

## Antibacterial Activity of Pyridine Nucleus-Containing Schiff Bases and their Copper and Cobalt Complexes

Cordelia Ukamaka Dueke-Eze, Tolulope Mojisola Fasina, and Oluwole Babafemi Familoni

Received: 13 February 2026/Accepted: 06 May 2026 /Published: 14 May 2026

<https://dx.doi.org/10.4314/cps.v13i5.9>

**Abstract:** Pyridine is a valuable nitrogen-containing heterocyclic compound widely present in numerous naturally occurring bioactive molecules and extensively utilized in pharmaceutical drug design and development. In this study, three pyridine-based Schiff bases, namely 2-((pyridine-4-ylimino)methyl)phenol (L1), 4-nitro-2-((pyridine-4-ylimino)methyl)phenol (L2) and 4-bromo-2-((pyridine-4-ylimino)methyl)phenol (L3). Their corresponding copper and cobalt complexes were synthesized and characterized using melting point determination, FTIR spectroscopy, NMR spectroscopy, and elemental analysis. The Schiff bases acted as bidentate ligands, coordinating through the imine nitrogen and phenolic oxygen atoms. The *in vitro* antibacterial activity of the synthesized compounds was evaluated against *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Results revealed that antibacterial activity increased with concentration. Notably, the cobalt complexes demonstrated pronounced antibacterial efficacy, particularly against *S. aureus*, suggesting their potential as antibacterial agents. However, additional toxicological and formulation studies would be required before considering practical applications such as hospital antiseptic formulations.

**Keywords:** Schiff bases, pyridine-nucleus, Copper complex, cobalt complex, antibacterial

**Cordelia U. Dueke-Eze\***

Department of Chemistry, Faculty of Physical and Earth Sciences, University of Lagos, Lagos, Nigeria.

Email: [cdueke-eze@unilag.edu.ng](mailto:cdueke-eze@unilag.edu.ng)  
<https://orcid.org/0000-0002-4635-0570>

**Tolulope M. Fasina**

Department of Chemistry, Faculty of Physical and Earth Sciences, University of Lagos, Lagos, Nigeria.

Email: [tfasian@unilag.edu.ng](mailto:tfasian@unilag.edu.ng)  
<https://orcid.org/0000-0001-7615-9083>

**Oluwole B. Familoni**

Department of Chemistry, Faculty of Physical and Earth Sciences, University of Lagos, Lagos, Nigeria.

Email: [familonio@unilag.edu.ng](mailto:familonio@unilag.edu.ng)  
<https://orcid.org/0000-0002-5480-232X>

### 1.0 Introduction

The rapid emergence and spread of antimicrobial resistance has become a major global health concern, significantly reducing the effectiveness of existing antibiotics. In response, scientists have remained actively engaged in the discovery and development of novel antibacterial agents with improved efficacy and new mechanisms of action. Particular attention has been given to heterocyclic compounds, especially those containing the pyridine nucleus, due to their wide range of biological activities. Pyridine, which is a nitrogen-containing heterocyclic compound that occurs in various analogues, holds great importance in the arena of medicinal chemistry as an extremely valuable source of pharmacologically active molecules (Marinescu & Popa, 2022; Kumar *et al.*, 2023). The nitrogen-containing heterocyclic compound pyridine and its various derivatives have frequently been included in drugs approved by the FDA (De *et al.*, 2022; Yousef *et al.*, 2023). Pyridine and its derivatives have

been extensively reported in recent literature to exhibit diverse pharmacological properties, including antibacterial (Islam *et al.*, 2023; Rani & Reddy, 2018), antifungal (Balaes *et al.*, 2025; Elsayed, Elsayed & Sroor, 2024) anti-inflammatory (Sroor *et al.*, 2025) and anticancer activities (Yousef *et al.*, 2023; Nasif, & Sayin, 2025). This has made the pyridine scaffold a valuable pharmacophore in modern drug design and medicinal chemistry. Its structural versatility allows for chemical modification that can enhance binding interactions with biological targets, thereby improving therapeutic potential. Building on these findings, Schiff base derivatives of pyridine have attracted increasing attention due to their structural versatility and enhanced biological activity arising from the azomethine linkage (Joshi, 2023).

Schiff bases are a class of organic compounds characterized by the presence of an azomethine (-C=N-) functional group formed through the condensation of primary amines with aldehydes or ketones. The azomethine moiety serves as an important pharmacophore and metal-binding site, contributing significantly to the biological and coordination properties of these compounds (Raczuk *et al.*, 2022). Owing to their structural resemblance to naturally occurring biomolecules, Schiff bases exhibit diverse biological activities and have attracted considerable attention in medicinal chemistry (Hamdan, Hamdan & Aljabawi, 2024; Obeid *et al.*, 2025). Schiff bases constitute an important class of compounds with diverse pharmacological and biological activities, including antitumoral, antimicrobial, antimalarial, antioxidant, neuroprotective, antidiabetic, antidepressant, and anti-inflammatory effects (Alyamani, 2023; Dueke-Eze *et al.*, 2022, 2024; Dueke-Eze & Fasina, 2023; Yuldasheva *et al.*, 2022; Hamid & Salih, 2022).

