

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF METAL (II) COMPLEXES WITH SCHIFF BASE DERIVED FROM PROPIONALDEHYDE WITH ANILINE

IM. Wakil^{1*}, MB. Abubakar², GA. Mala³, S. Hassan⁴, A. Abubakar¹ and I. Waziri³

¹Department of Chemistry, Umar Ibn Ibrahim El- Kanemi College of Edu. Sci. and Tech. Bama, Borno State, Nigeria.

²Department of Microbiology and Parasitology, University of Maiduguri, P.M.B.1069, Maiduguri, Borno State, Nigeria.

³Department of Chemistry, University of Maiduguri, P.M.B.1069, Maiduguri, Borno State, Nigeria.

⁴Department of Chemistry, Umar Suleiman College of Education, Gashua, P.M.B. 02, Gashua, Yobe State, Nigeria.

ABSTRACT

Complexes of Mn(II), Cu(II) and Ni(II) with Schiff base ligand (HL) derived from condensation of propionaldehyde with aniline were synthesized in ethanolic medium. The complexes were characterized on the basis of melting point, conductivity, solubility, IR and UV/Visible spectral studies. The *in-vitro* antibacterial activities of the complexes were tested against different strains of bacteria such as Gram positive (*Staphylococcus aureus*, *Streptococcus pyogenes*), Gram negative (*Escherichia coli*, *Salmonella typhi*) and fungus *Candida albicans*. The complexes formed in moderate yields (36-66%) and they are of various colors, ranging from buff to brown and black. The IR spectral data revealed that the complexes coordinated through azomethine nitrogen and phenolic oxygen of the ligands. Further conclusive evidence of the coordination of the Schiff base with the metal ions was shown by the appearance of new bands due to $\nu(M-N)$ and $\nu(M-O)$ in the metal complexes. The UV/visible electronic spectra further revealed that Mn(II), Cu(II) and Ni(II) complexes are octahedral. Measured molar conductance (100.50×10^{-3} - 177.00×10^{-3}) showed that the complexes are non-electrolytes. The results of the anti-microbial study showed that the complexes had more potent activities than their free ligands.

Keywords: Schiff base, propionaldehyde, aniline, synthesis and antimicrobial evaluation.

1.0 INTRODUCTION

A Schiff base is a functional group that contains carbon-nitrogen double bond with nitrogen connected to an aryl or alkyl group but not hydrogen (Antony *et al.*, 2016; Joginder *et al.*, 2017). The general formula of Schiff bases is $R_1R_2C=NR_3$ where R may be an aliphatic or aromatic group (Brodowska and Chruscinska, 2014). They are usually formed by condensation of a primary amine with a carbonyl compound either aldehydes or ketones (Ndahi and Wakil, 2015; Antony *et al.*, 2016). Schiffbases were first reported by Hugo Schiff in 1864 (Antony *et al.*, 2016; Joginder *et al.*, 2017). The compounds

containing an azomethine group (-CH=N-) are known as imines, anils or Schiff bases (Hossain *et al.*, 2017). In azomethine derivatives, the C=N linkage is essential for biological activity, several azomethine has been reported to possess remarkable antibacterial, antifungal, anticancer and antimalarial activities (Rishu *et al.*, 2013). Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of applications in many fields, examples include: biological, inorganic and analytical chemistry. Among the organic reagents actually used, Schiff bases possess excellent coordination characteristics, structural similarities with

natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties (Wakil *et al.*, 2017; Rizwana and Santha, 2012). It is well known that N and S atoms play a key role in the coordination of metals at the active sites of numerous metallobimolecules. They serve as models for biologically important species and find applications in catalytic reactions. Chelating ligands containing N, S and O donor atoms show broad biological activity (Fugu *et al.*, 2013) and are of special interest, because of the variety of ways in which they are bonded to metal ions. It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities (Rizwana and Santha, 2012).

