

Synthesis and characterization of novel binuclear complexes

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Abstract

Interaction of 3,4-dihydroxy benzaldehyde and p-phenylene diamine in 2:1 molar ratio resulted in the formation of new Schiff base ligand 4,4'-(1,4-phenylene bis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-1-ylidene)-1,2-diol; (H_4L). From the direct reaction of the ligand (1) with Co(II), Ni(II) and Cu(II) chlorides and Fe(III) and Zn(II) nitrates in 2M:1L molar ratio, the five new neutral complexes were prepared. The characterization of the newly formed compounds was done by 1H NMR, U.V-Vis and IR spectroscopy and elemental analysis. The data showed tetrahedral geometry for Co, Ni, Cu and Zn complexes (3, 4, 5 and 6, respectively) and octahedral geometry for Fe complex (2). The in-vitro antibacterial activity against G +ve bacteria (*B. subtilis* and *S. aureus*), G -ve bacteria (*E. coli* and *P. aeruginosa*) and antifungal activity against (*C. albicans* and *A. niger*) of the metal complexes were studied and compared with that of free ligand. Also MIC of the compounds against test microorganisms was detected.

Key words: Complexes, Schiff bases, Synthesis, 3,4-dihydroxy benzaldehyde, MIC of biological evaluation

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1. Introduction

Some Schiff bases were tested for fungicidal activity, which is related to their chemical structure [1], there metal complexes are important in biochemical process. For example, the transamination reactions are catalyzed by metals ions through the formation of intermediate Schiff bases containing vitamin B6 [2]. In the area of bioinorganic chemistry interest in Schiff base complexes has centered on the role of such complexes in providing synthetic models for the metal containing sites in metallo-proteins and enzymes [3]. Schiff base ligands are potential anticancer drugs [4] and the anticancer activity of these metal complexes are enhanced in comparison to their free ligands [5]. 3,4-dihydroxybenzaldehyde, (Protocatechuaaldehyde, PCA) derivatives were evaluated and showed inhibition for bacteria growth [6], antioxidants [7], antitumor [8], anticorrosion [9] and reagent in simple, rapid and highly sensitive analysis of Cr(VI) and (V) [10].

In the present work, new Schiff base derived from condensation of PCA and p-phenylene diamine and its complexes were prepared and investigated using the elemental analysis and UV-Vis, IR, 1H -NMR spectral analysis as well as TGA and the biological activities including MIC were studied.

2. Materials and methods

2.1. Materials and reagents

The analytical reagent grade (AR) 3,4-Dihydroxy benzaldehyde, 1,4-phenylene diamine, $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, $CuCl_2 \cdot 2H_2O$, $Fe(NO_3)_3 \cdot 9H_2O$, $Zn(NO_3)_2 \cdot 6H_2O$ are Merck or Aldrich was used and Organic solvents used (methanol, ethanol, diethyl ether and acetone) were HPLC or extra pure grades and were used without further purification.

2.2. Instruments

Percentages of C, H and N were determined in the Microanalytical Laboratory. IR spectra were recorded using KBr pellets on a Perkin-Elmer 1430 Spectrometer for the region (200-4000 cm^{-1}). Electronic spectra were measured in UV-Vis range (195-1100 nm) using a Perkin-Elmer lambda 35 UV/Vis. The 1H -NMR spectra were recorded on DEITAZ NMR 500 MHZ Spectrometer at the National Research Centre. The mass spectra were recorded on GC-MSA-QP 5050A Shimadzu. Magnetic susceptibility measurements were carried out at room temperature on a Sherwood Scientific Magnetic Balance. Antimicrobial activity experiments were carried out.

2.3. Synthesis of Schiff base ligand (H_4L) (1)

The Schiff base ligand (H_4L , 1) was prepared by dropwise addition of hot ethanolic solution (25ml) 3, 4-dihydroxy benzaldehyde (1.381g, 0.005mole) to hot

ethanolic solution of 1,4-phenylene diamine (0.5405g, 0.005mole). The reaction mixture was heated under reflux for 3 hr., evaporation of solvent at r.t. allowed to appear of fine dark orange crystals, filtered, washed with ethanol, acetone and diethyl ether and air dried. M.p.160°C; M. wt. 348.0; Anal. Calc. for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.59; N, 8.0 %, found: C, 68.67; H, 4.60; N, 7.75%; Main IR Peaks (KBr, cm^{-1}): $\nu(OH)$ 3380, $\nu(C=N)$ 1592.

2.4. General procedures for the Preparation of complexes

The solid complexes; Figs. (10 and 11) were prepared by drop wise addition of an ethanolic solution of metal salts to an ethanolic solution of the ligand in 2:1 molar ratio metal salt: ligand, the reaction mixture refluxed for 3hr., the obtained precipitate was filtered and washed with ethanol, acetone and diethyl ether and air dried.

2.4.1. The complex, $Fe_2L(H_2O)_6(NO_3)_2 \cdot 2H_2O$; (2)

Black solid. M.p.>300°C; M.wt. 723.68; Anal. Calc. for $C_{20}H_{28}Fe_2N_4O_{18}$: C,33.19; H,3.86; N,7.7; Fe,15.43%; found: C,33.48; H,3.4; N,6.77; Fe,15.00; Main IR Peaks (KBr, cm^{-1}): $\nu(C=N)$ 1580.

