

ORIGINAL ARTICLE

Synthesis and Antibacterial Activity of Cu(II),Pd(II) and Co(II) Complexes of Schiff Base Derived from L-Methionine and 2-Hydroxy-1-naphthaldehyde

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ABSTRACT

Condensation 2-hydroxy-1-naphthaldehyde with L-methionine yielded E-((2)-((2-hydroxynaphthalene-1-yl)ethylene)amino)-4-(methylthio) butanoic acid **1** in a good yield. Metal complexes of Schiff base **1** have also been derived with Cu(II), Pb(II), and Co(II) metal salts were synthesized. Elemental analysis (CHN), IR, <sup>1</sup>H, <sup>13</sup>C, and NMR spectroscopy were used to characterize the synthesized compounds. The synthesized compounds were screened for antibacterial activity against gram-positive and negative bacteria. Novel compounds showed strong antibacterial action against Streptococcus pneumonia, but only modest activity against E. coli and Klebsiella pneumonia.

Key words: Schiff base, antibacterial activity, metal complexes, methionine

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INTRODUCTION

In humans, methionine is a necessary amino acid. Other amino acids, such as cysteine and taurine, use it as a substrate. Many animals, including humans, rely on methionine for their metabolism. Excessive consumption of methionine, the methyl group donor in DNA methylation, has been associated with cancer progression in several studies [1]. In addition to their vital significance in catalysis and organic synthesis, amino acid Schiff bases are an important class of ligands because their metal complexes have a variety of uses including biological, clinical, analytical, and industrial relevance [2, 3].

Singh *et al* prepared complexes of Schiff base derived from histidine and methionine [4]. The ligand, methionine salicylidene was synthesized by the condensation reaction of methionine and salicylaldehyde. The Co(II), Ni(II), and Cu(II) complexes were prepared with the synthetic ligand [5].

In recent years, our interest has focused on preparing several Schiff bases compounds and studying their biological effectiveness as anti-bacterial[6], anti-fungal [7], antioxidant [8], and anti-mitotic [9]. In this work, we synthesized some new metal complexes of Schiff-base derived from methionine and 2-hydroxy naphthaldehyde.

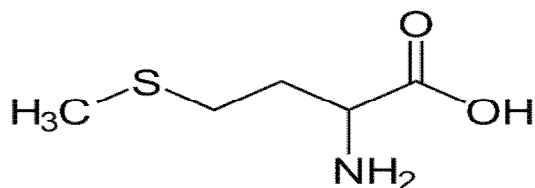


Figure 1: Chemical structure of methionine

**MATERIAL AND METHODS****Instrumentation**

IR spectra were recorded using KBr discs on a Pye-Unicam SP3-300 spectrometer in the range 4000-200 cm<sup>-1</sup> at the Polymer Research Centre, University of Basrah, Basrah, Iraq. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were obtained on a Bruker at 600 MHz with TMS as an internal reference at Konstanz University in Germany. The melting point was determined using a Philip Harris melting point apparatus at the University of Basrah, College of Veterinary Medicine

**Synthesis****Synthesis of 2-((Z)-[(1-hydroxynaphthalen-2-yl)methylidene]amino)-4-(methylsulfonyl)butanoic acid 1 [10]**

In a 10 ml ethanolic solution of 2-Hydroxy naphthaldehyde, 2-amino-4-(methylsulfonyl)butanoic acid (L-Methionine) (5.0 mmol, 0.74 g) was added to a hot ethanolic solution of 2-Hydroxy naphthaldehyde (5.0 mmol, 0.86 g). Three drops of glacial acetic acid were added, and the resulting solution was refluxed for three hours before being refrigerated overnight. The product was recrystallized using chloroform: methanol (8:2, v:v) to get orange crystals of 2-((Z)-[(1-hydroxynaphthalen-2-yl)methylidene]amino)-4-(methylsulfonyl)butanoic acid. Color: Pale-yellow Yield: 78%.

