

## Preparation, Characterization and Antimicrobial Activities of N'-(3-(hydroxyimino) butan-2-ylidene)-2 (phenylamino) acetohydrazide and Its Metal Complexes

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**A** SERIES of thirteen metal complexes was synthesized by reaction a new acetohydrazide oxime ligand with some metal ions ( $\text{Cu}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Ru}^{3+}$ ,  $\text{UO}_2^{2+}$  and  $\text{VO}_3^-$ ). The ligand, N'-(3-(hydroxyimino) butan-2-ylidene)-2-(phenylamino)acetohydrazide was prepared by refluxing an equimolar amount of phenyl amino acetohydrazide with 2,3-butanedione monoxime. The synthesized compounds were characterized using elemental and thermal analyses, NMR, IR, U.V spectroscopy, magnetic and conductance measurements. The results demonstrated that complexes (2), (3), (5-7), (10) and (12) were formed in 1L:1M molar ratio. Complexes (4), (8), (9), (13) and (14) were found to afford  $\text{M}_2\text{L}$  formulae while complex (11) adopted  $\text{ML}_2$  formulae. The ligand acted as a neutral (bidentate [11], tridentate [6,7], monobasic (tridentate [2,3,5,12]), dibasic (tridentate [10], tetradentate[4,8,9,13,14]) chelating to the metal ions via nitrogen atoms of aceto-amino and azomethine groups, carbonyl oxygen atom in its enolic or ketonic form and/or protonated or deprotonated oximino nitrogen atom, adopting an octahedral, tetrahedral or square planar geometry around metal ions. The antimicrobial activity of the ligand, as well as the metal complexes, was examined using Amphotericin B and Amoxicillin as drug-standards against *Aspergillus niger* (*A.niger*) and *Escherichia coli* (*E. coli*), respectively. The ligand demonstrates a high cytotoxicity against *A.niger* whereas it recorded a moderate activity against *E. coli*. It is interestingly found that zinc(II) complex (6), copper(II) complexes (8) and (10) recorded higher activities than the Amphotericin B drug with 122%, 116% and 111.1% percentages respectively against *A.niger*. Zinc(II) complex (6) was also the most sensitive complex against *E. coli* with (94.1 %) comparable to Amoxicillin.

**Keywords:** Acetohydrazide, Oxime, Metal complexes, 2,3-Butanedione monoxime.

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Schiff bases possess an outstanding importance in inorganic, analytical and medicinal chemistry because of their versatility to form a large variety of stable complexes upon coordination with different transition metal ions[1-5]. Hydrazone ligands represent a class of Schiff base with an extra function group characterized by a nitrogen-nitrogen covalent bond that enhances their capability to form more stable metal complexes via reaction with most of the transition metal ions[6,7]. Both hydrazide and hydrazone compounds have drawn much concern in order to investigate their structures as well as their enormous biomedical activities as: antioxidant [8,9], analgesic, anti-inflammatory [10], antimalarial, anti-leishmanial and anti-trypanosomal[11], anti-convulsant [(12)], antibacterial[13,14], antiplatelet [15], antitumor[16] and antiviral[17,18] activities. The presence of active azomethine  $\text{NHN}=\text{CH}$ - protons in these compounds imparts them a major importance as good candidates for the development of new drugs [19-21]. For this behavior, hydrazone derivatives are widely used in organic synthesis as well as designing of new drugs. In parallel to the growing biochemical applications of hydrazide compounds, oxime-containing ligand derivatives represent another esteemed category with high biological implications. Oximes are recognized by presence oxygen atom attached directly to a nitrogen atom containing a pair of free electrons. The recognized biological activity of oxime derivatives is evidently related to the N-OH groups which enhance their ability to chelate metal ions. The  $-\text{N}-\text{OH}$  moiety appears to be flexible to be oxidized, reduced, and conjugated with inorganic and organic moieties. The  $\alpha$ -adjacent atom has free electrons imparts oxime character of being involved in nucleophilic displacements reactions via the anionic form  $\text{N}=\text{O}^-$ . The oximes ligands remarkable ability to form stable metal complexes with a large number of metal ions, along with the N-OH group affinity to produce a nitroxide radical, defines to a great extent, but not exclusively, the biological as well as the toxicological activity of oximes. For these characteristic, oxime containing compounds demonstrated effective activities in several biomedical applications as: antimicrobial, antimalarial, and anticancer drugs[22-29]. Based on the unique characteristics of oxime, there is a growing interest related to synthesizing as well as structural investigating of oximes derivatives in order to develop novel therapeutic medications. Costanzo *et al.* reported that oximes can inhibit the activity of arginase enzyme. He related that to the ability of the N-OH groups of the oxime to bind the active centers  $\text{Mn}^{2+}$  in the enzyme structure [30]. In another study, new binary and ternary Cu(I) complexes derived from Benzyl-thiourea ligand have been synthesized and their antibacterial activity on Gram-negative and Gram-positive strains have been evaluated. The prepared metal complexes demonstrated a profound cytotoxicity against both types of bacteria[31]. It was reported that the combination of both oxime and amide groups in the same molecule leads to the formation of more stable chelators by coordination to the metal ions [32,33]. In the light of this consideration, we reported herein synthesis of new binary metal complexes derived from  $\text{N}'$ -((3-(hydroxyimino)butan-2-ylidene)-2-(phenylamino)acetohydrazide). The synthesized compounds were characterized by spectral and analytical techniques. The

fungicidal and bactericidal ability of the ligand as well as its metal complexes were evaluated toward *A.niger* and *E. Coli*.