Propionaldehyde (figure 1.1) is an aldehyde also known as propanal, propionic aldehyde or methylacetaldehyde, with a boiling point of 49°C and a melting point 81°C. Propionaldehyde is a colourless liquid with a suffocating, fruity-like odour. It is highly flammable and soluble in water. It is used in the manufacture of propionic acid, polyvinyl and other plastics. It is also used in the synthesis of rubber chemicals as a disinfectant and preservative. Propionaldehyde can form explosive peroxides and may polymerize with the addition of acids, bases, amines and oxidants, resulting in a fire or explosion hazard. It decomposes on burning, producing toxic gases and irritating fumes (Poirier *et al.*, 2002).

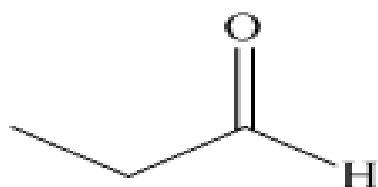


Fig. 1.1: Propionaldehyde

1.1 Aniline

Aniline (figure 1.2) is a toxic organic compound known as phenylamine or aminobenzene. Consisting of a phenyl group attached to an amino group, aniline is the prototypical aromatic amine. It has a melting point -6.3°C and a boiling point 186°C . Aniline is a colourless, oily liquid which darkens on exposure to air and light. It has a characteristic amine odour and burning taste. Aniline is miscible with alcohol, benzene, chloroform, carbon tetrachloride, acetone and most organic solvents. It ignites readily, burning with a smoky flame characteristic of aromatic compounds. Aniline is

used in rubber accelerators and antioxidants, dyes and intermediates, photographic chemicals, as isocyanates for urethane foams, in pharmaceuticals, explosives, petroleum refining and in production of diphenylamine, phenolics, herbicides, pesticides, fungicides and fibers (Anthony, 2007).

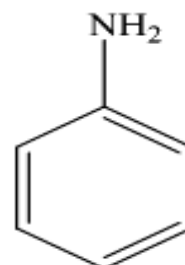


Fig. 1.2: Aniline

2.0 MATERIALS AND METHODS

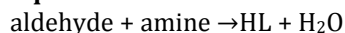
All the chemicals and solvents used were of Analar(AR) grade and were used without further purification. They are propionaldehyde, aniline, $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, methanol, ethanol, acetone, chloroform, ethyl acetate, benzene, petroleum ether and concentrated sulphuric acid. Melting point of all compounds were determined using Griffin melting point apparatus. The solubility of the complexes was determined in some polar and non-polar solvents such as water, methanol, ethanol, acetone, chloroform, ethyl acetate, benzene and petroleum ether and then warmed over a water bath for complexes that did not dissolve in cold solvents. Molar conductivity was measured by using metler P163 conductivity meter in methanol solution (10^{-3}M) at 25°C , in the Department of Soil Science, University of Maiduguri. The infrared (IR) spectra were recorded as NaBr disc on Perkin Elmer 1310(IR) at Multi-User Laboratory, Faculty of Science, Abubakar Tafawa Balewa University, (ABTU) Bauchi, in the range of $(200-4000)\text{cm}^{-1}$ for the ligand and their complexes. Electronic spectra of all the complexes were measured in methanol solution (10^{-3}M) at 25°C using UV-2550PC Series Shimadzu Spectrophotometer in the wavelength range of 250–800 nm at the National Research Institute for Chemical Technology (NARICT), Federal Ministry of Science and Technology, Zaria, Nigeria.

2.1 Synthesis of Schiff base ligand (HL)

The Schiff base ligand (HL) was synthesized using a standard literature procedure described by (Nageshet *et al.*, 2015; Kiran *et al.*, 2016). This was done by the condensation of 20ml of propionaldehyde (7.21ml, 0.1mol) with aniline

(9.11ml, 0.1mol) in ethanol (1:1 molar ratio). 2-3 drops of conc. H_2SO_4 was added. The resulting mixture was refluxed for 3-4 hours. On cooling, the solid product obtained was filtered, washed with ethanol and dried in a desiccator containing calcium chloride ($CaCl_2$).

