

Research Article

Synthesis, Characterization and Antibacterial Activity of Schiff Base, 4-Chloro-2-{(E)-[(4-Fluorophenyl)imino]methyl}phenol Metal (II) Complexes

F. K. Ommenya ^(b),¹ E. A. Nyawade,¹ D. M. Andala,² and J. Kinyua³

¹Department of Chemistry, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000, Nairobi 00200, Kenya ²Department of Chemistry, Multimedia University of Kenya, P.O. Box 15653, Nairobi 00503, Kenya ³Department of Biochemistry, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000, Nairobi 00200, Kenya

Correspondence should be addressed to F. K. Ommenya; ommenya@gmail.com

Received 18 November 2019; Revised 14 February 2020; Accepted 20 February 2020; Published 30 March 2020

Academic Editor: Marcelino Maneiro

Copyright © 2020 F. K. Ommenya et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

A new series of Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes of the Schiff base ligand, 4-chloro-2-{(E)-[(4-fluorophenyl) imino]methyl}phenol (C_{13} H₉ClFNO), was synthesized in a methanolic medium. The Schiff base was derived from the condensation reaction of 5-chlorosalicylaldehyde and 4-fluoroaniline at room temperature. Elemental analysis, FT-IR, UV-Vis, and NMR spectral data, molar conductance measurements, and melting points were used to characterize the Schiff base and the metal complexes. From the elemental analysis data, the metal complexes formed had the general formulae [M(L)₂(H₂O)₂], where L = Schiff base ligand (C_{13} H₉ClFNO) and M = Mn, Co, Ni, Cu, and Zn. On the basis of FT-IR, electronic spectra, and NMR data, "O" and "N" donor atoms of the Schiff base ligand participated in coordination with the metal (II) ions, and thus, a six coordinated octahedral geometry for all these complexes was proposed. Molar conductance studies on the complexes indicated they were nonelectrolytic in nature. The Schiff base ligand and its metal (II) complexes were tested *in vitro* to evaluate their bactericidal activity against Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and Gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus typhi*) using the disc diffusion method. The antibacterial evaluation results revealed that the metal (II) complexes exhibited higher antibacterial activity than the free Schiff base ligand.

1. Introduction

The chemistry of metal complexes with Schiff base ligands containing oxygen and nitrogen as donor atoms has continued to attract the attention of researchers. These ligands are known to coordinate to metal atom in different ways under different reaction conditions. The ligands are derived from the condensation reaction of aldehydes and primary amines [1].

One of the major areas of research on the Schiff base metal complexes is their biological activity with the main aim being the discovery of safe and effective therapeutic agents for the treatment of bacterial infections and cancers. A number of Schiff base metal complexes have a diverse spectrum of biological and pharmaceutical activities. For instance, transition metal complexes of Schiff base ligands bearing "O" and "N" donor atoms are very important because of their biological properties such as antibacterial, antifungal, anti-inflammatory [2], analgesic [3, 4], anticonvulsant [5], antitubercular [6], antioxidant [7], and anthelmintic [8]. The Schiff base transition metal complexes have also been used as biological models to understand the structure of biomolecules and biological processes [9].

Manganese, cobalt, nickel, copper, and zinc are life-essential metallic elements and exhibit greater biological activity when associated with certain metal protein complexes, participating in oxygen transport, electronic transfer reactions, or the storage of ions [10]. This has created enormous interest in the study of systems containing these metals.

Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes of the Schiff base, 4-chloro-2-{(E)-[(4-fluorophenyl)imino] methyl}phenol, which to the best of our knowledge has neither been synthesized nor antibacterial activities carried out, was studied in our laboratories. The antibacterial activity of the new Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) complexes of the Schiff base ligand, 4-chloro-2-{(E)-[(4fluorophenyl)imino]methyl}phenol (C₁₃H₉ClFNO) has been investigated and is now reported in this article. The antibacterial evaluation results revealed that the metal complexes, with a proposed six coordinated octahedral geometry, exhibited higher antibacterial activity than the free Schiff base ligand against Gram-negative bacteria (E. coli and P. aeruginosa) and Gram-positive bacteria (B. subtilis and S. typhi).

2. Experimental Section

2.1. Materials and Methods. The chemicals and solvents used in this research work were of analytical grade sourced from Sigma Chemicals Company. Synthesis of Schiff base ligand was carried out in pure solvent using standard literature methods [11]. Melting points were recorded on a Gallenkamp apparatus and are uncorrected. FT-IR spectra of synthesized compounds (in a KBr matrix) were recorded in the 4000-400 cm⁻¹ region on a SHIMADZU FTIR-8400 spectrophotometer. The ¹H NMR and ¹³C NMR spectra of the Schiff base ligand and its diamagnetic metal (II) complexes were recorded in deuterated DMSO on a Bruker Avance III HD Nanobay 400 MHz NMR spectrometer equipped with a 5 mm BBO probe at room temperature. Tetramethylsilane was used as an internal standard, and chemical shift is given in δ . Elemental analysis (C, H, and N%) was recorded on a LECO CNHS-932 microanalyzer. The electronic spectra of the synthesized compounds were recorded on a AOE Instruments UV-1800 PC spectrophotometer in the 200-800 nm range, with a quartz cuvette (path length, 1 cm) and studies performed in HPLC grade acetonitrile. Conductivity measurements of the Schiff base ligand and its metal (II) complexes were carried out on a SIBATA Conductivity meter Model SC-17A, at room temperature. A mass spectrum was recorded on a Shimadzu GCMS QP 2010SE spectrometer.

The synthesized compounds were screened *in vitro* for their antibacterial activities against *E. coli*, *P. aeruginosa*, *B. subtilis*, and *S. typhi* using the disc diffusion method [12].

2.2. Synthesis of Schiff Base Ligand, L. The Schiff base ligand (L) (Scheme 1) was prepared according to literature methods with a few modifications [11].