M.p.: 177-179 °C.

FT-IR(KBr, cm<sup>-1</sup>), 3252(OH), 3080(C-H, aromatic), 2905, 2885(C-H, aliphatic), 1871(C=O carboxylic), 1620(C=N), 1604(C=C), 1558, 1327 (CO<sub>2</sub>H). <sup>1</sup>H NMR(DMSO-d<sub>6</sub>): δ 14.47(s, 1H, CO<sub>2</sub>H), 10.80(s, 1H, OH-Ar), 9.22(s, 1H, CH=N), 7.92-6.83(m, 6H, Harom.), 4.51(s, 1H, CH-CO<sub>2</sub>H), 2.66-2.51 (m, 2H, SCH<sub>2</sub>(cis+trans)), 2.23-2.14(m, 2H, CH<sub>2</sub>(cis+trans)), 2.05(s, 3H, SCH<sub>3</sub>). <sup>13</sup>C NMR(DMSO-d<sub>6</sub>): 193.6(CO<sub>2</sub>H), 170.3 (C-Ar-OH), 160.1 (CH=N); 133-113.7 (Carom.), 61.6 (CH-CO<sub>2</sub>H), 39.4 (C-CH<sub>2</sub>), 30.9(C-SCH<sub>2</sub>), 15.2(C-SCH<sub>3</sub>). Anal. calc. for C<sub>16</sub>H<sub>17</sub>NO<sub>3</sub>S(303.38): C, 63.35; H, 5.65; N, 4.62. Found: C, 62.89; H, 5.31; N, 4.73.

**Synthesis of metal complexes**

The metal complexes were synthesized by mixing a hot ethanolic solution of the appropriate metal chloride (1 mmole) with a hot ethanolic solution of the ligand (0.606 g, 2 mmoles). The resulting mixture was refluxed for 3 hours, after which the colorful precipitation appeared. They were collected through filtration, washed numerous times with ethanol and chloroform to purify them further, and then dried under a vacuum.

**Synthesis of Cu(II) complex 2**

Color: Green-black

Yield: 67%.

M.p.: 198-201 dec. °C.

FT-IR(KBr, cm<sup>-1</sup>), 3243(OH), 3087(C-H, aromatic), 2915, 2887(C-H, aliphatic), 1865(C=O carboxylic), 1677(C=N), 1601(C=C), 1564, 1320 (CO<sub>2</sub>H).

<sup>1</sup>H NMR(DMSO-d<sub>6</sub>): δ 11.99(s, 2H, CO<sub>2</sub>H), 8.91(s, 2H, CH=N), 8.12-7.21(m, 12H, Harom.), 3.68 (s, 2H, CH-CO<sub>2</sub>H), 2.60 (t, 4H, SCH<sub>2</sub>), 2.25(t, 4H, CH<sub>2</sub>), 2.05(s, 6H, SCH<sub>3</sub>). <sup>13</sup>C NMR(DMSO-d<sub>6</sub>): 192.25(CO<sub>2</sub>H), 163.34 (CH=N); 131.12-111.85 (Carom.), 63.6 (CH-CO<sub>2</sub>H), 34.4 (C-CH<sub>2</sub>), 30.7(C-SCH<sub>2</sub>), 15.8(C-SCH<sub>3</sub>). Anal. calc. for C<sub>32</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub> Cu (667.54): C, 57.52; H, 4.79; N, 4.19. Found: C, 57.23; H, 4.51; N, 3.88.

**Synthesis of Pd(II) complex 3**

Color: Brown

Yield: 78%

M.p.: 224-227 dec. °C.

FT-IR(KBr, cm<sup>-1</sup>), 3241(OH), 3079(C-H, aromatic), 2909, 2882(C-H, aliphatic), 1871(C=O carboxylic), 1652(C=N), 1608(C=C), 1557, 1329 (CO<sub>2</sub>H).