2.4.2. The complex, $Co_2L(H_2O)_4 \cdot 5H_2O$; (3)

Dark brown solid. M.p. 290°C; M.wt.623.8; Anal.Calc for $C_{20}H_{30}Co_2N_2O_{13}$: C,38.48 ;H,4.85; N,4.48; Co,18.9%; found: C,38.45; H,4.25; N,4.95; Co,18.25%; Main IR Peaks (KBr, cm^{-1}): $\nu(C=N)$ 1596.

2.4.3. The complex, $Ni_2L(H_2O)_4 \cdot 3H_2O$; (4)

Dark brown solid, M.p. >300°C; M.wt.587.4; Anal.Calc. for $C_{20}H_{26}Ni_2N_2O_{11}$: C,40.82 ;H,4.4; N,4.70; Ni,19.95%; Found: C,40.56;H,4.06;N,4.75;Ni,19.1%; Main IR Peaks (KBr, cm^{-1}): $\nu(C=N)$ 1592.

2.4.4. The complex, $Cu_2L(H_2O)_4 \cdot 5H_2O$; (5)

Black solid. M.p. >300°C; M.wt.649.0; Anal.Calc. for $C_{20}H_{30}Cu_2N_2O_{14}$: C,36.94 ;H,4.62; N,4.30; Cu,19.50%; Found: C,36.75; H,4.45; N,3.73; Cu,19.0%; Main IR Peaks (KBr, cm^{-1}): $\nu(C=N)$ 1612.

2.4.5. The complex, $Zn_2L(H_2O)_4 \cdot 3H_2O$; (6)

Brown solid. M.p.190°C; M.wt.608.8; Anal.Calc. for $C_{20}H_{26}Zn_2N_2O_{11}$: C,39.94; H,4.35; N,4.60; Zn,21.72%; found: C,40.07; H,4.75; N,4.15; Zn,21.0; Main IR Peaks (KBr, cm^{-1}): $\nu(C=N)$ 1593.

3. Results and Discussion

The present Schiff base ligand H_4L ; Fig. (1) was prepared by refluxing in ethanol an equimolar mixture of PCA and 1,4-phenylene diamine. The structure of formed Schiff base was established by IR, 1H -NMR, mass and U.V-vis spectra as well as elemental analysis. All complexes were prepared by direct reaction between Schiff base ligand H_4L and corresponding salts. The obtained complexes are stable in air and have melting points above 150°C .They are insoluble in organic solvents such as diethyl ether and

acetone, but soluble in DMF and DMSO. The elemental analysis data of the Schiff base and complexes (Section 2) are in well agreement with the expected structure.

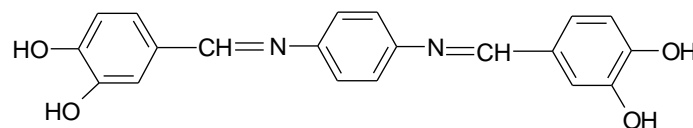


Fig. 1. Proposed structure of (H_4L)

The molar conductance values of the synthesized complexes were determined using 10^{-3} M concentration in DMF as solvent, are in the range of $0.83 - 1.65 \Omega^{-1} cm^2 mol^{-1}$. These values suggest non-electrolyte nature for these complexes [11].

3.1. Characterization of ligand (H_4L)

The infrared spectrum of the Schiff base ligand (H_4L) in the region $200-4000 cm^{-1}$ showed a medium absorption band at $1592 cm^{-1}$ assigned to the $C=N$ stretching vibrations, indicating the formation of the Schiff base linkage. Furthermore, the absence of $C=O$ and $-NH_2$ stretching vibration in the spectra of the ligand related to aldehyde and amine, respectively, indicated the occurrence of Schiff base condensation [12].

The spectrum showed that a broad medium intensity band occurred at $3380 cm^{-1}$ assigned to νOH and the phenolic $\nu C-OH$ stretching vibration was observed at $1287 cm^{-1}$. The two weak intensity bands at 3929 and $2840 cm^{-1}$ corresponding to $\nu(C-H)_{ar}$ and $\nu(C-H)_{aliph}$ stretching vibration. $\nu Ph-N$ gave medium intensity band at $1172 cm^{-1}$. The 1H -NMR spectrum of the Schiff base ligand (Fig. 2a, b) showed signals lying at range $8.9-9.7 ppm$ were due to the resonance hydroxyl groups, the signals of OH groups lying at higher field side could be attribute to the contribution of the OH group intramolecular and intermolecular hydrogen bonds. Addition of D_2O to the pervious solution results disappearing the signal due to proton exchange. The resonance of imine proton downfield shifted to ($9.6 ppm$) due to the strong shielding effect of the hydroxyl groups. Also the multiple signals lying in range $6.3-7.6 ppm$ were attributed to resonance of aromatic protons.

The electronic spectrum of the ligand in DMF displayed bands below $330 nm$ which were attributed to intra ligand $\pi-\pi^*$ and $n-\pi^*$ transitions of the benzene ring and azomethine group. The mass spectrum of the free Schiff base ligand (Fig. 3) showed its molecular ion peak at $m/e=348$ which was coincidence with its formula weight.

