

Synthesis, Characterization and Antimicrobial Evaluation of Mn(II) and Zn(II) Schiff base Complexes with p-hydroxypropiophenone moiety

Agbese, S.A. *, Shallangwa, G.A. and Idris, S.O.

Department of Chemistry,
Ahmadu Bello University Zaria, Nigeria

*Corresponding Author: sagbese@yahoo.com; sagbese@redstarplc.com

Abstract

The Schiff base was synthesized by condensing 4-aminopyridine with 4-hydroxypropiophenone. The synthesized ligand was characterized by proton and carbon-13 NMR spectroscopy, electronic spectroscopy and FTIR. The result of the FTIR showed the presence of a band at 1643.41 cm^{-1} assigned to the azomethine bond, also the result of the $^1\text{H NMR}$ and $^{13}\text{C NMR}$ gave credence to the successful synthesis of the Schiff base. The Mn(II) and Zn(II) complexes were characterized by UV-visible analysis, FTIR, molar conductivity measurement and magnetic susceptibility test. The results of the FTIR suggest that the metal complexes possess coordinated water molecules and the shift in the wavenumber of the azomethine linkage in the spectra of the complexes shows that the nitrogen of the imine bond participated in the coordination to the metal centre. The magnetic susceptibility measurement shows that the metal complexes possess octahedral geometry. The molar conductivity test shows that the complexes are non-electrolytic in nature and the metal to ligand ratio is 1:2. The synthesized ligand and the metal complexes were evaluated for biological activities against some organisms. The Zn(II) complex showed significant activity against the test organisms.

Key words: Schiff base, $^1\text{H NMR}$, $^{13}\text{C NMR}$, FTIR, UV-visible, metal complexes, antimicrobial.



Introduction

Schiff bases are formed when a primary amine reacts with an aldehyde or a ketone under specific conditions. Structurally, a Schiff base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group (C=O) has been replaced by an imine or azomethine group (Ahmed *et al.*, 2015). Schiff bases are considered as 'privileged ligands' because of their capability to stabilize different metals in various oxidation states and their metal chelates are widely studied owing to the synthetic flexibility, sensitivity and selectivity towards various metal ion (Spinu and Kriza, 2000). Schiff bases are generally bidentate, tridentate, tetradentate or polydentate ligands capable of forming very stable complexes with transition metals. Some Schiff bases are easily synthesized and form complexes with almost all metal ions. Schiff bases have been shown to exhibit a broad range of biological activities, including; antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral and antipyretic properties (Da Silva *et al.*, 2011) and also as catalyst in several reactions such as polymerization reaction, reduction of ketones, aldol reaction, Henry reaction, epoxidation of alkenes, hydrosilation of ketones and Diels-alder reaction.

The coordination of bioactive molecules to metal ions is a common strategy to improve the therapeutic potency and/or to reduce the toxicity of drug molecules. The resulting metal complexes frequently possess superior lipophilicity profiles compared to the free ligands, allowing them to move easily pass through the cell membranes to exert their biological effects. The biological activities may be related to the redox properties of the metal complex (Mruthyunjayaswamy *et al.*, 2015). Extensive researches in the field of metal complexes and their Schiff bases have been reported. Their preparation, chemical and physical properties have been described by various workers and also their antimicrobial, antifungal, antiviral, anti-inflammatory, antitubercular, anti-HIV and

herbicidal. Their chelation increases the lipophilic nature of the central atom which subsequently favours its permeation through the lipid layer of the cell membrane (Rehman *et al.*, 2008). The present study discusses the synthesis, characterization and antimicrobial evaluation of Schiff base formed by condensation of p-hydroxypropiophenone and 4-aminopyridine and its Mn(II) and Zn(II) complexes.

Materials and Methods

All chemicals were of analytical grades and were used as received from suppliers without further purification.

Instruments

Melting points were determined on a Stuart automatic melting point apparatus model SMP40 using open capillary tubes with temperature of 40°C at a temperature ramp of 15°C, FTIR spectra were obtained using Shimadzu FTIR-8400S Spectrophotometer within the wavenumber of 4000-650cm⁻¹. Electronic spectra for compounds in UV-Visible region 200-800nm were recorded using UV-Visible 2012PC Spectrophotometer. ¹H NMR and ¹³C NMR were obtained using Agilent-NMR-vnmrs400 Spectrometer, Conductivity measurements were performed using Jenway 4010 conductivity meter while magnetic moments were obtained using Sherwood Scientific AUTOMagnetic susceptibility Guoybalance.