Reports of Schiff bases with much greater antimicrobial effects when complexed with metal ions than as free ligands are well documented (Thakur *et al.*, 2024). The type of

metal that is incorporated in the complex and type of Schiff base have great impact on their activity profile (Zhang *et al.*, 2011; John, Joseyphus & Joe, 2020; Meeran *et al.*, 2022; Abu-Yamin, *et al.*, 2022; Lacopetta *et al.*, 2023; Guo *et al.*, 2024; Mannaa *et al.*, 2025). Despite the growing body of literature on pyridine-derived Schiff bases and their metal complexes, limited information is available regarding the antibacterial properties of substituted N-(2-hydroxybenzylidene)pyridine-4-amine derivatives containing electron-withdrawing substituents such as nitro and bromo groups. Furthermore, comparative studies evaluating the influence of Cu(II) and Co(II) coordination on the antibacterial activity of these ligands against both Gram-positive and Gram-negative bacteria remain scarce. Consequently, the structure-activity relationships associated with ligand substitution and metal complexation in this class of compounds are not yet fully understood.

Our group has previously synthesized derivatives of N-(2-hydroxybenzylidene)pyridine-4-amine (L1–L3), which exhibited significant *in vitro* inhibitory activity against *Mycobacterium tuberculosis* H37Rv. Their Cu(II), Co(II), and Ni(II) complexes also demonstrated enhanced antitubercular activity relative to the free ligands (Dueke-Eze & Fasina, 2023a). These promising findings suggest that coordination of pyridine-based Schiff bases with transition metal ions may enhance biological activity through increased lipophilicity, improved membrane permeability, and altered modes of interaction with microbial targets. However, their antibacterial activities against clinically relevant bacterial pathogens have not yet been investigated. Therefore, this study aimed to synthesize and characterize a series of substituted pyridine-based Schiff bases and their Cu(II) and Co(II) complexes and to evaluate their antibacterial activities against selected Gram-positive and Gram-negative



bacterial strains. Particular emphasis was placed on determining the effects of ligand substitution and metal coordination on antibacterial efficacy. The findings of this study are expected to contribute to the development of new metal-based antibacterial agents and provide insights into the structure-activity relationships of pyridine-derived Schiff base complexes.

## 2.0 Materials and Methods

All reagents and solvents used in this study were of analytical grade and were obtained from Sigma-Aldrich and other commercial suppliers. The chemicals were used without further purification unless otherwise stated. Melting points were determined using a Stuart SMP3 melting point apparatus and are uncorrected. Fourier-transform infrared (FTIR) spectra were recorded on a Digilab FTS 7000 spectrometer equipped with an attenuated total reflectance (ATR) diamond-selenium accessory over the range 4000–400  $\text{cm}^{-1}$ . The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian 300 MHz spectrometer using  $\text{CDCl}_3$  as solvent and tetramethylsilane (TMS) as the internal standard. Elemental analyses (CHN) were carried out using a Perkin-Elmer 2400 CHNS/O elemental analyzer. Antibacterial studies were conducted at the Nigeria Institute of Medical Research (NIMR), Yaba, Lagos, Nigeria.

### 2.1 Standard procedure for the preparation of Schiff bases (L1-L3)

The degassed solution containing 4-aminopyridine (0.80 mmol), aldehyde (0.80 mmol), and p-toluene sulfonic acid monohydrate (10 mg) in toluene (100 ml) was refluxed for 24 h under a nitrogen atmosphere in a Dean-Stark apparatus. After removal of the solvent under reduced pressure, the crude product was purified by recrystallization from toluene to obtain the Schiff base (Dueke-Eze & Fasina, 2023<sup>a</sup>)

#### 2.1.1. 2-((pyridine-4-ylimino)methyl)phenol (L1)



Deep yellow solid, yield: 12.80 mg (81%); mp: 77–78 $^{\circ}\text{C}$ ;  $R_f$ : 0.55. IR ( $\text{cm}^{-1}$ ): 3324, 1587, 1557, 1398, 1339, 1271, 1214, 1148, 1121, 1056, 930, 845, 801, 730, 679;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.95–7.05 (m, 2H), 7.14 (d,  $J$  6.6 Hz, 2H), 7.46 (t,  $J$  15.6 Hz, 2H), 8.61 (s, 1H), 8.65 (d,  $J$  5.4 Hz, 2H), 12.57 (s, 1H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 116.10, 151.15, 155.46, 117.50, 118.64, 119.45, 132.92, 134.37, 161.29, 165.68. Anal. calcd.:  $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}$ : C, 72.71, H, 5.08, N, 14.10. Found: C, 72.62, H, 5.02, N, 13.96.

#### 2.1.2. 4-nitro-2-((pyridine-4-ylimino)methyl)phenol (L2)

Yellow solid, yield: 14.60 mg (75%); mp: 193–194 $^{\circ}\text{C}$ ;  $R_f$ : 0.32. IR ( $\text{cm}^{-1}$ ): 1652, 1584, 1524, 1471, 1354, 1280, 1228, 1173, 1081, 947, 888, 820, 751, 718, 639;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 7.09–7.22 (m, 3H), 8.30–8.44 (m, 2H), 8.56 (s, 1H), 8.717 (t,  $J$  8.4 Hz, 2H), 10.01;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 115.94, 118.58, 119.04, 128.95, 129.30, 129.67, 131.63, 151.44, 164.14, 166.39. Anal. calcd.:  $\text{C}_{12}\text{H}_9\text{N}_3\text{O}_3$ : C, 59.26, H, 3.77, N, 17.28. Found: C, 58.96, H, 3.63, N, 17.06.

