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Green synthesis of thioxoimidazolidine derivative ligand: Spectroscopic, thermal and biological assignments of new Cu(II), Co(II), and Ni(II) chelates in neutral system

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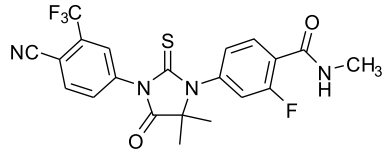
Eco-friendly synthesis of ethyl 3-(4-oxo-3-(1-(pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin-1-yl)propanoate (**4**) ligand (L) using microwave irradiation technique was described. The structure of thioxoimidazolidine derivative ligand compound has been established based on different types of analyses such as infrared, ^{1}H-NMR, ^{13}C-NMR, and mass spectra as well as elemental analysis. The copper, cobalt, and nickel(II) complexes with molecular formula $[M(L)(H_2O)_4]Cl_2$ (where M = Co(II), Ni(II), and Cu(II), L = thioxoimidazolidine derivative ligand), have been prepared and well-characterized using microanalytical, conductivity measurements, magnetic, spectroscopic, and physical analyses. Upon the outcome results of analyses, the stoichiometry of the synthesized complexes is 1:1 (M:L). The molar conductance values concluded that the behavior of metal complexes was electrolytes. The 3-(4-oxo-3-(1-(pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin-1-yl)propanoate chelate acts as a monovalent bidentate fashion via nitrogen and oxygen atoms of both thioxoimidazolidine and propanoate ester moieties. The geometric structures of the synthesized metal complexes are an octahedral configuration based on spectroscopic and magnetic moment studies. The thermogravimetric assignments deduced that the presence of four coordinated water molecules. The synthesized copper(II), cobalt(II), and nickel(II) complexes were biologically checked against G+ and G- bacteria and two species of fungi (*Aspergillus Nigaer*, and *Penicillium Sp*.).

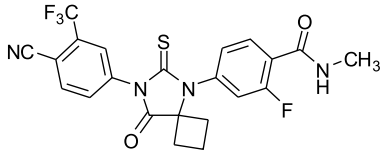
Keywords: Imidazolidine; Microwave irradiation; Coordination; Biological activity.

INTRODUCTION

Thiohydantoins are the sulfur isotopes of hydantoins in which both carbonyl groups or one of them are replaced by thiocarbonyl groups[1]. Enzalutamide, midazolidine-4-one-2-thion, is a drug used to treat Metastatic Castration Resistant Prostate Cancer (CRPC)[2]. Also, enzalutamide is used to treat patients with mCRPC[3]. Apalutamide, is an anti-androgen drug that is also used to treat prostate cancer[4–6] (Figure 1).Thioxoimidazolidin-4-one derivatives prevent the α-amylase and α-glucosidase enzymes activities and used for the treatment of diabetes-related diseases[7]. Moxonidine is a new generation antihypertensive drug containing imidazole moiety[8]. Tipifarnib is an imidazole derivative which used for treatment of acute myeloid leukemia (AML)[8]. Thiohydantoins, is well known due their amazing applications as human immunodeficiency virus (HIV)[9, 10], antimutagenic[12, 13], anticarcinogenic[14], anti-microbial[15–17], anti-viral[18], hypolipidemic[19, 20], anti-thyroidal[21–23] and tuberculosis[24], anti-ulcer, anti-inflammatory agents[25], and pesticides[26]. In addition,



Enzalutamide



Apalutamide

Figure 1. Biologically active thioxoimidazolidine derivatives

2-thiohydantoins are used as a reference standard for developing the C-terminal protein sequence[27, 28], and are also used as a reagent for developing pigments[29, 30]. It is used also in textile printing, polymerization catalysis and metal cation complexation and[31].

In the literature survey, much attention was devoted to the study metal-to-ligand complexes that contain donor bonds to nitrogen, oxygen, and sulfur due to their diverse biological activities, such as antimicrobial[32, 33] anti-inflammatory[34], antipyretic, herbicides[35] anticancer[36] and anti-ulcer[37]. These also play an interesting role in the activation of enzymes and are used for the storage and transport of active substances[38]. The study of formation transition metal complexes is relevant in the field of analytical chemistry because the use of metal complexes allows the development of methods with increased selectivity and sensitivity. It is also of great importance in the field of biological and environmental chemistry[39]. These facts prompted us to synthesize new cobalt, nickel and copper transition metal complexes, to study the effect of antimicrobial activity of organic moieties in combination with metal ions.

EXPERIMENTAL

Instruments and biological experiment

The antimicrobial efficiency of the tested samples was assessed by a modified Kirby-Bauer disc diffusion method[40–43].

Tools and instruments used in compounds identifications are listed in Table 1.

Table 1. Methods and instruments used to identify new compounds

Analysis	Model of Instruments
Melting points	"Electrothermal IA 9100 series"
FTIR spectra	"Perkin-Elmer 1650 spectrometer"
^{1}H- and ^{13}C-NMR spectra	"Bruker AC-400 Hz instrument"
Elemental analysis	"Perkin Elmer 2400 CHN analyzer"
Mass spectra	"Shimadzu GC-MS-QP 1000 EX spectrometer"
Electronic spectra	"UV2 Unicam UV/Vis Spectrophotometer"
Magnetic moments	"Guoy balance"
Molar conductivities	"Jenway 4010 conductivity meter"
Metal contents	"gravimetrically method"
Thermogravimetric analysis	"TGA/DTA–50H Shimadzu thermal analyzer"
Electron spin resonance	"Jeol, JES-FE2XG, ESR-spectrometer"

Synthesis of thioxoimidazolidine derivative ligand

All chemicals were received from Sigma (NY, USA) and used without further purification.