4-fluoroaniline (0.3549 g; 3.19 mmol) was added to a 30 mL magnetically stirred ethanolic solution of 5-chlorosalicylaldehyde (0.5000 g; 3.19 mmol) in a 50 mL roundbottomed flask at room temperature. Two drops (0.2 mL) of glacial acetic acid was added to the mixture, to adjust its pH to ~6, upon which a thick yellow orange precipitate formed instantly. The precipitate was separated by filtration and purified by recrystallization from ethanol. Shiny, needle-like vellow-orange crystals were formed. The crystals were washed with cold ethanol and diethyl ether to remove unreacted amine and aldehyde. The crystals were dried in air. Yield: 92.0%, 0.7336 g, colour: yellow orange, $m.p = 133 - 135^{\circ}C,$ and molar conductance $(\Lambda) =$ $5 \text{ Ohm}^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$. Elemental analysis data for C₁₃H₉ClFNO (FW = 249.67) found: C, 62.63%; H, 3.59%; N, 5.50% calculated: C, 62.48%; H, 3.60%; N, 5.61%. FT-IR (KBr, disc cm⁻¹) 3386.4 v(O-H), 1601.0 v(HC=N), 1277.0 v(C-O). UV-Vis (acetonitrile) λ_{max} (nm) 225.3, 269.1, and 345.1. ¹H NMR (ppm d_6 -DMSO, 400 MHz): δ 8.92 (s, 1H, CH=N), 12.85 (s, 1H, OH), 7.43–7.49 (m, 7ArH). ¹³C NMR (ppm d₆-DMSO): 123-117 (Ar, C=C), 163 (HC=N), 133(C-O). MS: m/z 249 [M⁺ + 1].

2.3. Synthesis of the Schiff Base Metal (II) Complexes, C. The Schiff base metal (II) complexes (C) (Scheme 1) were prepared by reacting the Schiff base with the metal (II) ions as per the literature methods [11].

A solution of hydrated metal (II) chloride (0.1 mmol) in 10 mL hot methanol at 50°C was added dropwise to a solution of the Schiff base ligand (L) (0.2 mmol) in 20 mL of hot methanol at 50°C in a 50 mL round-bottomed flask. The resulting mixture was magnetically stirred and refluxed for 3 hours on an oil bath at 65°C whereupon a precipitated product formed. The precipitate was separated by filtration and washed with methanol, hot ethanol, and diethyl ether to remove unreacted Schiff base and metal (II) salt chloride.

2.3.1. Manganese (II) Complex, C1. Yield: 65.03%, 0.0383 g, colour: grey, m.p > 350°C, and molar conductance (Λ) = 21 Ohm⁻¹·cm²·mol⁻¹. Elemental analysis data for C₂₆H₂₀Cl₂F₂MnN₂O₄ (FW = 588.28) found: C, 53.08%; H, 3.43%; N, 4.72% calculated: C, 53.04%; H, 3.40%; N, 4.76%. FT-IR (KBr, disc cm⁻¹) 3423.0 v(O-H), 1596.2 v(HC=N), 1212.7 v(C-O), 697.0 v(H₂O), 526.6 v(Mn-N), 489.1 v(Mn-O). UV-Vis (acetonitrile) λ_{max} (nm) 221.4, 251.8, and 342.1.

2.3.2. Cobalt (II) Complex, C2. Yield: 70.99%, 0.4210 g, colour: dark brown, m.p > 350°C, and molar conductance $(\Lambda) = 19 \text{ Ohm}^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$. Elemental analysis data for $C_{26}H_{20}Cl_2F_2CoN_2O_4$ (FW = 592.27) found: C, 52.69%; H, 3.35%; N, 4.88% calculated: C, 52.68%; H, 3.38%; N, 4.73%. FT-IR (KBr, disc·cm⁻¹) 3427.1 v(O-H), 1597.4 v(HC=N), 1213.3 v(C-O), 692.6 v(H_2O), 530.6 v(Co-N), 488.3 v(Co-O). UV-Vis (acetonitrile) λ_{max} (nm) 249.1 and 401.9.

2.3.3. Nickel (II) Complex, C3. Yield: 61.05%, 0.0362 g, colour: red brown, m.p > 350°C, and molar conductance (Λ) = 20 Ohm⁻¹·cm²·mol⁻¹. Elemental analysis data for C₂₆H₂₀Cl₂F₂NiN₂O₄ (FW = 592.03) found: C, 52.68%; H, 3.36%; N, 4.70% calculated: C, 52.70%; H, 3.38%; N, 4.73%. FT-IR (KBr, disc cm⁻¹) 3415.7 v(O-H), 1595.7 v(HC=N), 1210.8 v(C-O), 697.9 v(H₂O), 526.4 v(Ni-N), 489.2 v(Ni-O). UV-Vis (acetonitrile) λ_{max} (nm) 245.2, 325.1 and 421.9. ¹H NMR (ppm *d*₆-DMSO, 400 MHz): δ 8.87 (s, 1H, CH=N),



Where M = Mn(II), Co(II), Ni(II), Cu(II) and Zn(II)

SCHEME 1: Synthesis of Schiff base ligand metal (II) complexes.

7.12–7.15 (m, 7ArH); ¹³C NMR (ppm d_6 -DMSO): 122–118 (Ar, C=C), 162 (HC=N), 132(C-O).

2.3.4. Copper (II) Complex, C4. Yield: 73.91%, 0.0442 g, colour: brown, m.p > 350°C, and molar conductance (Λ) = 16 Ohm⁻¹·cm²·mol⁻¹. Elemental analysis data for C₂₆H₂₀Cl₂F₂CuN₂O₄ (FW = 596.89) found: C, 52.21%; H, 3.34%; N, 4.65% calculated: C, 52.27%; H, 3.35%; N, 4.69%. FT-IR (KBr, disc cm⁻¹) 3446.6 v(O-H), 1597.1 v(HC=N), 1214.7 v(C-O), 694.8 v(H₂O), 530.1 v(Cu-N), 488.7 v(Cu-O). UV-Vis (acetonitrile) λ_{max} (nm) 229.1, 266.1 and 349.7.