Synthesis of Schiff base ligand

The synthesis of the Schiff base ligand was carried out according to the method reported by Mruthyunjayaswamy *et al.*, 2015. Equimolar quantities of 4-aminopyridine (0.02mol, 4.71g) and 4-hydroxypropiophenone (0.02mol, 7.38g) were dissolved in hot ethanol (40ml). Acetic acid (2 drops) was also added to the solution. The solution was refluxed for 8 hours on a water bath. The crystals formed was filtered and washed with distilled water and then recrystallized from methanol, air dried and kept in a desiccator for further analysis.

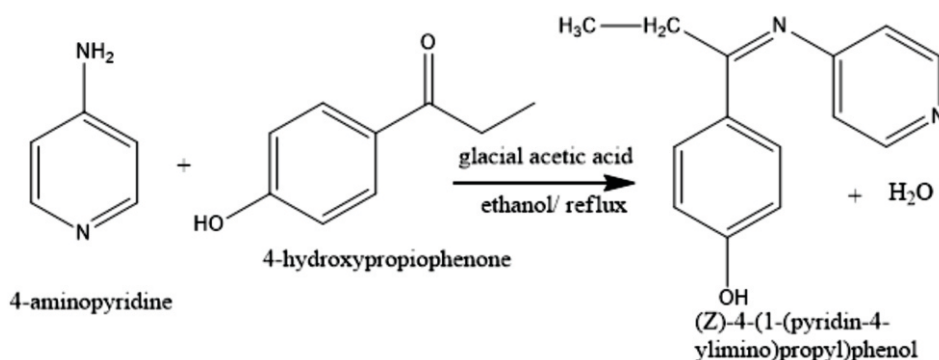


Figure 1: Synthetic route of the Schiff base ligand

Synthesis of Schiff base metal complexes

The synthesis of the Schiff base metal complex was carried out according to the method reported by Nagesh *et al.*, 2015. The newly synthesized Schiff base ligand (0.010mol) in ethanol (20 ml) was added a hot ethanolic solution (15 ml) of the respective metal chlorides (0.005mol) i.e. 1:2 metal to ligands ratio. The reaction mixture was heated under reflux for 3 hours until complete precipitation and the precipitate was separated by filtration, purified by washing several times with distilled water and dried in a dessicator.

Antimicrobial Screening

The antimicrobial test was carried out in accordance with the Laboratory Standard as reported by Offiong and Martelli, (1994). The test microorganisms were of clinical strains, which were obtained, identified and characterized at the Department of Microbiology, Ahmadu Bello University Zaria. The isolates included two gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*), two gram negative bacteria (*Escherichia coli* and *Proteus vulgaris*) and two fungal strains (*Aspergillus flavus* and *Aspergillus niger*).

Results

Physicochemical Properties

Table 1: Physicochemical properties of Schiff base ligand and its Mn(II) and Zn(II) complexes

Compound	Colour	Texture	Molecular Weight(g/mol)	Melting Point(°C)	%Yield
Ligand	Pale yellow	crystalline	226.11	122	89.90
Mn complex	Brown	solid	641.22	198-200	31.10
Zn complex	White	solid	651.22	137-140	44.70

Table 2: Characteristics FTIR bands in (cm⁻¹) of the Schiff base and its metal complexes

Schiff base ligand	Mn(II)complex	Zn(II)complex	Frequency assignment
-	3757.46	3826.90	$\nu(\text{H}_2\text{O})$ str
3425.69	3417.98	3441.12	$\nu(\text{O}=\text{H})$ str
1643.41	1651.12	1620.26	$\nu(\text{C}=\text{N})$ azomethine
1527.67	1527.67	1527.67	$\nu(\text{C}=\text{N})$ heterocyclic
1234.48	1226.77	1222.95	$\nu(\text{C}-\text{O})$ str
-	949.01	902.72	$\nu(\text{H}_2\text{O})$ bend
-	794.70	709.83	$\nu(\text{M}-\text{O})$

Table 3: Electronic spectra of Schiff base ligand and its Mn(II) and Zn(II) complexes

Compound	Absorption wavelength(nm)	Magnetic moment(BM)	Molar conductivity (? ⁻¹ mol ⁻¹ cm ²)
Schiff base ligand	308 348	-	-
Mn(II) complex	308 320 327	5.60	42.50
Zn(II) complex	306	-	11.34