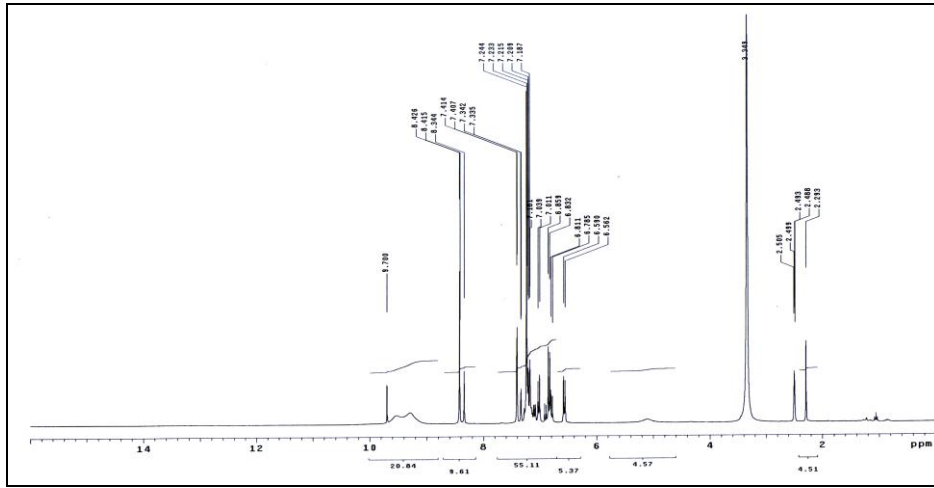


Fig.2a. The ^1H -NMR spectrum for (H_4L) in (DMSO)

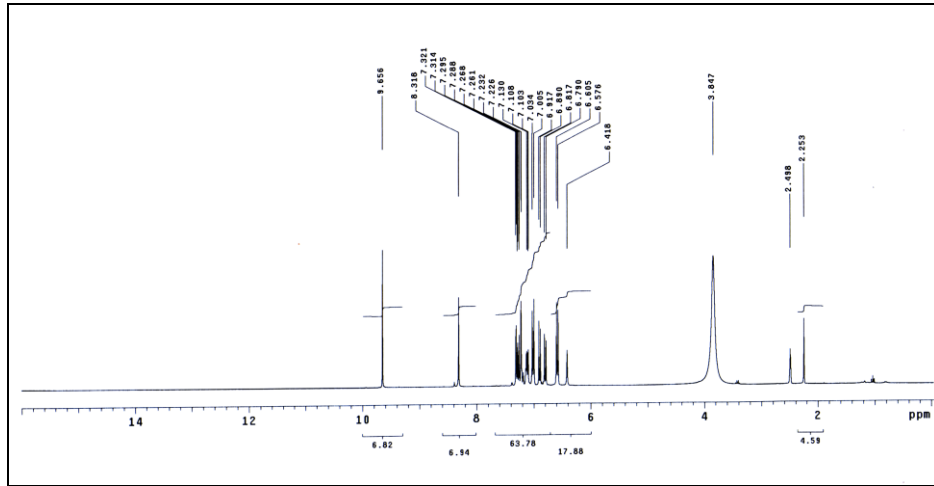


Fig.2b. The ^1H -NMR spectrum for (H_4L) in $(\text{DMSO} + \text{D}_2\text{O})$

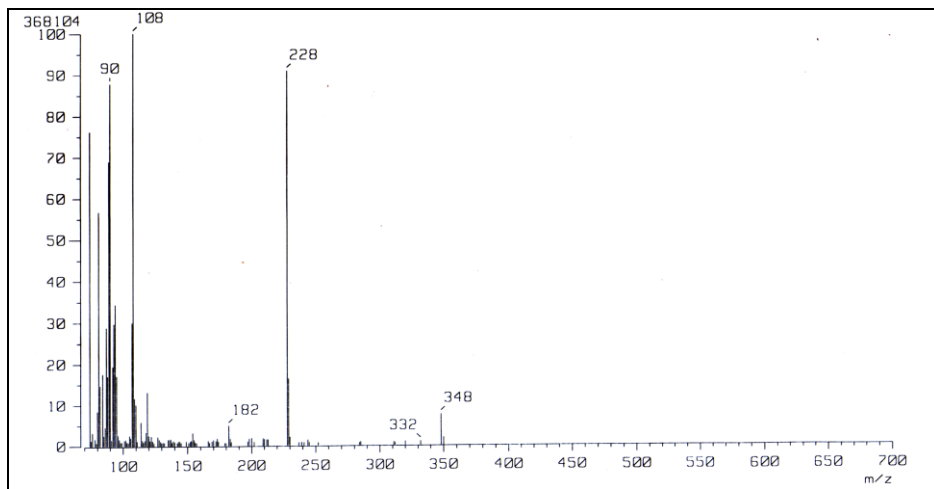


Fig. 3. The mass spectrum for (H_4L)

3.2. Characterization of the complexes

3.2.1. Infrared spectra

The infrared spectra (Table 1) of the complexes provide some information about the bonding in the complexes. The band in the IR spectrum of the ligand at 1592 cm^{-1} is found to be unaffected; this is characteristic feature for uncoordination through azomethine group [13]. Also, the $\nu\text{M-N}$ bands were not appearing, due to uncomplexation via azomethine group. Deprotonation of all phenolic functions was confirmed by the lack of phenolic O-H stretching bands at 3380 indicating the participation with the metal ion as $-\text{O}^-$, on the other hand very broad bands observed in the spectra of the complexes in the range $3390\text{--}3427\text{ cm}^{-1}$ considerably support the presence of water molecules in the complexes [14]. The band at 1287 cm^{-1} in the free ligand ascribed to the phenolic C-O stretching vibration, this band was shifted to lower frequencies ($1185\text{--}1216\text{ cm}^{-1}$) due to O- metal coordination [15]. The weak bands appeared in the far IR spectra between $555\text{--}583\text{ cm}^{-1}$ were attributed to $\nu\text{M-O}$.