2.3.5. Zinc (II) Complex, C5. Yield: 63.11%, 0.0378 g, colour: light yellow, m.p = 265–268°C, and molar conductance (Λ) = 19 Ohm⁻¹·cm²·mol⁻¹. Elemental analysis data for C₂₆H₂₀Cl₂F₂ZnN₂O₄ (FW = 598.73) found: C, 52.09%; H, 3.30%; N, 4.64% calculated: C, 52.11%; H, 3.34%; N, 4.68%. FT-IR (KBr, disc cm⁻¹) 3417.2 v(O-H), 1596.6 v(HC=N), 1214.3 v(C-O), 699.7 v(H₂O), 527.8 v(Zn-N), 489.7 v(Zn-O). UV-Vis (acetonitrile) λ_{max} (nm) 223.4, 303.2 and 343.9. ¹H NMR (ppm *d*₆-DMSO, 400 MHz): δ 8.55 (s, 1H, CH=N), 7.18–7.39 (m, 7ArH); ¹³C NMR (ppm *d*₆-DMSO): 124–116 (Ar, C=C), 162 (HC=N), 125(C-O).

2.4. Biological Assay. The synthesized ligand and its transition metal (II) complexes were screened in vitro for their antibacterial activities against E. coli, P. aeruginosa, B. subtilis, and S. typhi bacterial strains using the disc diffusion method [11, 13]. The disc diffusion method was used because of its convenience, efficiency, and low cost. The stock solutions (1 mgmL^{-1}) of the ligand and its metal complexes were prepared by dissolving 20 mg of the test compound in 20 mL of dimethyl sulfoxide (DMSO) solvent. From this stock solution, concentrations of 10, 20, 30, and $40 \,\mu gmL^{-1}$ were prepared by dilution with DMSO. The solvent (DMSO) was used as control for each dilution. The bacteria were subcultured in an agar nutrient medium. Standard antibacterial drugs (Amoxyclav, Nalidixic acid, and Gentamicin) were used as positive controls for comparison with the ligand and the synthesized metal complexes. Whatman filter paper (no. 1) discs of 7 mm diameter were sterilized in an autoclave and then soaked in the desired concentration of the synthesized compounds. The paper discs were placed aseptically in the petri dishes containing nutrient agar media seeded with *E. coli*, *P. aeruginosa*, *B. subtilis*, and *S. typhi* separately and then incubated for 24 hours at 37°C. The diameters of the zones of inhibition were measured after 24 hours of incubation. The antibacterial activities were calculated as mean \pm SD of three replicates (Table 1). The zones of inhibition (Figures 1 and 2) were measured using a Vernier caliper in millimeters (mm), and the following criteria were applied [12]; low activity (1–7 mm), moderate activity (7–10 mm), high activity (11–15 mm), very high activity (≥16), and no activity (0).

3. Results and Discussion

The Schiff base ligand in this study was first synthesized by Feng [14] using the reflux method. In this research, however, the ligand was prepared using the room temperature method which afforded a higher yield. The metal (II) complexes of the ligand are new and thus reported for the first time. The Schiff base ligand is soluble in hot ethanol and solvents such as DMF and DMSO. The imine and its metal (II) complexes are coloured solids which are stable in air. The complexes were insoluble in common organic solvents such as methanol, dichloromethane, ethanol, and acetone but soluble in DMSO and DMF.

The melting points of the complexes were higher than that of the Schiff base ligand indicating that the complexes are more stable than the ligand. The chemical equations showing the preparation of the Schiff base ligand and its metal (II) complexes are represented in Scheme 1.

3.1. Conductivity Measurements. The molar conductance values of the synthesized compounds in 10^{-3} M DMSO were measured at room temperature. The conductance values of the synthesized compounds were below 50 Ohm⁻¹·cm²·mol⁻¹, indicating their nonelectrolytic nature [15, 16]. This suggested that there were no anions present outside the coordination sphere of the complexes.

3.2. Electronic Spectral Analysis. The electronic spectral data of the Schiff base ligand and its metal (II) complexes are given in the experimental section. The Schiff base ligand