***3-((1-Aminocarbonothioyl)hydrazono)ethylpyridine* (2)**

Method A: a mixture of 2-acetylpyridine (1.21 gm, 0.01 mol) and thiosemicarbazide (0.9 gm, 0.01 mol) in glacial acetic acid (20 mL) stirred with reflux for 3h, the precipitate formed after cooling filtered and crystallized from methanol to give yellowish crystals (yield 59%), m.p. 243–245°C. *Method B*: In a glass beaker, a mixture of 2-acetylpyridine (1.21 gm, 0.01 mol) and thiosemicarbazide (0.9 gm, 0.01 mol), dissolved in methylene chloride (20 mL) then silica gel added (1.0 g, 200–400 mesh), the mixture stirred with glass rod till solvent evaporated, the dried mixture irradiated for 1.5–2.0 min in a domestic microwave oven (2450 MHz, 800 W). The product isolated from silica gel by dissolving in acetone and filtered off. The product formed after acetone evaporation crystallized from methanol to give pale yellow crystals. Yield 91%, m.p. 244–246°C. IR: 3289–3186 cm^{-1} (NH_2 and NH), 2666 cm^{-1} (C=S thiamide). ^{1}H NMR (DMSO-d_6, 300Mz): δ = 2.63 (s, 3H, CH_3), 7.07 (dd, 1H, pyridine C_5H), 7.50 (d, 1H, J = 9.00, pyridine C_4H), 7.58 (s, 2H, NH_2), 7.67 (d, 1H, J = 6.00, pyridine C_6H), 7.93 (s, 1H, pyridine C_2H), 10.17 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6, 75Mz): δ = 13.06 (CH_3), 121.4 (pyridine C_5), 134.8 (pyridine C_3), 138.5 (pyridine C_4), 145.7 (C=N), 149.8 (pyridine C_6), 153.3 (pyridine C_2), 173.7 (C=S). Anal. Calcd for $C_8H_{10}N_4S$ (194.26): C, 49.46; H, 5.19; N, 28.84; S, 16.51; Found: C, 49.12; H, 5.61; N, 28.74; S, 16.32. MS *m/z* (int. %): 194 (100), 169 (49.4), 168 (64.6), 141 (17.7), 140 (71.0), 129 (20.0), 115 (31.7), 114 (28.6), 113 (64.0), 112 (20.29), 100 (15.9), 99 (21.76), 88 (50.6), 87 (64.6), 86 (34.5), 85 (25.3), 76 (38.0), 75 (39.4), 71 (34.5), 64 (45.8), 63 (61.8), 62 (71.1).

***1-(1-(Pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin--4-one* (3)**

Method A: a mixture of **1** (1.94 gm, 0.01 mol) and ethyl chloroacetate (1.22 gm, 0.01 mol) in DMF (15 mL) refluxed with stirring for 4h, the reaction mixture cooled, poured onto ice-watering and the crude precipitate formed filtered and crystallized from methanol to give orange crystals (yield 74%), m.p. 261–263°C. *Method B*: In a glass beaker, a mixture of **1** (1.94 gm, 0.01 mol) and ethyl chloroacetate (1.22 gm, 0.01 mol), dissolved in methylene chloride (20 mL) then silica gel added (1.0 g, 200–400 mesh), the mixture stirred with glass rod till solvent evaporated, the dried mixture irradiated for 3.0–3.5 min in a domestic microwave oven (2450 MHz, 800 W). The product isolated from silica gel by dissolving in acetone and filtered off. The product formed after acetone evaporation crystallized from methanol to give orange crystals. Yield 89%, m.p. 262–264°C. IR: 3177 cm^{-1} (NH), 2640 cm^{-1} (C=S thiamide), 1645 cm^{-1} (C=O amide). ^{1}H NMR (DMSO-d_6, 300Mz): δ = 2.37 (s, 3H, CH_3), 4.40 (s, 2H, imidazolidine CH_2), 7.09 (dd, 1H, pyridine C_5H), 7.51 (d, 1H, J = 9.00, pyridine C_4H), 7.60 (d, 1H, J = 6.00, pyridine C_6H), 7.95 (s, 1H, pyridine C_2H), 10.28 (s, 1H, NH). ^{13}C-NMR (DMSO- d_6, 75Mz): δ = 15.15 (CH_3), 63.96 (CH_2), 121.8 (pyridine C_5), 134.9 (pyridine C_3), 135.5 (pyridine C_4), 138.7 (C=N), 142.9 (pyridine C_6), 153.3 (pyridine C_2), 164.3 (C=O), 170.7 (C=S). Anal. Calcd for $C_{10}H_{10}N_4OS$ (234.28): C, 51.27; H, 4.30; N, 23.91; S, 13.69; Found: C, 51.03; H, 4.11; N, 23.81; S, 13.60. MS *m/z* (int. %): 234 (45.5), 206 (31.2), 185 (73.3), 175 (47.1), 157 (11.51), 146 (3.80), 129 (9.14), 118 (8.53), 103 (32.93), 90 (14.83), 76 (67.56), 64 (100), 55 (59.05).

