

Synthesis, Characterization, Thermal study and Biological Evaluation of Transition Metal Complexes Supported by ONNNO – Pentadentate Schiff Base Ligand

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Abstract Schiff base ligand H₄L [N₁,N₃-bis(2,4 – dihydroxydeneimino)diethylenetriamine], was synthesised by the condensation reaction of 2,4 – dihydroxybenzaldehyde and diethylenetriamine in 2:1 molar ratio. The ligand which exhibits N₃O₄ donor set and transition metal complexes of V^{III}, VO^{II}, ZrO^{II}, Pd^{II}, Rh^{III} and Cd^{II} ions were synthesized and characterized by ¹HNMR, fourier transform infrared (FT-IR), UV – vis, mass spectroscopy, elemental analysis (CHNO), thermo gravimetric analysis (TGA), magnetic susceptibility and molar conductivity measurements. Antibacterial activity of the ligand and metal complexes against four kinds of bacteria (two gram + and two gram -) were investigated.

Keywords Schiff base, Transition metals, 2,4 – dihydroxybenzaldehyde, N₃O₄ ligand

1. Introduction

Schiff base and their 3d – 4f metal complexes containing nitrogen and oxygen donor atoms play an important role in biological and inorganic research and have been studied extensively due to their unique coordination and biological properties. They readily yielding stable and intensely colored metal complexes, some of which have been shown to exhibit interesting physical and chemical properties and potentially useful biological activities [1]. Many Schiff bases have a second functional group, generally an OH, near the imine function. This proximity of the functional groups permits the formation of five or six member chelate rings when coordinated with metal ions. Schiff bases have a diversified structure with nitrogen and oxygen donor systems. Due to the various synthetic procedures, numerous Schiff bases of various structural types have been synthesized [2].

Probably the best known Schiff base is N,N'-ethylenebis (salicylideneiminato) or salen, which is a bifunctional and tetradentate (ONNO) ligand. The more general term salen-type is used in the literature to describe the class of [O, N, N, O] bis-Schiff base ligands. The properties of salen-type ligands can be altered by fine-tuning the electronic and steric effects of substituent groups [3, 4]. The doubly deprotonated ligand contains strong donors, namely phenolato oxygen atoms as well as imine nitrogen atoms bearing excellent coordination ability with transition/intertransition metal

ions through its N₃O₂ donor set.

Schiff bases are widely used as pigments and dyes, catalysts, intermediates in organic synthesis, and as polymer stabilizers [5]. Schiff bases have also been shown to exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties [6–9].

In this paper a new pentadentate dianionic Schiff base ligand, H₄L [N₁,N₃-bis(2,4 – dihydroxy deneimino) diethylenetriamine], that exhibits a N₃O₄ donor set and some transition metal complexes were synthesized and investigated.

2. Materials and Methods

All chemicals were analytical grade and used without any modification. ¹HNMR spectra were obtained using a Bruker 500 MHz and d₆ –DMSO as a solvent at University of Al Albait, Amman, Jordan. Fourier transform infrared (FT-IR) spectra were recorded on a Shimadzu spectrophotometer. Elemental analysis for the ligand and metal complexes were carried out using CHNS—elemental analyzer and atomic absorption using Shimadzu model 6809. Mass spectra were recorded by electron impact mass spectrometry (EIMS) using a Direct Injection Probe on a Shimadzu GCMS – QP5050A Spectrometer, Electronic spectra using Varian UV–visible spectrophotometer, Molar conductivity of the complexes were measured in DMSO as a solvent in 0.001M solutions using a CON 510 bench conductivity meter with 2-ring stainless steel conductivity electrode (cell constant, K = 1.0) were carried out at the Chemistry Department,

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College of Science, Mustanseriya University, Baghdad, Iraq. Magnetic susceptibility measurements were carried out using the Faraday method with balance magnetic susceptibility model MSB-MKI in the Chemistry Department, College of Science, Al-Nahrain University, Baghdad, Iraq. Thermal stability (weight changes) of the samples was recorded by Mettler Toledo TGA851 and STA 6000 in the temperature up to 1000°C at Ibn-Sina Company, Baghdad, Iraq. Bacterial strains and Mueller Hinton agar were supplied from Department of Biology, College of Science, Mustanseriya University.