#### 2.1.3. 4-bromo-2-((pyridine-4-ylimino)methyl)phenol (L3)

Orange crystals. Yield: 18.60 mg (84%); mp: 139–141 $^{\circ}\text{C}$ ;  $R_f$ : 0.42. IR ( $\text{cm}^{-1}$ ): 1615, 1582, 1550, 1472, 1411, 1354, 1328, 274, 1183, 1078, 985, 916, 867, 804, 781, 738, 689;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$ : 6.96 (d,  $J$  8.7 Hz, 2H), 7.13 (d,  $J$  5.4 Hz, 2H), 7.48–7.54 (m, 2H), 8.54 (s, 1H), 8.66 (s, 2H), 12.57 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$ : 110.88, 116.05, 119.53, 119.97, 134.80, 136.93, 151.26, 154.93, 160.27, 164.38. Anal. calcd.:  $\text{C}_{12}\text{H}_9\text{BrN}_2\text{O}$ : C, 52.01, H, 3.27, N, 10.11. Found: C, 52.16, H, 3.18, N, 9.82.

## 2.2. Procedure for the synthesis of metal complexes

A stirred ethanolic solution (10 ml) of the ligands (1.1 mmol) was gradually mixed with a solution of each chloride metal salt (0.5 mmol)

dissolved in either ethanol or water. The mixture was refluxed for four to six hours, and after cooling, the solid result was filtered and repeatedly cleaned with a 1:1 ethanol to water mixture. In a desiccator, the substance was dried on silica gel.

### 2.2.1. *Cu-2-((pyridine-4-ylimino)methyl)phenol (Cu-L1)*

Yield: 2.07 mg (60 %); mp: 244 °C (dec.). IR (cm<sup>-1</sup>): 3464, 1594, 1581, 1527, 1438, 1372, 1147, 1058, 1027, 902, 869, 748, 655, 528, 489. Anal. calcd.: C<sub>12</sub>H<sub>11</sub>ClCuN<sub>2</sub>O<sub>2</sub>: C, 45.87, H, 3.53, N, 8.92, Cu, 20.22. Found: C, 46.32, H, 3.00, N, 8.40, Cu, 20.74.

### 2.2.2. *Cu-4-nitro-2-((pyridine-4-ylimino)methyl)phenol (Cu-L2)*

Yield: 1.67 mg (39%); mp: >349 °C. IR (cm<sup>-1</sup>): 3212, 1597, 1508, 1424, 1373, 1246, 1101, 1087, 1003, 850, 826, 720, 622, 508, 482, 444. Anal. calcd.: C<sub>12</sub>H<sub>10</sub>ClCuN<sub>3</sub>O<sub>4</sub>: C, 40.12, H, 2.81, N, 11.70, Cu, 17.69. Found: C, 40.07, H, 2.61, N, 10.78, Cu, 18.19.

### 2.2.3. *Cu-4-bromo-2-((pyridine-4-ylimino)methyl)phenol (Cu-L3)*

Yield: 2.33 mg (59%); mp: 248 °C (dec.). IR (cm<sup>-1</sup>): 2359, 1739, 1598, 1517, 1452, 1391, 1333, 1316, 1279, 1168, 1028, 933, 874, 700, 626, 563, 464, 439. Anal. Calcd: C<sub>12</sub>H<sub>10</sub>BrClCuN<sub>2</sub>O<sub>2</sub>: C, 36.66, H, 2.56, N, 7.13, Cu, 16.16. Found: C, 38.49, H, 2.17, N, 6.63, Cu, 16.00.

### *Cobalt (II) complexes of the Schiff bases*

### 2.2.4. *Co-2-((pyridine-4-ylimino)methyl)phenol (Co-L1)*

Yield: 3.33 mg (54 %); mp: 298-303 °C. IR (cm<sup>-1</sup>): 1590, 1524, 1491, 1462, 1444, 1387, 1351, 1319, 1174, 1124, 1056, 1027, 980, 866, 834, 753, 735, 445, 414. Anal. calcd.: C<sub>24</sub>H<sub>22</sub>CoN<sub>4</sub>O<sub>4</sub>: C, 58.90, H, 4.53, N, 11.45, Co, 12.04. Found: C, 60.64, H, 4.02, N, 10.81, Co, 13.17.

### 2.2.5. *Co-4-nitro-2-((pyridine-4-ylimino)methyl)phenol (Co-L2)*

Yield: 4.93 mg (58%); mp: 248-251 °C. IR (cm<sup>-1</sup>): 3421, 1597, 1574, 1507, 1456, 1395, 1369, 1335, 1216, 1196, 1160, 1084, 1055, 922, 855, 804, 696, 490, 428. Anal. Calcd: C<sub>24</sub>H<sub>20</sub>CoN<sub>6</sub>O<sub>8</sub>: C, 49.75, H, 3.48, N, 14.51, Co, 10.17. Found: C, 50.26, H, 3.02, N, 15.8,5 Co, 9.71.

### 2.2.6. *Cu-4-bromo-2-((pyridine-4-ylimino)methyl)phenol (Cu-L3)*

Yield: 4.78 mg (66 %); mp: >349 °C. IR (cm<sup>-1</sup>): 3060, 1597, 1554, 1470, 1334, 1279, 1211, 1170, 1081, 987, 913, 870, 848, 818, 781, 628, 529, 523, 429. Anal. calcd.: C<sub>24</sub>H<sub>24</sub>Br<sub>2</sub>CoN<sub>4</sub>O<sub>6</sub>: C, 42.19, H, 3.54, N, 8.20, Co, 8.63. Found: C, 41.54, H, 2.79, N, 7.56, Co, 8.51.