Zone of inhibition in mm* against bacterial strains					
Sample	Conc. (µg/mL)	Gram-positive		Gram-negative	
		E. coli	P. aeruginosa	B. subtilis	S. typhi
L	10	7.3 ± 0.5	8.4 ± 0.5	7.7 ± 0.9	8.4 ± 0.5
	20	7.5 ± 0.5	8.7 ± 0.5	7.9 ± 0.9	8.6 ± 0.5
	30	7.7 ± 0.5	8.9 ± 0.8	8.5 ± 0.8	8.8 ± 0.5
	40	8.0 ± 0.5	10.0 ± 0.8	9.0 ± 0.8	8.9 ± 0.5
$[Mn(L)_2(H_2O)_2]$	10	8.1 ± 0.5	10.7 ± 0.8	9.7 ± 0.5	9.3 ± 0.5
	20	8.6 ± 0.5	11.0 ± 0.8	10.3 ± 0.8	9.6 ± 0.5
	30	8.9 ± 0.5	12.±0.5	10.9 ± 0.5	9.8 ± 0.5
	40	9.7 ± 0.5	14.7 ± 0.5	11.7 ± 0.5	10.2 ± 0.5
$[\mathrm{Co}(\mathrm{L})_2(\mathrm{H}_2\mathrm{O})_2]$	10	9.0 ± 0.9	9.7 ± 1.2	8.3 ± 0.5	9.4 ± 1.2
	20	9.2 ± 0.8	10.7 ± 1.4	8.9 ± 0.9	9.7 ± 0.5
	30	9.8 ± 0.5	11.3 ± 1.2	9.3 ± 0.5	11.0 ± 0.8
	40	10.0 ± 0.8	12.0 ± 0.8	10.2 ± 0.5	11.7 ± 0.5
[Ni(L) ₂ (H ₂ O) ₂]	10	9.5 ± 0.8	11.3 ± 0.5	9.7 ± 0.5	8.6 ± 0.5
	20	10.0 ± 0.8	11.8 ± 0.5	9.9 ± 0.5	8.8 ± 0.5
	30	10.4 ± 0.8	12.4 ± 0.5	10.8 ± 0.5	9.0 ± 0.8
	40	11.3 ± 0.9	12.7 ± 1.2	11.0 ± 0.8	9.3 ± 0.8
$[Cu(L)_2(H_2O)_2]$	10	8.1 ± 0.8	10.3 ± 1.2	8.6 ± 0.5	8.7 ± 0.5
	20	8.3 ± 0.5	10.6 ± 1.2	9.3 ± 0.5	8.9 ± 0.5
	30	8.6 ± 0.5	10.9 ± 1.2	10.0 ± 0.8	9.3 ± 0.5
	40	8.9 ± 0.9	11.7 ± 1.2	10.7 ± 0.5	9.6 ± 0.5
$[Zn(L)_2(H_2O)_2]$	10	7.6 ± 0.9	10.0 ± 0.5	8.4 ± 0.9	10.1 ± 0.9
	20	7.8 ± 0.5	10.4 ± 1.4	8.9 ± 0.9	10.3 ± 0.9
	30	8.1 ± 0.5	10.9 ± 1.2	9.7 ± 0.5	11.0 ± 1.2
	40	8.3 ± 0.5	11.4 ± 0.8	9.9 ± 0.9	11.6 ± 1.4
Amoxyclav (AMC)		8.0 ± 0.0			
Nalidixic acid (NA)		12.0 ± 1.0	20.0 ± 2.0	13.0 ± 1.0	30.5 ± 0.5
Gentamicin (GEN)		9.0 ± 0.0	14.0 ± 0.0	9.5 ± 0.5	10.5 ± 1.5

TABLE 1: Antibacterial screening data for the Schiff base ligand and its metal (II) complexes at concentrations of 10, 20, 30, and 40 µg/mL.

L =Schiff base ligand, 4-chloro-2-{(E)-[(4-fluorophenyl)imino]methyl}phenol (C₁₃H₉ClFNO) * = average of three replicates ± SD.



FIGURE 1: Zone of inhibition of [CuL₂(H₂O)₂] against B. subtilis.

showed three bands at 225.3 nm (44385.26 cm⁻¹), 269.1 nm (37160.91 cm⁻¹), and 345.1 nm (28977.11 cm⁻¹). The band at 225.3 nm is due to the π - π * transition in benzene. The band appearing at 269.1 nm is assignable to n- π * transition of nonbonding electrons present on the nitrogen of the azomethine group (-HC=N). The band at 345.1 nm is due to n- π * transition of the phenolic group [17, 18].



FIGURE 2: Zone of inhibition of [NiL₂(H₂O)₂] against *E. coli*.

The UV-Vis spectra of the Schiff base metal (II) complexes (Figure 3) displayed similar absorption spectra as the ligand but have either undergone a blue shift or red shift.

The bands in the electronic spectrum of the Mn (II) complex shifted towards shorter wavelength and gave three bands at 221.4 nm (45167.12 cm^{-1}), 251.8 nm (39714.06 cm^{-1}), and 342.1 nm (29231.22 cm^{-1}). The band at 221.4 nm and 251.8 nm was due to intraligand transition, and the band at



FIGURE 3: UV-Vis spectra of Schiff base ligand and its metal (II) complexes.

342.1 nm was as a result of d-d low-spin transition for ${}^{6}A_{1g} \longrightarrow {}^{4}E_{g}$ which is suggestive of octahedral geometry around Mn (II) ion [19, 20].

In the Co (II) complex, two bands were observed at 249.1 nm (40144.52 cm⁻¹) and 401.9 nm (24881.81 cm⁻¹). This was a shift towards longer wavelength with respect to the spectrum of the Schiff base ligand. The band at 249.1 nm was due to intraligand transition, and the band at 401.9 nm was as a result of d-d transition for ${}^{3}T_{1g}(F) \longrightarrow {}^{3}T_{2g}$ which is within the range for octahedral configuration as reported in many octahedral cobalt (II) complexes [20–22].

The electronic spectrum of Ni (II) complex showed three bands at 245.2 nm (40783.03 cm⁻¹), 325.1 nm (30759.77 cm⁻¹), and 421.9 nm (23702.30 cm⁻¹). The band at 245.2 nm was probably due to intraligand transition, while the band at 325.1 nm was due to charge transfer. The observed band at 421.9 nm was as a result of d-d transition for ${}^{3}A_{2g} \longrightarrow {}^{3}T_{2g}$ which favours an octahedral geometry for the Ni (II) complex [19].

The copper (II) complex spectrum showed three bands at 229.1 nm (43649.06 cm⁻¹), 266.1 nm (37579.86 cm⁻¹), and 349.7 nm (28595.94 cm⁻¹), which were all shifted to longer wavelength. The band at 229.1 nm and 266.1 nm was due to intraligand transition, and the one at 349.7 nm was as a result of d-d spin allowed transition for ${}^{3}T_{1g} \longrightarrow {}^{3}T_{2g}$. This transition is suggestive of octahedral geometry around Cu (II) ion [23].