Syntheses of H₄L [N₁, N₃-bis(2,4 – dihydroxy deneimino) diethylenetriamine]

2,4 – dihydroxybenzaldehyde (1.12 g, 10 mmol) dissolved in ethanol (20ml) was added to diethylene triamine (0.50 g, 5 mmol) in ethanol (20ml). Few drops of glacial acetic acid was added as catalyst, and then refluxed for 4hrs. The Schiff base ligand was isolated by column chromatography over silica gel (E. Merck) 60–120 mesh size, using a mixture of light petroleum and ethyl acetate (v/v, 1:1). The elute yielded pure was evaporated under reduced pressure to yield a gummy mass, which was dried and stored *in vacuum* over silica gel for subsequent use (Scheme 1). Yield: 68%, m.p. 73 – 75°C. Elemental analysis for C₁₈H₂₁N₃O₄, M.wt. 343; calculated (%) C 62.97, H 6.12, N 12.24, O 18.65; found (%) C 63.34, H 6.32, N 12.45, O 18.97.

Synthesis of complexes: The appropriate quantity of solid Schiff base ligand H₄L (0.686 g, 2 mmol) was dissolved in ethanol (20ml). This ligand solution was added dropwise with stirring to 2mmol of an ethanolic solution of; VCl₃, VOSO₄.H₂O, ZrOCl₂, PdCl₂, RhCl₃ and CdCl₂. Adjust the

pH to 7 and reflux for 2hr to complete the crystal precipitation process, cooled and filtered. Recrystallization took place from hot ethanol to afford the appropriate precipitate with 53–85% yield, see table 1.

Antimicrobial tests: The ligand H₄L and some of their corresponding metal complexes were screened *in vitro* for their antibacterial activity against two Gram-negative (*Escherichia coli* and *Klebsiella pneumoniae*) and two Gram-positive (*Enterococcus faecalis* and *Staphylococcus aureus*) bacterial strains using agar well diffusion method and Primaxin drug as standard. The results of antibacterial studies are presented in Table 1. The tested compounds were dissolved in DMF to get concentrations of 50µg/mL. 0.1 mL from the specific concentration of dissolved tested compounds was carefully placed on incubated agar surface. After incubation for 24 h at 37°C, inhibition of the organisms which evidenced by clear zone surround each disk was measured and used to calculate mean of inhibition zones.

3. Results and Discussion

FT – IR spectra: The (FT-IR) spectra were recorded in the region 4000–400 cm⁻¹ using KBr disc.

The ligand (H₄L) shows two absorption band at 3570 and 3357cm⁻¹ attributed to ν (OH₁) and (OH₂) groups respectively. The low frequency for (OH₂) is probably due to the considerable amount of H-bonding to the adjacent (>C=N) group [10, 11]. Strong band located at 1639 cm⁻¹ corresponding to imine (C=N) stretching frequency, ν (Ar–O) at 1283 cm⁻¹. Three Bands appeared at 2922 and 1459 cm⁻¹ for aromatic ν (C–H, C=C), and at 2853 cm⁻¹ for aliphatic ν (C–H) [12].

Table 1. Some measured physical data of the ligand and complexes

No.	Compound	color	m.p.C ^o	%Yield	M% calc.(found)
1	C ₁₈ H ₂₁ N ₃ O ₄ [H ₄ L]	orange	73 – 75	78%	-----
2	[VH ₂ L(H ₂ O)]Cl.H ₂ O	green	215*	85%	10.99 (10.36)
3	[VOH ₂ L].H ₂ O	olive	250*	63%	11.91 (11.36)
4	[ZrOH ₂ L].H ₂ O	page	241*	70%	19.48 -----
5	[PdH ₂ L(H ₂ O)].H ₂ O	brown	287*	58%	21.93 (21.46)
6	[RhH ₂ L(H ₂ O)]Cl.H ₂ O	page	212*	53%	20.68 ----
7	[CdH ₂ L(H ₂ O)].H ₂ O	orange	230*	70%	22.98 (22.52)

Table 2. Major Infra – red absorption bands of H₄L and complexes (cm⁻¹)

Compound	ν(NH)	ν(C=N)	ν(C-O)	ν(M-NH), ν(M-N)	ν(M-O)
H ₄ L	3147	1635	1283	-----	-----
[VH ₂ L(H ₂ O)]Cl.H ₂ O	3263	1608	1230	551, 528	470
[VOH ₂ L] H ₂ O	3128	1604	1230	551, 528	451
[ZrOH ₂ L] H ₂ O	3232	1600	1228	578, 532	445
[PdH ₂ L(H ₂ O)] H ₂ O	3205	1600	1219	551, 528	462
[RhH ₂ L(H ₂ O)]Cl. H ₂ O	3176	1606	1225	563, 524	457
[CdH ₂ L(H ₂ O)] H ₂ O	3128	1600	1222	559, 540	462