### 2.3 *Antibacterial Activity*

The antibacterial activity of the synthesized Schiff bases and their metal complexes was evaluated against *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli* and *Pseudomonas aeruginosa* using the agar diffusion method according to the standard protocols of the Nigeria Institute of Medical Research, Yaba, Lagos. Fresh bacterial cultures were prepared and standardized prior to inoculation. Sterile nutrient agar plates were seeded with the test organisms and wells were aseptically bored into the agar medium. Solutions of the test compounds were prepared in dimethyl sulfoxide (DMSO) at concentrations of 40, 20, 10 and 5 mg mL<sup>-1</sup> and introduced into the wells. The plates were incubated at 37 °C for 24 h and antibacterial activity was assessed by measuring the zones of inhibition around the wells. Appropriate positive and negative controls were included and all experiments were carried out in triplicate (Dueke-Eze & Fasina, 2023<sup>b</sup>)

### 3.0. Results and Discussion

#### 3.1. Synthesis

The Schiff bases were obtained in good yields (75–84%), indicating that the condensation reactions proceeded efficiently under the



reaction conditions employed. Complexation with Cu(II) and Co(II) ions resulted in compounds with significantly higher melting or decomposition temperatures than the corresponding ligands, suggesting increased thermal stability arising from metal–ligand coordination. The elemental analysis data were

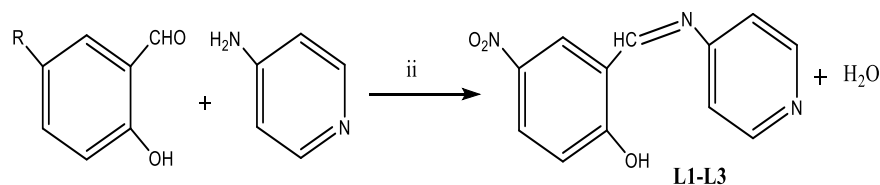
generally consistent with the proposed molecular formulae.

The ligands L1, L2 and L3 were synthesized by direct condensation reaction of 4-aminopyridine with 2-hydroxybenzaldehyde (L1), 5-nitro-2-hydroxybenzaldehyde (L2) and 5-bromo-2-hydroxybenzaldehyde (L3) (Scheme 1).

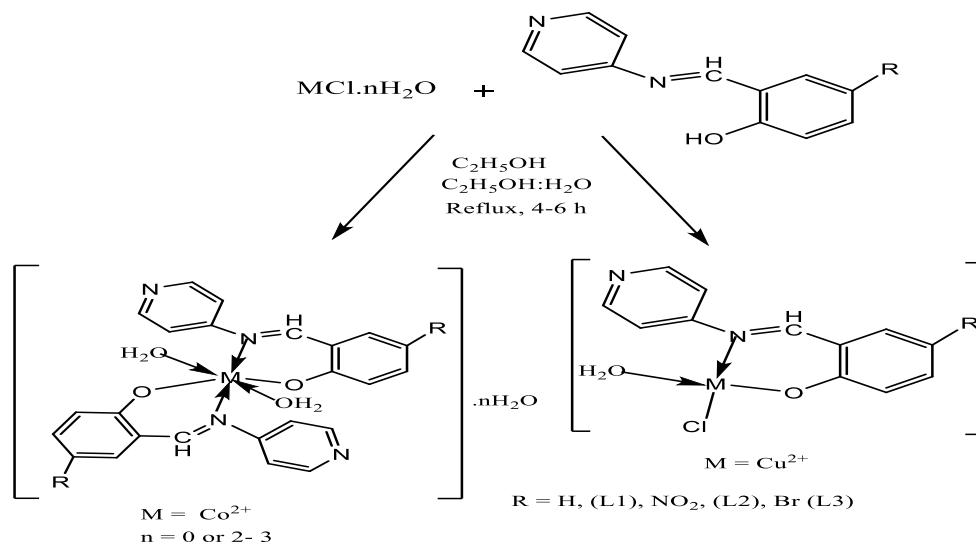
### Scheme 1: Synthetic route to the Schiff base formation

The compounds' analytical and physical properties are displayed in Table 1. The synthesis of these compounds was successful as evidenced by the fact that they formed in reasonable yields, and the elemental analyses confirmed the molecular formulae. The

significant difference from the melting points of the metal complexes and their corresponding ligand suggest that the metal complexes were synthesized. Each metal complex's elemental analysis supported the proposed molecular formula.



Reagents and conditions: (ii)  $C_6H_8O_4S$ , toluene,  $N_2(g)$ , heat, 24 h  
R = H, (L1),  $NO_2$ , (L2), Br, (L3)