The infrared spectra of complexes (2) and (6) exhibited bands around 1543 , 1289 and 1125 cm^{-1} due to $\nu(\text{N}=\text{O})$, $\nu_{\text{asym}}(\text{NO}_2)$ and $\nu_{\text{sym}}(\text{NO}_2)$, respectively which were corresponding to nature of coordinated monodentate nitrate group [16].

3.2.2. Electronic spectra

The electronic spectrum of Fe^{+3} complex (2) in DMF, exhibited two bands at 440 and 320 nm assignable to the spin allowed electronic absorption of $\text{T}_{2g}(\text{F})$ to 5E_g transition in octahedral configuration and charge transfer, respectively. The magnetic moment (5.60 B.M) infers the presence of octahedral geometry around the central Fe^{+3} ion [17]. The electronic spectrum of $\text{Co}(\text{II})$ complex (3) in DMF showed the low intensity shoulders at 590 and 654 . the former bands is probably due to ${}^4\text{A}_2(\text{F})$ to ${}^4\text{T}_1(\text{P})$ and ${}^4\text{A}_2(\text{F})$ to ${}^4\text{T}_1(\text{F})$ which indicating tetrahedral geometry of this complex [18]. The magnetic moment of 4.27 BM sustained this configuration. The spectrum of the $\text{Ni}(\text{II})$ complex (4) in DMF showed a very broad band at 600 nm indicating the ${}^3\text{T}_1$ to ${}^3\text{T}_1(\text{P})$ corresponding to the tetrahedral configuration of this complex. The magnetic moment (3.2 B.M) indicated the tetrahedral geometry of the ligand around Ni^{+2} ion [19]. The spectrum of $\text{Cu}(\text{II})$ complex (5) in DMF gave broad band at 517 nm , hence, the copper complex appear to be in tetrahedral geometry. The μ_{eff} value (1.7 B.M) was corresponding to tetrahedral geometry arrangement of the ligands around the Cu^{+2} ion [20]. The electronic absorption spectrum of $\text{Zn}(\text{II})$ complex (6) in DMF showed only charge transfer transition which can be assigned to charge transfer from the ligand to the metal and vice versa and no d-d transition are expected for d^{10} $\text{Zn}(\text{II})$ complexes [21].

3.2.3. The ${}^1\text{H-NMR}$ spectra

The ${}^1\text{H-NMR}$ spectrum of the zinc complexes (Fig.4a) recorded in DMSO-d_6 at room temperature. In the spectrum of the complex the phenolic proton signals

observed at δ $8.9\text{--}9.7$ ppm in the spectrum of the free ligand was found to be absent, confirming subsequent involvement of deprotonated hydroxyls in chelation to the metal ions. The strong broad signal appeared at δ 4.4 ppm which not found in the spectrum of the free ligand due to resonance of protons of coordinated water molecules. Addition of D_2O to the previous solution showed the absence of the signal due to proton exchange (Fig. 4b).

3.2.4. Thermal analysis

The thermo gravimetric analysis (TGA); Figs. (5-8), curves for complexes (2, 3, 4 and 5), respectively were obtained at a heating rate of $10^\circ\text{C}/\text{min}$ and flowing nitrogen atmosphere over a temperature range of $20\text{--}100^\circ\text{C}$ and recorded in table (2). The decomposition temperature and the weight losses of the complexes were calculated from TGA data.

3.2.5. ESR Spectra

The ESR spectrum of complex 5 ; Fig.(9) is axial shape and having symmetric bands with two "g" value, $g_{\parallel} = 2.25$, $g_{\perp} = 2.08$, while $g_{\parallel} > g_{\perp} > 2.0027$ characteristic of complex with ${}^2\text{B}_1(d_{x^2-y^2})$ orbital ground state. The average g values were calculated according to the equation $g_{\text{av.}} = 1/3[g_{\parallel} + 2 g_{\perp}]$, which was equal to 2.14 . The 5 complex exhibit $g_{\parallel} < 2.3$, suggesting covalent character of copper - ligand in present complex. The complex 5 having $G = 3.12$, So there are exchange coupling between $\text{Cu}(\text{II})$ centers in the solid state. The g factor derivates strongly from complex (5) because of strong spin - orbit coupling. The ESR spectral parameter of $\text{Cu}(\text{II})$ in complex having tetrahedral geometry around $\text{Cu}(\text{II})$ ion. These data are well consistent with other reported values [22].

4. Antimicrobial Activity

Screening for the antimicrobial activity of the ligand H_4L and its complexes was tested. The testing was carried out using the classical agar diffusion method. Antimicrobial disk diffusion was performed as described by the National Committee for Clinical Laboratory Standard [23, 24]. The data in table (3) show that all tested compounds have an appropriate activity against Gram-positive bacteria represented by *Bacillus subtilis*, the most active of them was compound number 1 (recorded 23.0 mm inhibition zone) and the compounds 3 & 5 showed activity against *Staphylococcus aureus* and were recorded as 21.5 mm . Also, the compounds showed activity against Gram-negative bacteria represented by *Escherichia coli* (the most active compound 3 shown 21.0 mm) and *Pseudomonas aeruginosa* (the most active compound 5 shown 20.0 mm inhibition zone). In turn, compound 3 have a good and highest activity against unicellular fungi represented by *Candida albicans* (compound 3 recorded 26.0 mm zone diameter) and filamentous fungi represented by *Aspergillus niger* (compounds 5, 1, 6 and 3 showed a good activity and recorded 30 , 27.0 , 26.5 and 25.0 mm zone diameter, respectively).