The FT-IR spectra of all complexes contain strong peaks characteristic of C=N bands, confirming the complexation of the metal ions. Indeed, upon coordination to the metal center, the imine C=N stretching frequency in the IR spectra dropped from 1639 cm^{-1} in the free ligand to $1600 - 1608\text{ cm}^{-1}$ in the complexes. This is further supported by the appearance of new bands at $520 - 530\text{ cm}^{-1}$ due to $\nu(\text{M-N})$ bond. [13]. The presence of coordinated water molecule along with OH₁ group was indicated by the appearance of a broad band at $3255 - 3570\text{ cm}^{-1}$ and two weak bands (for water molecule) in the region $755-787\text{ cm}^{-1}$ and $709-718\text{ cm}^{-1}$ due to (-OH) rocking and wagging mode of vibrations, respectively. Ligand coordination to the metal centre is substantiated by another two bands at approximately $550 - 570$ and $440 - 455\text{ cm}^{-1}$ corresponding to $\nu(\text{M-NH})$ and $\nu(\text{M-O})$ respectively. For VO^{II} complex the infra red spectrum showed an absorption band at 968 cm^{-1} attributed to stretching frequency of V=O [14], while the Zirconyl complexes exhibit one strong band in the region 849 cm^{-1} which can be attributed to the $\nu(\text{Zr=O})$ [15]. Comparison of the infrared spectra of the prepared complexes can lead us to the conclusion that the Schiff base ligand was coordinated in the same manner for all complexes (Table 2).

Electronic spectra: The UV-Vis absorption spectrum of the ligand in ethanol is composed of two main absorption bands. The high energy one (272 nm), is probably related to $\pi \rightarrow \pi^*$ transitions centred on the benzene moiety. The second absorption band was observed at 347nm probably assignment to $n \rightarrow \pi^*$ transitions. The low energy of this band may have a pronounced charge transfer transition character.

Electronic Spectrum of VO (II) complex showed two low intensity absorption bands at 11350 and 16710 cm^{-1}

respectively attributed to the transitions ${}^2\text{B}_2 \rightarrow {}^2\text{E}(\nu_1)$ and ${}^2\text{B}_2 \rightarrow {}^2\text{B}_1(\nu_2)$. The third band, ${}^2\text{B}_2 \rightarrow {}^2\text{A}_1(\nu_3)$ transition is not observed, being often buried beneath a high intensity charge transfer band. These bands are characteristic to distorted octahedral geometry [16]. Spectrum of V(III) complex showed two electronic absorption bands at 13100 and 20490 cm^{-1} transition probably assigned to ${}^3\text{T}_1(\text{F}) \rightarrow {}^3\text{T}_2$ and ${}^3\text{T}_1(\text{F}) \rightarrow {}^3\text{T}_1(\text{P})$, respectively. These transitions can be fit with the analytical equations for an octahedral complex [17]. The spectrum of Rh(III) complex gave weak band at 12117 cm^{-1} assigned to a spin forbidden transition, and a shoulder at 24173 cm^{-1} , these two bands were assigned to ${}^1\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}$ and ${}^1\text{A}_{1g} \rightarrow {}^1\text{T}_{2g}$ transitions respectively and they correspond to octahedral Rh (III) complex [18, 19].

Mass spectra: Mass spectra were recorded using a Direct Injection Probe. The mass spectral features of the ligand H₄L as illustrated in Figure 1 was described by molecular ion peak at $m/z = 343$ which confirm the molecular weight m/z value of 343 that agree with the empirical formula of the ligand (C₁₈H₂₁N₃O₄). The intensity was 100% for the base peak 57 which is assign to the cleavage of $[\text{CH}_2\text{CH}_2\text{N}=\text{CH}]^+$ character in the molecule. The peak at 149 (parent peak) is assign to the cleavage of $(\text{OH}_1)\text{OH}_2\text{Ar}-\text{CH}=\text{NCH}_2^+$. The peak at 71 is assign to the cleavage of $[\text{CH}_2\text{CH}_2-\text{NH}-\text{CH}_2\text{CH}_2]^+$, and the parent peak at 307 is assign to the arrangement of losing two water molecules. Several other peaks for the mass spectrum of the ligand were shown in figure 1.