### Scheme 2: Synthetic route to Schiff base metal formation



Table 1: Physical and analytical data of L1-L3

Ligand code	Molecular Wt. (M.wt. (g/mol))	mp:(°C)	Yield(%)	Microanalysis:			
				%Calculated			(Found)
				C	H	N	M
<b>L1</b>	C <sub>12</sub> H <sub>10</sub> N <sub>2</sub> O (198)	77-78	81	72.71 (72.62)	5.08 (5.02)	14.10 (13.96)	
<b>Cu(L1)</b>	C <sub>12</sub> H <sub>11</sub> ClCuN <sub>2</sub> O <sub>2</sub> (314)	244 (dec.)	60	45.87 (46.32)	3.53 (3.00)	8.92 (8.40)	20.22 (20.74)
<b>Co(L1)</b>	C <sub>24</sub> H <sub>22</sub> CoN <sub>4</sub> O <sub>4</sub> (489)	298-303	54	58.90 (60.64)	4.53 (4.02)	11.45 (10.81)	12.04 (13.17)
<b>L2</b>	C <sub>12</sub> H <sub>9</sub> N <sub>3</sub> O <sub>3</sub> (243)	193-194	75	59.26 (58.96)	3.77 (3.63)	17.28 (17.06)	
<b>Cu(L2)</b>	C <sub>12</sub> H <sub>10</sub> ClCuN <sub>3</sub> O <sub>4</sub> (359)	>349	39	40.12 (40.07)	2.81 (2.61)	11.70 (10.78)	17.69 (18.19)
<b>Co(L2)</b>	C <sub>24</sub> H <sub>20</sub> CoN <sub>6</sub> O <sub>8</sub> (579)	248-251	58	49.75 (50.26)	3.48 (3.02)	14.51 (15.15)	10.17 (9.71)
<b>L3</b>	C <sub>12</sub> H <sub>9</sub> BrN <sub>2</sub> O (277)	139-141	84	52.01 (52.16)	3.27 (3.18)	10.11 (9.82)	
<b>Cu(L3)</b>	C <sub>12</sub> H <sub>10</sub> BrClCuN <sub>2</sub> O <sub>2</sub> (393)	248 (dec)	59	36.66 (38.49)	2.56 (2.17)	7.13 (6.63)	16.16 (16.00)
<b>Co(L3)</b>	C <sub>24</sub> H <sub>24</sub> Br <sub>2</sub> CoN <sub>4</sub> O <sub>6</sub> (683)	>349	66	42.19 (41.54)	3.54 (2.79)	8.20 (7.56)	8.63 (8.51)

### 3.2 Spectroscopic Analysis of L1-L3

#### 3.2.1. Nuclear Magnetic Resonance (NMR)

The imine (HC=N) and hydroxyl (OH) protons are responsible for the singlet  $\delta_H$  8.61 and 12.57 ppm (L1),  $\delta_H$  8.56 and 10.01 ppm and  $\delta_H$  8.54 and 12.57 ppm (L3) resonances in the ligands' <sup>1</sup>H NMR spectra. The <sup>13</sup>C NMR spectrum included all of the carbon atom signals. Therefore, the ligand's structure is supported by the NMR data. The appearance of

singlet signals at  $\delta_H$  8.54–8.61 ppm corresponding to the azomethine proton confirms successful condensation of the aldehydes with 4-aminopyridine. The phenolic OH resonances observed between  $\delta_H$  10.01 and 12.57 ppm are characteristic of intramolecular hydrogen bonding commonly observed in salicylaldehyde-derived Schiff bases.

Table 2: Characteristic <sup>1</sup>H and <sup>13</sup>C NMR bands of L1-L3

Ligand code	Chemical shift (ppm)			
	HC=N		C-OH	
	$\delta_H$	$\delta_C$	$\delta_H$	$\delta_C$
<b>L1</b>	8.61	161.29	12.57	165.68
<b>L2</b>	8.56	164.14	10.01	166.39
<b>L3</b>	8.54	160.27	12.57	164.38





additional bands at 414-489 (M-N) and 445-529 (M-O) (Rani *et al.*, 2020).

### 3.1.3. Antibacterial Activity

The synthesized compounds exhibited concentration-dependent antibacterial activity,

with metal complexes generally showing enhanced activity compared with the free ligands and greater efficacy against Gram-positive bacteria than Gram-negative bacteria.

**Table 3: Characteristic IR (cm<sup>-1</sup>) bands of L1-Co-L3**

Code	Formula	$\nu\text{OH}$	$\nu\text{C}=\text{N}$	$\nu\text{C}-\text{O}$	$\nu\text{Py}$	$\nu\text{H}_2\text{O}$	$\nu\text{M}-\text{O}$	$\nu\text{M}-\text{N}$
L <sub>1</sub>	C <sub>12</sub> H <sub>10</sub> N <sub>2</sub> O	3324	1587	1271	1056	–	–	–
Cu-L <sub>1</sub>	[CuDL1·Cl·H <sub>2</sub> O]	–	1581	1372	1058	869	528	489
Co-L <sub>1</sub>	[Co(DL1) <sub>2</sub> ·2H <sub>2</sub> O]	–	1590	1319	1056	866	445	414
L <sub>2</sub>	C <sub>12</sub> H <sub>9</sub> N <sub>3</sub> O <sub>3</sub>	–	1650	1280	1081	–	–	–
Cu-L <sub>2</sub>	[CuDL2·Cl·H <sub>2</sub> O]	–	1597	1373	1087	850	482	444
Co-L <sub>2</sub>	[Co(DL2) <sub>2</sub> ·2H <sub>2</sub> O]	–	1597	1335	1084	855	490	428
L <sub>3</sub>	C <sub>12</sub> H <sub>9</sub> BrN <sub>2</sub> O	–	1615	1274	1078	–	–	–
Cu-L <sub>3</sub>	[CuL3·Cl·H <sub>2</sub> O]	–	1598	1279	1080	874	464	439
Co-L <sub>3</sub>	[Co(L3) <sub>2</sub> ·2H <sub>2</sub> O]·2H <sub>2</sub> O	–	1597	1279	1081	870	523	429

**Abbreviations:**  $\nu\text{OH}$  = O–H stretching vibration;  $\nu\text{C}=\text{N}$  = azomethine C=N stretching;  $\nu\text{C}-\text{O}$  = C–O stretching;  $\nu\text{Py}$  = pyridine ring C=N stretching;  $\nu\text{H}_2\text{O}$  = coordinated water vibration;  $\nu\text{M}-\text{O}$  = metal–oxygen vibration;  $\nu\text{M}-\text{N}$  = metal–nitrogen vibration. All values are in cm<sup>-1</sup>.