Zn (II) complex displayed absorption bands at 223.4 nm $(44762.76 \text{ cm}^{-1})$, 303.2 nm $(32981.53 \text{ cm}^{-1})$, and 343.9 nm $(29078.22 \text{ cm}^{-1})$. The band at 223.4 nm and 303.2 nm was due to intraligand transition, and the band at 343.9 nm was assignable to the metal to ligand charge transfer (MLCT) transition. An octahedral geometry is proposed for this complex based on its analytical, conductance, and spectral data. This is further supported by its diamagnetic nature and absence of d-d band, due to its complete d¹⁰ electronic configuration [9, 24, 25].

The absence of any band below $10,000 \text{ cm}^{-1}$ eliminates the possibility of a tetrahedral environment in these

complexes [26]. It can also be concluded that a shift in the spectral bands of the complexes, with respect to the spectrum of the Schiff base ligand, bathochromically or hyp-sochromically, indicated coordination.

3.3. FT-IR Spectral Analysis. The binding mode of the Schiff base ligand to the metal ions in complexes was determined by comparing the FT-IR spectrum of the free ligand with the spectra of the metal (II) complexes.

The stretching frequency for the azomethine C=N bond, v(C=N) was observed at 1601.0 cm⁻¹ for the free ligand. The C=N stretching frequencies in the metal (II) complexes were observed at 1596.2, 1597.4, 1595.7, 1597.1, and 1596.6 cm⁻¹ for Manganese (II), Cobalt (II), Nickel (II), Copper (II), and Zinc (II) complexes, respectively, a shift to lower wave numbers. This indicated coordination of Schiff base through the azomethine nitrogen [27]. Moreover, the appearance of additional weak bands in the region 526.4–530.6 cm⁻¹ and 488.3–489.7 cm⁻¹ attributed to v(M-N) and v(M-O), respectively [28], further confirmed complexation [29]. This showed that the Schiff base ligand coordinated to the metal via "N" and "O" atoms.

The FT-IR spectra of the complexes also showed strong bands in the $3140.3-3446.6 \text{ cm}^{-1}$ region, suggesting the presence of coordinated/lattice water in the complexes. This was further confirmed by the appearance of nonligand band in the 692.6-699.7 cm⁻¹ region, assignable to the rocking mode of water [29].

In the free Schiff base ligand, the band at 1277 cm^{-1} due to v(C-O, phenolic) shifted to lower wave number by 62.3–66.2 cm⁻¹ in the complexes indicating the coordination of the phenolic oxygen atom to the metal ion [30]. Therefore, it can be concluded that coordination took place via phenolic oxygen and azomethine nitrogen of the Schiff base ligand molecule.

3.4. Elemental Analysis. The microanalysis data suggested that all the complexes were mononuclear where two moles of the ligand and two moles of water molecules were coordinated to the central metal atom. The data, therefore, suggested that the metal to ligand ratio in the complex was 1:2 and the general formula for the complexes as $[M(L)_2(H_2O)_2]$ (M = Mn (II), Co (II), Ni (II), Cu(II), Zn (II); L = deprotonated imine) [31, 32]. The theoretical (calculated) values were found to be in good agreement with the experimental values.

3.5. NMR Spectral Analysis. The ¹H and ¹³C NMR spectra of the Schiff base ligand and its diamagnetic Ni (II) and Zn (II) complexes were recorded in DMSO- d_6 .

The ¹H NMR spectrum of the Schiff base showed a singlet peak at $\delta = 8.92$ ppm corresponding to the azomethine proton (-N=CH-) [30, 31], an indication that the Schiff base was formed during the condensation reaction. Observation of a peak at $\delta = 162.82$ ppm in the ¹³C NMR spectrum was further proof that the ligand was successfully synthesized [33].

The azomethine proton peak of Schiff base shifted upfield in the ¹H NMR spectra of the Ni (II) and Zn (II) complexes $(\delta = 8.87 - 8.90 \text{ ppm} \text{ and } 8.55 \text{ ppm}, \text{ respectively})$. The upfield shifting of azomethine proton in Ni (II) and Zn (II) complexes was attributed to the discharging of electronic cloud towards the Ni (II) and Zn(II) ion indicating coordination through the azomethine nitrogen to the metallic ion [34]. The expected ¹H NMR peak, at $\delta = 12.85$ ppm, assignable to the phenolic proton in the free Schiff base ligand [35] was absent in the spectra of the two complexes. This confirmed the deprotonation of the phenolic group and coordination of the negatively charged oxygen species to the metal cation. This observation further proves the neutral nature of the metal (II) complexes and explains the nonelectrolytic behavior of the complexes. The ¹³C NMR peaks for the azomethine carbon atom and phenolic group carbons of the coordinated Schiff base ligand were, respectively, observed at $\delta = 165$ ppm and 162 ppm, in the spectra of the Ni (II) complex, a 2 ppm upfield shift from that observed for the free ligand, due to coordination [33, 36]. Thus, the ¹H NMR and ¹³C NMR spectra confirmed the monobasic bidentate nature of the ligand, already suggested by the FT-IR spectral studies. Furthermore, the number of protons calculated from the integration curves and obtained values of the expected C H N analysis agreed well with each other [34, 37].

3.6. Mass Spectra. The mass spectrum of the Schiff base ligand showed a molecular ion peak at m/z 249 (M⁺+1) which is consistent with the molecular weight of the Schiff base ligand 249.

3.7. Antibacterial Activity. The antibacterial activity tests were conducted according to standard procedures using two Gram-positive and two Gram-negative bacterial strains [13, 38]. The results were recorded as shown in Table 1.

The ability of the Schiff base ligand and its metal (II) complexes to inhibit the growth of the bacteria was compared to that of the known standard antibacterial drugs, Amoxyclav (AMC), Nalidixic acid (NA), and Gentamicin (GEN). The Schiff base ligand and its metal (II) complexes demonstrated abilities to inhibit bacterial growth. Research has shown that coordination of a ligand, with the potential to inhibit bacterial growth, evokes antibacterial growth inhibition ability [39].