¹HNMR spectra: NMR spectra were recorded for the ligand, ZrO^{II} and Cd^{II} complexes using DMSO as solvent and TMS was used as an internal standard. Chemical shifts were reported in parts per million (ppm) and coupling constants were given in Hertz (Hz).

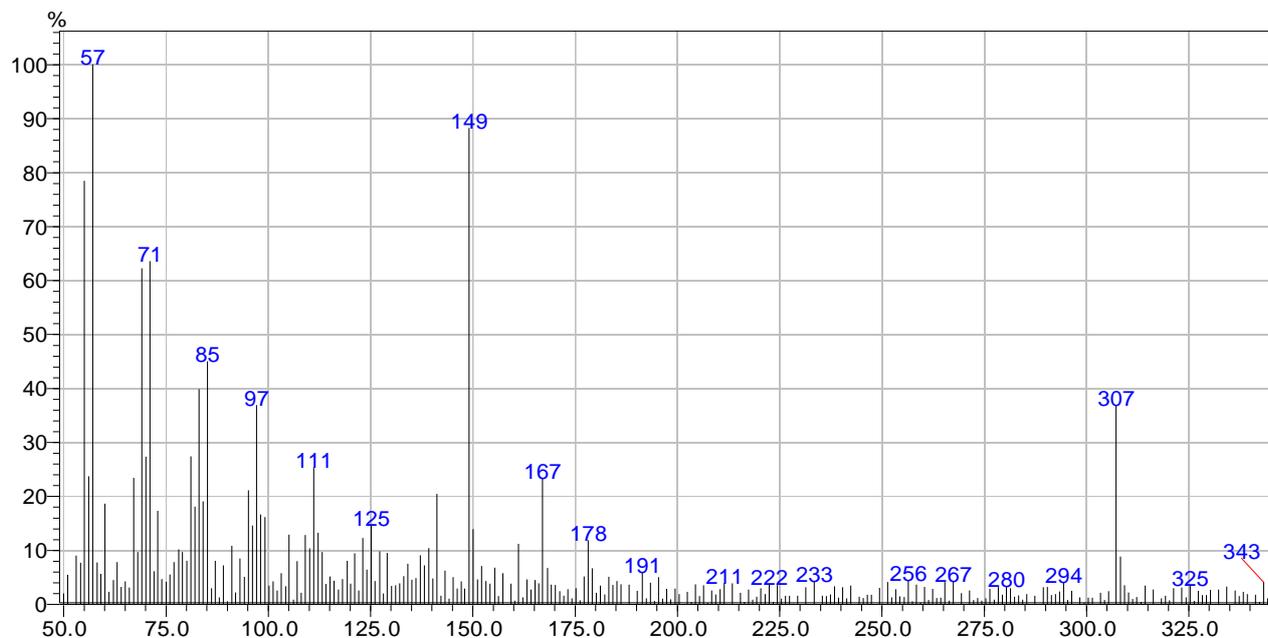


Figure 1. Mass spectrum of the ligand H₄L

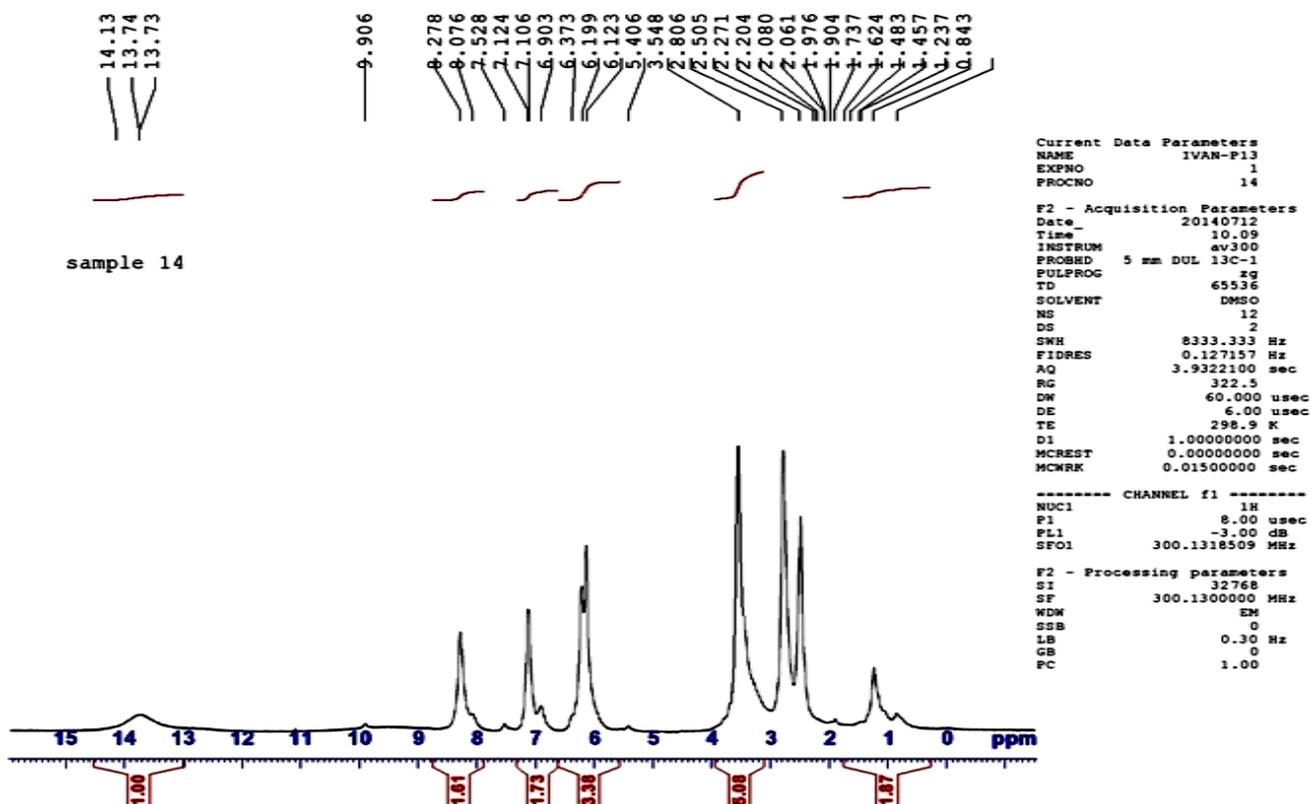


Figure 2. ^1H NMR spectrum of H_4L

The spectrum of the ligand showed a broad peak at 14.13 – 13.74 δ ppm probably assigned to combined signals of –NH – proton and OH_1 respectively. Two signals observed at 9.90 δ ppm for OH_2 and at 8.27 δ ppm for –CH=N clearly indicates that the magnetic environment is equivalent for such proton. Multiples signals of aromatic protons appeared at the range 6.01 – 7.50 δ ppm, while the aliphatic protons peaks were recorded at 1.23– 3.54 δ ppm. ^1H NMR. spectra for ZrO^{II} and Cd^{II} complexes showed the disappearance of OH_1 peak, while the signal of –NH – proton was shifted to 12.47 δ ppm probably due to coordination effects of the metal ion. Other signals of the ligand were slightly shifted towards low field when compared to those of the free ligand (see figure 2). These results suggest the behavior of the ligand as pentadentate through two deprotonated phenolic oxygen and azomethine nitrogen along with amine –NH – group [20, 21].

Magnetic measurements: Magnetic susceptibility was measured for all the complexes at room temperature by use of Curie balance.

The magnetic moment for the V^{III} complex was $\mu_{\text{eff}} = 2.46$ B.M; this is very close to the spin-only value and is indicative of octahedral geometry ($t_2g^2eg^0$) [22]. The same geometry were suggested for VO^{II} complex with magnetic moment ($\mu_{\text{eff}} = 1.66$) and Rh^{III} diamagnetic complex (0.00 B.M) [23].

Molar conductivity measurements: Using DMSO as a solvent with the concentration of 10^{-3} M, all metal complexes behaved as non-electrolyte except V^{III} and Rh^{III} complexes

which their conductance, 42.6 and 37.8 ($\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$) respectively which indicate the 1:1 electrolyte type, and these results fit with the geometry of mononuclear complexes [24].

Thermogravimetric analysis: Thermo gravimetric analyses (weight changes) were performed for complexes in the temperature range from room temperature up to 900°C using helium as inert gas at the heating rate of 20°C/min.