Among all compounds investigated, Co-L1 exhibited the highest antibacterial activity against *S. aureus*, maintaining strong activity even at lower concentrations. In contrast, Cu-L3 displayed comparatively weaker activity. The enhanced performance of cobalt complexes relative to the corresponding copper complexes suggests a favorable role of cobalt coordination in promoting antibacterial activity.

Activity was more pronounced against Gram-positive bacteria (*S. aureus* and *E. faecalis*) than Gram-negative bacteria (*E. coli* and *P. aeruginosa*). The greater susceptibility of Gram-positive bacteria may be associated with the absence of an outer lipopolysaccharide

membrane, allowing easier penetration and interaction of the compounds with cellular components, unlike Gram-negative bacteria which possess an additional permeability barrier.

This trend was evident in the activity against *S. aureus*, where all compounds showed inhibitory effects at varying concentrations, while incorporation of metal ions further enhanced activity, particularly among the cobalt complexes. The enhanced antibacterial activity observed upon incorporation of metal ions, particularly in the cobalt complexes, may be attributed to the chelation effect, which reduces the polarity of the ligand and increases the lipophilic character of the complexes



Table 4: Antibacterial Activity of L1-Co-L3

	Gram Positive				Gram negative					
	<i>S.aureus</i>				<i>E.Feacalis</i>	<i>E. coli</i>				<i>p. aeruginosa</i>
Conc. Mg/ml	40	20	10	5	40-5	40	20	10	5	40-5
L1	2+	2+	1+	0	0-0	1+	1+	0	0	0-0
Cu-L1	3+	3+	1+	1+	0-0	1+	0	0	0	0-0
Co-L1	3+	3+	3+	0	0-0	2+	1+	1+	0	0-0
L2	3+	2+	2+	2+	0-0	1+	0	0	0	0-0
Cu-L2	3+	2+	2+	2+	0-0	2+	1+	1+	0	0-0
Co-L2	3+	3+	2+	1+	0-0	3+	1+	1+	1+	0-0
L3	2+	2+	1+	1+	0-0	1+	0	0	0	0-0
Cu-L3	2+	1+	1+	0	0-0	2+	1+	0	0	0-0
Co-L3	3+	3+	1+	1+	0-0	3+	0	0	0	0-0
Control	0	0	0	0	0-0	0	0	0	0	0-0

Inhibition values = 1 - 5 m m = 1+ (less active); 6 - 11 m m = 2+ (moderate active); >12 m m = 3+ (highly active), 0 = not detected

This facilitates better penetration through the bacterial cell membrane, resulting in improved interaction with intracellular targets and enhanced antibacterial efficacy. Additionally, metal coordination may alter the electronic properties of the ligand and promote stronger binding to microbial biomolecules, thereby increasing biological activity. The observed trend in antibacterial activity followed the order CoL1 > CoL2 = CoL3 = CuL1 > Cu-L2 > L2 > L1 = L3 > Cu-L3.

#### 4.0. Conclusion

A series of pyridine-based Schiff bases and their copper and cobalt complexes were successfully synthesized and structurally characterized. The coordination behavior of the Schiff bases through the imine nitrogen and phenolic oxygen atoms contributed to the formation of stable metal complexes with improved antibacterial performance. The observed concentration-dependent antibacterial activity, particularly the pronounced efficacy of the cobalt complexes against *Staphylococcus aureus*, highlights the influence of metal coordination on enhancing

biological potency. These findings demonstrate the potential of pyridine-containing Schiff base metal complexes as promising antibacterial scaffolds and provide a basis for further studies aimed at developing novel antiseptic agents, supported by future toxicological and biological investigations.

#### Acknowledgement

The authors are grateful to the Department of Microbiology, Nigeria Institute of Medical Research (NIMR), Yaba, Lagos State, Nigeria, for facilitating and supporting the biological studies reported in this work.

#### 5.0 References

- Abu-Yamin, A. A., Abduh, M. S., Saghir, S. A. M. & Al-Gabri, N. (2022). Synthesis, Characterization and Biological Activities of New Schiff Base Compound and Its Lanthanide. *Pharmaceuticals (Basel)*, 15, 4, 454. <https://doi.org/10.3390/ph15040454>
- Aggoun, D., Fernández-García, M., López, D., Bouzerafa, B., Ouenoughi, S., Setifi, F. & Ourari, A. (2020). New nickel(II) and copper(II) bidentate Schiff base



