



# Synthesis, physicochemical and *in-vitro* antibacterial properties of some novel metal(II) complexes of 3-[[[(6-methoxyppyridin-3-yl)imino]methyl]naphthalen-2-ol

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The tridentate Schiff base, 3-[[[(6-methoxyppyridin-3-yl)imino]methyl]naphthalen-2-ol, formed by condensation of 5-amino-2-methoxyppyridine and 2-hydroxy-1-naphthaldehyde coordinates to some Metal(II) ions, forming complexes of the type  $[M(L_2)]\frac{1}{2}H_2O$  {where M = Mn, Co, Ni, Cu, Zn, Pd}. These complexes are characterized by percentage metal, melting point, conductance measurements, electronic and IR spectroscopies. The IR data confirms that coordination is via the imine nitrogen and naphthalenol oxygen atoms; while electronic data support a 4-coordinate tetrahedral/squareplanar geometry for the metal complexes. The complexes are air-stable solids which melt/decompose on heating in the temperature range 196-232°C; and none is an electrolyte in nitromethane. The *in-vitro* antibacterial activities of the complexes against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella oxytoca* are reported. Notably, the Pd(II) complex exhibits broad-spectrum antibacterial activity against these bacteria with the exception of *Pseudomonas aeruginosa* with inhibitory zones range in the range 8.0-12.0 mm.

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**Introduction**

Schiff bases have received great attention from scientists worldwide including our research group due to their ease of synthesis, as precursors in metal-organic chemical vapor depositions (MOCVD), and as catalysts in various reactions [1-6]. Moreover, (chloropyridinyl) thiazolidine Schiff bases have potent antifungal activities against *Candida albicans* which are comparable with the renowned drug griseofulvin [7]; and various (methoxyphenyl)-3-chloroazetidin-2-one have good antihelmintic activity against the earthworm *Perituma posthuma* [8]. Furthermore, the Schiff base (N,N-dimethyl-N'(2-pyridyl)ethylenediamine picrate is a histamine antagonist [9], while (pyridinyl)methylthio-4H-triazole Schiff base induced apoptosis in human hepatocarcinoma cell SMMC-7721 [10]. Detailed literature search shows that the Schiff base derived from the condensation of 2-hydroxy-1-naphthaldehyde and 5-amino-2-methoxyppyridine, 3-[[[(6-methoxyppyridin-3-yl)imino]methyl]naphthalen-2-ol, and its metal chelates have not yet been reported [1-15]. Thus, the aim of this work is to synthesize, characterize and investigate the electronic and antibacterial properties of the Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and Pd(II) complexes of the Schiff base, 3-[[[(6-methoxyppyridin-3-yl)imino]methyl]naphthalen-2-ol; for a better understanding of geometries and its probable use as active ingredients in surface cleaning agents. These metal complexes and its ligand are new, being reported here for the first time.

**Experimental details****Materials and Physical Measurements**

Reagent grade 2-hydroxy-1-naphthaldehyde, 5-amino-2-methoxyppyridine, manganese(II) nitrate hexahydrate, cobalt(II) nitrate hexahydrate, nickel(II) nitrate hexahydrate, copper(II) nitrate hexahydrate, zinc(II) nitrate hexahydrate and palladium(II) chloride were purchased from BDH and Aldrich

chemicals and were used as received. Solvents were distilled and dried before use according to standard procedures. Melting points (uncorrected) were determined using the Stuart scientific melting point SMP1 machine and conductivities of  $10^{-3}$  M solutions of the complexes were measured in nitromethane at 25°C using a HANNA HI 991300 conductivity meter. The solid reflectance spectra were recorded on a Perkin-Elmer  $\lambda$ 20 spectrophotometer, while infrared spectra were measured as KBr discs on a Perkin-Elmer FTIR paragon 1000 spectrometer in the range 4000-400  $cm^{-1}$ . The percentage manganese, cobalt, nickel, copper, zinc and palladium were determined titrimetrically [16].

**Preparation of 3-[[[(6-methoxyppyridin-3-yl)imino]methyl]naphthalen-2-ol**

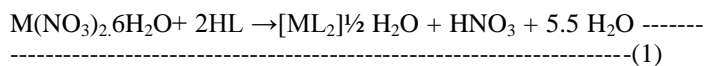
A 20 mL solution of  $1.2 \times 10^{-2}$  mol (1.44 g) 5-amino-2-methoxyppyridine in absolute ethanol, was added drop wise to a stirring solution of  $1.2 \times 10^{-2}$  mol (2.0 g) of 2-hydroxy-1-naphthaldehyde in 40 mL of absolute ethanol. The resulting yellow-colored solution was refluxed for 4 h after the addition of 4 drops of acetic acid. The yellow product formed on cooling to room temperature was filtered, and recrystallized from ethanol. The yield of the title compound was 2.34 g (70%).