## Experimental

### Materials

All chemicals used in this work were of the analytical grade available and used without further purification. 2,3-Butanedione monoxime (assay  $\geq 98\%$ ) was provided from Sigma-Aldrich company; DMSO (assay 99.7%); absolute ethanol (assay  $\geq 99.8\%$ ). Metal salts;  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$ ,  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}$ ,  $\text{Cu}(\text{SO}_4) \cdot 5\text{H}_2\text{O}$ ,  $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{Mn}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  were provided from SIGMA-ALDRICH company with purity ranged from 98 % to 99.995 %.  $\text{UO}_2(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$  (assay  $\geq 99.9\%$ ),  $\text{UO}_2(\text{NO}_3)_2$  (assay  $\geq 99.9\%$ ),  $\text{NH}_4\text{VO}_3$  (assay  $\geq 99.99\%$ ),  $\text{RuCl}_3 \cdot 3\text{H}_2\text{O}$  (assay  $\geq 99.9\%$ ) were provided from American-Elements. Ethyl (phenylamino) acetate and 2-(phenylamino) acetohydrazide were synthesized according to a published procedures[29,34,35]. TLC was utilized to assert the purity of obtained compounds.

### Instrumentation and measurement

The C, H and N content in the obtained compounds was analyzed on VARIO EL III GERMANY at the Microanalytical Center, Faculty of Science, Cairo University. Metal ion content was determined using complexometric titration. Ethylenediaminetetraacetic acid (EDTA) in the form of its disodium dihydrate salt was used as the complexing agent and murexide as an indicator[36]. FT-IR SPECTROMETER 4100 JASCO Fourier transform infrared spectrophotometer covering the range 400-4000  $\text{cm}^{-1}$  was used to record FT-IR spectra of the ligand and its metal complexes using KBr discs at the Microanalytical center, Faculty of Science, Cairo University. The nujol mull electronic absorption spectra (UV-Vis) were recorded on a Perkin-Elmer 550 spectrophotometer 200-900 nm range using Whatman filter paper No. 1 and referenced against similar filter paper saturated with paraffin oil at the Central Lab. National Research Centre. The thermal analysis (TG) was recorded at the Chemistry Department, Central Lab. Faculty of Science, El-Menoufia University, on a Shimadzu DT-30 thermal analyzer in the temperature range from (room temperature to 800  $^{\circ}\text{C}$ ) at a heating rate of 10  $^{\circ}\text{C}/\text{min}$ . Gouy method using mercuric tetrathiocyanatocobaltate(II) as the magnetic susceptibility standard was applied to study the magnetic susceptibilities at 25  $^{\circ}\text{C}$  on a Johnson Matthey Magnetic susceptibility Balance at the Chemistry Department, Faculty of Science, El-Menoufia University, the Diamagnetic corrections were estimated from Pascal's constant[37]. Values of magnetic moments were derived from the equation:

$$\mu_{eff} = 2.84 \sqrt{\chi_M^{corr} \cdot T}$$

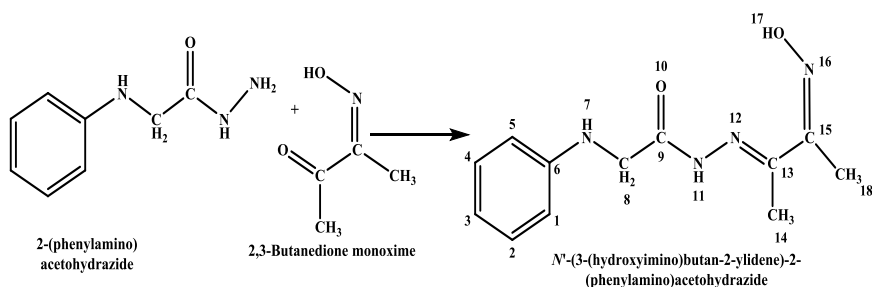
The molar conductance of  $10^{-3}$  M solution of the complexes in DMSO was measured at 25°C with a Bibbyconductometer type MCl at the Chemistry Department, Faculty of Science, El-Menoufia University. The resistance measured in ohms and the molar conductivities were calculated according to the equation:

$$\Lambda_M = \frac{V \times K \times g}{Mw * \Omega}$$

where:  $\Lambda_M$  = molar conductivity / $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$ , V = volume of the complex solution/ mL, K = cell constant (0.92/  $\text{cm}^{-1}$ ), Mw = molecular weight of the complex, g = weight of the complex/g,  $\Omega$  = resistance/ $\Omega$ .  $^1\text{H}$  NMR spectrum was obtained on a JEOL EX-270 MHz FT-NMR spectrometer (The Central Lab. National Research Centre) in  $d_6$ -DMSO as solvent. The chemical shifts in NMR analysis are relative to the TMS peak.