The nickel (II) complex had the highest activity against *E. coli* and *P. aeruginosa*, while the manganese (II) complex showed maximum inhibition zone against *B. subtilis* at 40 μ g/mL. The zinc (II) complex was slightly active than the ligand against *E. coli*. The cobalt (II) complex had a slightly higher activity than the ligand against *P. aeruginosa* and *B. subtilis*. The nickel (II) complex performed better than the ligand against *S. typhi* at 40 μ g/mL.

It is worth noting that the Schiff base and its metal (II) complexes inhibited the growth of Amoxyclav-resistant *P. aeruginosa, B. subtilis* and *S. typhi.*

Overall, the inhibition zones of the Schiff base ligand and its complexes at different concentrations showed that the complexes had enhanced bactericidal activity than the ligand [40] and the standard drug Amoxyclav (AMC) against all the bacterial strains studied. The antibacterial activities of the metal complexes are directly proportional to their concentration.

The biological activity of various transition metal coordination compounds has been explained using various theories. The increase in the antibacterial activity of the metal (II) complexes may be due to the effect of the metal ion on the normal state of the bacterial cell process [41]. Research has shown that the structural components possessing additional (C=N) bond with nitrogen and oxygen donor systems inhibit enzyme activity due to their deactivation by metal coordination [42, 43]. According to Tweedy's chelation theory, polarity of the metal ion is greatly reduced as a result of overlap of the ligand orbital and partial sharing of positive charge of metal ion with donor groups [44]. This enhances the delocalization of the pi electrons over the entire complex ring thereby promoting the lipophilicity of the chelate. Therefore, chelation enhances the lipophilic character of the central metal ion, hence increasing the hydrophobic character and liposolubility of the complex. This favors the complex permeation through the lipid layers of the cell membrane of the bacteria. Once it penetrates the cell, the complexes block the metal binding sites on enzymes of microorganisms. This in turn disturbs the respiration process of the cell by curtailing the synthesis of proteins, which restricts further growth of the organism [45, 46]. Thus, there is hope that these complexes could reasonably be used in designing more potent antibacterial agents for the treatment of some common diseases caused by E. coli, P. aeruginosa, B. subtilis, and S. typhi.

4. Conclusions

The Schiff base ligand 4-chloro-2-{(E)-[(4-fluorophenyl) imino]methyl}phenol (C₁₃H₉ClFNO) and its metal (II) complexes, $[M(L)_2(H_2O)_2]$ (*M* = Mn, Co, Ni, Cu, and Zn), were successfully synthesized and characterized. The deprotonated bidentate Schiff base ligand coordinated to the metal (II) ion via the azomethine nitrogen and phenolic oxygen resulting in the formation of a stable six-membered chelate ring. An octahedral geometry has been proposed for the metal (II) complexes based on the electronic spectra. The complexes formed are neutral with no free anions outside the coordination sphere. The metal (II) complexes exhibited better antibacterial properties than the parent Schiff base ligand under the same experimental conditions. It can also be deduced from this study that the antibacterial growth inhibition ability of the synthesized compounds increased with increasing concentration.

Data Availability

The data supporting the findings of the study are already given within the text.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

The authors wish to appreciate the technical teams at the Departments of Chemistry and Botany of the Jomo Kenyatta University of Agriculture and Technology for their invaluable assistance during this research work.

References

- H. Schiff, "Mittheilungen aus dem Universitätslaboratorium in Pisa: Eine neue Reihe organischer Basen," Annalen der Chemie und Pharmacie, vol. 131, no. 1, pp. 118-119, 1864.
- [2] B. S. Sathe, E. Jayachandran, V. A. Jagtap, and G. M. Sreenivasa, "Synthesis and antibacterial, antifungal activity of novel analogs of fluoro benzothiazole Schiff bases," *Journal of Chemical and Pharmaceutical Sciences*, vol. 3, no. 4, pp. 216-217, 2010.
- [3] S. M. Sondhi, N. Singh, A. Kumar, O. Lozach, and L. Meijer, "Synthesis, anti-inflammatory, analgesic and kinase (CDK-1, CDK-5 and GSK-3) inhibition activity evaluation of benzimidazole/benzoxazole derivatives and some schiff's bases," *Bioorganic & Medicinal Chemistry*, vol. 14, no. 11, pp. 3758–3765, 2006.
- [4] R. M. Mishra, S. Pandey, and R. Saxena, "Homozygous hemoglobin D with alpha thalassemia: case report," *The Open Hematology Journal*, vol. 2, pp. 1–4, 2011.
- [5] C. Ajit Kumar and S. N. Pandeya, "Synthesis and anticonvulsant activity (chemoshock) of schiff and mannich bases of isatin derivatives with 2-amino pyridine (mechanism of action)," *International Journal of PharmTech Research*, vol. 4, no. 2, pp. 590–598, 2012.
- [6] T. Aboul-Fadl, F. A.-H. Mohammed, and E. A.-S. Hassan, "Synthesis, antitubercular activity and pharmacokinetic studies of some schiff bases derived from 1- alkylisatin and isonicotinic acid hydrazide (inh)," *Archives of Pharmacal Research*, vol. 26, no. 10, pp. 778–784, 2003.
- [7] D. Wei, N. Li, G. Lu, and K. Yao, "Synthesis, catalytic and biological activity of novel dinuclear copper complex with Schiff base," *Science in China Series B*, vol. 49, no. 3, pp. 225–229, 2006.
- [8] P. G. Avaji, C. H. Vinod Kumar, S. A. Patil, K. N. Shivananda, and C. Nagaraju, "Synthesis, spectral characterization, invitro microbiological evaluation and cytotoxic activities of novel macrocyclic bis hydrazone," *European Journal of Medicinal Chemistry*, vol. 44, no. 9, pp. 3552–3559, 2009.
- [9] Z. H. Chohan, J. L. Wardell, J. N. Low, P. R. Meehan, and G. Ferguson, "Tetraethylammonium bromo(1,3-dithiol-2one-4,5-dithiolato)diethylstannate(1-)," Acta Crystallographica Section C Crystal Structure Communications, vol. 54, no. 10, 1998.
- [10] K. Shoaib, W. Rehman, B. Mohammad, and S. Ali, "Proteomics and bioinformatics synthesis, characterization and biological applications of transition metal complexes of [no] donor schiff bases," *Journal of Proteomics & Bioinformatics*, vol. 6, no. 7, pp. 153–157, 2013.
- [11] K. H. Kailas, J. P. Sheetal, P. P. Anita, and H. P. Apoorva, "Four synthesis methods of schiff base ligands and preparation of their metal complex with Ir and antimicrobial investigation," *World Journal of Pharmacy and Pharmaceutical Sciences*, vol. 5, no. 2, pp. 1055–1063, 2016.
- [12] M. R. S. Zaidan, A. Noor Rain, A. R. Badrul, A. Adlin, A. Norazah, and I. Zakiah, "In vitro screening of five local medicinal plants for antibacterial activity using disc diffusion

