



International Journal of **Biological Chemistry**

ISSN 1819-155X



Academic
Journals Inc.

www.academicjournals.com

Biological Activity of Copper (II), Cobalt (II) and Nickel (II) Complexes of Schiff Base Derived from O-phenylenediamine and 5-bromosalicylaldehyde

T.M. Fasina, O. Ogundele, F.N. Ejiah and C.U. Dueke-Eze
Department of Chemistry, University of Lagos, Akoka, Lagos State, Nigeria

Corresponding Author: T.M. Fasina, Department of Chemistry, University of Lagos, Akoka, Lagos State, Nigeria

ABSTRACT

Complexes of cobalt, nickel and copper ions with Schiff base derived from 5-bromosalicylaldehyde and o-phenylenediamine were synthesized and characterized using elemental analyses, molar conductance measurements, infrared and electronic spectroscopy. Elemental analysis data suggest the stoichiometry to be 1:1 [M:L] ratio formation in all complexes. The molar conductance measurements reveal the presence of non-electrolytic complexes. Comparison of the IR spectra of the Schiff base and the metal complexes indicate that the Schiff base is tetradentate and coordinates using the N_2O_2 chromophore. The electronic spectra data support octahedral geometry for cobalt (II) complex, square planar geometry for nickel (II) and copper (II) complexes. The growth inhibitory potential of the Schiff base and the metal complexes against some clinically important bacteria, namely *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Enterococcus faecalis* (ATCC 29212) and *Salmonella typhi* show that the metal complexes are more potent than the parent Schiff base ligand against all tested bacterial strains.

Key words: Schiff base metal complexes, o-phenylenediamine, biological activity

INTRODUCTION

Schiff base metal complexes have remained an intense area of research due to their simple synthesis, versatility and diverse range of applications (Yamada, 1999). Schiff bases played a key role in the development of coordination chemistry as they readily form stable complexes with most transition metals (Taylor *et al.*, 2004). Metal complexes of Schiff bases are specifically of interest in bioinorganic chemistry because many of these complexes provide biological models for use in understanding the structure of biomolecules and biological processes (Abd El-Wahab and El-Sarrag, 2004). These complexes may statistically mimic the spectroscopic or other physical properties of the enzyme (Albrecht *et al.*, 1999; Nanda *et al.*, 1997; Beissel *et al.*, 1996).

Earlier work have shown that some drugs exhibit increased activity when administered as metal chelates rather than organic compound (Singh *et al.*, 1975; Mahindru *et al.*, 1983) and that the coordinating possibility of o-phenylenediamine has been improved by condensing with variety of carbonyl compounds. Cobalt, palladium and lanthanide complexes derived from Schiff bases of 5-bromosalicylaldehyde and o-phenylenediamine have been reported to exhibit photo-luminescence and catalytic activity (Uh *et al.*, 2009; Joseph *et al.*, 2001; Chang *et al.*, 2004). However, their biological activity has not received much attention. In line with this, we herein report the synthesis and *in vitro* antibacterial activity of some Co (II), Ni (II) and Cu (II) complexes with symmetric Schiff base ligand derived from 5-bromosalicylaldehyde and o-phenylenediamine.

MATERIALS AND METHODS

Chemicals and solvents were of reagent or analytical grade and used without further purification.

The o-phenylenediamine, 5-bromosalicylaldehyde, copper (II) chloride, cobalt (II) chloride and nickel (II) chloride were purchased from Aldrich Sigma company and used as supplied.

Elemental analysis data were obtained on a Perkin Elmer model 2400 series II CHNS/O analyzer. Infrared (IR) spectra of the compounds were recorded as KBr discs on a Perkin-Elmer Spectrum RX1 spectrophotometer in the range 400 to 4000 cm^{-1} .

The ^1H NMR spectrum of the ligand was recorded in DMSO- d_6 solution on a Bruker Avance III 400 MHz spectrometer with chemical shifts reported in ppm relative to TMS as internal standard. The electronic absorption spectra of all the complexes were recorded in DMSO on a PGT80/T80⁺ UV-VIS spectrophotometer in 1 cm quartz cell at room temperature immediately after preparing the solution. Conductivity measurements were obtained using DMF as solvent. Melting points ($^{\circ}\text{C}$) were determined with aid of Gallenkamp melting-point apparatus.

Synthesis of schiff base (L): The Schiff base was prepared by dissolving (0.01 mole, 1.08 g) of o-phenylenediamine in 50 mL of ethanol and (0.02 mol, 4.02 g) of 5-bromosalicylaldehyde in 50 mL of ethanol. The solution was refluxed at 70°C for 4 h and cooled to room temperature. The yellow solid product obtained was filtered, dried and re-crystallized from ethanol.