**Preparation of the metal (II) complexes**

The various complexes were prepared by gradual addition of 0.54 mmol (0.10-0.16 g)  $M(NO_3)_2 \cdot 6H_2O$  {M = Mn, Co, Ni, Cu, Zn} neat to a stirring 1.08 mmol (0.3 g) of the ligand in 30 mL of absolute ethanol. The resulting solutions were then buffered with 1.08 mmol (0.11 g) of triethylamine and refluxed for 6 h during which the products formed. The precipitated solids were filtered, washed with ethanol and dried over anhydrous calcium chloride.

**Results and Discussion**

The generalised equation for the formation of the complex is:



{where M = Zn(II), Cu(II), Mn(II), Co(II), Ni(II)}.



All the complexes adopt  $[ML_2] \cdot \frac{1}{2} H_2O$  stoichiometry, with the exception of the Pd(II) complex which is anhydrous. Proposed structures for the ligand and the metal(II) complexes are provided in Figure 1. The formation of this ligand is confirmed by IR spectroscopy. The colors, melting points and conductance values are presented in Table 1. The molar conductances of the complexes are in the range  $10.0-22.0 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$  in nitromethane, proving their covalent nature. A value in the range  $60-115 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$  is expected for a 1:1 electrolyte [17].

#### Infrared spectra

The relevant infrared bands of the compounds are presented in Table 2. The strong band at  $3435 \text{ cm}^{-1}$  in the ligand, which is conspicuously absent in the spectra of the metal(II) Schiff base complexes is assigned as  $\nu\text{OH}$  stretching frequency; and it confirms the involvement of the naphthalenol O in chelation [1]. The new broad band at  $3500 \text{ cm}^{-1}$  in the spectra of all the complexes with the exception of the Pd(II) complex is assigned to the  $\nu\text{OH}$  frequency of crystallization  $H_2O$ . The uncoordinated  $C=N$  and  $C=C$  stretching vibrations, are expectedly coupled between  $1657-1424 \text{ cm}^{-1}$  in the ligand [11-12], and are hypsochromic shifted to  $1660-1425 \text{ cm}^{-1}$  in the metal complexes. This is an indication of the involvement of N atom of  $C=N$  in coordination to the metal ions. Further evidence of coordination is the appearance of bands due to  $\nu(M-O)$  and  $\nu(M-N)$  at  $470-402$  and  $598-513 \text{ cm}^{-1}$  respectively, these bands are absent in the ligand [7].

#### Electronic spectra

The electronic spectral data for the complexes are presented in Table 2. The Mn(II) Schiff base complex, shows two absorption bands at 18.80 and 21.05 kK respectively, consistent with a four-coordinate, tetrahedral geometry and are assigned to  ${}^6A_1 \rightarrow {}^4E_1 (\nu_1)$  and  ${}^6A_1 \rightarrow {}^4A_1 (\nu_2)$  transitions [18]. The cobalt(II) Schiff base complex gives an absorption band at 15.13 and a shoulder at 18.20 kK indicative of a four coordinate tetrahedral geometry and are assigned to  ${}^4A_2 \rightarrow {}^4T_1(P) (\nu_2)$  and  ${}^4A_2 \rightarrow {}^4T_1(P) (\nu_3)$ . The transition  ${}^4A_2 \rightarrow {}^4T_2 (\nu_1)$  in the range 5-7 kK is not observed as usual since it lies in the infrared region [19]. Nickel(II) complexes are known to exhibit complicated equilibria between coordination numbers six (octahedral) to four (square planar/tetrahedral). The Ni(II) Schiff base complex, exhibits two absorption bands at 16.05 and 20.70 kK typical of a 4-coordinate tetrahedral geometry assigned to  ${}^3T_1(F) \rightarrow {}^3T_2 (\nu_2)$  and  ${}^3T_1(F) \rightarrow {}^3A_2 (\nu_3)$  transitions [20].

The copper(II) complex, displays a single band at 14.71 kK assigned to  ${}^2T_2 \rightarrow {}^2E_2$  transition of 4-coordinate, distorted tetrahedral geometry [13].

The Zn(II) complex expectedly shows only charge transfer transition from  $M \rightarrow L$  as no d-d transition, is expected at 20.79 kK indicative of tetrahedral geometry [20]; while the Pd(II) complex shows an absorption band at 20.83 kK and a shoulder at 19.23 kK, typical of square planar geometry and are assigned to  ${}^1A_{1g} \rightarrow {}^1B_{1g}$  and  ${}^1A_{1g} \rightarrow {}^1E_{2g}$  transitions [15].