Proton (¹H) and ¹³C NMR studies of the Schiff base ligand

Table 4: Proton NMR spectra of the ligand

Peaks(ppm)	Assignments
7.735	Aromatic proton(2Hs), -CH=N-
7.415	Aromatic proton of the pyridine(2Hs), -CH=C-
6.422	Aromatic proton β to the C carrying -OH group(2Hs)
6.127	Aromatic proton α to the C carrying -OH group(2Hs)
5.748	Phenolic (1Hs), -OH
2.129	Methylene proton -CH ₂ -
0.629	Methyl proton -CH ₃

s-singlet, m-multiplet, d-doublet, t-triple

Table 5: Carbon-13 NMR spectra

Peaks(ppm)	Assignments
200.459	C=N azomethine
163.322	Carbon bearing the –OH group
155.715	Carbon beta to the C=N heterocyclic
148.700	C=N heterocyclic
131.151	Carbon gamma to the phenolic carbon
128.232	Carbon beta to the phenolic carbon
116.113	Carbon alpha to the phenolic carbon
109.682	Carbon alpha to the C=N heterocyclic
31.342	Methylene Carbon-CH ₂ -
9.099	Methyl Carbon-CH ₃

Discussions

The results of the physical characterization of the ligand and its Mn(II) and Zn(II) complex are presented in Table 1. The molecular formula of the Schiff base ligand and the metal complexes are in accordance with the physical data and analytical data. The synthesized Schiff base ligand and the Mn(II) and Zn(II) complexes are solid and stable at room temperature. Their sharp melting points suggest fairly pure compounds were synthesized.

Infrared spectral studies

The ligand displays band characteristics of hydroxyl group at 3425.69cm^{-1} , the disappearance of band at that region in the Mn(II) and Zn(II) complexes in FTIR spectra indicates a deprotonation and coordination of the phenolic oxygen group (Ifemelunma, 2014). The complexes display bands in the region 3700cm^{-1} and 3800cm^{-1} which is indicative of presence of coordinated water molecules in the structure of the metal complex. This is confirmed by the presence of bands in 949.01cm^{-1} and 902.72cm^{-1} in the Mn(II) and Zn(II) complexes respectively (Abdulghani *et al.*, 2015). The presence of band in the 794.70cm^{-1} and 709.83cm^{-1} in the Mn(II) and Zn(II) complex but not in the Schiff base spectrum can be attributed to the coordination of the ligand to the metal ion through the oxygen atom from the phenolic group (Ifemelunma, 2014). The formation of Schiff base azomethine linkage is confirmed by the formation of azomethine band at 1643.41cm^{-1} which shift upon complexation to 1651.12cm^{-1} and 1620.26cm^{-1} in the Mn(II) and Zn(II) complexes respectively (Abdulghani *et al.*, 2015).

Magnetic susceptibility studies

The magnetic moment gives an outline of the electronic state of the metal ion in the complex and the geometry of the complex. The magnetic moment was carried out at 35°C . The magnetic moment for Mn(II) was found to be 5.60BM, while Zn(II) complex is diamagnetic since it has no unpaired electron. The observed magnetic

moments are in accordance with the observed values for the first transition series in an octahedral environment (Housecroft *et al.*, 2005).

Molar conductivity studies

Molar conductivity was measured to show if the complex formed is electrolytic or non-electrolytic in nature and this will help to determine the extent of dissociation of the complex and hence the stability of the complex in solution, the reactivity and the ease of conversion to other species.

The low molar conductivity for the complexes (Table 3) implies that the complexes are non-electrolytic in nature leading to the proposition of $[\text{ML}_2 \cdot 2\text{H}_2\text{O}]$ as structure for the complexes. In contrast, complexes of higher molar conductivity values of range 106-311 implies presence of ions outside the coordination sphere which is indicative of electrolytic complex (Refat *et al.*, 2013)

Electronic spectral studies

The electronic spectra of the Schiff base and its metal complex were obtained using UV 2012PC Spectrophotometer in the range 200-800nm and are presented in Table 2. The electronic spectrum of the Schiff base ligand exhibited two high intensity bands with absorption maxima at 308nm and 328nm which can be attributed to $\pi-\pi^*$ transition of the aromatic ring and $n-\pi^*$ transition between the π -orbital localized on the azomethine bond respectively (Dueke-Eze, *et al.* 2010). The Mn(II) complex displayed four bands at 308 nm ($\pi-\pi^*$), 320 nm, 323nm and 325nm corresponding to charge transfer transitions. The effect of the charge transfer mask the effect of d-d transition which is expected to appear above 500nm thus the band due to d-d transition is not seen in the spectrum (Housecroft, *et al.* 2005). In the Zn(II) complex the d-d transition band was not observed in the spectrum which is quite common with diamagnetic d^{10} complexes (Abdulghani, *et al.* 2015).