Equation for the reaction



Where HL= Schiff-base

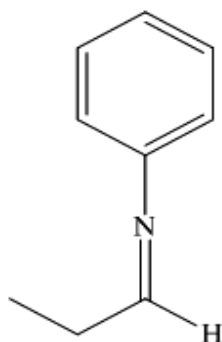
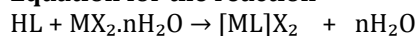


Fig. 1.3: Proposed structure of Schiff base (HL)

2.2 Synthesis of the Complexes

An ethanolic (20 ml) solution of Schiff base ligand (0.01mol, 2.66g) was added drop wise to 25ml of the metal(II)salts (1.977g, 0.01mol) of $MnCl_2 \cdot 4H_2O$, (2.377g, 0.01mol) of $NiCl_2 \cdot 6H_2O$, and (1.704g, 0.01mol) of $CuCl_2 \cdot 2H_2O$ in boiling ethanol (78.3°C). The reactions took place in 2:1 (ligand-metal). The reaction mixture was refluxed for 2 hours, cooled, filtered, washed with ethanol/acetone/ether and the product obtained was dried in a desiccator containing calcium chloride ($CaCl_2$).

Equation for the reaction



Where HL = Schiff base, M = Mn(II), Ni(II) and Cu(II), X = Cl, n = 2, 4, or 6

2.3 Antimicrobial test

Antibacterial activities of the ligand and the metal complexes were screened against different strains of organisms such as Gram positive (*Staphylococcus aureus*, *Streptococcus pyogenes*), Gram negative (*Escherichia coli*, *Salmonella typhi*) and fungus (*Candida albicans*) using a standard method described by (Mounika et al., 2010; Kiran et al., 2016). For the detection of the antimicrobial activities, the filter paper disc agar diffusion method was used. A disc of blotting paper was impregnated with a known volume and appropriate concentration of the ligand and the metal complexes, this was placed on a plate of sensitivity testing agar uniformly inoculated with the test organism at 37°C for 24 hours. The ligand and the complexes diffused from the disc that was related to the sensitivity of the organisms. Strains sensitive to the ligand/complexes were inhibited at a distance from the disc whereas resistant strains have smaller zones of inhibition or grow up to edge of the disc. After incubation, the average inhibition zone was measured and recorded.

3.0 RESULTS AND DISCUSSION

The Schiff base ligand (HL), on interaction with Mn(II), Cu(II) and Ni(II) formed complexes with moderate yields (36-66 %) corresponding to the general formula $M(L^1-L^1)_2X_2$ where M = Mn(II), Cu(II) and Ni(II), L-L deprotonated Schiff base ligand and X = Cl. All the complexes are air stable and have sharp melting points (125-162°C). The sharp melting point indicates that the complexes are probably pure (Sunil et al., 2011). The molar conductivity of the complexes were within the range of $(100.50 \times 10^{-3} - 177.00 \times 10^{-3} \text{Scm}^2\text{mol}^{-1})$. The values indicate the non-electrolytic behaviour of these complexes (Zahid et al., 2001; Mounika et al., 2010; Fugu et al., 2013). The solubility of the complexes and the ligand were determined at room temperature (37 °C) in polar and non-polar solvents. The complexes are either soluble or slightly soluble in some of the solvents except petroleum ether and ethyl acetate.

