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## SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES ON SCHIFF BASE DERIVED FROM 2-AMINOPYRIDINE AND 2-METHOXYBENZALDEHYDE AND ITS COBALT (II) AND NICKEL (II) COMPLEXES

Sani U<sup>1</sup> and Iliyasu S M<sup>2</sup>.

<sup>1</sup>Department of Pure and Industrial Chemistry, Bayero University Kano,

<sup>2</sup>Kano State College of Education and Preliminary Studies, Kano

\*saidiliyasumusa07@gmail.com; sumar.chm@buk.edu.ng, nababaagwa@yahoo.com.

### ABSTRACT

A Schiff base ligand has been synthesized by the condensation of 2-aminopyridine and 2-methoxybenzaldehyde. Metal complexes of the Schiff base were prepared by the reaction of the Schiff base and metal (II) chlorides of cobalt and nickel in ethanol. The complexes were isolated, washed and dried. The Schiff base is pale yellow, while cobalt and nickel complexes are blue and light green respectively. The Schiff base and its metal (II) complexes were characterized by solubility test, melting and decomposition temperature determination, FTIR, magnetic susceptibility, molar conductance gravimetric analysis and UV spectroscopy. Solubility test carried on the Schiff base and the complexes showed that they are all soluble in DMSO and DMF, but insoluble in water. From the FTIR result, a peak at  $1577\text{cm}^{-1}$  is assigned to the azomethine of the Schiff base which shifted to  $1637$  and  $1622\text{cm}^{-1}$  in cobalt (II) and nickel (II) complexes respectively. The complexes are high spin, non electrolytic in nature and have high thermal stability. Job's method of continuous variation suggests 1:2 metal to ligand ratio. The Schiff base is inactive against *Staphylococcus aureus* at all concentrations while the complexes were found to be active and the activity increases with increase in concentration. The Schiff base and its complexes are found to be active against *E. coli* at all concentrations. The antifungal study revealed that the Schiff base and its complexes are active against *Candida albican* at all concentrations, but inactive against *Mucor specie* at all concentrations.

**KEY WORDS:** 2-aminopyridine, 2-methoxybenzaldehyde, Ligand, Characterization, Antimicrobial activity

### INTRODUCTION

Schiff bases are the compounds containing azomethine group (-HC=N-). They are condensation products of ketones or aldehydes with primary amines and were first reported by Hugo Schiff in 1864. Nowadays, Schiff bases are used as intermediates for the synthesis of amino acids or as ligands for preparation of metal complexes having a series of different structures (Kumar *et al.*, 2013). Schiff bases with aryl substituent are more stable and readily synthesized, whereas those containing alkyl substituent are relatively unstable (Kumar *et al.*, 2013). Schiff bases of aliphatic aldehydes are unstable and readily polymerizable while those with aromatic aldehydes having effective conjugation are more stable (Chigurupati, 2015). Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial, antifungal and antitumor activity (Kumar *et al.*, 2013). A large number of Schiff bases and their complexes have been studied for their interesting and important properties, example, their ability to

reversibly bind oxygen, catalytic activity in hydrogenation of olefins and transfer of an amino group, photochromic properties, and complexing ability towards some toxic metals (Kumar *et al.*, 2013). The mode of interaction and inhibition effectiveness of Schiff bases with bacteria and fungi is expected to depend on the molecular structure of the compounds. Thus, advances in this field will require analysis of structure activity relationships of Schiff bases along with investigation of the mechanism of action of these compounds (Ejiah *et al.*, 2013). 2-aminopyridine compounds are well known class of compounds for a long time, and still are interestingly considerable due to their application in various fields (Olfa, 2013). Current literature reveals that these pyridine compounds possess a variety of biological activities, such as vasodilator, bronchodilator, antiatherosclerotic, geroprotective, hepatoprotective, antidiabetic, antimalarial, anti-inflammatory, antiasthmatic, antibacterial, and tyrosine kinase inhibiting agents (Ushirani *et al.*, 2013).

Schiff bases appeared to be important intermediate in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate. One of the most important types of catalytic mechanism is the biochemical process which involves the condensation of a primary amine in an enzyme usually that of a lysine residue, with a carbonyl group of the substrate to form an imine, or Schiff base (Arulmurugan *et al.*, 2010). Chelating ligands containing O and N donor atoms show broad biological activity and are of special interest because of the variety of ways in which they are bonded to the metal. The synthesis of schiff base ligands and their metal complexes have been extensively studied because of their interesting biological activities (Sikarwar *et al.*, 2016)

Organic reagents play vital role in modern analytical devices in order to enhance the selectivity and sensitivity of optical and electrochemical sensors as well as in many chromatographic methods. Schiff bases have excellent features and structural similarities among these reagents. The facile method of preparation and synthetic simplicity of imines enables to design suitable structural properties. In coordination chemistry, azomethine moiety form complexes with a variety of metals (Fareed *et al.* 2013). Schiff bases are also used as versatile components in nucleophilic addition with organometallic reagents and in cycloaddition reactions (Suresh *et al.*, 2012). In the present work, we report a synthesis, characterization, antibacterial and antifungal studies of a Schiff base derived from 2-