#### Synthesis of ligand

The ligand, ( $\text{H}_2\text{L}$ ) was synthesized by the addition of (1.65 g, 0.01 mol) phenyl aminoacetohydrazide to 2,3-butanedione monoxime (1.01 g, 0.01 mol) in 20 mL of absolute ethanol [Scheme 1]. The mixture was stirred and refluxed for three hours, then left to cool to room temperature. The solid product was filtered off, washed with cold ethanol, followed by recrystallization from ethanol and finally dried under vacuum over anhydrous  $\text{CaCl}_2$ . Yield: 90%, Color: Pale yellow. *Elemental Anal.* Calc.: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.21; H, 6.12; N, 22.41. IR, (KBr,  $\text{cm}^{-1}$ ): 3390, 3338, 3290, 3260  $\nu(\text{OH})$ ,  $\nu(\text{NH})$ , 1678  $\nu(\text{C}=\text{O}_{\text{Acetyl}})$ , 1641  $\nu(\text{C}=\text{N}_{\text{imine}})$ , 1605  $\nu(\text{C}=\text{N}_{\text{oxime}})$ , 1144, 1025  $\nu(\text{N}-\text{OH})$ , 992  $\nu(\text{N}-\text{N})$ ;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 270 MHz): 11.08 (s,  $\text{OH}^{17}$ ), 10.50, 9.1 (s,  $\text{NH}^{11,7}$ ), 6.43-7.01 ppm (m, 5  $\text{H}^{1-5}$ , aromatic protons), 4.01 (s, 2H, ( $^8\text{CH}_2$ )), 1.81 (s, 3 H, ( $^{18}\text{CH}_3$ )), 1.19 (s, 3H, ( $^{14}\text{CH}_3$ )).  $^{13}\text{C}$ -NMR [ $\text{DMSO}-d_6$ ,  $\delta/\text{ppm}$ ]: 169.50 (C9); 153.47 (C15); 150.00 (C13); 147.09 (C6); 77(C8); 129.6 (C2&4); 117.02 (C3); 113.99 (C1&5); 12.4 (C18); 7.90 (C14).



**Scheme 1. Preparation of Ligand, N'-(3-(hydroxyimino) butan-2-ylidene)-2-(phenylamino)acetohydrazide**

#### Synthesis of metal complexes

Metal complexes, (2), (3), (5-7) (10) and (12) were synthesized by reaction of an equimolar amount of the following salts:  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$ ,  $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{Mn}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{UO}_2(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{Cu}(\text{SO}_4)_2 \cdot 5\text{H}_2\text{O}$  and  $\text{RuCl}_3 \cdot 3\text{H}_2\text{O}$  respectively with a suitable amount of the ligand in ethanol solution, 5 drops of triethylamine (TEA) was added to the reacting solution after two hours then the refluxing process continued for another one hour. The formed precipitates were filtered off, washed with ethanol, then with diethyl ether and dehydrated under vacuum over anhydrous  $\text{CaCl}_2$ . The same procedures were used to prepare complexes; (4), (8), (9) and (13-14) using the following metal salts  $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}$ ,  $\text{NH}_4\text{VO}_3$  or  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  respectively but in (2 metal: 1 ligand) molar ratio. Complex (11) was obtained by reaction of  $\text{UO}_2(\text{NO}_3)_2$  salt with the ligand in (1 metal: 2 ligand) molar ratio in absence of triethylamine (TEA).

#### *In-vitro antimicrobial activities*

The antimicrobial activity evaluation of the compounds was carried out in the Botany Department, Lab. of microbiology, Faculty of Science, El-Menoufia University using Well Diffusion Method [38]. The antibacterial and antifungal activities were evaluated against strands of *E. coli* and *A.niger* respectively, at 200  $\mu\text{g}/\text{mL}$  concentrations in DMSO. A disc of poured DMSO was used as a negative control. The bacteria were subcultured in nutrient agar medium prepared using ( $\text{g} \cdot \text{L}^{-1}$  distilled water) NaCl (5 g), peptone (5 g), beef extract (3 g), agar (20 g) while the fungus was subcultured in CzapekDox's medium prepared using ( $\text{g} \cdot \text{L}^{-1}$  distilled water) yeast extract (1g), sucrose (30 g),  $\text{NaNO}_3$ , agar (20 g), KCl (0.5 g),  $\text{KH}_2\text{PO}_4$  (1 g),  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  (0.5 g) and trace of  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ . This medium was then sterilized by autoclaving at 120 °C for 15 min. After cooling to 45 °C the medium was poured into 90 mm diameter Petri dishes and incubated at 28 °C. After agar solidification, Petri dishes were stored at 4 °C for few hours. Microorganisms were spread over each dish by using sterile bent Loop rod. Disks were cut by sterilized Cork borer and then taken by sterilized needle. The resulted pits are sites for the tested compounds of known concentration. Standard antibacterial (Amoxicillin), and antifungal drugs (Amphotricene B), as well as solutions of metal salts, were also screened under similar conditions for comparison. Plates were allowed to stand in a refrigerator for two hours before incubation to allow the tested compounds to diffuse through the agar. The Petri dishes were incubated for 48 hr at 28. The growth inhibition zones around the holes were observed, indicating that the examined compound inhibits the growth of a microorganism. The inhibition zone was measured in millimeters carefully. All determination was made in duplicate for each of the compounds. An average of the two independent readings for each compound was recorded. The activity index for the complexes was calculated by following formula[39].

### Results and Discussion

The obtained metal complexes are colored, air-stable and insoluble in water, ethanol and non-polar solvents. They demonstrated a good solubility character in polar solvents *i.e.* DMF and DMSO. All prepared metal complexes showed a non-electrolytes nature. The proposed configuration structures (Fig. 1-3) goes inconsistent with the elemental, thermal and spectral analyses (Tables 1-3). We have not managed to grow diffractable single crystals till now. Complexes (2), (3), (5-7) and (10) and (12) were found to be formed in 1L:1M molar ratio, complexes (4), (8), (9) (13) and (14) were found to adopt  $M_2L$  formulae while complex (11) adopted  $ML_2$  configuration.