Proton and ^{13}C NMR studies of the Schiff base ligand

The Proton (^1H) and ^{13}C NMR spectra (figures 3 and 4) of the Schiff base ligand (HL) was recorded in d_6 -dimethylsulfoxide (DMSO) using TMS as internal standard. Table 4 shows consistency with that expected for the ligand. The ^1H NMR peak at 3.792 ppm can be attributed to the HOD/water because deuterated DMSO is hygroscopic and highly miscible with water, thus it absorbs water over time. The peak at 2.485 is due to residual DMSO- d_6 (Hugo, *et al.* 1997).

The assignments of the chemical shift in the ^{13}C NMR spectrum (Table 5) was done putting into consideration the effect of electronegativity of the atoms, the electron density and the effect of π -

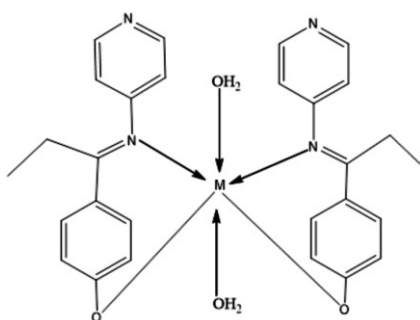


Figure 2: Proposed structure for the metal complexes Where M = Mn(II) and Zn(II) ions

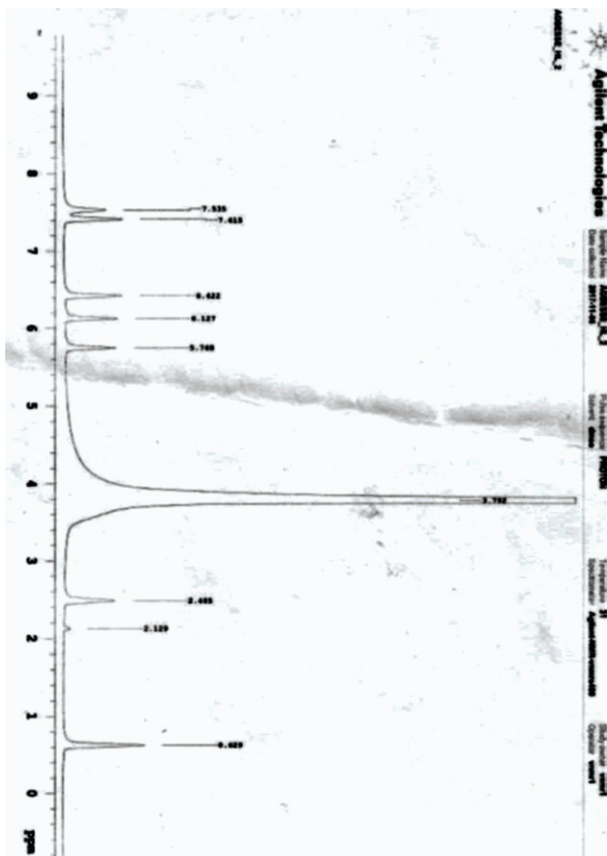


Figure 3: ^1H NMR spectra for Schiff base ligand

electrons system in addition to aromaticity of the attached groups. The spectrum is consistent with the proposed structure of the ligand. The septet peak at 39.995–38.728 ppm in the ^{13}C NMR spectra is assigned to the solvent DMSO used (Hugo, *et al.* 1997). There was no uncharacterized peak in the spectrum of both the ^1H NMR and ^{13}C NMR which further give credence to the agreement of the spectra with the assigned structure.

Based on the spectral data obtained, the molecular formulae of the Schiff base and its metal complex is $\text{C}_{14}\text{H}_{14}\text{ON}_2$ and $[\text{ML}_2 \cdot 2\text{H}_2\text{O}]$, respectively. The proposed structure for the metal complex is given in figure 2 and the proposed structures for the metal complexes indicates that the metal-ligand ratio is 1:2