The thermogram of complexes exhibits three clear cut stages [Figures 3 and 4]. The first step showed the initial weight loss in the temperature range of 85 - 115°C corresponding to the loss of water molecules. The loss of water molecules in this temperature range indicates that the water molecules are of lattice type [25, 26]. The second step occurred around 250°C due to loss of coordinated water molecules [27]. For $\text{VO}(\text{II})$ complex the second step did not start below 370°C and do not show any weight loss below this temperature which indicated that these complexes are devoid of coordinated water in the coordination sphere. The anhydrous complexes remain stable up to 475°C then the complexes show rapid degradation presumably due to decomposition of organic constituents of the complex molecules as indicated by the steep fall in the percentage weight loss. The final residue with attaining a constant weight roughly corresponds to metallic oxide [28].

Biological activity study: A comparative study of the ligand and metal complexes indicates that most of the metal complexes exhibit higher antimicrobial activity than that of the free ligand, while V^{III} and Cd^{II} complexes showed higher

activity than the control; see table 3. Hence complexation increases antimicrobial activity [29]. The higher activity of the metal complexes may be owing to the effect of metal ions on the normal cell membrane. Metal chelates bear polar and nonpolar properties together; this makes them suitable for

permeation to the cells and tissues. Changing hydrophilicity and lipophilicity probably leads to bring down the solubility and permeability barriers of cell, which in turn enhances the bioavailability of chemotherapeutics on one hand and potentiality at another [30-32].