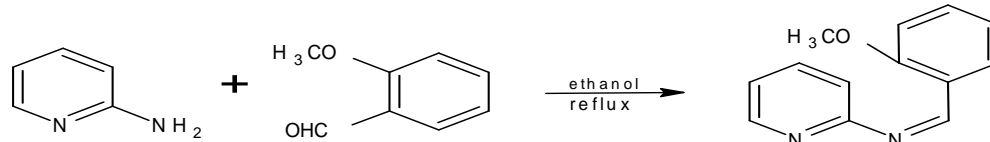
aminopyridine and 2-methoxybenzaldehyde and its cobalt (II) and nickel (II) complexes.

## MATERIALS AND METHODS

The reagents used in this work are of analytical grade and were used as purchased without purification. Glass wares were washed and dried in an oven at 110°C overnight before use. FTIR was carried out using Fourier Transform Infrared spectroscopy machine (Carry 630 by Agilent Technology) from 400 to 4000cm<sup>-1</sup>, melting point of the Schiff base and decomposition temperature of the complexes were determined using Stuart (SMP110) melting point apparatus, Conductivity of the complexes was determined using Jenway 4010 conductivity, UV visible was conducted using Parkin Elmer λ-35 for the Job's method and magnetic susceptibility was determined using Sherwood Scientific Magnetic Susceptibility Balance MK1. Bacterial and fungal isolates were obtained from Malam Aminu Kano Teaching Hospital Kano (AKTH) and identified at Microbiology Department, Bayero University Kano. Nutrient Agar and Potato Dextrose Agar were used as media for the bacterial and fungal isolates respectively.

### Preparation of the Schiff base

Equimolar ratio (0.03mol) of 2-aminopyridine (2.8236g) and 2-methoxybenzaldehyde (3.63ml) were dissolved in ethanol (50 ml). The mixture was refluxed at 70°C for 3hrs. The reaction mixture was concentrated, cooled to room temperature to afford the crystalline product which was re-crystallized from hot ethanol and collected by filtration, and dried in a dessicator over CaCl<sub>2</sub> for 18 hours (Ejiah *et al.*; 2013).



Scheme 1: preparation of the Schiff base

### Synthesis of the complexes

The complexes were prepared by dissolving 0.003mol of the Schiff base in 25ml hot ethanol and 0.0015mol of MCl<sub>2</sub>.nH<sub>2</sub>O (where M = Co or Ni) in 25ml hot ethanol solution. The two solutions were mixed together and refluxed with constant stirring for 2hrs at 70°C. On cooling, coloured solids were precipitated out. The products were filtered, washed with cold methanol, cold ethanol and pet. ether, and then dried in a dessicator over CaCl<sub>2</sub> for 18 hours (Kumar *et al.*, 2013).

### Antimicrobial activity

The antimicrobial activity of the Schiff base and its complexes were studied using two bacterial isolates: *Staphylococcus aureus* and

*Escherichia coli* and two fungi: *Mucor specie* and *Candida albicans* using Agar well diffusion method. The solidified culture media were inoculated with the test microorganisms and wells were dug in the nutrient agar (NA) medium for bacteria and potato dextrose agar (PDA) medium for fungi with the help of a sterile cork borer. The compounds were dissolved (0.06g) in DMSO (1.0ml) to give a stock solution (500,000µg/ml). Various concentrations of the test compounds were made (60, 30 and 15µg/ml) and introduced into the well by means of a micro syringe and incubated for 24 hours at 35°C. The zones of inhibition were measured in mm (Temitope and Temitope, 2015).

## RESULTS AND DISCUSSION

Table 1 shows some physical properties of the Schiff base and its complexes, the Schiff base was crystallized as pale yellow crystal with a good yield of 64.5%, while the cobalt (II) and nickel (II) complexes were obtained as blue and light green crystal powder respectively with a good yield of 69% and 72% for the cobalt and nickel complexes respectively. The Schiff base has a high thermal stability with a high melting point of 168°C and the complexes show better stability to heat than the Schiff base with a sharp decomposition temperature of 233°C and 237°C for the cobalt (II) and nickel (II) complexes respectively.

Table 2 shows the solubility of the Schiff base and its complexes, the Schiff base was found to be insoluble in water, petroleum ether, chloroform and acetone, but soluble in ethanol, DMSO, DMF and methanol, therefore, ethanol was used as solvent for the synthesis of the complexes. Similarly, the complexes were all found to be insoluble in water, petroleum ether, chloroform and acetone, but soluble in ethanol, DMSO and DMF.