Table 1. The IR Spectra data for compounds (1-6)

Compound	$\nu(\text{OH})$	$\nu(\text{H}_2\text{O})$	$\nu(\text{CH})$ ar.	$\nu(\text{CH})$ aliph.	$\nu(\text{C}=\text{N})$	$\nu(\text{C}-\text{OH})$	$\nu(\text{Ph}-\text{N})$	$\nu(\text{M}-\text{O})$
1	3380	-	2929	2840	1592	1287	1172	-
2*	-	3414	2928	2863	1580	1216	1125	583
3	-	3390	2926	2853	1596	1200	1126	584
3	-	3391	2931	2840	1592	1203	1125	580
4	-	3427	2934	2842	1612	1199	1109	581
5*	-	3413	2927	2840	1593	1185	1122	555

*nitrate complexes

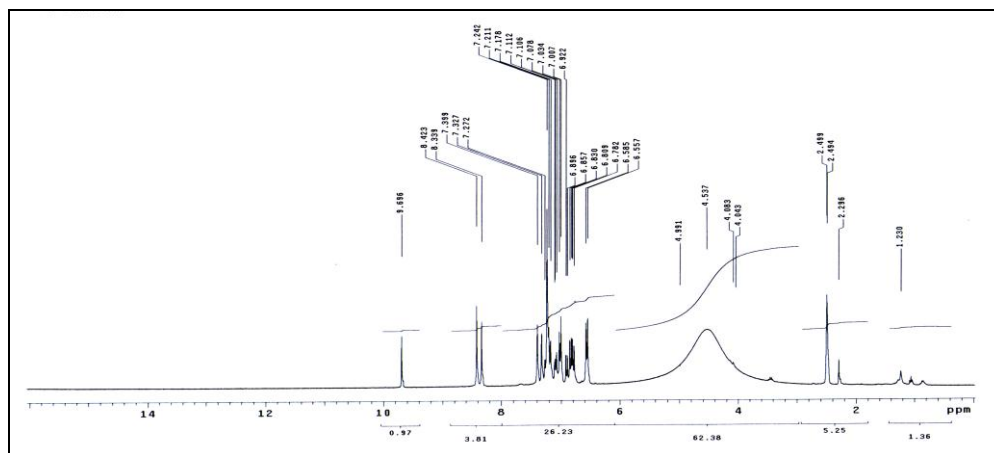


Fig. 4a. The ^1H -NMR for Zn(II) complex in (DMSO)

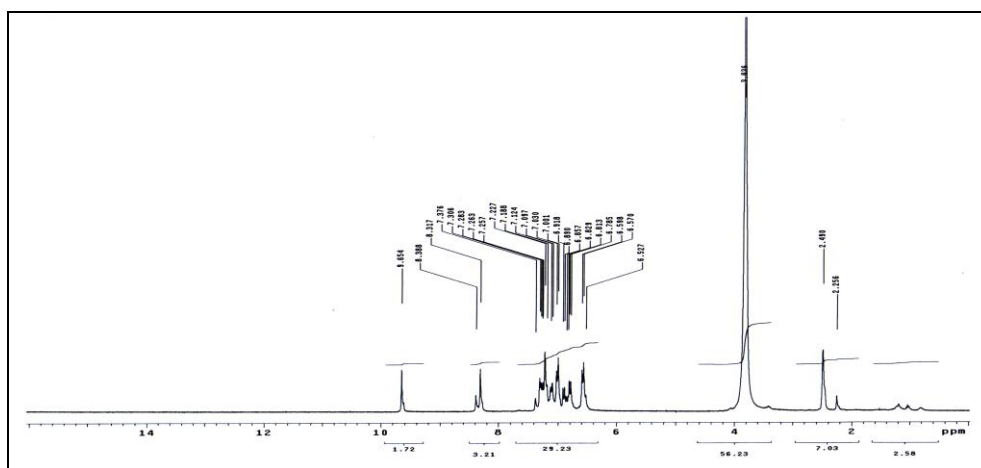


Fig. 4b. The ^1H -NMR for Zn(II) complex in (DMSO + D_2O)