Yield: 83.3% (m.p: 199°C); IR (Nujol, cm^{-1}) 3677, 1602, 1373; UV (nm) 269, 324; ^1H NMR: 6.09-7.87 (m, 12H, ArH), 8.89 (s, 2H, H-C = N); Anal calcd for $\text{C}_{20}\text{H}_{14}\text{Br}_2\text{N}_2\text{O}_2$ C: 50.66, H: 2.98, N: 5.91 found C: 50.51, H: 2.86, N: 5.86.

General synthesis of metal complexes: An ethanolic (40 mL) solution of Schiff base (0.003 mmol) was mixed with metal (II) chloride (0.003 mmol) in ethanol (40 mL) solution keeping ligand-metal ratio 1:1. The mixture was then refluxed for 2 h. The solid product obtained was filtered, washed with cold ethanol and dried in vacuo.

Cobalt: Yield 1.47 g (80.9%); M.P> $>300^{\circ}\text{C}$; IR (KBr, cm^{-1}): 1580, 1369, 1213, 749, 628; UV (nm) 287, 399, 484.

Anal. calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_6\text{CoCl}_2$, C: 39.63, H: 2.34, N: 4.64 found, C: 39.10, H: 2.43, N: 5.11.

Nickel: Yield 1.403 g (88.2%); M.P> $>300^{\circ}\text{C}$; IR (KBr, cm^{-1}) 1593, 1358, 754, 550; UV (nm) 319, 385, 496.

Anal. calcd for $\text{C}_{20}\text{H}_{12}\text{Br}_2\text{N}_2\text{O}_2\text{Ni}$, C: 45.06, H: 2.65, N: 5.28 found, C: 45.25, H: 2.17, N: 5.34.

Copper: Yield 1.402 g (71.1%); M.P> $>300^{\circ}\text{C}$; IR (Kbr, cm^{-1}) 1603, 1251, 737, 527, 641; UV (nm) 285, 330, 438.

Anal. calcd. for $\text{C}_{20}\text{H}_{12}\text{Br}_2\text{N}_2\text{O}_2\text{Cu}$, C: 44.68, H: 2.62, N: 5.21 found, C: 46.46, H: 2.26, N: 5.30.

Antimicrobial study: Antimicrobial activity was determined by the Agar-ditch method (Parekh *et al.*, 2005). The *in vitro* biological screening effects of the investigated compounds were tested against *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis* and *Salmonella typhi*. The compounds were dissolved in dimethylformamide to obtain a final concentration of 5 mg mL^{-1} .

The bacterial strain was inoculated in 25 mL of Mac Conkey agar and incubated for 24 h at 37°C in order to activate the bacterial strain. A solution of the activated bacterial strain was prepared in normal saline the turbidity was adjusted using 0.5 McFarland standards. Molten Mueller-Hinton agar was poured over sterile 90 mm Petri dishes and 1 mL of the activated strain was inoculated into the media when it reached a temperature of 40-45°C. The medium was allowed to solidify. A well was made in the plates with the help of a cork-borer (0.85 cm) which was then filled with the test sample solutions. Controls were run for each bacteria and the solvent. The plates were incubated at 37°C for 24 h and the zones of inhibition formed by these compounds were measured at the end of the incubation period.

RESULTS AND DISCUSSION

Synthesis: The Schiff base ligand, L was isolated in good yield as a yellow solid from the reaction of o-phenyldiamine and 5-bromosalicylaldehyde in a 1:2 stoichiometric ratio. The ¹H NMR spectrum of the Schiff base ligand exhibits a singlet signal at 8.89 d (s, 1H) and a multiple at 6.90-7.87 (m, Ar-H).

Treatment of the ligand L, with Cu (II), Co (II) and Ni (II) chlorides, yielded complexes corresponding to metal: Ligand ratio of 1:1. Analytical and physical data are presented in Table 1.