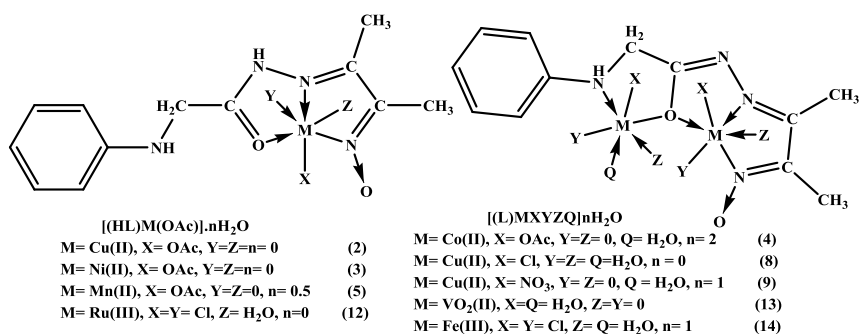


Fig.1. Structure representation of complexes (2-5), 8, 9 and 12-14.

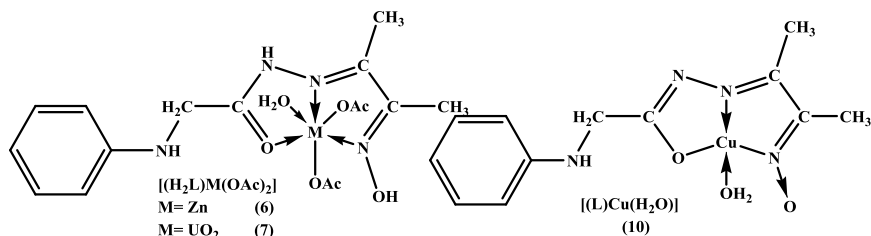


Fig. 2. Structure representation of complexes 6, 7 and 10.

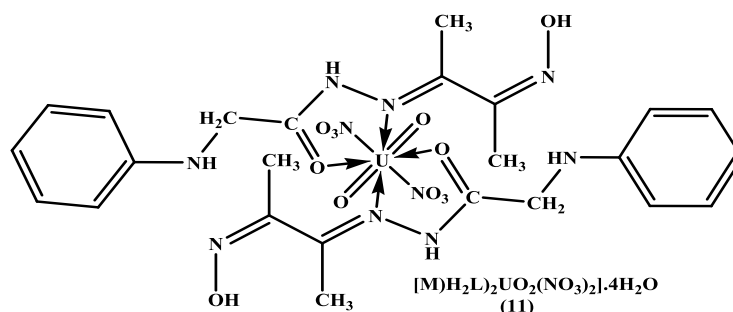


Fig. 3. Structure representation of uranyl(II) complex 11 .

#### Conductivity measurements

The values of molar conductance for 0.001 M of the metal complexes (2-14) at 25 °C in DMSO are depicted in Table 1. The 4.76-37.52  $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$  values referred to a non-electrolytic nature of these complexes[40].

#### NMR Spectra

The  $^1\text{H-NMR}$  spectrum of the ligand was recorded at room temperature using DMSO- $d_6$  as a solvent. The absence of the amino group ( $-\text{NH}_2$ ) signal characteristic to starting material (hydrazide) refers to its involvement in the condensation process to form the ligand. Three sets of chemical shifts were observed along the ligand. The first one was detected: as a singlet at  $\delta$  11.08 ppm (s, 1H), 10.5 ppm (s, 1H) and 9.1 ppm (s, 1H) which is assignable to the oxime hydroxyl ( $\text{C}=\text{N-OH}^{17}$ ), imine ( $^1\text{HN-C}=\text{O}$ ) and ( $^7\text{HN-CH}$ ), protons, respectively. The existence of these peaks is characteristic to hydrazone-oximes compounds[41,42]. The considerable high  $\delta$  of these hydrogen chemical shifts is related to the proton-attachment to high electronegative atoms (oxygen and nitrogen). This assignment is supported by the apparent intensity decrease of these signals in the deuterated ligand spectrum[43-45]. These findings clarified that the ligand exhibits the keto form only and no evidence for the presence of the enol form. This assumption was supported by the absence of the OH of the enolic form. The second set of peaks was observed as multiple ones in 6.43-7.01 ppm ranges, which can be assigned to the aromatic protons[41,42,46]. The third chemical shift which appeared at 4.01 could be attributed to methine proton ( $^8\text{CH}_2$ ). The final set of chemical shifts observed at  $\delta$  1.8 and 1.19 ppm was ascribed to the two methyl groups of the oxime moiety ( $^{18}\text{CH}_3$ ) and ( $^{14}\text{CH}_3$ ) respectively[41,42]. The  $^{13}\text{C-NMR}$  spectrum of the ligand showed a signal at 169.5 ppm which could be assigned to carbonyl carbon  $\text{C}^9=\text{O}$ . The chemical shift appeared at 153.27 and 150 ppm is assignable to azomethine carbon atoms ( $\text{C}^{13,15}$ ) [41,42,46]. While the chemical shifts of the methane carbon ( $\text{C}^8$ ) were observed at  $\delta = 77$ . However, the peaks observed at  $\delta$  147.09, 129.6, 117.02, 113.99 ppm were assigned to the aromatic carbons  $\text{C}^6$ ,  $\text{C}^{2,4}$ ,  $\text{C}^3$  and  $\text{C}^{1,5}$ , respectively. The two peaks appearing at  $\delta$  12.4 and 7.9 ppm could be due to the two methyl carbons the oxime moiety.