method antibacterial activity using disc diffusion method," *Tropical Biomedicine*, vol. 22, no. 2, pp. 165–170, 2006.

- [13] P. R. Murray, E. J. Baron, M. A. Pfaller, F. C. Tenover, and R. H. Yolke, *Manual of Clinical Microbiology*, ASM, Washington, DC, USA, 1995.
- [14] T.-J. Feng, "4-Chloro-2-[(E)-(4-fluorophenyl)iminomethyl] phenol," Acta Crystallographica Section E Structure Reports Online, vol. 70, no. 1, p. 42, 2014.
- [15] W. J. Geary, "The use of conductivity measurements in organic solvents for the characterisation of coordination compounds," *Coordination Chemistry Reviews*, vol. 7, no. 1, pp. 81–122, 1971.
- [16] L. Chen, K. Thompson, N. Bridson, and L. Chenvol, "Dinuclear copper(II) and copper (I) complexes of tetradentate (N4)thio-diazine ligands; synthetic, structural, magnetic and electrochemical studies: in situ oxidation of copper(I) complexes to produce dinuclear hydroxo-bridged copper(II) complexes," *Inorganica Chimica Acta*, vol. 214, pp. 67–76, 1993.
- [17] A. M. Shaker, L. A. E. Nassr, M. S. S. Adam, and I. M. A. Mohamed, "Hydrophilicity and acid hydrolysis of water-soluble antibacterial iron(II) Schiff base complexes in binary aqueous solvents," *Russian Journal of General Chemistry*, vol. 83, no. 12, pp. 2460–2464, 2013.
- [18] D. M. Boghaei, E. Askarizadeh, and A. Bezaatpour, "Synthesis, characterization, spectroscopic and thermodynamic studies of charge transfer interaction of a new water-soluble cobalt (II) Schiff base complex with imidazole derivatives," *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, vol. 69, no. 2, pp. 624–628, 2008.
- [19] I. Bertini, *Inorganic and Bio-Inorganic Chemistry*, EOLSS, Oxford, UK, 2009.
- [20] A. A. Abou-Hussein and W. Linert, "Synthesis, spectroscopic, coordination and biological activities of some organometallic complexes derived from thio-Schiff base ligands," *Spectrochim Acta-Part A Mol Biomol Spectrosc*, vol. 117, 2014.
- [21] A. A. El-Sherif, M. R. Shehata, M. M. Shoukry, and M. H. Barakat, "Thermodynamic investigation and mixed ligand complex formation of 1,4-Bis-(3-aminopropyl)-piperazine and biorelevant ligands," *Bioinorganic Chemistry* and Applications, vol. 2012, Article ID 984291, 10 pages, 2012.
- [22] G. G. Mohamed, M. A. Zayed, and S. M. Abdallah, "Metal complexes of a novel Schiff base derived from sulphametrole and varelaldehyde. Synthesis, spectral, thermal characterization and biological activity," *Journal of Molecular Structure*, vol. 979, no. 1–3, pp. 62–71, 2010.
- [23] M. S. Nair, D. Arish, and R. S. Joseyphus, "Synthesis, characterization, antifungal, antibacterial and DNA cleavage studies of some heterocyclic Schiff base metal complexes," *Journal of Saudi Chemical Society*, vol. 16, no. 1, pp. 83–88, 2012.
- [24] J. H. Aupers, Z. H. Chohan, P. J. Cox et al., "Syntheses and structures of diorgano(halo- orpseudohalo-)(1,3-dithiole-2-thione-4,5-dithiolato)-stannates (1-), [Q][R²SnX(dmit)] (Q = onium cation; X = halide orpseudohalide)," *Polyhedron*, vol. 17, no. 25-26, 1998.
- [25] P. W. Selwood, *Magnetochemistry*, Interscience, London, UK, 1956.
- [26] A. H. Chohan, A. I. Che-Ani, M. M. Tahir, N. A. G. Abdullah, N. M. Tawil, and S. N. Kamaruzzaman, "Housing and analysis of design defects: a post occupational evaluation of private housing in Malaysia," *International Journal of Physical Sciences*, vol. 6, no. 2, pp. 193–203, 2011.
- [27] M. Alias, H. Kassum, and C. Shakir, "Synthesis, physical characterization and biological evaluation of Schiff base

M(II) complexes," Journal of the Association of Arab Universities for Basic and Applied Sciences, vol. 15, no. 1, pp. 28–34, 2014.