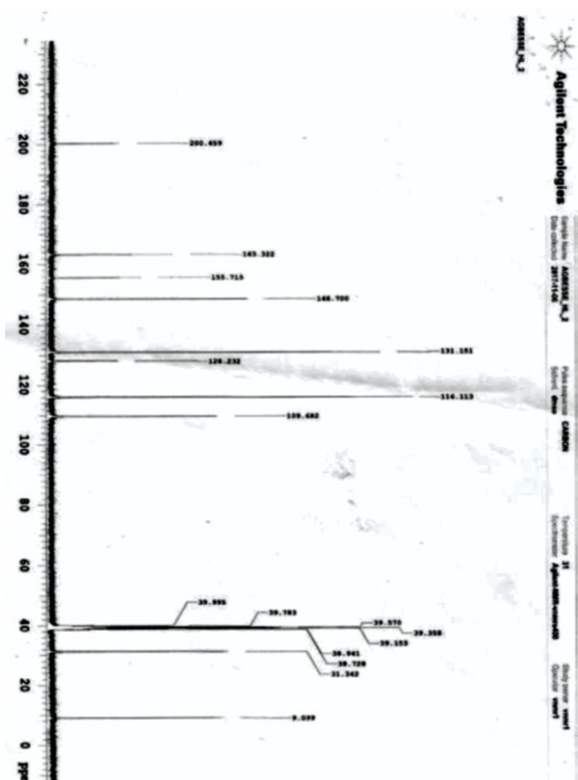


Figure 4: ^{13}C NMR spectra for Schiff base ligand

Results of Antimicrobial Screening

Table 6: Sensitivity test for Schiff base ligand, Mn(II) and Co(II) complex Zone of inhibition(mm) at varying concentration (mg/ml)

Test organism	Schiff base ligand				Mn(II) complex				Zn(II) complex				control
	50	25	12.5	6.25	50	25	12.5	6.25	50	25	12.5	6.25	
<i>S.aureus</i>	NS	NS	NS	NS	16	12	10	NS	19	18	24	11	35
<i>B.subtilis</i>	-	-	-	-	NS	NS	NS	-	16	12	10	NS	32
<i>E.coli</i>	-	-	-	-	-	-	-	-	12	10	NS	-	37
<i>P.vulgaris</i>	-	-	-	-	-	-	-	-	15	13	-	-	39
<i>A.niger</i>	-	-	-	-	-	-	-	-	16	14	12	10	35
<i>A.flavus</i>	-	-	-	-	-	-	-	-	NS	NS	NS	NS	35

NS-not sensitive

Table 7: Minimum Inhibition Concentration (MIC) of the compounds

Test Organism	Minimum Inhibition Concentration MIC (mg/ml)		
	Schiff base ligand	Mn(II) complex	Zn(II) complex
<i>S.aureus</i>	ND	12.500	3.125
<i>B.subtilis</i>	ND	ND	3.125
<i>E.coli</i>	ND	ND	12.5
<i>P.vulgaris</i>	ND	ND	6.25
<i>A.niger</i>	ND	ND	25
<i>A.flavus</i>	ND	ND	ND

Table 8: Minimum Bactericidal Concentration MBC (mg/ml)

Test Organism	Schiff base ligand	Mn(II) complex	Zn(II) complex
<i>S.aureus</i>	ND	NIL	6.25
<i>B.subtilis</i>	ND	ND	6.25
<i>E.coli</i>	ND	ND	NIL
<i>P.vulgaris</i>	ND	ND	12.5
<i>A.niger</i>	ND	ND	NIL
<i>A.flavus</i>	ND	ND	ND

ND-Not determined, NIL-No MBC

Discussions

The biological activities of the Schiff base ligand and its metal complexes were compared with ciprofloxacin (antibacterial agent) and fluconazole (antifungal agent). The data in Table 6 show that the Schiff base ligand did not show activity against the test organism while the Zn complexes showed significant activities against the test organisms, except *A. flavus*. The Mn(II) complex was only sensitive to *S. aureus* at higher concentration. This implies that the activity of the Schiff base ligand is enhanced on chelation with biologically active metals, such increased activity of the complexes can be explained on the basis of Overtone's concept (Anjaneyula, *et al.* 1986) and Tweedy's Chelation theory (Dharamaraj, *et al.* 2001). According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favours the passage of only the lipid-soluble materials due to which liposolubility is an

important factor, which controls the antifungal activity. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization π -electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of the proteins that restricts further growth of the organism. Furthermore, the mode of action of the compound may involve formation of a hydrogen bond through the azomethine group with the active centre of cell constituents, resulting in interference with the normal cell process. The MIC and MBC results of the Zn(II)

complex is shown in Table 7 and Table 8, the result shows that *B.subtilis* and *A.niger* growth was only inhibited by the Zn(II) complex but the test organisms was not killed by the metal complex. Thus, Zn(II) complex is bacteriostatic with respect to this *A.niger* and *B.subtilis*. While, the Zn(II) complex is bactericidal with respect to *S.aureus*, *E.coli* and *P.vulgaris*.

Conclusion

The Mn(II) and Zn(II) complexes of the synthesized Schiff base were prepared and characterized by various physicochemical techniques. The results of the physicochemical analysis show that the complexes possess octahedral geometry and based on the results the structure in figure 2 was proposed for the complexes. The Zn(II) complex shows significant activity against the test microorganisms.

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