- complexes derived from dihalogenated salicylaldehyde and alkylamine: Synthesis, spectroscopic, thermogravimetry, crystallographic determination and electrochemical studies. *Polyhedron*, 187, 114640. <https://doi.org/10.1016/j.poly.2020.114640>
- Alyamani, N. M. (2023). New Schiff Base–TMB Hybrids: Design, synthesis and antiproliferative investigation as potential anticancer agents. *Symmetry*, 15, 609. <https://doi.org/10.3390/sym15030609>
- Balaeş, T., Mangalagiu, V., Antoci, V., Amariuca-Mantu, D., Diaconu, D. & Mangalagiu, I. I. (2025). Hybrid Bis-(Imidazole/Benzimidazole)-Pyridine Derivatives with Antifungal Activity of Potential Interest in Medicine and Agriculture via Improved Efficiency Methods. *Pharmaceuticals (Basel)*, 18, 4, 495. <https://doi.org/10.3390/ph18040495>
- Carreño, A., Morales-Guevara, R., Cepeda-Plaza, M., Páez-Hernández, D., Preite, M., Polanco, R., Barrera, B., Fuentes, I., Marchant, P. & Fuentes, J. A. (2024). Synthesis, Physicochemical Characterization, and Antimicrobial Evaluation of Halogen-Substituted Non-Metal Pyridine Schiff Bases. *Molecules*, 29, 19, 4726. <https://doi.org/10.3390/molecules29194726>
- De, S., Kumar, A., Shah, S., Sabnaz, K., Nandan, S., Banerjee, S. & Dey, S. (2022). Pyridine: The scaffolds with significant clinical diversity. *RSC Advances*, 12, pp. 15385–15406. <https://doi.org/10.1039/D2RA01571D>
- Dueke-Eze, C. U., Fasina, T. M. & Familoni, O. B. (2023). Metal complexes of 4-aminopyridine Schiff bases: Potent molecules in the design of antituberculosis agents. *Communication in Physical Sciences*, 9, 3, pp. 203–212.
- Dueke-Eze, C. U. and Fasina, T. M. (2023). Schiff bases of salicyl diene-2-aminopyridine: Synthesis, UV–Vis study and antibacterial study. *International Journal of Basic Science and Technology*, 9, 2, pp. 85–91. <https://doi.org/55555/DHHP4380>
- Dueke-Eze, C. U., Ajiboye, D. D., Ebojoh, O. G., Kemabonta, K. K. & Fasina, T. M. (2024). Exploring the Larvicidal Potential of Schiff Bases and Their Cobalt Complexes: New perspective on Malaria Vector Control. *FUW Trends in Science & Technology Journal*, 9, 3, pp. 119–126.
- Dueke-Eze, C. U., Madueke, N. A., Iroha, N. B., Maduelosi, N. J., Nnanna, L. A., Anadebe, V. C. & Chokor, A. A. (2022). Adsorption and inhibition study of N-(5-methoxy-2-hydroxybenzylidene)isonicotinohydrazide Schiff base on copper corrosion in 3.5% NaCl. *Egyptian Journal of Petroleum*, 31, pp. 31–37. <https://doi.org/10.1016/j.ejpe.2022.05.001>
- Elsayed, M. A., Elsayed, A. M. & Sroor, F. M. (2024). Novel biologically active pyridine derivatives: Synthesis, structure characterization, in vitro antimicrobial evaluation and structure-activity relationship. *Medicinal Chemistry Research*, 33, pp. 476–491. <https://doi.org/10.1007/s00044-024-03188-1>
- Guo, Y. N., Hu, X. B., Zhang, H. G., Han, Y. F. & Wang, H. (2024). Synthesis, Crystal Structure, Photophysical Properties, and Antibacterial Activities of the Copper(II) Complex Derived from 4-Chloro-2-[(2,6-Dimethylphenyl)Imino]Methyl}Phenol. *Journal of Structural Chemistry*, 65, 5, pp. 868–881. <https://doi.org/10.1134/S0022476624050020>
- Hamdan, I. A. A., Hamdan, A. A. A. & Aljabawi, R. A. A. (2024). Synthesis, Spectral Identification of Some New Schiff Bases, and Evaluation of Their Antibacterial Activity and Inhibitory Effect on Proinflammatory Cytokines (IL-1 $\beta$ , TNF), and DNA Ligase. *Russian Journal of Bioorganic Chemistry*, 50, pp. 138–146.