Table 1: Physical characteristics for the ligand and their metal(II) complexes

Compounds	Molecular formula (Molar mass)	Colour	Melting point (°C)	Yield (%)	Molar conductivity ($\text{scm}^2\text{mol}^{-1}$)
HL	$C_9H_{11}N$ (133.2)	Buff	156	36	130.40×10^{-3}
$Mn(L^1-L^1)_2X_2$	$Mn[(C_{19}H_{15}NO_2)_2]Cl_2$ (392.24)	Dark brown	125	53	177.00×10^{-3}
$Cu(L^1-L^1)_2X_2$	$Cu[(C_{19}H_{15}NO_2)_2]Cl_2$ (400.8)	Black	136	66	100.50×10^{-3}
$Ni(L^1-L^1)_2X_2$	$Ni[(C_{19}H_{15}NO_2)_2]Cl_2$ (396.0)	Light brown	162	58	127.60×10^{-3}

3.1 Infrared Spectra

The selected vibrational frequencies for the Schiff base ligand and its metal complexes are presented in Table 2. The IR spectral data of the free ligand showed a band at 1540 cm^{-1} which is characteristics of the azomethine nitrogen present in the Schiff base ligand (HL) (Dagade *et al.*, 2012; Kotkar and Harjeet, 2013). In all the complexes, the bands for azomethine group underwent a bathochromic shift (highervalues)(1560-1720 cm^{-1}) indicating coordination of azomethine nitrogen with the metal ion (Raman *et al.*, 2004; Sadeek *et al.*, 2013). Both the ligand and their metal complexes showed broad bands at 3520 cm^{-1} – 3600 cm^{-1} which is assigned to $\nu(\text{OH})$ (Rizwana and Santha, 2012). The $\nu(\text{C-O})$ phenolic stretching frequencies of the ligand was observed at 1370 cm^{-1} . This band was shifted to a lower frequency range (1110 – 1220 cm^{-1}) in the complexes, and this is indicative of bonding through phenolic oxygen (Mounika *et al.*, 2010; Dagade *et al.*, 2012). The ligand (HL) also showed strong band at 1270 cm^{-1} which was assigned to $\nu(\text{C-N})$ stretching. The band was shifted to 1160 cm^{-1} – 1360 cm^{-1} region in all the complexes. The $\nu(\text{M-N})$ bands was observed at 480 cm^{-1} – 620 cm^{-1} as new bands. This occurrence indicates that there is coordination between the metal and the lone pair of electron on the nitrogen atom of the ligand (Sadeek *et al.*, 2013). Also, bands observed at 550 cm^{-1} – 640

cm^{-1} indicates the formation of $\nu(\text{M-O})$ bond for the complexes (Rizwana and Santha, 2012; Sadeek *et al.*, 2013). These bands were absent in the spectra of the free ligand. (Table 2: Relevant vibrational bands for the Schiff base ligand and their metal(II) complexes)

3.2 Electronic Spectra

UV-VIS spectra of the Mn(II), Cu(II) and Ni(II) complexes were recorded at 250 – 800 nm using methanol as a solvent. The absorption regions, band assignment and the proposed geometries of the complexes are given in Table 3. The UV/Visible spectra of $\text{Mn}(\text{L}^1\text{-L}^1)\text{X}_2$ complex showed a broad band in the visible and a shoulder at 13623 cm^{-1} and 34246 cm^{-1} which were assigned to ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{n})$ transition and ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g(\text{G})$ respectively. The bands observed in $[\text{Cu}(\text{L}^1\text{-L}^1)\text{X}_2]$ complex at 13661 cm^{-1} , 28089 cm^{-1} and 28571 cm^{-1} were tentatively assigned to ${}^2\text{T}_{2g} \rightarrow {}^2\text{E}_g$ and ${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_{1g}$ transition respectively.

The UV/Visible spectrum of $[\text{Ni}(\text{L}^1\text{-L}^1)\text{X}_2]$ complex showed the following broad bands at 26115 cm^{-1} , and 26292 cm^{-1} respectively. The band at 26115 cm^{-1} corresponds to ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ transition, while 26292 cm^{-1} corresponds to ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ transition respectively (Gehad *et al.*, 2006; Zahid *et al.*, 2006; Chandra *et al.*, 2009). (Table 3: Electronic absorption spectral data for the ligand and their metal(II) complexes)

Table 2: Relevant vibrational bands for the Schiff base ligand and their metal(II) complexes