<sup>1</sup>H NMR(DMSO-d<sub>6</sub>): δ 12.01(s, 2H, CO<sub>2</sub>H), 8.92(s, 2H, CH=N), 8.33-7.24 (m, 12H, Harom.), 4.51(s, 1H, CH-CO<sub>2</sub>H), 2.61 (t, 4H, SCH<sub>2</sub>), 2.27 (t, 4H, CH<sub>2</sub>), 2.07(s, 6H, SCH<sub>3</sub>). <sup>13</sup>C NMR(DMSO-d<sub>6</sub>): 190.1(CO<sub>2</sub>H), 162.8 (CH=N); 138.3-112.3 (Carom.), 59.9(CH-CO<sub>2</sub>H), 39.8 (C-CH<sub>2</sub>), 32.5(C-SCH<sub>2</sub>), 15.5(C-SCH<sub>3</sub>). Anal. calc. for C<sub>32</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub> Pd (710.42): C, 54.05; H, 4.50; N, 3.94. Found: C, 53.89; H, 4.21; N, 3.67

**Synthesis of Co(II) complex 4**

Color: Brown

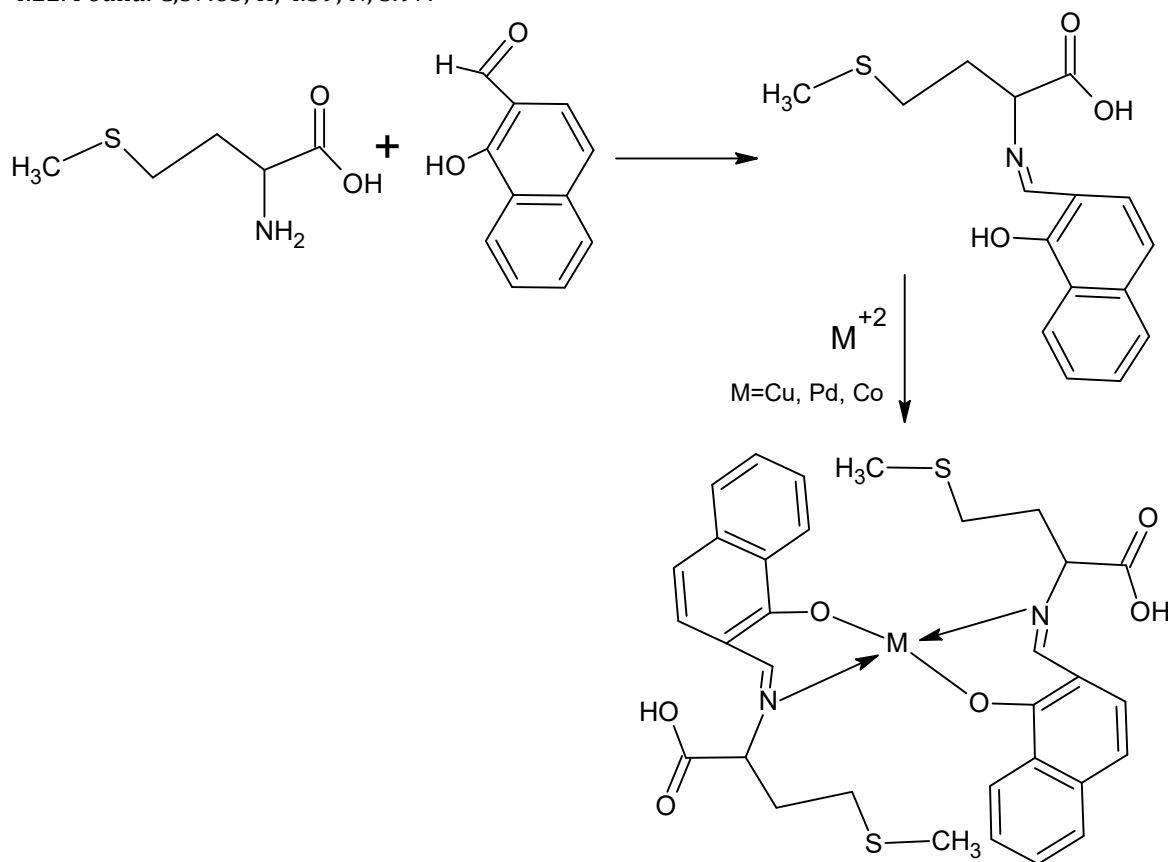
Yield: 76%.

