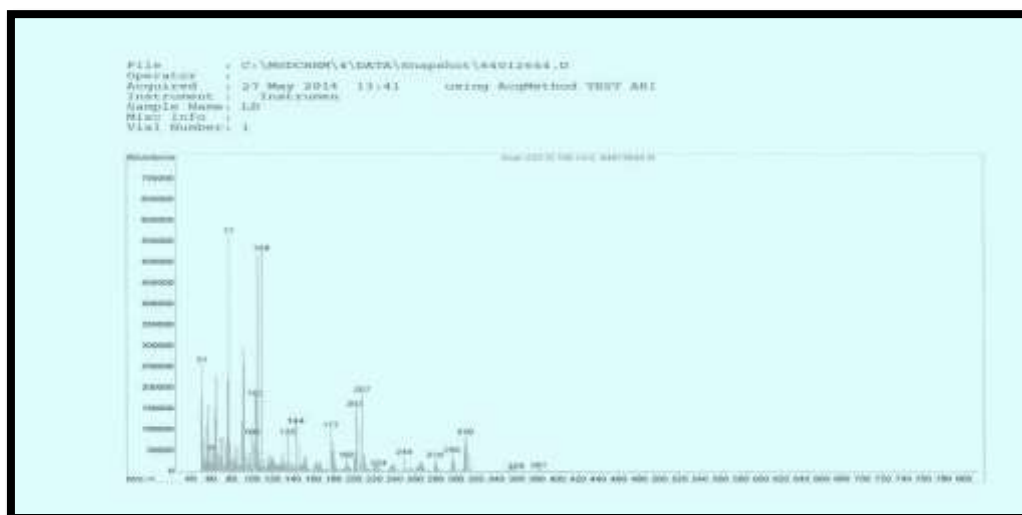
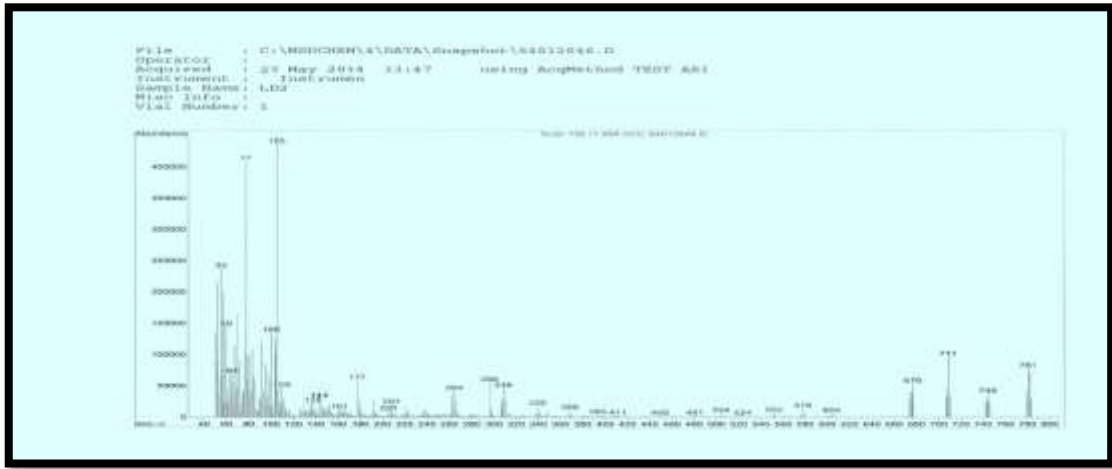