*Infrared spectra*

Table 2 collected IR spectral data of the ligand and its metal complexes, The ligand spectrum exhibits three bands located at 3390, 1678, and 992  $\text{cm}^{-1}$  ascribed to  $\nu(\text{OH})$ ,  $\nu(\text{C}=\text{O})$  and  $\nu(\text{N}-\text{N})$ , respectively [47,48]. Two bands observed at 1641 and 1605  $\text{cm}^{-1}$  related to the two  $\text{C}=\text{N}$  of imine and oxime groups [49], while the bands observed at 1144 and 1025  $\text{cm}^{-1}$  were attributed to the  $\nu\text{N}-\text{O}$  group [50]. The Presence of NH groups was supported by the bands recorded at 3338, 3290 and 3260  $\text{cm}^{-1}$  [51-53]. Based on variation in the IR spectra of the metal complexes in comparison to that of the ligand, it could be presumed that the ligand performed either as a neutral (bidentate or tridentate), or monobasic (tridentate) or dibasic (tridentate or tetradentate). The spectra of complexes [(HL)Cu(OAc)], [(HL)Ni(OAc)], [(HL)Mn(OAc)] $\cdot$ 0.5H<sub>2</sub>O and [(HL)RuCl<sub>2</sub>(H<sub>2</sub>O)] showed i) complete absence of the  $\nu(\text{OH})$  group ii) a negative shift in the position and intensity of two  $\text{C}=\text{N}$  groups iii) a negative shift in the position and intensity of the carbonyl group by (2-29  $\text{cm}^{-1}$ ). These findings suggest the bonding of the ligand the metal ions takes a monobasic tridentate mode via de-protonation of an oxime moiety, azomethine and carbonyl groups. The participation of the OH group of the oxime via loss of the hydrogen atom is accompanied by a strengthening in NO double bond, which is declared in the positive shift of the two NO bands to the regions (1148-1175), (1037-1096)  $\text{cm}^{-1}$  [49,54]. The spectra of complexes (6) and (7) show similar patterns except the still presence of the OH group of the oxime, although this band was subjected to shifting by a (10-13  $\text{cm}^{-1}$ ), which suggested the chelating of the ligand to metal ions in a neutral tridentate mode in these two complexes (Fig. 2). This mode of bonding is further supported by the new bands observed in the 638-575, 581-497 and 456-504 ranges related to  $\nu(\text{M}\leftarrow\text{O})$ , two  $\nu(\text{M}\leftarrow\text{N})$  respectively [55]. The spectra of the bimetallic complexes (4), (8-9) and (13-14) suggested the chelation of the ligand in a dibasic tetradentate fashion bonding two metal ions by the three nitrogen atoms of amino, imine and oxima to groups and the enolic oxygen atom, which is supported by i) complete disappearance of the band of both hydroxyl of the oxime as well as the carbonyl group of the acetohydrazide moiety. ii) a negative shift in the position of the NH bands iii) the appearance of an additional band in the range 1500-1527 assigned to the emerging of a new  $\text{C}=\text{N}$  group. The IR spectral findings go consistently with the elemental analyses results suggesting that this group of metal complexes adopts  $\text{M}_2\text{L}$  formulae (Fig. 1). This proposed coordination mode is reinforced by the appearance of new bands in the 1500-1527 and 1210-1235  $\text{cm}^{-1}$  ranges corresponding to  $\nu(\text{N}=\text{C}-\text{O})$ , and  $\nu(\text{C}-\text{O})$  of the acetohydrazide moiety, respectively [56,57]. In the spectrum of complex (10), the ligand behaved as a dibasic tridentate, coordinates to the metal ion via the C-O oxygen atom, (C=N) imino and the oxima to (C=N $\rightarrow$ O) nitrogen atoms with the formation of two five-member rings. This type of coordination proved by disappearing of C=O, NH, OH bands, appearance of C=N band new and negative shifts in  $\nu(\text{N}=\text{C}-\text{O})$  and an increase in the vibration range of (N $\rightarrow$ O) band which is observed at 1175  $\text{cm}^{-1}$ . The spectrum of complex (11) revealed a neutral bidentate mode of the ligand. The shifting to lower wavenumber in the bands characteristic to carbonyl and C=N imine referring that, the bonding occurred through these two groups. Two medium new bands at 951 and 849  $\text{cm}^{-1}$



were detected in spectra of complexes (7) and (11) credited to  $\nu_s$  and  $\nu_{as}$   $\nu(\text{O}=\text{U}=\text{O})$  respectively [58-60]. The IR spectral findings of this complex go inconsistent with the elemental analyses results suggesting that complex (11) adopts  $\text{ML}_2$  formulae (Fig. 3). The two emerged bands in the 1542-1570 and 1370-1393  $\text{cm}^{-1}$  ranges in metal complexes (2-7) were assigned to  $\nu_{as}(\text{COO}^-)$  and  $\nu_s(\text{COO}^-)$  of the acetate groups [61]. The observed separation value ( $\Delta$ ) (159-200)  $\text{cm}^{-1}$  between asymmetric and symmetric ( $\text{COO}^-$ ) groups indicate that the ligand acts as a mono-dentate in these complexes [62]. IR spectrum of the nitrate complexes (9,11) showed new bands at  $\nu_5$  (1432, 1412) and  $\nu_1$  (1366, 1329)  $\text{cm}^{-1}$  respectively referring presence of nitrate group in a coordination mode with the metal ion. The difference between ( $\nu_5 - \nu_1$ ) was in the range (74-81)  $\text{cm}^{-1}$  indicating that, the nitrate group bonded to the M(II) ion is uni-dentate fashion [61,63,64]. The dioxovanadium complex (13) displayed a medium vibrational band at 997 and 956 correspond to the  $\nu_{as}(\text{O}=\text{V}=\text{O})$  and  $\nu_s(\text{O}=\text{V}=\text{O})$  vibrational modes [4,58]

Table 1.