***Ethyl 3-(4-oxo-3-(1-(pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin-1-yl) propanoate* (4)**

Method A: a mixture of **2** (2.34 gm, 0.01 mol) and ethyl chloropropionate (1.36 gm, 0.01 mol) in DMF (20 mL) refluxed with stirring for 4h, the reaction mixture cooled, poured onto ice-water and the crude precipitate formed filtered and crystallized from methanol to give yellow crystals (yield 62%), m.p. 196-198°C. *Method B*: In a glass beaker, a mixture of **2** (2.34 gm, 0.01 mol) and ethyl chloropropionate (1.36 gm, 0.01 mol), dissolved in methylene chloride (25 mL) then silica gel added (1.0 g, 200–400 mesh), the mixture stirred with glass rod till solvent evaporated, the dried mixture irradiated for 3.0–3.5 min in a domestic microwave oven (2450 MHz, 800 W). The product isolated from silica gel by dissolving in acetone and filtered off. The product formed after acetone evaporation crystallized from methanol to give yellow crystals. Yield 93%, m.p. 274°C. IR: 821 cm^{-1} (C=S thiamide), 1629 cm^{-1} (C=O amide). ^{1}H NMR (DMSO-d_6, 300Mz): δ = 1.73 (t, 3H, J = 6.0, $CH_2C\underline{H}_3$), 2.76 (s, 3H, CH_3), 2.87 (q, 2H, $C\underline{H}_2CH_3$), 4.06 (s, 2H, imidazolidine CH_2), 4.13 (t, 2H, J = 9.0 $NCH_2C\underline{H}_2$), 4.23 (t, 2H, J = 6.0 $NC\underline{H}_2CH_2$), 7.10 (dd, 1H, pyridine C_5H), 7.16 (d, 1H, J = 9.00, pyridine C_4H), 7.23 (d, 1H, J = 6.00, pyridine C_6H), 7.27 (s, 1H, pyridine C_2H). ^{13}C-NMR (DMSO- d_6, 75Mz): δ = 13.29 (N=C-CH_3), 13.93 ($CH_2\underline{C}H_3$), 31.15 ($NCH_2\underline{C}H_2$), 50.74 ($N\underline{C}H_2CH_2$), 58.22 (imidazolidine CH_2), 60.39 ($\underline{C}H_2CH_3$), 122.3 (pyridine C_5), 134.8 (pyridine C_3), 135.5 (pyridine C_4), 149.7 (C=N), 153.3 (pyridine C_6), 155.5 (pyridine C_2), 164.0 (imidazolidine C=O), 170.7 ($CH_2CH_2\underline{C}$=O), 173.7 (imidazolidine C=S). Anal. Calcd for $C_{15}H_{18}N_4O_3S$ (334.39): C, 53.88; H, 5.43; N, 16.75; S, 9.59; Found: C, 53.63; H, 5.38; N, 16.71; S, 9.48. MS *m/z* (int. %): $(M^+ + 1)$ 335 (1.9), M^+ 334 (25.8), 305 (8.8), 233 (21.7), 234 (15.4), 232 (11.5), 119 (10.9), 118 (10.0), 105 (29.1), 104 (34.9), 103 (19.7), 77 (56.8), 76 (21.0), 63 (11.9), 62 (11.9), 59 (11.5), 58 (11.4), 52 (44.3), 51 (100.0), 50 (92.5).

Synthesis of Cu(II), Co(II), and Ni(II) thioxoimidazolidine complexes

An equimolar volume of $CuCl_2$, $CoCl_2 \cdot 6H_2O$, and $NiCl_2 \cdot 6H_2O$ metal salts was dissolved in 10 mL distilled water. A methanol solution of ethyl 3-(4-oxo-3-(1-(pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin-1-yl) propanoate (**4**) ligand (L) was mixed to an aqueous solution of metal chloride with continuously stirring for about 2–3 hrs. The solid complex was separated, filtered, washed with methanol, diethyl ether and dried in an oven at 80°C and then stored in a desiccator under *vacuum* over anhydrous calcium chloride. The metal to thioxoimidazolidine ligand ratio is 1:1 stoichiometric proportion. Anal. Calcd for copper (II) complex: C, 33.31; H, 4.85; N, 10.36; Found: C, 33.24; H, 4.81; N, 10.11, Anal. Calcd for cobalt (II) complex: C, 33.59; H, 4.89; N, 10.45; Found: C, 33.30; H, 4.77; N, 10.40; and Anal. Calcd for nickel (II) complex: C, 33.61; H, 4.89; N, 10.45; Found: C, 33.45; H, 4.79; N, 10.39.

RESULTS AND DISSICATIONS

Interpretation of thioxoimidazolidine derivative (4) ligand

Attempts were carried out for synthesis of compound ethyl 3-(4-oxo-3-(1-(pyridin-3-yl) ethylideneamino)--2-thioxoimidazolidin-1-yl)propanoate (4) with different methods, using the traditional method and microwave technique, for improving the quality of the product and increase the yield, if possible, and finally using the final product to form metal ion complex with different metals. Firstly, 3-Acetylpyridine reacted with thiosemicarbazide in glacial acetic acid, as traditional technique, and they reacted under microwave irradiation over silica gel (200–400 mesh) with a domestic microwave oven (2450 MHz, 800 W) as an improvement technique (Figure 2), the products formed in the two methods showed the effectiveness of the microwave technique in improving the yield and increasing the melting point of the product.

The structure of the 3-((1-Aminocarbonothioyl)hydrazono)ethylpyridine **2** was elucidated from its NMR and IR spectra along with the mass fragmentation. The IR showed the disappearance of the C=O of the acetyl group in the acetylpyridine with the appearance of the NH_2, NH and C=S bands due to the condensation of the thiosemicarbazide with acetylpyridine. The IR of compound **2** showed bands at the range 3289–3186 cm^{-1} due to NH_2 and NH, also, showed a band at 830 cm^{-1} due to C=S. The ^1H NMR supported the structure, where, it showed a singlet signal at δ = 7.58 ppm due to NH_2 group and another singlet at δ =10.17 ppm due to NH. The ^1H NMR chart for compound **2** is shown in Fig. 3. The ^{13}C NMR showed also, a peak at 173.7 due to the carbon of the C=S as illustrated in Fig. 4.