M.p.: 204-207 dec. °C.

FT-IR(KBr, cm<sup>-1</sup>), 3239(OH), 3074(C-H, aromatic), 2911, 2887(C-H, aliphatic), 1867(C=O carboxylic), 1668(C=N), 1605(C=C), 1555, 1327 (CO<sub>2</sub>H).

<sup>1</sup>H NMR(DMSO-d<sub>6</sub>): δ 12.12(s, 2H, CO<sub>2</sub>H), 8.97(s, 2H, CH=N), 8.16-7.18(m, 12H, Harom.), 4.47(s, 1H, CH-CO<sub>2</sub>H), 2.63 (t, 4H, SCH<sub>2</sub>), 2.26 (t, 4H, CH<sub>2</sub>), 2.02(s, 6H, SCH<sub>3</sub>). <sup>13</sup>C NMR(DMSO-d<sub>6</sub>): 195.4(CO<sub>2</sub>H), 162.3 (CH=N); 133.4-113.1 (Carom.), 60.7(CH-CO<sub>2</sub>H),

37.2(C-CH<sub>2</sub>), 30.2(C-SCH<sub>2</sub>), 15.9(C-SCH<sub>3</sub>). Anal. calc. for C<sub>32</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub> Co (663.12): C, 57.90; H, 4.82; N, 4.22. Found: C,57.65; H, 4.59; N, 3.97.



**Scheme1:** Synthesis of Cu(II),Pd(II) and Co(II) complexes of Schiff base derived from L-Methionine and 2-Hdroxy-1-naphthaldehyde

## RESULTS AND DISCUSSION

### Chemistry

The reaction of equimolar amino acid (L-Methionin) and aldehyde (2-Hydroxy-1-naphthaldehyde) was yielded Schiff base derivative as a ligand to prepare some new metal complexes in 2:1ligand to metal molar ratio. According to wavelenghts of maximum absorbance, the color of the produced chemicals varies from brown to green to black. High melting points were displayed in the complexes due to strong network of bonding created between the ligand and the metal ions. The IR spectrum confirms the existence of the azomethine group (CH = N) of the ligand **1** extending about 1620 cm<sup>-1</sup> with a sharp area, on complexation with central metal(II) ions, which moved to a lower frequency by 1652-1677 cm<sup>-1</sup>, indicating that coordination happens via azomethine. [11].

In the <sup>1</sup>H NMR spectrum of ligand, the two singlet at δ 14.47 and 10.80 ppm were assigned to CO<sub>2</sub>H and OH protons respectively and singlet at δ 14.01-13.77 ppm assigned to CO<sub>2</sub>H for compounds **2-4** which the signals of OH protons was disappeared. While the singlet at δ 9.22 ppm was attributed to the azomethine proton (CH=N) for ligand and singlet at δ 8.97-8.91 ppm for complexes compounds **2-4**. The multiplet at the region δ 8.23-6.83 ppm was belonged to the aromatic protons for all synthesized compounds **1-4**. All synthesized compounds showed signals due to the methylene protons SCH<sub>3</sub> and SCH<sub>2</sub>CH<sub>2</sub> were appeared as two multiplets at the regions δ 2.66-2.51 and 2.23-2.14 ppm, respectively.