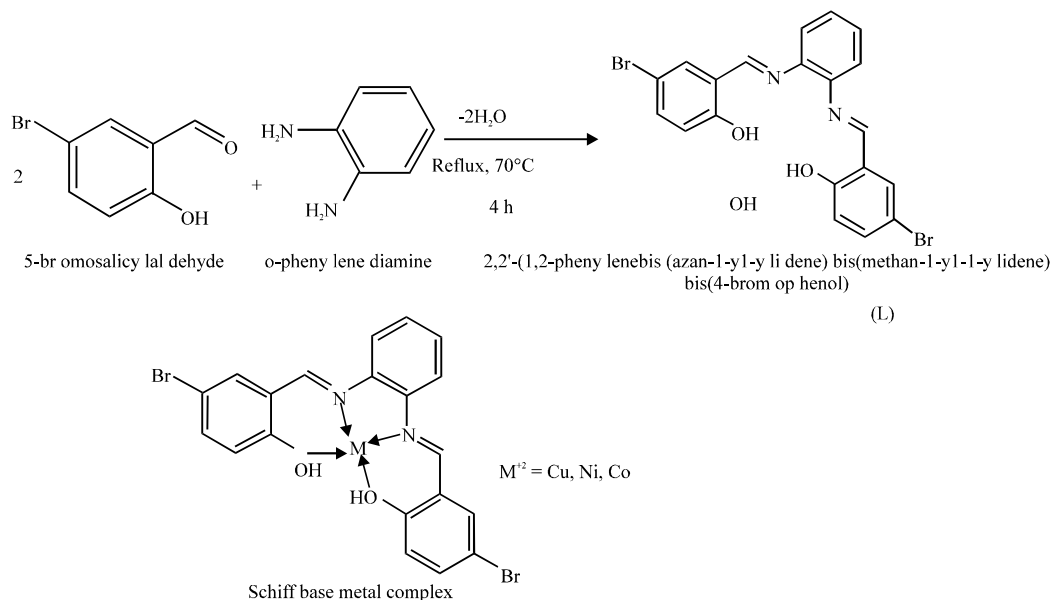


Table 1: Analytical and physical data of compounds

Compound	Empirical formula	Formula weight	Colour (% yield)	m.p (°C)	Microanalysis (calcd.)		
					C	H	N
L	C ₂₀ H ₁₄ BrN ₂ O ₂	474	Yellow (83.3)	199	50.51 (50.66)	2.86 (2.98)	5.86 (5.91)
CoL	C ₂₀ H ₁₂ BrN ₂ O ₂ CoCl ₂	603	Brown (80.9)	>300	39.10 (39.63)	2.42 (2.32)	5.11 (4.64)
NiL	C ₂₀ H ₁₂ BrN ₂ O ₂ Ni	530	Brick red (88.2)	>300	45.25 (45.06)	2.17 (2.28)	5.34 (5.28)
CuL	C ₂₀ H ₁₂ BrN ₂ O ₂ Cu	533	Brown	>300	46.46 (44.84)	2.26 (2.26)	5.30 (5.23)

The metal complexes are soluble in common organic solvents such as DMF and DMSO. The low molar conductance values of the complexes reveal their non-electrolytic nature (Geary, 1971).

IR spectra: In order to determine the binding mode of Schiff base to metal in the complexes, IR spectrum of the free ligand was compared with the spectra of the metal complexes. Diagnostic IR spectral bands of the ligands and their metal complexes are presented in Table 2. The characteristic absorption bands of the ligand occurred at 1602 and 1373, 1270 cm^{-1} due to C = N and C-O vibrations, respectively. The band at 1602 cm^{-1} due to the azomethine nitrogen atoms of the Schiff base underwent a shift to lower frequency 1580 cm^{-1} upon complexation, indicating the involvement of nitrogen of the azomethine group in coordination (Aranha *et al.*, 2007). The C-O band which occur at 1373 and 1270 cm^{-1} for the ligand appeared at lower frequencies after complexation due to coordination of the phenolic oxygen of the ligand to the metal ion (Abd-Elza, 2001). Thus, it can be concluded that the Schiff base is a tetradentate ligand coordinating via the azomethine N and the phenolic O. In the spectra of Co (II) complex, the broad band at 3434 cm^{-1} , together with new band at 628 cm^{-1} indicating the presence of coordinated water. This indicates an octahedral geometry for Co (II) complex. A square planer geometry is suggested for Cu (II) and Ni (II) complexes due to the absence of coordinated water molecules. The nature of metal-ligand bond is confirmed by the newly formed band in the region 646-754 assigned to (M-N) and 496-628 attributed to (M-O).