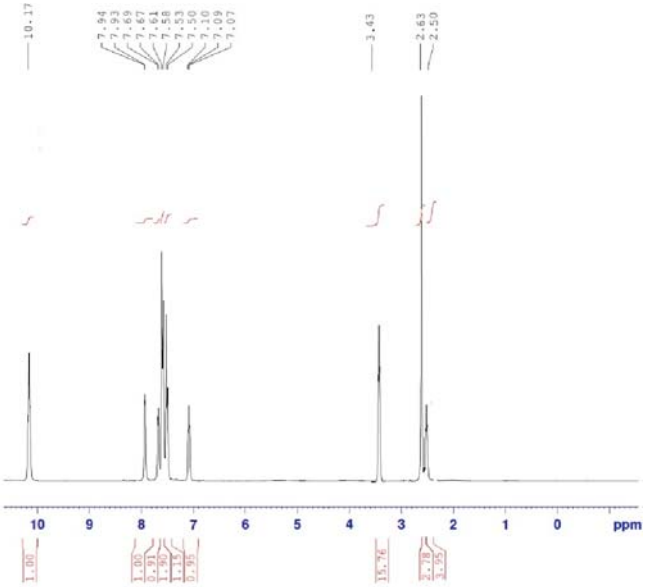


Figure 3. ^1H NMR of compound **2**

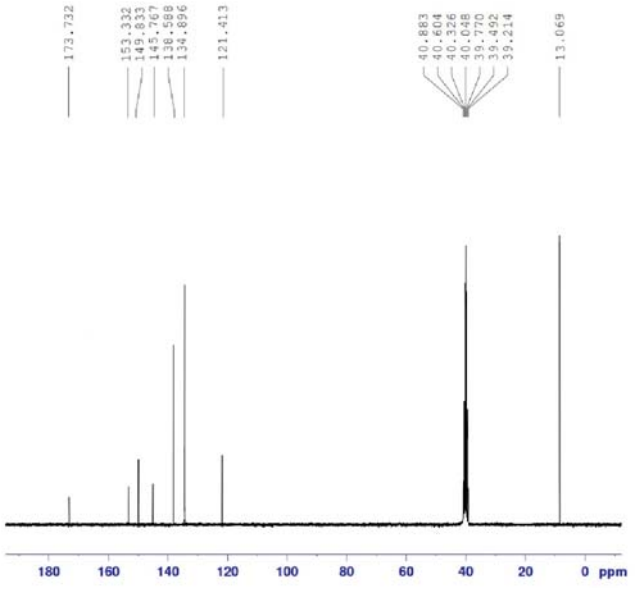


Figure 4. ^{13}C NMR of compound **2**

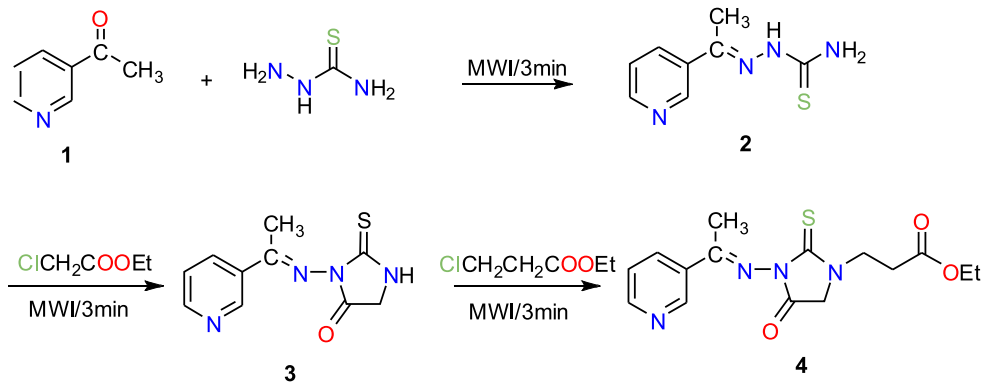


Figure 2. Synthesis of imidazolidine derivative

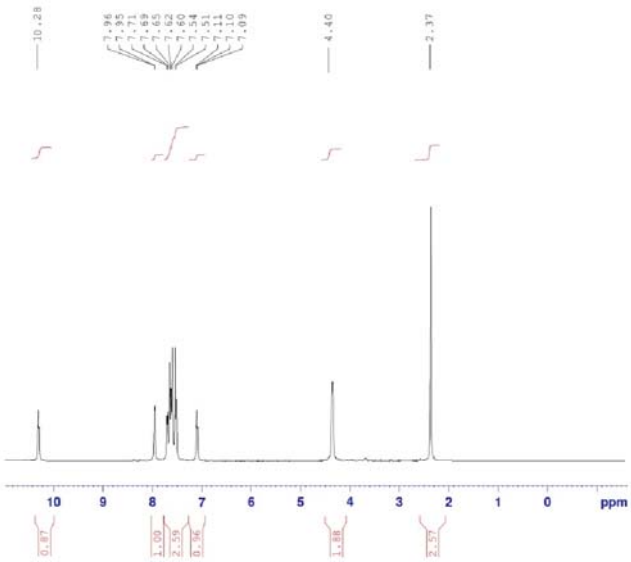


Figure 5. ^{1}H NMR of compound **3**

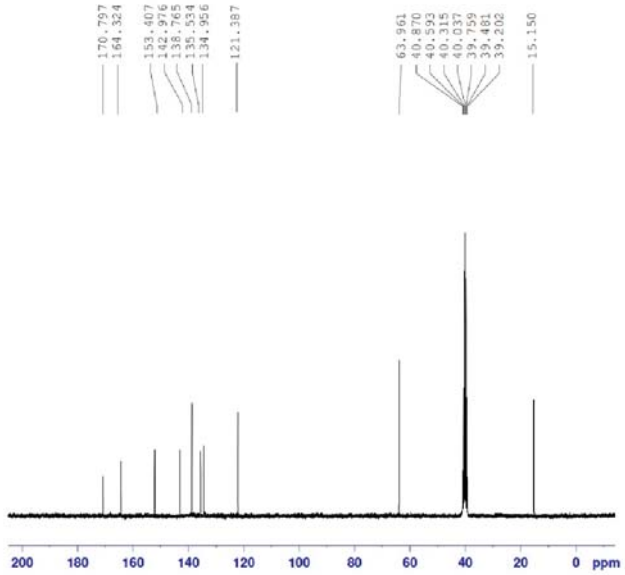


Figure 6. ^{13}C NMR of compound **3**

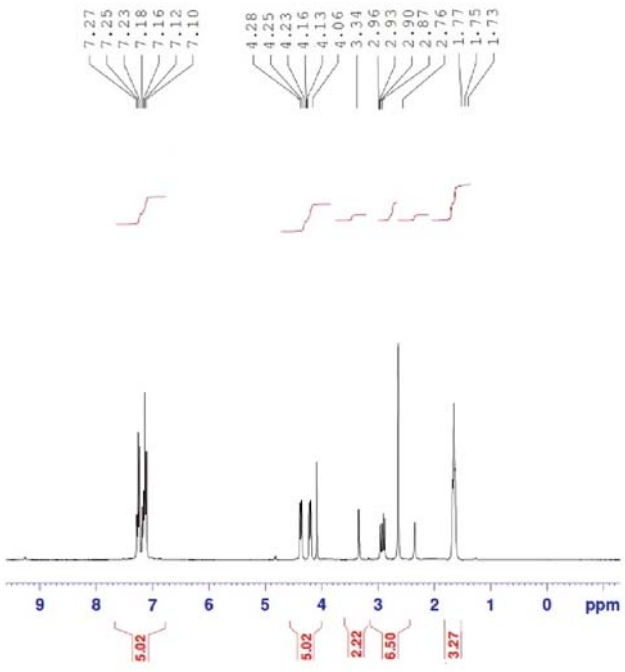


Figure 7. ^{1}H NMR of compound **4**

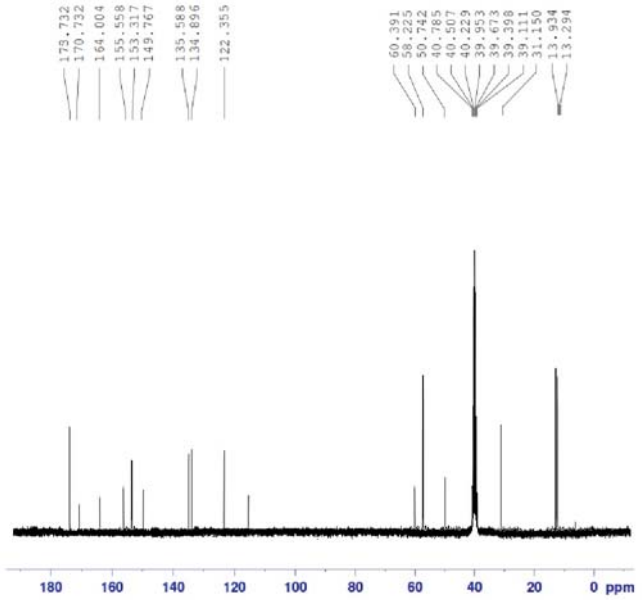


Figure 8. ^{13}C NMR of compound **4**

With the same methods, compound **2** reacted with ethyl chloroacetate in DMF under reflux and the same reaction carried out under microwave irradiation, the products formed in the two techniques showed, also, an improvement of the yield and melting point of the product. The 1-(1-(Pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin-4-one **3** formed showed in its ^{1}H NMR spectrum the presence of imidazolidine CH_2 protons at δ = 4.40 ppm Fig. 5. Also, ^{13}C NMR showed new peaks due to the carbon of imidazolidine CH_2 and C=O at δ = 63.96 and 164.3 ppm, respectively, Fig. 6.

Finally, compound **3** reacted in boiling DMF with ethyl chloropropionate and the reaction, also, repeated in microwave with the same previous manner to give compound **4**. The structure of compound **4,** Ethyl 3-(4-oxo-3-(1-(pyridin-3-yl)ethylideneamino)-2-thioxoimidazolidin-1-yl) propanoate, proved with its ^{1}H, ^{13}C NMR, IR, and mass spectra. ^{1}H NMR of compound **4** (Fig. 7), showed two triplets due to two CH_2 groups of propionate moiety with quartet and triplet due to the ethyl group at δ = 4.13, 4.23, 1.73 and 2.87 ppm, respectively. The ^{13}C NMR of compound **4** (Fig. 8), showed signals due to the propionate moiety at δ = 13.93, 31.15, 50.74 and 60.39 ppm due to CH_3, and 3 CH, respectively. The mass fragmentation chart and pattern for compound **4** are shown in Fig. 9 and Fig. 10. respectively.