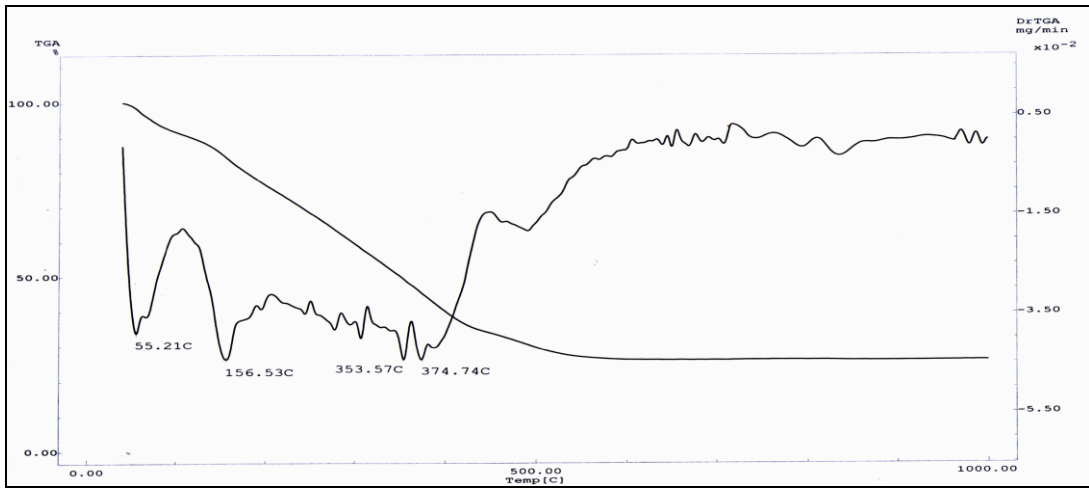


Fig. 5. TG and DTG of complex (2)

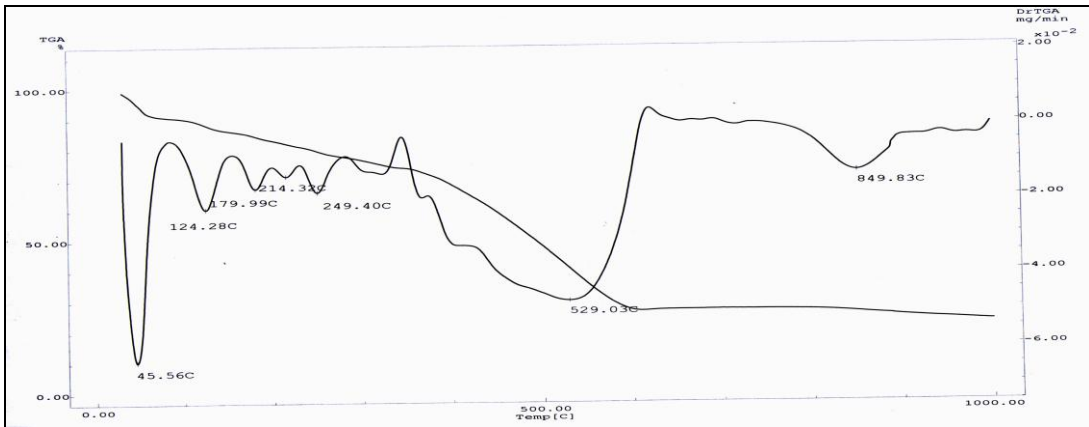


Fig. 6. TG and DTG of complex (3)

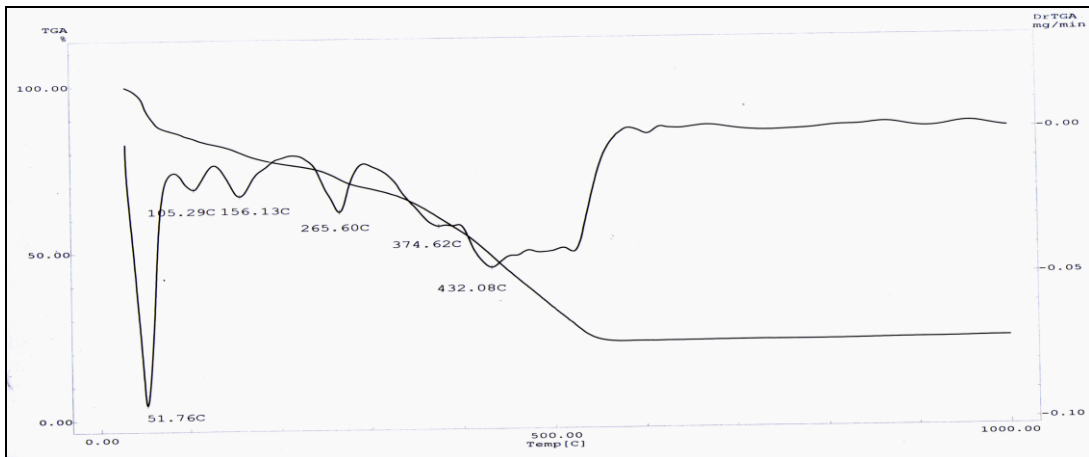


Fig. 7. TG and DTG of complex (4)