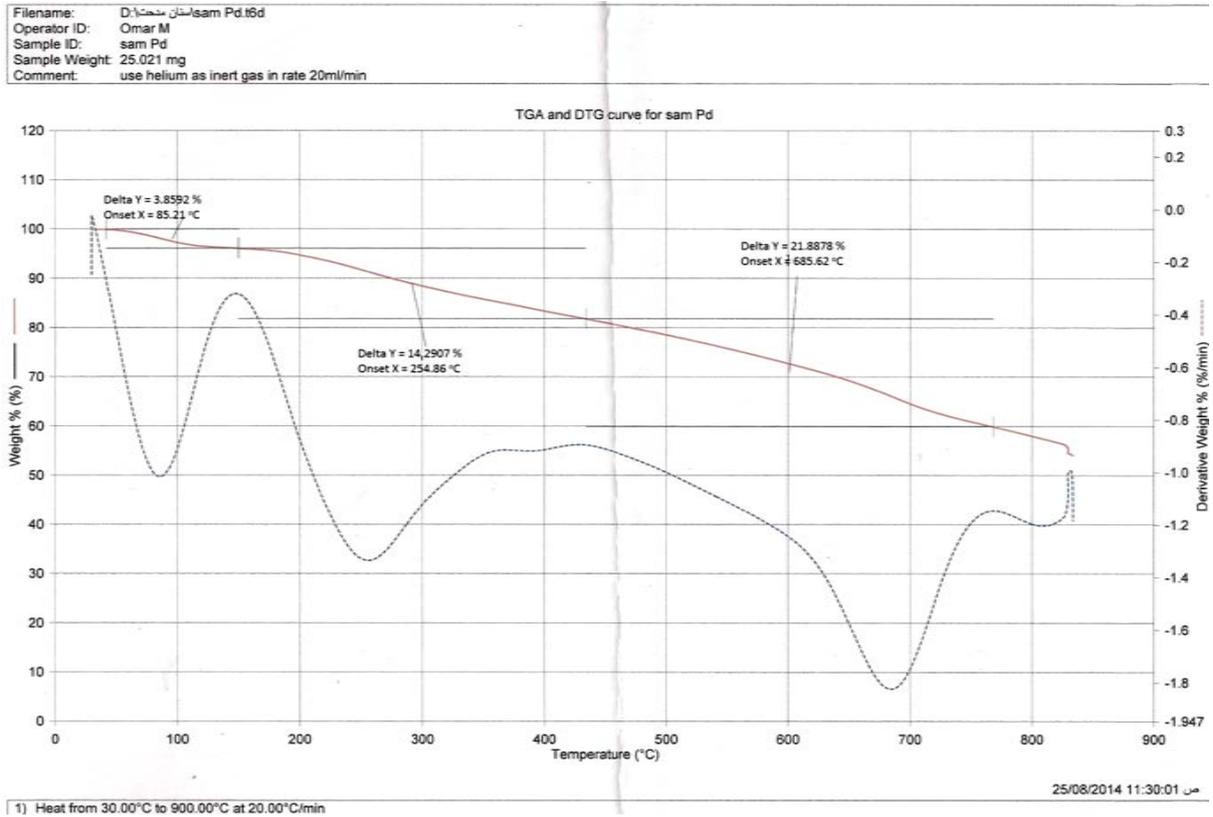


Figure 3. TGA of Pd^{II} complex

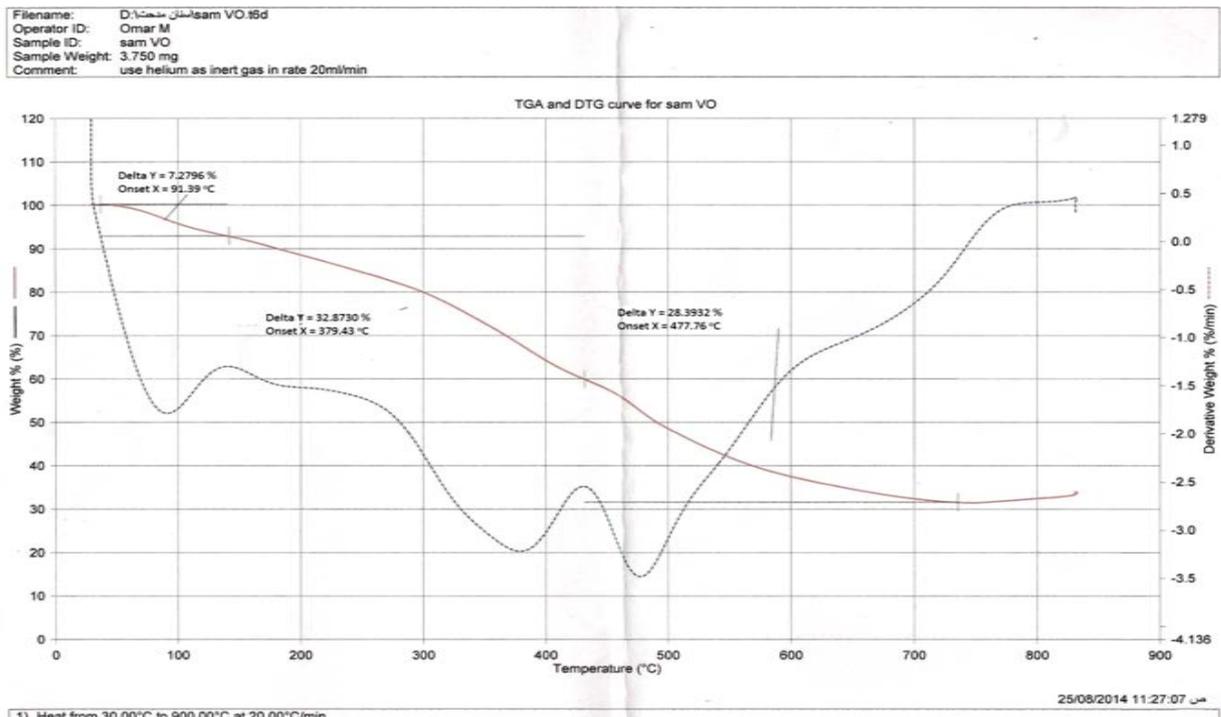


Figure 4. TGA of VO^{II} complex

Table 3. Results of antibacterial assay (concentration used 50µg/mL of DMSO)

No.	Compound	Gram + bacteria		Gram – bacteria	
		<i>Staph.aureus</i>	<i>Entrococus</i>	<i>E. coli</i>	<i>Klebsila</i>
1	[H ₄ L]	14	6	15	20
2	[VH ₂ L(H ₂ O)]Cl.H ₂ O	32	19	18	33
3	[VOH ₂ L].H ₂ O	19	13	20	24
4	[ZrOH ₂ L].H ₂ O	11	10	15	17
5	[PdH ₂ L(H ₂ O)].H ₂ O	16	9	10	15
6	[CdH ₂ L(H ₂ O)].H ₂ O	30	32	27	28
7	SD*	29	31	30	26

SD* standard drug –Primaxin; <10: weak, Between 10 and 16: Moderate, >16: Significant

4. Conclusions

An acyclic Schiff base ligand containing N₃O₄ donor atoms and its mono nuclear transition metal complexes were prepared. The investigation of the analytical data observed suggested the complexes formed with six coordination number as the ligand behaves as pentadentate donor atoms with an additional oxygen atom for VO^{II}, ZrO^{II} and one coordinated water molecule for the others.

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