- [28] J. Ferraro, "Low Frequency vibration of inorganic and coordination compound," Plenum press, New York, NY, USA, 1971.
- [29] K. Nakamoto, Infrared Raman Spectra of Inorganic and Coordination Compounds, John Wiley & Sons, New York, NY, USA, Third edition, 1992.
- [30] J. P. Tandon, A. J. Crowe, and F. Road, "Synthesis and structural studies of TIN(II) complexes of semicarbazones and thiosemicarbazones," *Polyhedron*, vol. 5, no. 3, pp. 739– 742, 1986.
- [31] A. M. Hammam, Z. A. Khafagi, and S. A. Ibrahim, "Synthesis and characterization of some new antimicrobial transition metal complexes with 1, 2, 4-Traizole-3-thione schiff bases," *Journal of Materials and Environmental Science*, vol. 6, no. 6, pp. 1596–1605, 2015.
- [32] C. I. R. Sobana, G. A. R. Gnana, and M. A. Princela, "Synthesis and characterization of bioactive transition metal complexes of Zr(IV) and Th(IV) using di-α-formylmethoxy bis (3-penta decenyl phenyl) methane (DFMPM) derived from Cardanol," *AJCPR*, vol. 3, no. 1, pp. 208–214, 2015.
- [33] B. V. Agarwala, S. Hingorani, and V. Puri, "KCL. Physicochemical studies of (o-vanillin thiosemicarbazonato)-nickel(II) chelate," *Transition Metal Chemistry*, vol. 19, pp. 25–27, 1994.
- [34] H. Gunther, NMR Spectroscopy: Basic Principles, Concepts, and Applications in Chemistry, JohnWiley & Sons, Hoboken, NJ, USA, 2nd edition, 1995.
- [35] B. Manjula and S. Arul, "Preparation, characterization, antimicrobial activities and DNA cleavage studies of Schiff base complexes derived from 4-amino antipyrine," *Asian Journal* of Biochemical and Pharmaceutical Research, vol. 1, pp. 168– 178, 2013.
- [36] E. Canpolat, A. Yazici, and M. Kaya, "Studies on mononuclear chelates derived from substituted Schiff-base ligands (part 10): synthesis and characterization of a new 4-hydroxysalicylidenp-aminoacetophenoneoxime and its complexes with Co(II), Ni(II), Cu(II) and Zn(II)," *Journal of Coordination Chemistry*, vol. 60, no. 4, pp. 473–480, 2007.
- [37] R. A. Nyquist, Interpreting Infrared, Raman and Nuclear Magnetic Resonance Spectra, vol. 2, Academic Press, New York, NY, USA, 2001.
- [38] A. U. Rahman, M. I. Choudhary, and W. J. Thomson, *Bioassay Techniques for Drug Development*, Harwood Academic Publishers, Amsterdam, Netherlands, 2001.
- [39] E. A. Nyawade, H. B. Friedrich, B. Omondi, H. Y. Chenia, M. Singh, and S. Gorle, "Synthesis and characterization of new α, α' -diaminoalkane-bridged dicarbonyl(η 5-cyclopentadienyl) ruthenium(II) complex salts: antibacterial activity tests of η 5cyclopentadienyl dicarbonyl ruthenium(II) amine complexes," *Journal of Organometallic Chemistry*, vol. 799-800, pp. 138–146, 2015.
- [40] M. Revanasiddappa, T. Suresh, S. Khasim, S. C. Raghavendray, C. Basavaraja, and S. D. Angadi, "Transition metal complexes of 1, 4(2'-Hydroxyphenyl-1-yl) di-imino azine: synthesis, characterization and antimicrobial studies," *E-Journal of Chemistry*, vol. 5, no. 2, pp. 395–403, 2008.
- [41] H. Naeimi and M. Moradian, "Synthesis and characterization of nitro-schiff bases derived from 5-nitro-salicylaldehyde and various diamines and their complexes of Co (II)," *Journal of Coordination Chemistry*, vol. 63, no. 1, 2010.
- [42] A. A. Al-Amier, Y. K. Al-Majedy, H. H. Ibrahim, and A. A. Al-Tamimi, "Antioxidant, antimicrobial, and

theoretical studies of the thiosemicarbazone derivative schiff base 2-(2-imino-1-methylimidazolidin-4-ylidene)hydrazinecarbothioamide (IMHC)," *Organic and Medicinal Chemistry Letters*, vol. 2, no. 1, p. 4, 2012.

- [43] M. Jesmin, M. M. Ali, M. S. Salahuddin, M. R. Habib, and J. A. Khanam, "Antimicrobial activity of some schiff bases derived from benzoin, salicylaldehyde, aminophenol and 2,4 dinitrophenyl hydrazine," *Mycobiology*, vol. 36, no. 1, pp. 70–73, 2008.
- [44] K. Mahajan, N. Fahmi, and R. V. Singh, "Synthesis, characterization and antimicrobial studies of Sb (III) complexes of substituted thioimines," *Indian Journal of Chemistry Section A*, vol. 46, no. 8, pp. 1221–1225, 2007.
- [45] A. A. El-Sherif and T. M. A. Eldebss, "Synthesis, spectral characterization, solution equilibria, in vitro antibacterial and cytotoxic activities of Cu(II), Ni(II), Mn(II), Co(II) and Zn(II) complexes with Schiff base derived from 5-bromosalicylaldehyde and 2-aminomethylthiophene," *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, vol. 79, no. 5, pp. 1803–1814, 2011.
- [46] G. B. Bagihalli, P. G. Avaji, S. A. Patil, and P. S. Badami, "Synthesis, spectral characterization, in vitro antibacterial, antifungal and cytotoxic activities of Co(II), Ni(II) and Cu(II) complexes with 1,2,4-triazole Schiff bases," *European Journal* of Medicinal Chemistry, vol. 43, no. 12, pp. 2639–2649, 2008.