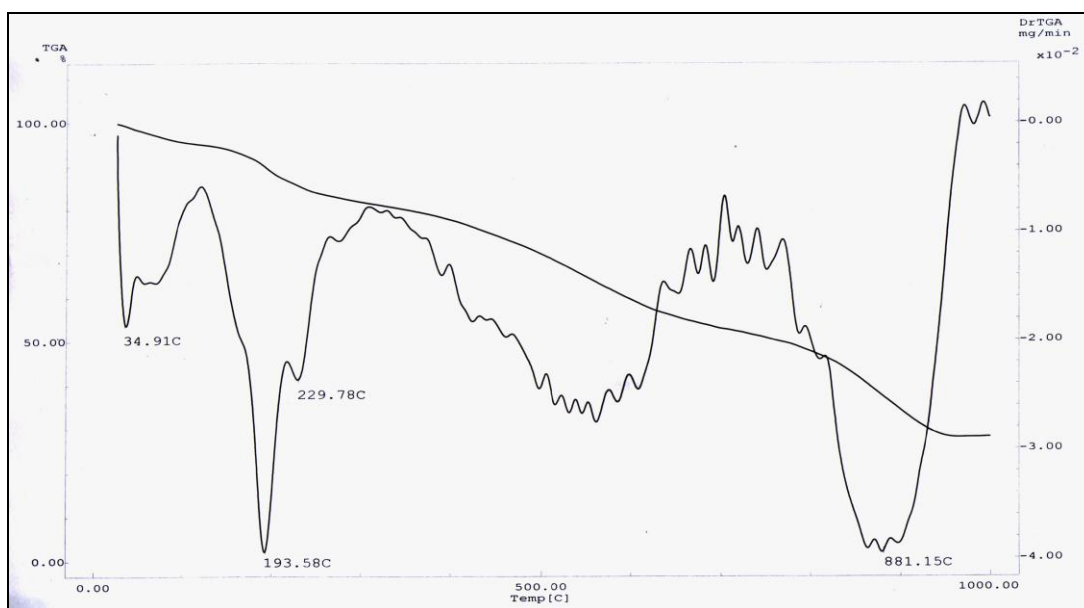


Fig. 8. TG and DTG of complex (6)

Table 2. Thermal gravimetric analysis for compounds (2, 3, 4 and 6)

Compound No.	Stages	Calculated	Found	Assignment
2	First Step	4.97	5.49	Two Crystalline H ₂ O
	Second Step	14.9	13.03	Six Coordinated H ₂ O
	Third and Fourth Step	56.31	55.03	Decomposition of Organic part of ligand + 2HNO ₃
	Residue	25.36	25.86	1.15 Fe ₂ O ₃
3	First Step	8.65	8.21	Three Crystalline H ₂ O
	Second Step	5.77	4.6	Two Crystalline H ₂ O
	Third and Fourth Step	13.14	12.18	Two Coordinated H ₂ O
	Fifth and Sixth step	50.33	51.21	2NO ₂ +
	Residue	24.00	23.5	2CoO
4	First Step	12.25	12.42	Three Crystalline H ₂ O + One Coordinated H ₂ O
	Second Step	6.1	4.80	Two Coordinated H ₂ O
	Third and Fourth Step	13.27	12.65	One Coordinated H ₂ O + 2NO
	Fifth Step	48.00	47.52	Decomposition of Organic part of ligand + 1HCl
	Residue	22.89	22.80	1.8 NiO
6	First Step	5.95	4.67	Two Crystalline H ₂ O
	Second Step	14.96	13.18	One Crystalline H ₂ O + Four Coordinated H ₂ O +
	Third and Fourth Step	52.65	53.76	Decomposition of Organic part of ligand
	Residue	27.1	28.23	2ZnO

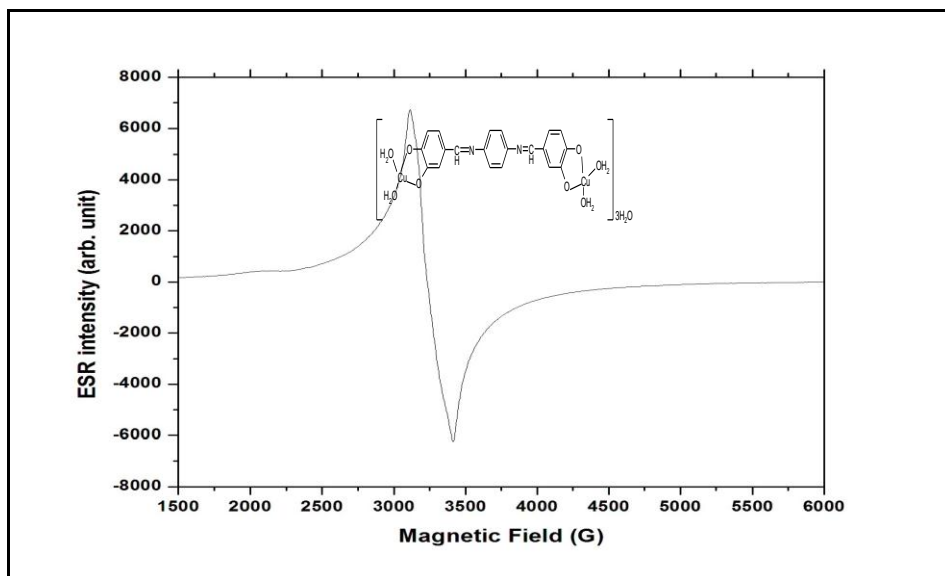


Fig. 9. ESR Spectrum of complex 5

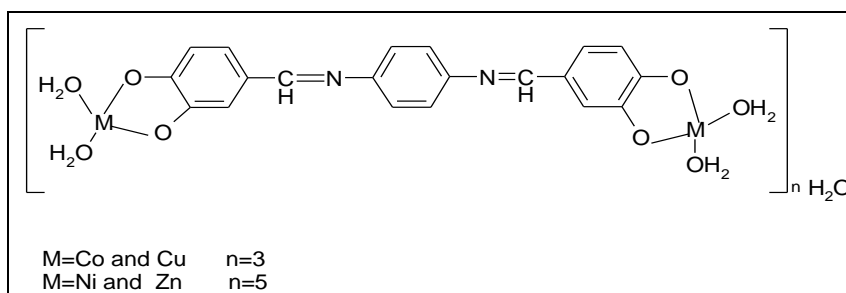


Fig. 10. Proposed structure of complexes 3,4,5 and 6

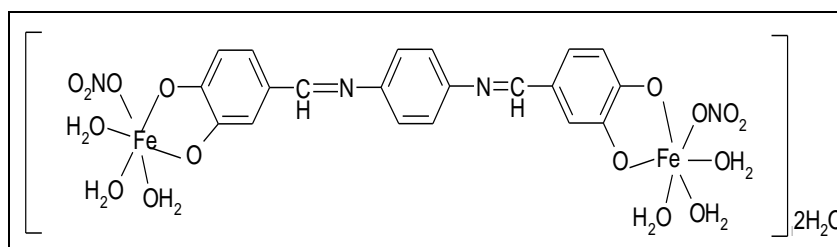


Fig. 11. Proposed structure of complex (2)