Electronic spectra: The electronic absorption spectra of the Schiff base and all the metal complexes were recorded in DMSO at room temperature. The electronic spectral data of the ligand and its complexes are presented in Table 2. The aromatic band of the ligand at 269 nm is attributed to benzene $\pi \rightarrow \pi^*$ transition. The band around 324 nm is due to the $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the nitrogen of the azomethine group in the Schiff base. The electronic spectra of Co (II) complex showed an intense absorption band at 484 nm assignable to ${}^4T_{1g} \rightarrow {}^4T_{1g}$ suggesting an octahedral geometry (Sonmez and Sekerci, 2007). The appearance of a band at 496 nm due to ${}^1A_{1g} \rightarrow {}^1B_{1g}$ favors a square planar geometry for Ni (II) complex (Raman *et al.*, 2003). Only one band was also observed at 438 nm in the electronic spectrum of the Cu (II) complex assigned to ${}^2B_{1g} \rightarrow {}^2A_{1g}$ which is in conformity to a square planar geometry (Raman *et al.*, 2003). All the complexes show an intense band at ca 330-399 nm which is assigned to $n \rightarrow \pi^*$ transition associated with the azomethine linkage.

Antimicrobial activity: The antimicrobial activity of the investigated compounds was tested against the microorganisms *E. coli*, *S. typhi*, *S. aureus* and *E. feacalis*. The compounds were tested at a concentration of 5 mg mL^{-1} using the agar ditch method (Parekh *et al.*, 2005). The growth inhibition zones were measured in diameter (mm) and the results are summarized in Table 3. A comparative study of the ligand and its metal complexes indicates that the complexes exhibited anti-microbial activity over the free ligand. The ligand showed no activity against *E. coli*, *S. typhi* and *S. aureus* but there was activity against *E. feacalis*. The metal complexes showed activity against all the tested organisms. The order of activity observed for the complexes reveal that the CoL exhibited high activity against the tested microbes with *S. aureus* being more susceptible to the complex. CuL and NiL Complexes exhibited similar activity, none of these complexes showed activity against *S. aureus* with the NiL exhibiting high activity against *E. coli* and *E. feacalis*. The similarity in the activity of the CuL and NiL towards the tested organisms can be attributed to the

Table 2: IR, UV and conductivity data of compounds

Compound	ν (O-H)	ν (C = N)	ν (C-O) _{sym}	ν (M-N)	ν (M-O)	Chemical shift δ (ppm) C = N	λ max (nm)	Conductivity ($\mu\text{s cm}^{-1}$)
L		1602	1373			8.89	269, 324	-
CoL	3434	1580	1327	749	628		287, 399, 484	8.75
NiL	-	1593	1358	754	550		319, 373, 479	5.81
CuL	-	1603	1251	737	641		285, 323, 420	9.02

Table 3: Antimicrobial activity of Schiff base ligand, L and their metal complexes (5 mg mL⁻¹)

Compound	Diameter of inhibition zone of bacteria (mm)			
	Gram positive		Gram negative	
	<i>S. typhi</i>	<i>S. aureus</i>	<i>E. feacalis</i>	<i>E. coli</i>
L	-	15	-	-
CoL	24	11	19	13
NiL	-	20	20	13
CuL	-	17	20	12
DMF	-	-	-	-

Control (DMF): No activity (there was no zone of inhibition)

structures of the complexes which exhibited square planer geometry against the CoL attributed octahedral geometry. This once again confirms earlier reports that antimicrobial activity is dependent on the molecular structure of the compound and the bacterial strain under consideration (Vaghasiya *et al.*, 2004).

It is generally observed that metal chelates have higher antibacterial activity than the free ligand. This is because of an increase in cell permeability. The lipid membrane which surrounds the cell favours the passage of only lipid soluble materials and it is known that liposolubility is an important factor controlling antimicrobial activity. Thus, in the present study the cell permeability was perhaps not affected and hence activity of the ligand is not visualized.

This study is of great importance as broad spectrum antimicrobial agents can be developed using the CoL which showed moderate to high activity against all tested organisms.

CONCLUSION

The design and synthesis of Schiff base ligand, obtained from the reaction of o-phenylenediamine and 5-bromosalicylaldehyde is described. Cu (II), Co (II) and Ni (II) complexes have been synthesized using the above Schiff base and characterized on the basis of analytical, IR and UV-Vis data. The Schiff base coordinates through its azomethine N and the phenolic O to the metal ion and acts as a tetradentate ligand. The electronic spectra exhibit two kinds of geometries; square planar for Cu (II) and Ni (II) complexes, octahedral for Co (II) complex. The antimicrobial results showed that the metal complexes were more active than the Schiff bases arising from the structure of the metal complex and cell permeability.

ACKNOWLEDGMENTS

The authors are grateful to Department of Medical Microbiology, College of Medicine, University of Lagos where the organisms were obtained.