Compounds	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{C-N})$	$\nu(\text{C-O})$	$\nu(\text{C-H})$	$\nu(\text{M-N})$	$\nu(\text{M-O})$
HL	3600br	1540w	1270w	1370sh	2960s	-	-
$\text{Mn}(\text{L}^1\text{-L}^1)\text{X}_2$	3580sh	1720w	1360sh	1120w	2920sh	620sh	580w
$\text{Cu}(\text{L}^1\text{-L}^1)\text{X}_2$	3520sh	1560w	1290sh	1220w	2820sh	580sh	640w
$\text{Ni}(\text{L}^1\text{-L}^1)\text{X}_2$	3580w	1620w	1160m	1110w	2920sh	480sh	550sh

Table 3: Electronic absorption spectral data for the ligand and their metal(II) complexes

Compounds	Absorption(cm^{-1})	Band assignments	Geometry
HL	33478	$\text{n} \rightarrow \pi^*$	
$\text{Mn}(\text{L}^1\text{-L}^1)\text{X}_2$	13623	${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{n})$	Octahedral
	34246	${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g(\text{G})$	
$\text{Cu}(\text{L}^1\text{-L}^1)\text{X}_2$	13661	${}^2\text{T}_{2g} \rightarrow {}^2\text{E}_g$	Octahedral
	28089	${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_{1g}$	
	28571	${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_{1g}$	
$\text{Ni}(\text{L}^1\text{-L}^1)\text{X}_2$	26115	${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$	Octahedral
	26292	${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$	

3.3 Antibacterial activity

The antimicrobial activity of the Schiff base ligand and their metal complexes [Mn(II), Cu(II) and Ni(II) complexes] at concentrations of 10, 20 and 30 µg/ml were evaluated against Gram positive (*Staphylococcus aureus*, *Streptococcus pyogenes*) and Gram negative (*Escherichia coli*, *Salmonella typhi*) bacteria as well as fungal species – *Candida albicans* are presented in table 4. The Schiff base ligand exhibited no activity against all the test microorganisms except *C. albicans* which showed moderate activity (Vlietinck et al., 1995) ($P < 0.001$) at concentration level of 10 and 20 µg/ml. On complexation, to form Mn(II) complexes, all the test organisms showed a very good activity (Vlietinck et al., 1995) against *S. aureus*, *S. pyogenes* and *C. albicans* except *E. coli* and *S. typhi* which showed no activity at all. Also Cu(L¹-L¹)X₂ complex was active against all the organisms at 10, 20 and 30 µg/ml except *E. coli* which was resistant to the Cu(II) complex. Very high activity was observed in the complex of

Ni(II) which is highly susceptible (Vlietinck et al., 1995) against *S. aureus*, *S. pyogenes*, *E. coli*, *S. typhi* and *C. albicans*. Based on the comparative study, Ni(L¹-L¹)X₂ yielded more activity as compared to Cu(II) and Mn(II) complexes. The activity of these complexes followed the order: Ni > Cu > Mn. In general, increase in concentrations increases the activity of the metal complexes (Singh and Rajesh, 2009; Shelke et al. (2011)). It is evident that the complexes have more potency related activities than their free ligand; hence, complexation increases the antimicrobial activity. Therefore, such increased activity of the metal complexes as compared to their parent ligands can be explained on the basis of Overtone's concept and Tweedy's chelation theory which explained that the lipid membrane that surrounds the cell favours the passage of only lipophilic substances (Mounika et al., 2010) which is considered to be an important factor that controls the antimicrobial activity of the agents.