In the absence of room temperature magnetic moment measurements and suitable crystals for single X-ray structural determination, the assignment of geometry is tentative. The ligand bands are three bands at 26.29, 27.67 and 40.32 kK respectively assigned to  $n-\pi^*$ ,  $\pi-\pi^*$  and Charge transfer

transitions. These bands are bathochromic/hypsochromic shifted in the metal complexes to 26.22 -26.39, 27.48-32.90 and 40.16-40.33 kK due to coordination [1].

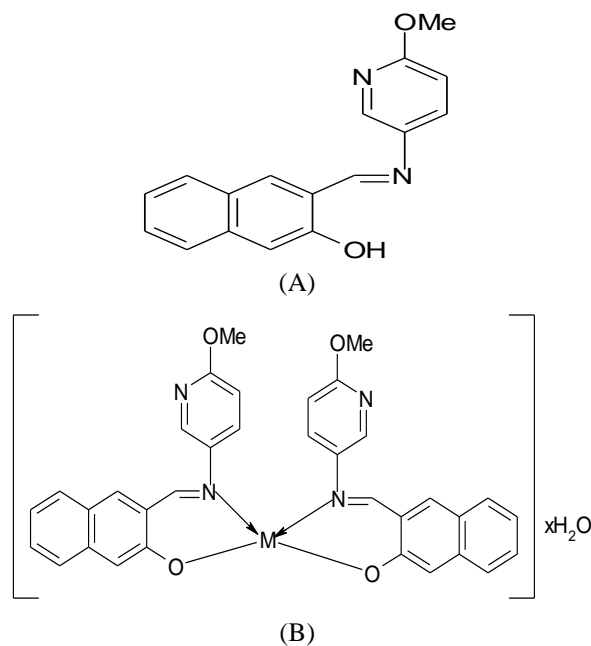


Figure 1: Proposed structure for the ligand (A) and its metal(II) complexes (B)

#### Antibacterial activities

The antimicrobial activities are presented in Table 3 and shown in Figure 2. The ligand and its metal complexes are not active against *P. aeruginosa*. The Pd(II) complex is the only one that is active against *S. aureus*. The resistance of *P. aeruginosa* to all the compounds is attributed to a concerted action of multidrug efflux pumps, and the low permeability of the bacterial cellular envelopes [22]; while the resistance of *S. aureus* has been attributed to the production of  $\beta$ -lactamase which inactivates the compounds [23].

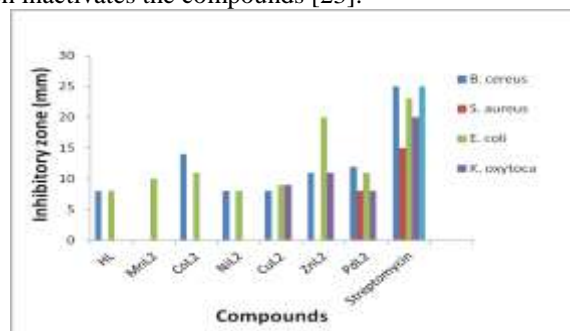


Figure 2: The comparative antibacterial activities of the complexes with the Streptomycin

Furthermore, *Klebsiella oxytoca* is sensitive to the Cu(II), Zn(II) and Pd(II) complexes, whereas it is resistant to the ligand and its Mn(II), Co(II) and Ni(II) complexes due to the production of extended-spectrum beta-lactamases (ESBL), which inactivates these compounds [24]. *E. coli* is sensitive to the ligand and all the metal complexes. The activities of the metal complexes are greater than that of the ligand and is in the range 9.0-20.0 mm except for the Ni(II) complex which has the same activity of 8.0 mm as the ligand, and the metal complexes are generally more active than the ligand. This is attributed to the chelation theory, which states that chelation increases antimicrobial activity, because of partial sharing of its positive charge with donor groups of the ligand and possible  $\pi$ -electron

delocalisation which increased the lipophilic character [25]. Similarly, *B. cereus* is sensitive to the ligand and its metal complexes exception for the Mn(II) complex. i.e. the Ni(II) and Cu(II) complexes have same activity of 8.0 mm as the ligand, while the Zn(II), Pd(II) and Co(II) complexes have higher activities of 11.0, 12.0 and 14.0 mm respectively. In all cases, the antibiotic (streptomycin) is more active than the metal complexes (8.0-20.0 mm) with an inhibitory zone range of 15.0-25.0 mm expectedly. The Zn(II) complex has the best activity against *E. coli* with inhibitory zone of 20.0 mm which is 80% that of streptomycin, and the Pd(II) complex exhibits broad-spectrum antibacterial activity against *B. cereus*, *S. aureus*, *E. coli* and *K. oxytoca* with inhibitory zones range of 8.0-12.0 mm, proving its usefulness as a broad-spectrum antibacterial agent.