**Table 2. IR spectral assignment for the ligand and its metal complexes.**

No.	$\nu(\text{OH})$	$\nu(\text{NH})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu(\text{N}-\text{N})$	$\nu(\text{N}-\text{O})$	$\frac{\nu(\text{N}=\text{C}-\text{O})}{\nu(\text{C}-\text{O})}$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$	$\nu(\text{CH}_3\text{COO})/\text{NO}_3$
(1)	3390	3338, 3290,3260	1678	1641,1605	992	1144 1025	--	--	--	--
(2)	--	3306,3265	1655	1603,1564	1021	1148,1096	575	512,486	512,486	1548,1373(175)
(3)	--	3300,3281	1649	1635,1604	1019	1160,1071	570	513,498	513,498	1570,1370(200)
(4)	--	3251	--	1611,1540	1007	1153,1121	1505, 1235	611,550	513, 467	1567,1393(174)
(5)	--	3360,3215	1676	1603,1595	1021	1160,1037	616	511,487	511,487	1550,1380(170)
(6)	3403	3286,3233	1677	1629,1600	1014	1195,1096	607	581,504	581,504	1542,1383(159)
(7)	3380	3310,3215	1635	1600,1588	1023	1141,1056	638	500,479	500,479	1553,1389(164)
(8)	--	3218	--	1609,1593	1001	1165,1076	1521, 1210	587,541	5110,489	--
(9)	--	3211	--	1607,1594	999	1190,1087	1500,1215	657,597	513, 477	1432,1356(76)
(10)	--	3205	--	1606,1580	1017	1175,1090	1527, 1223	617	506,484	--
(11)	3354	3234,3201	1630	1610,1593	1013	1180,1099	657	513	513	1412, 1329(83)
(12)	--	3290, 3180	1650	1606,1580	998	1175,1069	620	497, 456	497, 456	--
(13)	--	3250	--	1605,1595	1029	1155,1072	1501,1241	612,532	511, 491	--
(14)	--	3206	--	1604,1588	1030	1186,1067	1512,1213	600,551	505,480	--

#### *Electronic spectra and magnetic measurements*

The electronic spectral, as well as the magnetic data of the compounds, are depicted in Table 3. Three bands were observed in the spectrum of the ligand at 260, 310 and 340 nm. The first band at 260 nm is attributed to  $\pi \rightarrow \pi^*$  transition of phenyl ring of the ligand which is almost unchanged upon complexation, whereas the second and third bands are attributed to  $n \rightarrow \pi^*$  transitions of azomethine and carbonyl groups which were subjected to shifting in the spectra of metal complexes indicating participation of these groups in the complex formation [65,66]. In some complexes, new bands were observed in the 400-440 nm ranges, which may be attributed to charge transfer electronic transitions.

#### *Copper(II) complexes*

The electronic absorption spectra of the Cu(II) complexes (2, 9, 10) showed one additional band at 515, 550 and 560 nm, respectively assignable to the transition  ${}^2B_{1g} \rightarrow {}^2E_g$ . The magnetic moment values of copper(II) complexes (2) and (10) recorded 1.91 and 2.01 B.M, which are consistent with the presence of one unpaired electron of copper(II) ions in a square planar environment [66-68]. The lower magnetic moment of complex (9) than the expected values reported for square planar copper complexes is related to spin-spin interactions between the copper ions [69]. The electronic spectrum of copper complex (8) revealed the presence of two bands at 400 and 580 nm assignable to  ${}^2B_{1g} \rightarrow {}^2A_{1g}$  and  ${}^2B_{1g} \rightarrow {}^2B_{1g}$  transitions. While the magnetic moment of this complex recorded 0.98 BM which is lower than that reported for octahedral copper complexes, this is could be assigned to spin-spin interaction of copper(II) ions in an octahedral environment, support the bimetal nuclear nature of the complex [69].

#### *Ni(II), Co(II) and Mn(II) complexes*

The electronic spectra of the nickel(II) complex (3), cobalt(II) complex (4) and manganese(II) complex (5) showed two bands at 460, 630 nm; 465, 565; and 485, 550, respectively; these bands are attributed to  ${}^3T_1(F) \rightarrow {}^3A_2(v_2)$ ,  ${}^3T_1(F) \rightarrow {}^3T_1(P)$  ( $v_3$ ) transitions for Ni(II) complex;  ${}^4A_2 \rightarrow {}^4T_1(F)$  ( $v_2$ )  ${}^4A_2 \rightarrow {}^4T_1(P)$  ( $v_3$ ) transitions for Co(II) complex and  ${}^6A_1 \rightarrow {}^4E_1(F)$ ,  ${}^6A_1 \rightarrow {}^4T_1(F)$  transitions for Mn(II) complex. The magnetic moment recorded by these metal complexes were 3.11, 2.89, and 5.98 BM respectively, suggesting a tetrahedral environment around the Ni(II) ion and high spin tetrahedral environments around the Co(II) and Mn(II) ions [66,70]. The lower magnetic moment of the Co(II) complex than that reported for cobalt tetrahedral complexes could be assigned to spin-spin interactions between the Co(II) ions and clearly, support the bimetal nuclear nature of the complex [71,72].

#### *Ru(III) and Fe(III) complexes*

The electronic spectrum of ruthenium(III) showed one band at 505 nm which assigned to  ${}^2T_{2g} \rightarrow {}^2A_{2g}$  transition referring to a distorted tetragonal

octahedral structure. The magnetic moment of this complex was 1.65 BM, which is corresponding to a low spin octahedral environment around the Ru(II) ion. Also iron(III) complex (14) demonstrated an octahedral geometry around the Fe(III) ion, this is supported by the presence of three bands at 465, 550, 580 nm assignable to  ${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$ ,  ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$  and  ${}^6A_{1g} \rightarrow {}^4E_g(G)$  transitions [66,73]. The magnetic moment recorded by this complex was 6.01 BM referring to a high spin octahedral geometry around the Fe(III) ions [66,73].