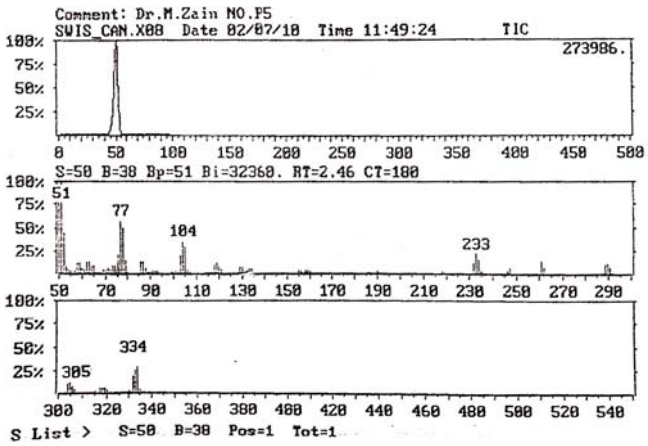


Figure 9. Mass fragmentation for compound **4**

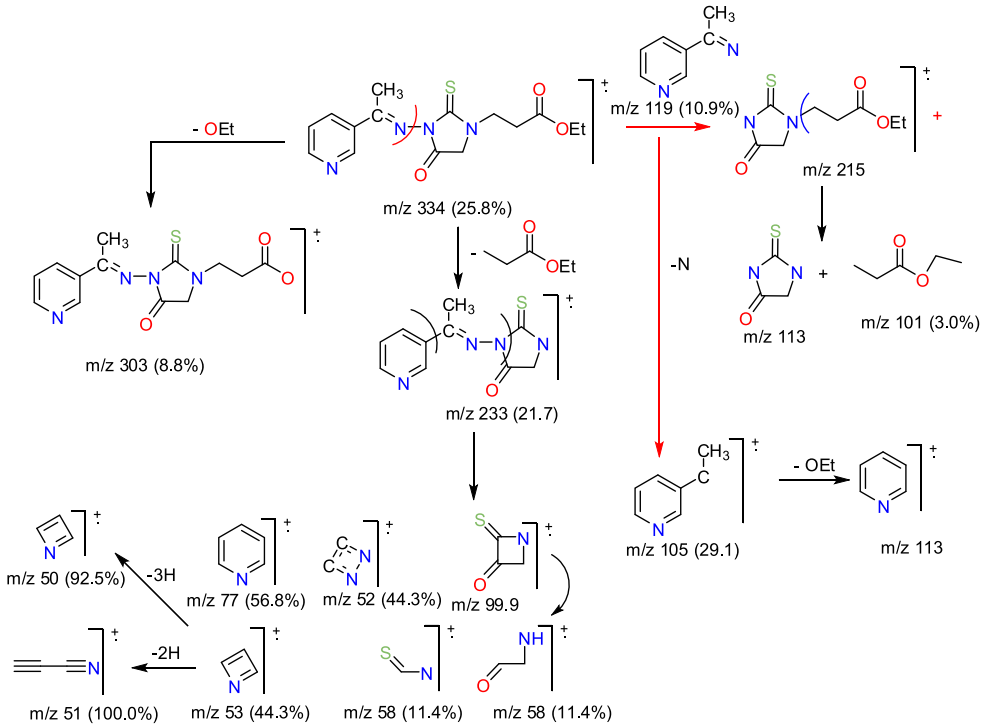


Figure 10. Mass fragmentation pattern for compound **4**

Interpretation of Cu(II), Co(II), and Ni(II) thioxoimidazolidine (4) ligand complexes

Microanalytical and molar conductance studies

The elemental, color, melting points (°C), magnetic susceptibility (B.M), and molar conductance ($ohm^{-1}cm^2mol^{-1}$) values are summarized in Table 2. The microanalytical data concluded that the stoichiometry between Metal: Ligand is (1:1) with speculated general formulae as $[M(L)(H_2O)_4]Cl_2$. The synthesized metal complexes have a higher melting point within 350–400°C temperature range. The Cu(II), Co(II), Ni(II) thioxoimidazolidine complexes are insoluble in H_2O, alcohols, and common organic solvents, but soluble in dimethyl sulfoxide (DMSO) and dimethyl formamide (DMF). The molar conductivity values are located within the range of 129–152 $ohm^{-1}cm^2$ mol^{-1} due to an electrolytic property.

Infrared spectra

The infrared spectra of thioxoimidazolidine derivative (**4**) ligand (Fig. 11a & Table 3) included four characteristic vibration bands at 1707 cm^{-1}, 1629 cm^{-1} [44], 1498 cm^{-1} and 821 cm^{-1} attributed to the ν(C=O) ester group, ν(C=O) thioxoimidazolidine ring, ν(N-C=S) thioxoimidazolidine ring, ν(C=S) group, respectively. Randall et al.[45] have been observed that a strong band presence within the range of 1471–1613 cm^{-1} in the case of thioxoimidazolidine ring is assigned to the stretching vibration motion of N-C=S group, while the stretching vibration of (C=S) group is present at 821 cm^{-1} [31].

In the case of the infrared spectra (Fig. 11b-d) of the synthesized Cu(II), Co(II), and Ni(II) complexes, the broad bands within the region of 3446–3345 cm^{-1} and medium-weak bands at ~ 900 cm^{-1} [44] can be assigned to the ν(O-H) stretching vibration and bending vibration δ(H_2O) of the four coordinated water molecules, respectively.

Regarding the infrared spectra of the synthesized complexes, a very strong band at 1707 cm^{-1} (free ligand) is absent or shifted by 56 cm^{-1} in case of copper(II) complex to lower wavenumbers, the shift in ν(C=O) ester group supported that the chelation of thioxoimidazolidine **4** ligand towards metal ion occurs through the oxygen atom.

The stretching vibration motion of ν(N-C=S) thioxoimidazolidine ring in case of the synthesized complexes is shifted to a lower frequency by 15–25 cm^{-1} (1483–1473 cm^{-1}), this shift is a second items supported also the involvement of nitrogen atom of thioxoimidazolidine ring in the coordination process. The new vibration bands presence in the spectra of metal complexes within the lower frequency region 543–518 cm^{-1} and 605–601 cm^{-1} also confirms the involvement of nitrogen and oxygen atoms of thioxoimidazolidine and ester groups, respectively, in the coordination to metal ion.

Both vibration motions of ν(C=O) and ν(C=S) of the thioxoimidazolidine ring haven't been shifted due to the did not share of oxygen and sulfur of thioxoimidazolidine ring in the chelation towards metal ion.

Table 2. Analytical data of thioxoimidazolidine derivative ligand **4** and its complexes

Compounds	Molecular formula (Mwt)	Color	M.p/°C	μ_{eff}/B.M	$\Lambda_m/ohm^{-1}cm^2mol^{-1}$
Ligand **4**	$C_{15}H_{18}N_4O_3S$ (334.39)	Yellow	274	–	6
Cu(II) complex	$C_{15}H_{26}Cl_2N_4O_7SCu$ (540.90)	Green	> 350	1.83	138
Co(II) complex	$C_{15}H_{26}Cl_2N_4O_7SCo$ (536.29)	Yellow	> 350	5.12	152
Ni(II) complex	$C_{15}H_{26}Cl_2N_4O_7SNi$ (536.05)	Green	> 350	3.85	129

Table 3. Infrared spectral assignments of thioxoimidazolidine derivative ligand **4** and its complexes

Assignments	Compounds			
	Ligand **4**	Cu(II) complex	Co(II) complex	Ni(II) complex
v(C=O) ester	1707	1652	–	–
v(C=O) thioxoimidazolidine	1629	1620	1612	1611
v(N-C=S) thioxoimidazolidine	1498	1483	1479	1473
v(C=S)	821	820	821	825
v(M-O)	–	605	601	600
v(M-N)	–	518	537	543