### Conclusion

The tridentate Schiff-base ligand coordinates to the Mn(II), Ni(II), Co(II), Cu(II), Pd(II) and Zn(II) ions in a tetradentate manner using the azomethine N<sub>2</sub>O<sub>2</sub> chromophores. The assignment of a 4-coordinate tetrahedral/square-planar geometry to metal(II) complexes is corroborated by infrared and electronic spectral measurements. The complexes are non-electrolyte in nitromethane. The antibacterial studies show that the ligand and its metal(II) complexes are active against *E. coli* with inhibitory zones range of 8.0-20.0 mm, and the Pd(II) complex exhibits broad-spectrum antibacterial activity against *B. cereus*, *S. aureus*, *E. coli* and *K. oxytoca* with inhibitory zones range of 8.0- 12.0 mm.

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**Table 1 Analytical data for the ligand and its complexes**

Compound (Empirical formula)	Formula mass	Color	% Yield	$\Lambda_m^*$	M.p (°C)	%Metal (Calc.)
HL	278.30	Yellow	80	-	142-144	-
[MnL <sub>2</sub> ] $\frac{1}{2}$ H <sub>2</sub> O	618.54	Green	70	16.0	196	8.79 (8.88)
[CoL <sub>2</sub> ] $\frac{1}{2}$ H <sub>2</sub> O	622.53	Peach	70	11.0	230 <sup>a</sup>	9.43 (9.47)
[NiL <sub>2</sub> ] $\frac{1}{2}$ H <sub>2</sub> O	622.31	Greenish Yellow	70	15.0	200 <sup>a</sup>	9.39 (9.43)
[CuL <sub>2</sub> ] $\frac{1}{2}$ H <sub>2</sub> O	627.15	Brown	70	10.0	210 <sup>a</sup>	9.97 (10.13)
[ZnL <sub>2</sub> ] $\frac{1}{2}$ H <sub>2</sub> O	628.63	Yellow	70	18.0	230-232	10.46 (10.39)
[PdL <sub>2</sub> ]	660.99	Brownish yellow	70	22.0	220 <sup>a</sup>	16.07 (16.10)

$\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ , a = decomposition temperature, Calc = calculated

**Table 2 Relevant infrared and electronic spectral data of the ligand and its complexes**

Compound	$\nu_{\text{OH}}$	$\nu(\text{C}=\text{N}) + \nu(\text{C}=\text{C})$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{O})$	Electronic transitions (kK)
HL	3435s	1657s 1424s	-	-	27.67, 26.29, 40.32
$[\text{Mn}(\text{L}_2)] \frac{1}{2}\text{H}_2\text{O}$	3500b	1659s 1425s	585m 532s	440m 410s	18.80, 21.05, 26.28, 27.93, 31.37.
$[\text{Co}(\text{L}_2)] \frac{1}{2}\text{H}_2\text{O}$	3500b	1659s 1425s	570s 527m	465m 405m	15.13, 18.87, 26.39, 27.70, 32.90, 40.16
$[\text{Ni}(\text{L}_2)] \frac{1}{2}\text{H}_2\text{O}$	3500b	1660s 1426s	585s 532s	450s 443s	16.05, 20.70, 26.25, 40.16
$[\text{Cu}(\text{L}_2)] \frac{1}{2}\text{H}_2\text{O}$	3500b	1658s 1427s	578s 519s	455s 402s	14.71, 26.29, 27.67, 40.32
$[\text{Zn}(\text{L}_2)] \frac{1}{2}\text{H}_2\text{O}$	3500b	1658s 1425s	550s 532m	470m 405m	20.79, 28.01, 40.16
$[\text{Pd}(\text{L}_2)]$	-	1659s 1425s	598m 513m	450m 420m	19.23, 20.83, 26.22, 27.48, 31.45, 40.16

Key: b = broad, m = medium, s = strong., 1kK = 1000 $\text{cm}^{-1}$

**Table 3 Zones of inhibition (mm) of the compounds against various bacteria isolates**

Complexes/ Organisms	HL	$[\text{MnL}_2]$	$[\text{CoL}_2]$	$[\text{NiL}_2]$	$[\text{CuL}_2]$	$[\text{ZnL}_2]$	$[\text{PdL}_2]$	Streptomycin
<i>B. cereus</i>	8.0±0	R	14.0±0.7	8.0±0.7	8.0±1.4	11.0±0	12.0±0.7	25.0±2.1
<i>S. aureus</i>	R	R	R	R	R	R	8.0±0	15.0±0.7
<i>E. coli</i>	8.0±0.7	10.0±0.7	11.0±0	8.0±0	9.0±0.7	20.0±1.4	11.0±0.7	23.0±1.6
<i>K. oxytoca</i>	R	R	R	R	9.0±0.7	11.0±0.7	8.0±1.0	20.0±1.4
<i>P. aeruginosa</i>	R	R	R	R	R	R	R	25.0±0.7

R= resistance