#### *Zn(II) complex*

Zinc(II) complex (6) showed diamagnetic character. They do not show d-d transitions, and the observed bands are only intra-ligand transitions. The zinc(II) complex (6) show band at 400 nm assignable to the ligand to metal charge transfer transitions (LMCT) [65].

#### *UO<sub>2</sub>(II) complexes*

Electronic absorption spectral data of the two dioxouranium(VI) complexes (7) and (11) in nujol mull are depicted in Table 3. The two complexes demonstrated a diamagnetic character. Five absorption bands were observed for each complex. The first three bands are assigned to intra-ligand transitions, while the other two electronic transitions observed at 410, 460 and 415, 480 for the two complexes respectively. The higher energy band (460 and 480) is ascribable to charge transfer from oxygen of uranyl moiety to f-orbital of the uranium(VI) ion (O→U). The broadness of this band indicates unequal energies of the O→U charge transfer in the two oxo cations. The other band observed at 410 and 415 nm is assignable to charge transfer from ligand to the uranium(VI) ion (LMCT) [51,65,74].

#### *Dioxovanadium(V) complex*

The electronic absorption spectra of the [(L)(VO<sub>2</sub>)<sub>2</sub>(H<sub>2</sub>O)<sub>3</sub>] complex (13) is recorded in nujol mull and data is depicted in Table 3. For dioxovanadium(V) complexes, no d-d bands are expected because of their 3d<sup>0</sup> configuration. The first three absorption bands at 255, 315, and 375 nm are assigned to intra-ligand transitions within the ligand. The additional peak at 440 nm is due to ligand to metal charge transfer (LMCT) transitions [75-78].

#### *Thermal analyses*

The thermal analyses data of metal complexes, depicted in Table 4, exhibited much insight about thermal stability, stoichiometric formulae as well as their chemical composition. (TGA/DTA) was carried out using thermogravimetric analysis in a static atmosphere of air and in the temperature range 20-800 °C. The thermal conduct of the metal complexes are compatible with the proposed formulae derived from the elemental analyses and spectral data. The thermal analyses data refer that all complexes are generally decomposed into multiple steps.

Table 3



The thermo-gram pattern of complex (4)  $[(L)Co_2(OAc)_2(H_2O)].2H_2O$  exhibits five decomposition steps within the 30–800 °C temperature range. The first two steps are assigned to losses of one hydrated and two coordinated water molecules with two endothermic peaks at 90 and 200 °C, respectively. The first step is accompanied by 6.76 % weight loss (calcd 6.72) while the second one is accompanied with 3.01 weight loss (calcd. 3.36). The third step with weight loss (21.77 %) was assigned to 2 acetate groups (calcd. 22.17%). This step is complemented by an endothermic peak at 285 °C. The fourth step was assigned to the melting complemented with exothermic peak at 600°C with weight loss (52.22, calcd. 53.78%), refers to decomposition of the complex ending up with the formation the metal oxide. Cu(II) complex (8)  $[(HL)Cu_2Cl_2(H_2O)_5]$  decompose in four steps. The first step was accompanied with an endothermic peak at 210 °C and a weight loss 16.52% corresponding to loss of five coordinated water molecules (Calcd. 16.86). The endothermic peak observed at 330 °C was assigned to the melting point of the metal complex, while the endo peak observed at 338°C accompanied with (12.11%) was ascribed to loss of 2 chloride ions (calcd.13.27%). The final step accompanied with exo thermic peak at 580 with weight loss (52.61, calcd. 54.99%), refers to decomposition of the complex ending up with formation the metal oxide. Complexes (9) and (14) showed five decomposition steps. The first one involves loss of one, two hydrated water molecules with weight loss 3.38 and 5.56 % respectively, these weight losses accompanied with two endo thermic peaks at 90 and 85 °C in the DTA pattern of complex (9) and (14) respectively. The removal of the coordinated water molecules (one for complex (9) and three for complex (14) was accompanied with endothermic peaks at 180 and 170 °C and weight losses 4.23 and 9.16 % (calcd. 3.38 and 9.33) respectively. The endothermic peaks observed at 315 and 370 °C were assigned to the melting points of two metal complexes respectively, while the endothermic peaks observed at 350 and 270°C accompanied by 23.25 and 23.03 % (calcd., 24.04) corresponding to loss of two nitrate and four chloride ions from complexes (9) and (14) respectively. The final step accompanied with exo-thermic peaks at 590 and 610 °C, with weight losses (54.29 and 45.02 % (calcd. 55.08 and 47.15%), refers to complexes (9) and (14) respectively ending up with the formation metal oxides. Complex(13) decomposes in only three steps; the first one related to loss of four molecules of coordinated water with weight loss 14.55 % (calcd. 14.88) and an endothermic peak located at 85 °C. The melting point of the complex was accompanied by an exothermic peak at 350 °C, while the final step was accompanied with exothermic peak at 620 °C and weight loss 47.39 (calcd. 49.39%), referring to decomposition of the complex ending up with formation the metal oxide ( $V_2O_5$ ).