- Hamid, S. J. & Salih, T. (2022). Design, synthesis, and anti-inflammatory activity of some coumarin Schiff base derivatives: In silico and in vitro study. *Drug Design, Development and Therapy*, 16, pp. 2275–2288.
- Islam, M. B., Islam, M. I., Nath, N., Emran, T. B., Rahman, M. R., Sharma, R. & Matin, M. M. (2023). Recent Advances in Pyridine Scaffold: Focus on Chemistry, Synthesis, and Antibacterial Activities. *BioMed Research International*, 2023, Article ID 9967591. <https://doi.org/10.1155/2023/9967591>
- John, L., Joseyphus, R. S. & Joe, I. H. (2020). Biomedical application studies of Schiff base metal complexes containing pyridine moiety: Molecular docking and a DFT approach. *SN Applied Sciences*, 2, 500. <https://doi.org/10.1007/s42452-020-2274-6>
- Joshi, K. (2023). Chemistry with Schiff Bases of Pyridine Derivatives: Their Potential as Bioactive Ligands and Chemosensors. In *Exploring Chemistry with Pyridine Derivatives*. IntechOpen. <https://doi.org/10.5772/intechopen.106749>
- Kumar, N., Kaur, H., Khanna, A., Kaur, K., Singh, J. V., Kaur, S., Bedi, P. M. S. & Singh, B. (2023). Pyridine as a potent antimicrobial agent and its recent discoveries. In *Recent Advances in the Synthesis and Applications of Pyridines*, Chapter 16, pp. 581–605. Elsevier.
- Lacopetta, D., Ceramella, J., Catalano, A., Mariconda, A., Giuzio, F., Saturnino, C., Longo, P. and Sinicropi, M. S. (2023). Metal Complexes with Schiff Bases as Antimicrobials and Catalysts. *Inorganics*, 11, 8, 320. <https://doi.org/10.3390/inorganics11080320>
- Mannaa, A. H., Gomaa, E. A., Zaky, R. R., Ghaith, E. A. and Abd El-Hady, M. N. (2025). Bivalent transition metal complexes of triazole pyridine Schiff base with theoretical and biological investigations. *Scientific Reports*, 15, 31192. <https://doi.org/10.1038/s41598-025-15782-3>
- Marinescu, M. & Popa, C.-V. (2022). Pyridine Compounds with Antimicrobial and Antiviral Activities. *International Journal of Molecular Sciences*, 23, 5659. <https://doi.org/10.3390/ijms23105659>
- Meeran, I. S., Raja, T. W., Dusthakeer, V. N. A., Ali, M. M. N., Tajudeen, S. S. & Shabeer, T. K. (2022). An insight into antimycobacterial and antioxidant potentials of INH-Schiff base complexes and in silico targeting of MtKasB receptor of *M. tuberculosis*. *New Journal of Chemistry*, 46, pp. 4620–4633.
- Nasif, V. & Sayin, K. (2025). Synthesis of new pyridine-based ONNO type Schiff bases and Cd(II) complexes: Investigation of structural, electronic and anti-cancer properties computationally and experimentally. *Journal of Molecular Structure*, 1322, 1, 140359. <https://doi.org/10.1016/j.molstruc.2024.140359>
- Obeid, A., Al-Aghbari, S. A., Al-Taifi, E. A., Alhamzi, E. H. L. & Rageh, Z. (2025). Syntheses, Characterization and Biological Effect Studies of Some New Heterocyclic Compounds Containing Pyrazole and Pyridazine Rings and Their Schiff Bases. *Open Access Library Journal*, 12, 1, pp. 1–10. <https://doi.org/10.4236/oalib.1112623>
- Raczuk, E., Dmochowska, B., Samaszko-Fiartek, J. & Madaj, J. (2022). Different Schiff Bases—Structure, Importance and Classification. *Molecules*, 27, 787. <https://doi.org/10.3390/molecules27030787>
- Rani, V. and Reddy, P. (2018). Synthesis and Antimicrobial Activity of New Pyridine Containing Substituted Phenyl Azetidene-2-One Derivatives. *Open Journal of Medicinal Chemistry*, 8, pp. 22–29. <https://doi.org/10.4236/ojmc.2018.82003>



- Rani, V., Kesavan, C. and Haseena, M. P. (2020). Bidentate Schiff Base Ligands Appended Metal(II) Complexes as Probes of DNA and Plasma Protein: In Silico Molecular Modelling Studies. *Applied Biochemistry and Biotechnology*, 191, pp. 1515–1532. <https://doi.org/10.1007/s12010-020-03270-5>
- Sroor, F. M., Ahmed, A. F., Soliman, A. A., Wagdy, K. B. & Khalil, K. M. (2025). Comparative Study of Pyridine and Pyrimidine Derivatives as Promising Anti-Inflammatory Agents: Design, Synthesis, and LPS-Induced RAW 264.7 Macrophages. *Drug Development Research*, 86, 6, e70146. <https://doi.org/10.1002/ddr.70146>.
- Thakur, S., Jaryal, A. and Bhalla, A. (2024). Recent advances in biological and medicinal profile of Schiff bases and their metal complexes: An updated version (2018–2023). *Results in Chemistry*, 7, 101350. <https://doi.org/10.1016/j.rechem.2024.101350>
- Vankar, S. D., Makwana, H. M. and Sharma, M. G. (2024). Rapid Synthesis of Schiff Bases via Pyridine-2-Carboxylic Acid as an Effective Catalyst. *ChemistrySelect*, 9, e202402376. <https://doi.org/10.1002/slct.202402376>
- Yousef, R. G., Eissa, I. H., Elwan, A. & El-Zahabi, M. A. (2023). Pyridine Derivatives as Anticancer Agents: FDA-Approved Drugs and Promising Reported Compounds. *Al-Azhar Journal of Pharmaceutical Sciences*, 68, 2, pp. 64–81. <https://doi.org/10.21608/ajps.2023.332167>
- Yuldasheva, N., Acikyildiz, N., Akyuz, M., Yabo-Dambagi, L., Aydin, T., Cakir, A. & Kazaz, C. (2022). The synthesis of Schiff bases and new secondary amine derivatives of p-vanillin and evaluation of their neuroprotective, antidiabetic, antidepressant and antioxidant potentials. *Journal of Molecular Structure*, 1270, 133883.
- Zhang, L. Z., Ding, T. and Chen, C. L. (2011). Biological activities of pyridine-2-carbaldehyde Schiff bases derived from S-methyl- and S-benzylthiocarbamate and their zinc(II) and manganese(II) complexes: Crystal structure of the manganese(II) complex of pyridine-2-carbaldehyde S-benzylthiocarbamate. *Russian Journal of Coordination Chemistry*, 37, pp. 356–361. <https://doi.org/10.1134/S1070328411040117>

**Declaration****Consent for publication**

Not applicable

**Availability of data**

Data shall be made available on demand.

**Competing interests**

The authors declared no conflict-of-interest

**Ethical Consideration**

Not applicable

**Funding**

The authors declared no source of funding

**Authors' contributions**

Cordelia U. Dueke-Eze and Tolulope M. Fasina and Oluwole B. Familoni designed, synthesized and characterized the compounds. Cordelia U. Dueke-Eze and Tolulope M. Fasina and Oluwole B. Familoni interpreted the results. Cordelia U. Dueke-Eze wrote the manuscript.