Figure 11: Mass spectra of [Cr (L)₂Cl₂]Cl



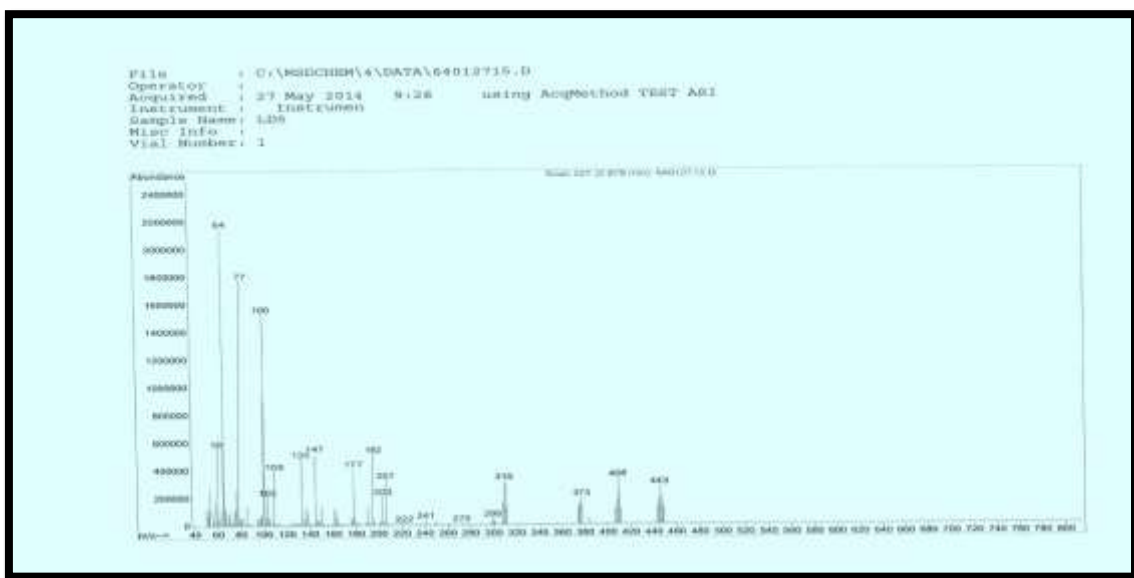
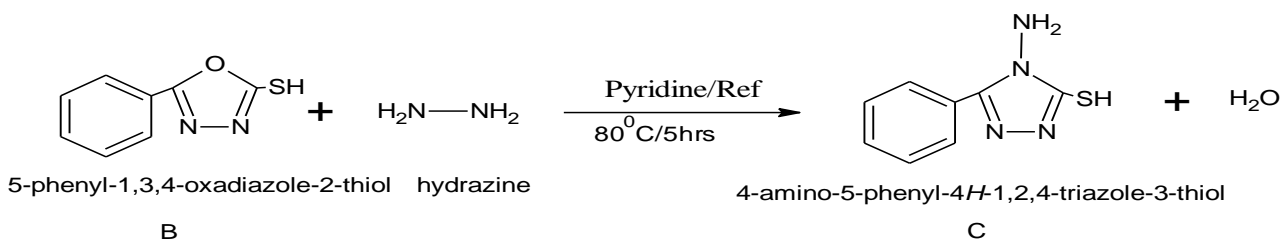
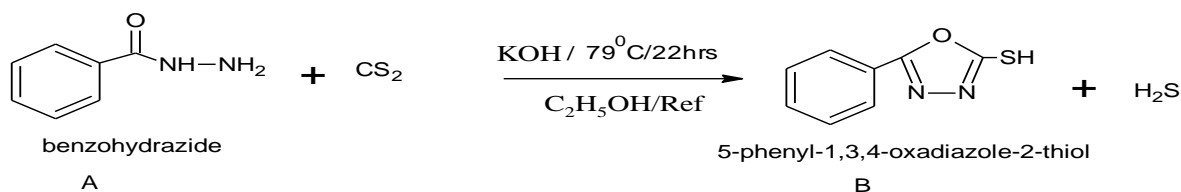
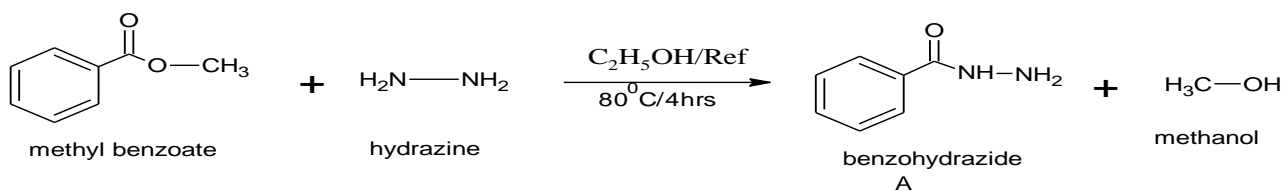
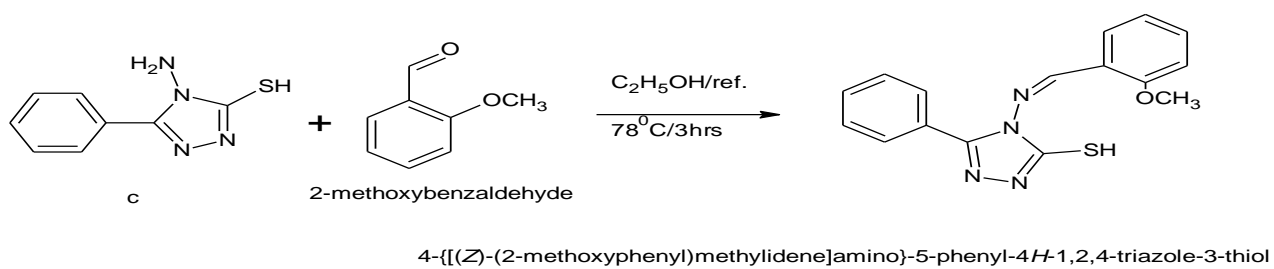


Figure 15: Mass spectra of [Cu(L)Cl₂]





Scheme (1)