*Antimicrobial activity*

The antimicrobial activity of the ligand and the metal complexes was examined against *A.niger* and *E. coli*. All tests were carried out in triplicate and the diameters of the inhibition zones were measured in millimeters. The Amphotericin B and Amoxicillin were taken as standard to compare the effectiveness of the tested compounds. The effectiveness of the compounds was compared the standard drug and depicted in a percentage value Table 5. The ligand showed a potent activity against *A.niger* whereas it recorded a moderate activity against *E. coli*. with 72.2 and 44.1 percentages, respectively. Investigation the antimicrobial activity of the metal complexes revealed: For *A.niger*, Zn(II) complex (6) represented the most sensitive complex with 22.3 mm (122.2 %) inhibition zone. Cu(II) complex (8) and Cu(II) complex (10) showed also higher activities than Amphotericin B with percentages 116.7 and 111.1 respectively. Most complexes showed moderate activities with percentages in the range (61.1-83.3). On the other hand, Mn(II) complex (5) and Ru(II) complex (12) recorded no activity against *A.niger*. For *E. coli*: Zn(II) complex (6) was also the most sensitive complex with 32 mm (94.1 %) inhibition zone against *E. coli*: Cu(II) complex (8) complex showed also potent activity with 73.5 percentage. Ni(II) complex (2), Co(II) complex (4), Cu(II) complex (10) and Ru(III) complex (12) showed moderate activities with percentages in the range (55.8-83.3). On the other hand, Co(II) complex (4) and Mn(II) complex (5) recorded no activity against *E. coli*. The orders of the antimicrobial activity were as follow: For *A.niger*: Zn(II) complex (6) > Cu(II) complex (8) > Cu(II) complex (10) > Standard drug > Co(II) complex (4) > Ni(II) complex (3) > ligand [H<sub>2</sub>L] = VO<sub>2</sub>(II) complex (13) > Cu(II) complex (2) > Cu(II) complex (9). For *E. coli*: Standard drug > Zn(II) complex (6) > Cu(II) complex (8) > Ni(II) complex (3) = Ru(III) complex (12) > Cu(II) complex (10) > VO<sub>2</sub>(II) complex (13) > Cu(II) complex (2) > ligand [H<sub>2</sub>L] > Fe(III) complex (14) > Cu(II) complex (9).

**Conclusion**

Novel acetohydrazide-oxime ligand, N'-((3-(hydroxyimino)butan-2-ylidene)-2-(phenyl-amino) acetohydrazide was synthesized. The structures of the ligand as well its metal complexes were investigated analytically and spectroscopically. The ligand acted as a bidentate, tridentate or tetradentate bonded to the metal ions via oxime, azomethine and carbonyl groups. Complexes (2), (3), (5-7) and (10) and (12) were formed in 1L:1M molar ratio; complexes (4), (8), (9), (13) and (14) adopted M<sub>2</sub>L formulae whereas complex (11) adopted ML<sub>2</sub> formulae. All metal complexes adopted mononuclear complexes except complexes (4), (8), (9), (13) and (14) that exhibits binuclear configuration. Both ligand and metal complexes demonstrates promising cytotoxicity against *A.niger* and *E.coli*. Zinc(II) complex (6), copper(II) complexes (8), (10) recorded outstanding activities by comparison with the



Amphotericin B standard drug with 122%, 116% and 111.1% percentages respectively against *A.niger*. Zinc(II) complex (6) was also the most sensitive complex against *E. coli* with (94.1 %) related to Amoxicillin.

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تشبيد و توصيف و دراسة النشاط البيولوجي المضاد للمكروبات لمتراكبات مشتقة من  
المترايط-2-(3-(hydroxyimino) butan-2-ylidene)-N'-(phenylamino)acetohydrazide

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تم تحضير سلسلة من ثلاثة عشر متراكباً بتفاعل مترايط جديد من الأسيتوهيدرازيد أوكزيم مع النحاس(II)، النيكل(II)، الكوبلت(II)، المنجنيز(II)، الحديد(III)، الزنك(II)، الروثنيوم(III)، اليورانيوم(VI) و الفاناديوم(V). تم تحضير المترايط بتفاعل كمية متكافئة من كلا من الفينيل أمينو أسيتو هيدرازيد مع 2،3 بيوتان داي أون أحادي الأوكزيم. تم توصيف المركبات المحضرة بواسطة كلا من التحاليل العنصرية والحرارية، طيف الأشعة تحت الحمراء و طيف الرنين النووي المغناطيسي و طيف الأشعة البنفسجية و المرئية و قياسات العزم المغناطيسي و التوصيل المولاري . أظهرت النتائج أن المترايط يتفاعل كمترايط ثنائي و ثلاثي و رباعي التشابك. وأن المتراكبات (10)، (5-7)، (3)، (2) (12) تتكون في في الصيغة المولارية ML في حين أن متراكبات (14)، (13)، (9)، (8)، (4) تتكون في صيغة ML<sub>2</sub> المولارية أما متراكب رقم (11) فوجد أنه يؤخذ الصيغة ML. فيما تبين أن الشكل الهندسي للمتراكبات ثمانى الأوجة و رباعي الأوجة و رباعي الأسطح. تم دراسة النشاط المضاد للميكروبات لكل من المترايط والمتراكبات المحضرة. حيث ابدى المترايط نشاط ملحوظاً مضاداً لفطر الاسبيرجليم نيجر في حين أظهر نشاطاً متوسطاً مضاداً لبكتريا الاشيريشيا كولاي. في حين أبدت متراكبات الزنك رقم (6) و النحاس رقم (8) و (10) نشاطاً مميزاً مضاداً لفطر الاسبيرجليم نيجر يفوق عيار أمفوتريسين المرجعي المضاد للفطريات بنسبة 122% ، 116% ، 111%، في حين كان متراكب الزنك رقم (6) الأكثر تأثيراً تجاه بكتريا الاشيريشيا كولاي مقارنة بعقار الأموكسيسيلين.