The <sup>13</sup>C NMR spectra of all synthesized compounds were obtained in DMSO-d<sub>6</sub>. The synthesis of these compounds was further supported by <sup>13</sup>C NMR spectra. For molecules **1-4**, the spectra revealed the existence of a -CH=N group around 158.01-163.3 ppm. The signal at δ 176.47 ppm due to C-OH in ligand **1**. The structure of synthesized substances is represented by the spectra data signals.

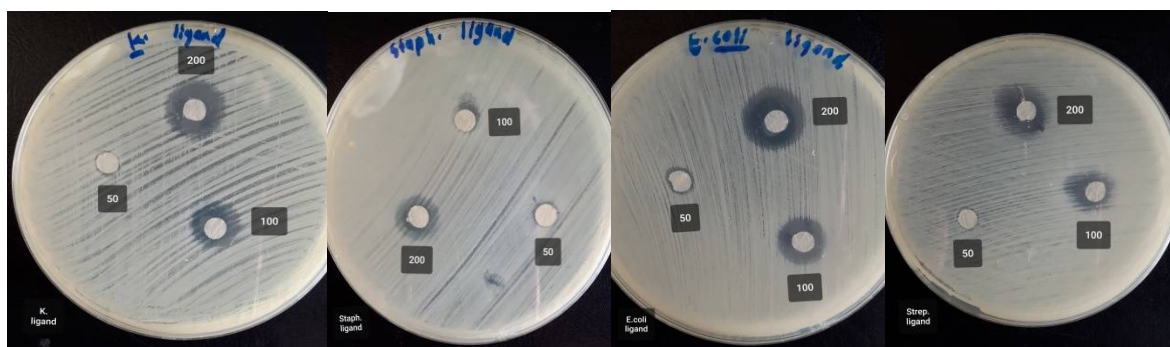
### Antibacterial activity

The potential antimicrobial efficacy of the ligand and their new complexes towards two different strains of bacteria two gram positive (*Staphylococcus aureus*, (*Streptococcus uberis*) and two gram negative (*Escherichia coli* and *Klebsiella pneumonia*) was checked. Antibacterial activity was measured using the paper disc-agar diffusion technique using Muller Hinton agar as a culture medium [12,13]. The

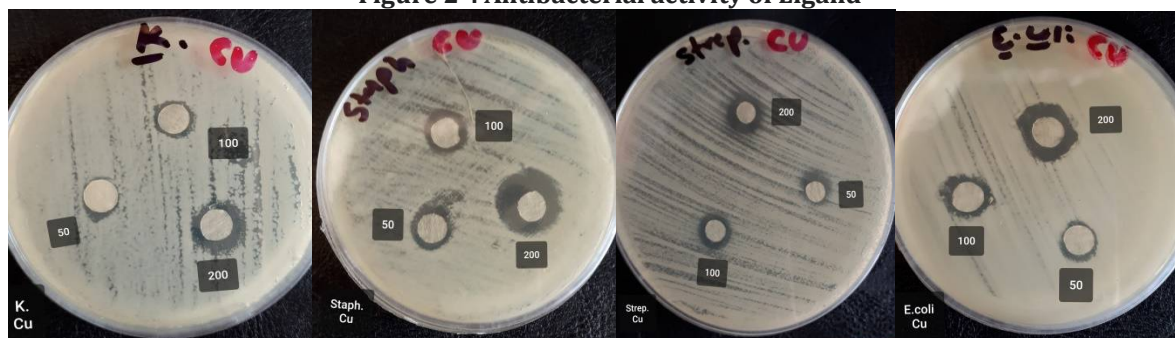
synthesized compounds were dissolved in Dimethyl sulfoxide (DMSO) solvent and recommended concentrations (50, 100 and 200 µg/mL). For all of the bacteria studied, petri plates containing 20 mL Mueller Hinton Agar were utilized. On the Petri plates were inserted sterile Whatman no. 1 filter paper disks (6mm in diameter) impregnated with the test solution in DMSO. In the case of bacteria, the plates were incubated at 37°C for 24 hours. The results of the antibacterial assays are given in Figures 2-5 and Table 1. The test compounds give good or moderate antibacterial activity against all the tested strains. The Cu complex 2 showed activity against all chosen microorganism aforementioned, despite the fact that compound 2 being inefficient with *staphylococcus*.