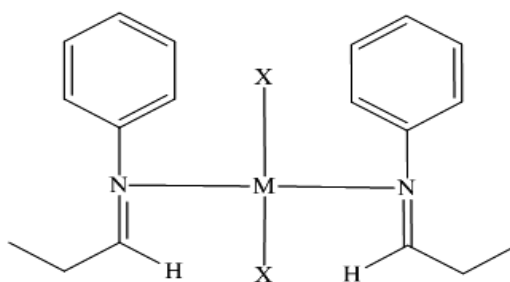


Fig.1.4: Proposed structure of the metal complexes
Where M = Mn(II), Ni(II) or Cu(II)

Table 4: Antimicrobial susceptibility studies of HL and its metal complexes

Compounds	Conc. (µg/ml)	Antimicrobial activity with zone of inhibition (mm)				
		<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>Escherichia coli</i>	<i>Salmonella typhi</i>	<i>Candida albicans</i>
HL	30	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a
	20	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a	14.33±0.58 ^{b,b'}
	10	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^a	11.33±0.58 ^{c,c'}
Mn(L ¹ -L ¹)X ₂	30	14.67±0.58 ^{b,b'}	18.67±0.58 ^{b,b'}	0.00±0.00 ^a	0.00±0.00 ^a	15.67±0.58 ^{d,d'}
	20	13.33±0.58 ^{c,c'}	14.67±0.58 ^{c,c'}	0.00±0.00 ^a	0.00±0.00 ^a	10.67±0.58 ^{b,b'}
	10	9.33±0.58 ^{d,d'}	12.00±0.00 ^{d,d'}	0.00±0.00 ^a	0.00±0.00 ^a	16.00±0.00 ^{e,c'}
Cu(L ¹ -L ¹)X ₂	30	13.33±0.58 ^{b,b',c'}	11.67±0.58 ^{e,d'}	0.00±0.00 ^a	9.33±0.58 ^b	16.00±0.00 ^{e,b'}
	20	10.67±1.15 ^{f,d'}	10.00±1.00 ^f	0.00±0.00 ^a	8.00±0.00 ^c	11.33±1.15 ^{h,c'}
	10	8.33±0.58 ^{g,d'}	7.00±0.00 ^g	0.00±0.00 ^a	0.00±0.00 ^a	9.00±0.00 ⁱ
Ni(L ¹ -L ¹)X ₂	30	28.00±0.00 ^h	19.67±0.58 ^{h,b'}	19.67±0.58 ^{b,b'}	18.33±1.15 ^d	20.67±0.58 ^{d,d'}
	20	24.33±1.15 ⁱ	16.67±0.58 ⁱ	15.00±0.00 ^c	15.67±0.58 ^{e,e'}	17.00±0.00 ^{k,b'}
	10	18.67±1.15 ^j	13.33±0.58 ^{j,d'}	10.67±0.58 ^d	12.67±0.58 ^f	13.00±0.00 ^{l,b'}
LZ	30	31.67±0.58 ^k	30.00±0.00 ^k	-	-	-
ER	30	0.00±0.00 ^a	24.67±0.58 ^l	-	-	-
GN	30	-	-	20.00±0.00 ^{e,b'}	15.00±0.00 ^{g,e'}	-
NR	30	-	-	22.00±0.00 ^f	34.00±0.00 ^h	-
KT	30	-	-	-	-	37.00±0.00 ^m

*Different superscript letters along the same column are significantly ($P < 0.05$) different.

Key: HL¹ = Schiff base ligand, X₂ = Cl, LZ = Linezolid, ER = Erythromycin, GN = Gentamicin, NOR = Norfloxacin, KET = Ketazolol.

4.0 CONCLUSION

In this paper the synthesis of a Schiff base ligand derived from condensation of propionaldehyde with aniline and its metal(II) complexes have been described. The Schiff base ligand coordinated through its azomethine nitrogen with the metal ion. This is supported by infrared spectral data. The electronic spectral bands observed are consistent with an octahedral geometry for Mn(II), Cu(II) and Ni(II). The molar conductivity data of the complexes in methanol indicated that they are non-electrolytes. All the complexes are air stable and soluble in some of the solvents used except petroleum ether and ethyl acetate. The *in-vitro* antimicrobial study shows that the complexes have higher degree of activities compared to the free ligand.

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