Table 3. The antimicrobial activity of the compounds (1-6)

Comp No.	Recorded zone diameter (mm) for each test microorganism					
	Bacteria				Fungi	
	Gram +ve		Gram -ve		Unicellular	Filamentous
	<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>C. albicans</i>	<i>A. niger</i>
1	23.00	19.00	17.00	15.50	17.50	27.00
2	18.50	16.00	15.50	15.00	14.00	20.00
3	18.50	21.50	21.00	19.50	26.00	25.00
4	14.50	15.50	15.00	16.00	20.00	20.00
5	21.00	21.50	13.50	20.00	21.00	30.00
6	18.00	15.50	15.00	13.50	18.00	26.5
St.	29.00	31.00	34.00	32.00	25.00	00.00

St. = Standard antibiotic (Amikacin)

Table 4. The MIC (in micrograms per milliliter) = minimum inhibitory concentration. i.e., the lowest concentration of drug which completely inhibites bacterial and fungal growth for compounds (1-6)

Comp No.	Recorded zone diameter (mm) For each test microorganism					
	Bacteria			Fungi		
	Gram +ve		Gram -ve	Unicellular		Filamentous
	<i>B. subtilis</i> NCTC 10400	<i>S. aureus</i> NCTC 7447	<i>E. coli</i> NCTC 10416	<i>P. aeruginosa</i> ATCC 10145	<i>C. albicans</i> IMRU3669	<i>A. niger</i> LIV131
1	2.5	5	5	5	5	1.25
2	5	5	1.25	5	2.5	2.5
3	5	2.5	1.25	1.25	1.25	1.25
4	1.25	2.5	5	5	2.5	2.5
5	1.25	1.25	1.25	2.5	5	0.625
6	1.25	5	1.25	5	1.25	2.5
St.	0.0195	0.0097	0.0195	0.00976	0.039	-

St. = Standard antibiotic (Amikacin)

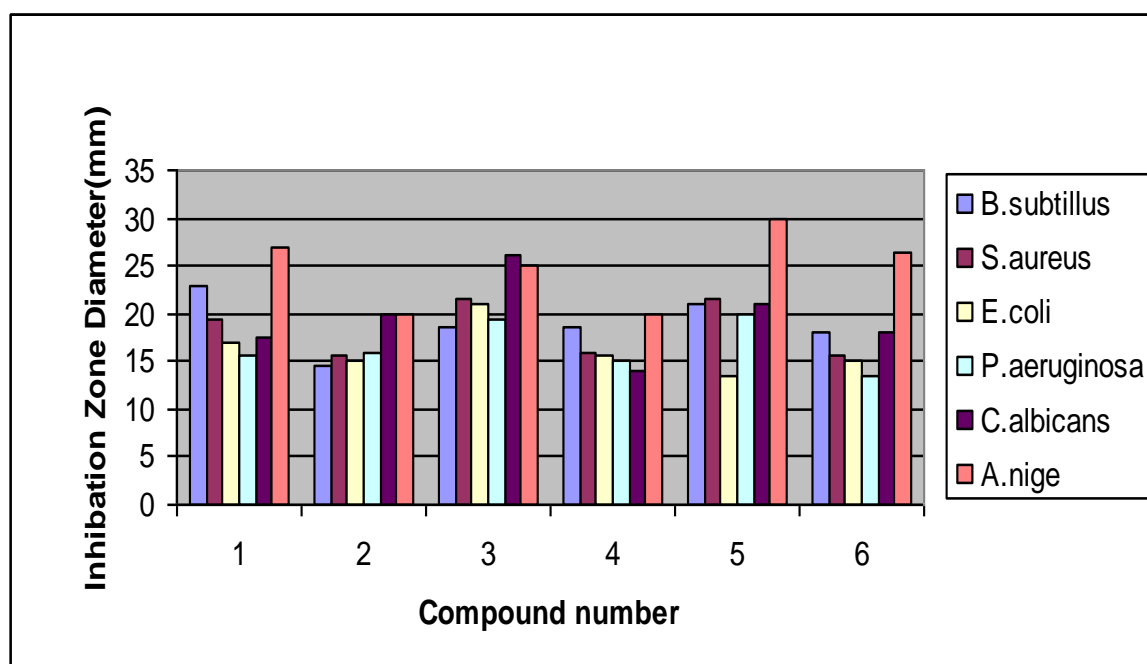


Fig. 12. Biological evaluation of (H₄L; 1) and its complexes

In sum, the most active compound among the six tested compounds against the six tested microorganisms was compound 3 due to its wide spectrum of activity and good activity against bacteria and fungi (Fig. 12). Also, the minimum inhibitory concentration values of the compounds against the growth of microorganisms were determined by means of standard dilution method and summarized in table (4).

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