REFERENCES

- Abd El-Wahab, Z.H. and M.R. El-Sarrag, 2004. Derivatives of phosphate schiff base transition metal complexes: Synthesis, studies and biological activity. *Spectrochim. Acta Part A: Mol. Biomol. Spectroscopy*, 60: 271-277.
- Abd-Elza, M.M., 2001. Spectroscopic characterization of some tetradentate Schiff bases and their complexes with nickel, copper and zinc. *J. Chin. Chem. Soc.*, 48: 153-158.
- Albrecht, M., K. Hubler, T. Scheiring and W. Kaim, 1999. Copper (I) and copper (II) complexes of the bidentate imidazole/thioether ligand 1-methyl-2-(methylthiomethyl)-1H-benzimidazole. *Inorg. Chim. Acta*, 287: 204-208.
- Aranha, P.E., M.P. dos Santo, S. Romera and E.R. Dockal, 2007. Synthesis, characterization and spectroscopic studies of tetradentate Schiff base chromium (III) complexes. *Polyhedron*, 26: 1373-1382.
- Beissel, T., T. Glaser, F. Kesting, K. Wiegardt and B. Nuber, 1996. Mono- and dinuclear transition metal complexes of the hexadentate ligand tris (4-tert-butyl-2-mercaptobenzyl) -1, 4, 7-triazacyclononane (L). *Inorg. Chem.*, 35: 3936-3947.
- Chang, K.H., C.C. Huang, Y.H. Liu, Y.H. Hu, P.T. Chou and Y.C. Lin, 2004. Synthesis of photo-luminescent Zn (II) Schiff base complexes and it's derivative containing Pd (II) moiety. *Dalton Trans.*, 2004: 1731-1738.
- Geary, W.J., 1971. The use of conductivity measurements in organic solvents for the characterization of coordination compounds. *Coord. Chem. Rev.*, 7: 81-122.
- Joseph, T., S.B. Halligudi, C. Satyanarayan, D.P. Sawant and S. Gopinathan, 2001. Oxidation by molecular oxygen using zeolite encapsulated Co (II) saloph complexes. *J. Mol. Catal. A: Chem.*, 168: 87-97.
- Mahindru, A.M., J.M. Fisher and M. Rabinovitz, 1983. Bathocuproine sulphonate: A tissue culture-compatible indicator of copper-mediated toxicity. *Nature*, 303: 64-65.
- Nanda, K.K., W.A. Addison, R.J. Butcher, M.R. McDevitt, N.T. Tao and E. Sinn, 1997. Structural demonstration of the role of ligand framework conformability in copper (II)/ copper (I) redox potentials. *Inorg. Chem.*, 36: 134-135.
- Parekh, J., P. Inamdhar, R. Nair, S. Baluja and S. Chanda, 2005. Synthesis and antimicrobial activity of some Schiff bases derived from 4-aminobenzoic acid. *J. Serbian Chem. Soc.*, 70: 1155-1161.
- Raman, N., V. Muthuraj, S. Ravichandran and A. Kulandaisamy, 2003. Synthesis, characterization and electrochemical behaviour of Cu (II), Co (II), Ni (II) and Zn (II) complexes derived from acetylacetone and p-anisidine and their antimicrobial activity. *Proc. Indian Acad. Sci. (Chem. Sci.)*, 115: 161-167.
- Singh, P., R.L. Goel and B.P. Singh, 1975. 8-acetyl-7-hydroxy-4-methyl coumarin as a gravimetric reagent for Cu²⁺ and Fe³⁺. *J. Indian Chem. Soc.*, 52: 958-959.
- Sonmez, M. and M. Sekerci, 2007. The template synthesis, spectral characterization and thermal behavior of new binuclear Schiff base complexes derived from N-aminopyrimidine with 2,3-butandion. *J. Serbian Chem. Soc.*, 72: 259-264.
- Taylor, M.K., J. Reglinski and D. Wallace, 2004. Coordination geometry of tetradentate Schiff's base nickel complexes: The effects of donors, backbone length and hydrogenation. *Polyhedron*, 23: 3201-3209.

- Uh, H., P.D. Badger, S.J. Geib and S. Petoud, 2009. Synthesis and solid state, solution luminescence properties of near-infrared-emitting neodymium (3+) complexes formed with ligands derived from salophen. *Helv. Chim. Acta*, 92: 2313-2329.
- Vaghasiya, Y., M. Soni, R. Nair, S. Baluja and S. Chanda, 2004. Synthesis, structural determination and antibacterial activity of compounds derived from vanilline and 4-aminoantipyrene *J. Serb. Chem. Soc.*, 69: 991-998.
- Yamada, S., 1999. Advancement in stereochemical aspects of Schiff base metal complexes. *Coord. Chem. Rev.*, 190-192: 537-555.