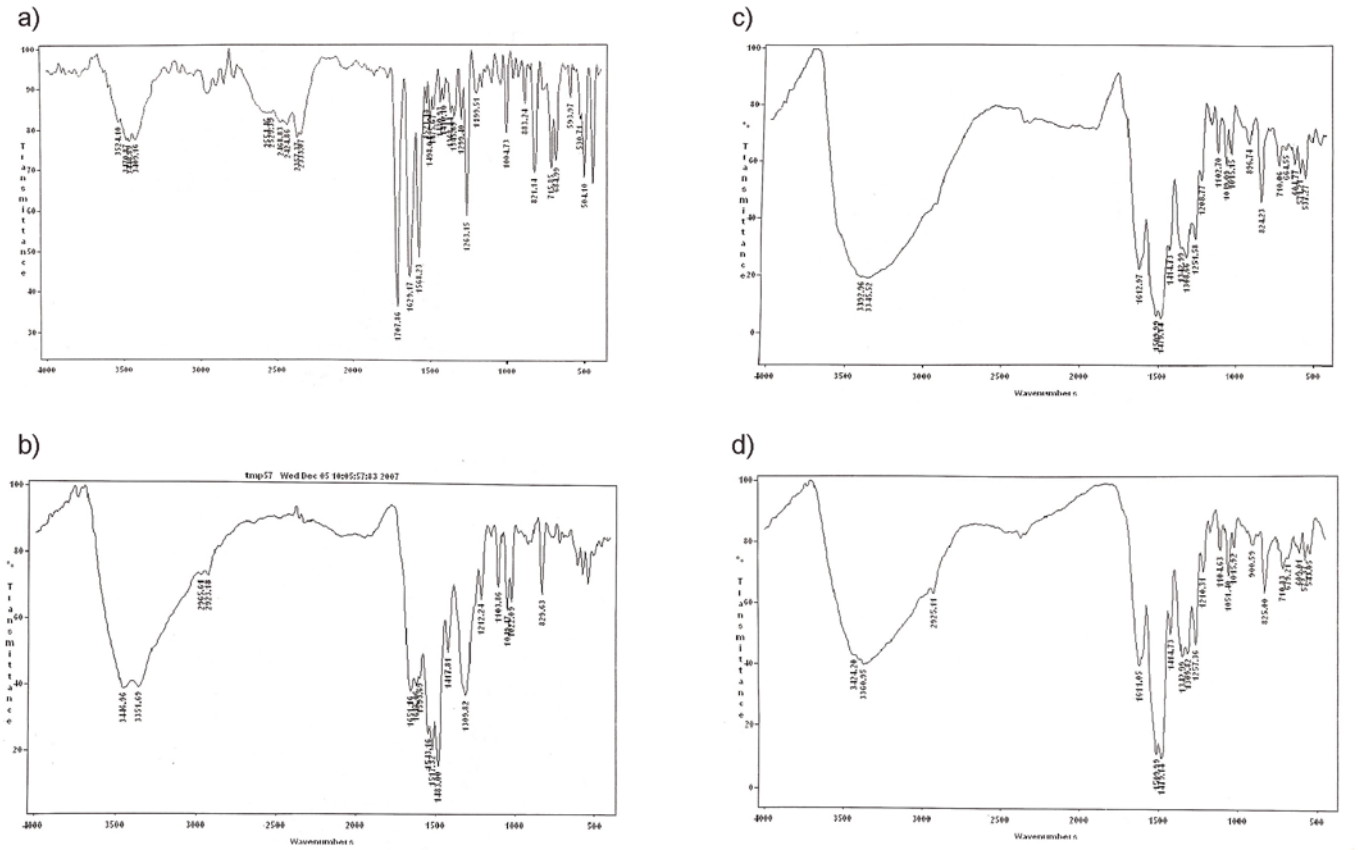


Figure 11. Infrared spectra of a-free ligand, b-Cu(II), c-Co(II), and d-Ni(II) complexes

Electronic, ESR spectra and magnetic measurements

The electronic spectrum of Cu(II) complex has a single broad band at 14.045 cm^{-1}, due to $^2E_g \rightarrow {}^2T_g$ electronic transition. The magnetic moment value of copper(II) complex is 1.83 B.M., which is matched with an octahedral geometry[32, 33]. Regarding the ESR analysis of the copper(II) complex, the spectral analysis are $g\| = 2.15$ and $g_\perp = 2.08$. The experimental $g\|$ value is less than 2.3 with consent to the covalent bond character. The experimental data of the copper(II) complex agrees with $g\| > g_\perp > 2.003$, These results proved that the unpaired electron is present in $d_{x^2-y^2}$ orbital around the Cu(II) metal ion and the spectral behavior are characteristic of axial symmetry. The octahedral Co(II) complex has a two electronic transition bands at 20.202 cm^{-1} and 11,765 cm^{-1}, these are assigned to $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3) and $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (ν_2) respectively[32]. The magnetic moment of cobalt(II) complex is 5.12 B.M which is matched with an octahedral geometry. Nickel(II) complex has a three electronic transition bands at 25.641 cm^{-1}, 16.949 cm^{-1} and 10.989 cm^{-1} due to $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ (ν_3), $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (ν_2), $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (ν_1)[46, 47] respectively. The distorted octahedral geometry of the Ni(II) complex has a magnetic moment 3.85 B.M., this high μ_{eff} value is due to the mixing of multiplet excited states in which spin orbit coupling is ratable[48]. Based on the above spectroscopic and magnetic results, it can be deduced that the thioxoimidazolidine complexes are formulated as $[M(L)(H_2O)_4]Cl_2$ (Fig. 12)

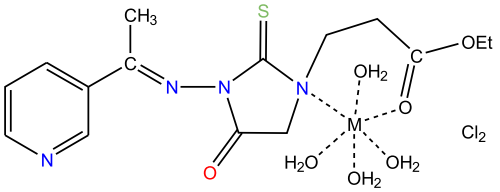


Figure 12. Suggested structures of the synthesized $[M(L)(H_2O)_4]Cl_2$ complex (M = Cu, Co, and Ni(II) metal ions)

Thermogravimetric analyses

The thermogravimetric (TGA) and the differential thermal analysis (DTA) data of the solid Cu(II), Co(II), and Ni(II) thioxoimidazolidine complexes are displayed in Fig. 13a–c and their assignments are summarized in Table 4.