**Table 1: Antibacterial activity of Schiff base and complexes compounds 1-4**  
inhibition zone diameters were measured in millimeters

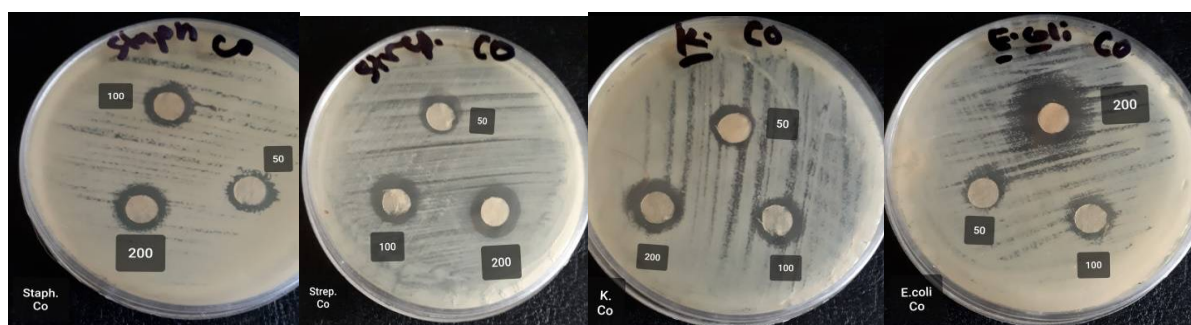
Bacteria types	Zone inhibition of antimicrobial sensitivity test of compounds (mm)											
	ligand			Cu complex			Pd complex			Co complex		
concentration µg/L	50	100	200	50	100	200	50	100	200	50	100	200
<i>K. pneumonia</i>	6	12	13	7	8	10	10	14	16	8	11	12
<i>E. coli</i>	8	12	14	8	9	12	7	14	18	8	10	15
<i>S. aureus</i>	7	8	11	9	10	13	9	10	18	9	10	10
<i>Streptococcus.uberis</i>	7	12	14	8	10	13	10	12	14	9	10	12



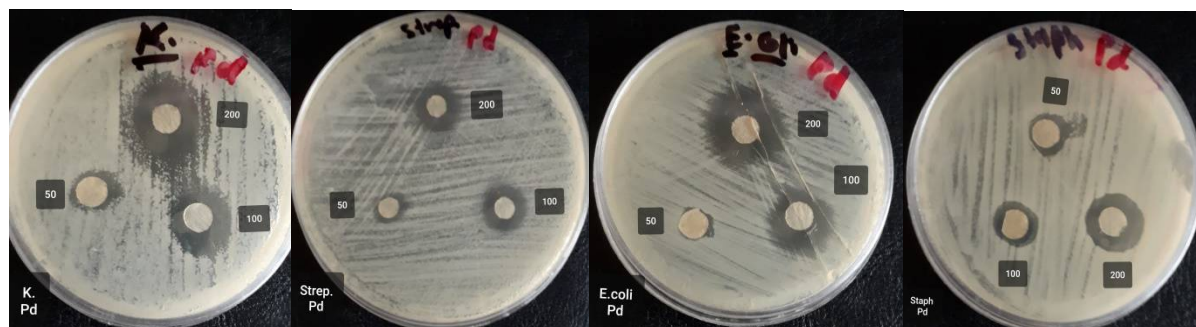
**Figure 2 : Antibacterial activity of Ligand**



**Figure 3 : Antibacterial activity of Cu(II) complex**



**Figure 4 : Antibacterial activity of Co(II) complex**



**Figure 5 : Antibacterial activity of Pd(II) complex**

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