Table 4. Thermal analyses of Cu(II), Co(II), and Ni(II) thioxoimidazolidine complexes

Complexes	DTA peak/°C	Temp. Range/°C	Weight loss		Assignments	
			Calcd.	Found	Loss species	Residual species found/(calcd.)
Cu(II)	255	25–400	75.14	75.82	$4H_2O$ $C_{15}H_{18}N_4O_3S$	$CuCl_2$ (24.18/(24.86))
Co(II)	325	25–400	75.79	74.94	$4H_2O$ $C_{15}H_{18}N_4O_3S$	$CoCl_2$ (25.06/(24.21))
Ni(II)	360	25–400	75.82	75.53	$4H_2O$ $C_{15}H_{18}N_4O_3S$	$NiCl_2$ (24.47/(24.18))

The thermal analysis discussions have confirmed the presence of four coordinated water molecules inside the coordination sphere. The representative of $[Cu(L)(H_2O)_2]Cl_2$, $[Co(L)(H_2O)_2]Cl_2$, and $[Ni(L)(H_2O)_2]Cl_2$ complexes are stable up to 400°C and after that, the mass losses are in the range of 74.94–75.82% (calcd. 74.94–75.82%) corresponding to the loss of four coordinated water molecules and thioxoimidazolidine ligand ($C_{15}H_{18}N_4O_3S$) moiety. In the final thermal decomposition step, the residues percentages are located within the range of 24.18–25.06% (calcd. 24.18–24.86%). The complexes under study have an anhydrous metal chlorides MCl_2 as a residual product.

Biological analyses

The ethyl 3-(4-oxo-3-(1-(pyridin-3-yl)ethylideneamino)--2-thioxoimidazolidin-1-yl)propanoate (**4**) ligand along with the Cu(II), Co(II), and Ni(II) complexes were tested for their antimicrobial activity G+ bacteria (*Bacillus Subtillis*, *Streptococcus Pneumonia*, and *Staphyloccoccus Aurease*), G- bacteria (*Escherichia coli*, and *Pesudomonas Sp*.) and fungi (*Aspergillus Nigaer*, and *Penicillium Sp*.) by paper disc diffusion method (Table 4). Dimethyl sulfoxide solvent was used as a control sample. The metal-ligand complexes show moderate activity rather than free ligand against all organisms except *Streptococcus Pneumonia*, and *Staphyloccoccus Aurease*. The synthesized Cu(II), Co(II), Ni(II) complexes show moderate antimicrobial activity against *Bacillus Subtillis*, *Escherichia coli*, *Pesudomonas Sp*. *Aspergillus Nigaer*, and *Penicillium Sp*. Copper(II) and cobalt(II) complexes have not possessed any activities against *Escherichia coli*. It was observed from these results that some metal compounds exhibit slightly higher free ligand activity against the same microorganisms and under similar conditions. The mode of action of the complexes may involve the formation of hydrogen bonds with microbials or ribosomes of microbial cells resulting in interference with normal cell processes.

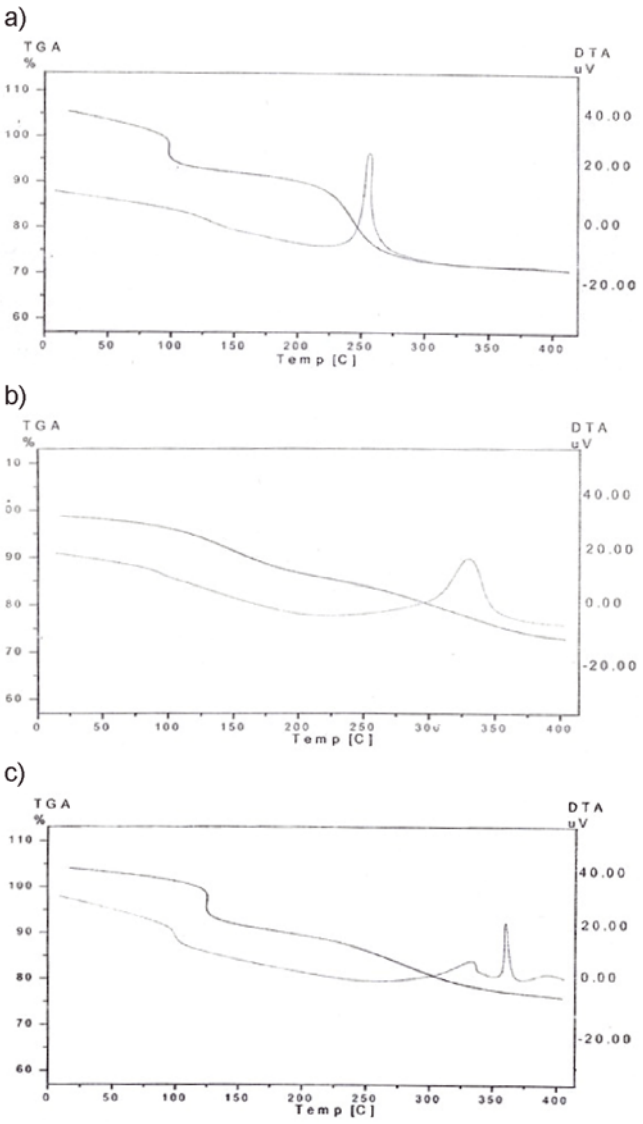


Figure 13 a-c. TGA-DTA curves of a-Cu(II), b-Co(II), and c--Ni(II) complexes

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Table 5. Antibacterial efficient of free ligand and its Cu(II), Co(II), and Ni(II) complexes

Compounds	G+ bacteria			G- bacteria		Fungi	
	Bacillus Subtillis	*Streptococcus Pneumonia*	*Staphyloccoccus Aurease*	*Escherichia coli*	*Pesudomonas Sp.*	*Aspergillus Nigaer*	*Penicillium Sp.*
Ligand	+	+++	++	–	–	–	+
Cu(II)	+	+++	++	–	+	–	+++
Co(II)	++	+++	++	–	++	+	++
Ni(II)	+++	+++	++	+	++	+	+++

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