Table 3 shows some selected Infrared spectral data of the ligand and its metal (II) complexes. In the FTIR spectra of the ligand and the

complexes, vibration frequencies were assigned for the ligand and the complexes. A peak at 1577  $\text{cm}^{-1}$  was assigned to azomethine (Jamuna *et al.*, 2011) which shifted to 1637  $\text{cm}^{-1}$  in cobalt (II) complex and 1657  $\text{cm}^{-1}$  in nickel (II) complex which indicate the coordination of the azomethine nitrogen to the metals (II) ions (Sabry *et al.*, 2016) and also 721  $\text{cm}^{-1}$  and 678  $\text{cm}^{-1}$  which were absent in the spectra of the ligand indicates the metal to nitrogen bond (Bharat *et al.*, 2015). Similarly 459  $\text{cm}^{-1}$  and 461  $\text{cm}^{-1}$  which were also not found in the spectra of the ligand indicates the coordination of the methoxide oxygen to the cobalt (II) and nickel (II) ions respectively. On a similar note, the peak at 1242  $\text{cm}^{-1}$  which shifted to 1232 and 1294  $\text{cm}^{-1}$  in Co (II) and Ni (II) complexes respectively were assigned to C-O bond of the methoxy group (Abdel-Latif *et al.*, 2006).

Table 4 shows magnetic susceptibility measurement of the complexes, The effective magnetic moment of the complexes, as determined from the magnetic susceptibility, were 4.51BM and 2.95BM for the cobalt (II) and nickel (II) complexes respectively, which suggests high spin complexes with octahedral geometry (Imran *et al.*, 2010).

Table 1: Physical properties of the Schiff base and the complexes

Compound	Molecular formular	colour	Percentage yield %	Melting Point °C	Decomposition Temperature
Ligand	$\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$	Pale Yellow	64.5	168	-
[CoL <sub>2</sub> ]	$\text{CoC}_{26}\text{H}_{24}\text{N}_4\text{O}_2\text{Cl}_2$	Blue	69	-	233
[NiL <sub>2</sub> ]	$\text{NiC}_{26}\text{H}_{24}\text{N}_4\text{O}_2\text{Cl}_2$	Light green	72	-	237

L = Ligand,  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$ 

Table 2: Solubility of the Schiff base in water and some organic solvents

Compound	Dist. water	Ethanol	Methanol	Pet.ether	Chloroform	Acetone	DMF	DMSO
Ligand	IS	S	SS	IS	IS	IS	S	S
[CoL <sub>2</sub> ]	IS	S	S	IS	IS	IS	S	S
[NiL <sub>2</sub> ]	IS	S	S	IS	IS	IS	S	S

L = Ligand,  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$ 

Table 3: Selected Infrared spectral data of the ligand and its metal (II) complexes

Compound	$\nu(\text{C}=\text{N})\text{cm}^{-1}$	$\nu(-\text{OCH}_3)\text{cm}^{-1}$	$\nu(\text{M}-\text{N})\text{cm}^{-1}$	$\nu(\text{M}-\text{O})\text{cm}^{-1}$
Ligand	1577	1242	-	-
[CoL <sub>2</sub> ]	1637	1232	718	459
[NiL <sub>2</sub> ]	1622	1294	674	589

L = Ligand,  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$

**Table 4:** Molar magnetic susceptibility, gram magnetic susceptibility and effective magnetic moments of the complexes

Compound	$X_g$ (ergG <sup>-2</sup> g <sup>-1</sup> )	$X_m$ (ergG <sup>-2</sup> mol <sup>-1</sup> )	$\mu_{eff}$ (B.M)
[CoL <sub>2</sub> ]	1.541 x 10 <sup>-5</sup>	8.544 x 10 <sup>-3</sup>	4.51
[NiL <sub>2</sub> ]	65.720 x 10 <sup>-7</sup>	3.642 x 10 <sup>-3</sup>	2.95

L = Ligand, C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O

Table 5 shows the molar conductance as determined from the electrical conductance in 0.003M DMSO solution of the complexes which suggest a non electrolytic nature.

Table 6 shows the percentage composition of the metals, chlorine and the ligand as obtained from gravimetric analysis. Within the limit of experimental error, the values obtained are consistent with the theoretical value and it suggest 1:2:2 M:L:Cl ratio.

Table 7 shows the percentage of water of crystallization in the complexes. All the complexes were found to be hydrated due to the presence of broad peak around 3200 cm<sup>-1</sup> in the IR spectra of the complexes, indicating water of hydration where Co (II) complex was found to be monohydrate and the Ni (II) complex dihydrate. To confirm the metal ligand reacting ratio, Jobs method of continuous variation was applied as reported by Samadi and Azizi, (2015). From the Job's plot giving in figures 1 and 2, the number of coordinated ligand was determined which indicate a 1:2 metal ligand ratio for the two metal complexes.

Table 8 shows the antibacterial activity of the Schiff base and its metal (II) complexes as

carried out against bacterial isolates (*Staphylococcus aureus* and *Escherichia coli*) using Ciprofloxacin (500mg) as control. The Schiff base shows no activity against *Staphylococcus aureus* at all concentrations, but show activity against *Escherichia coli*. The two metal complexes show activity against the two bacterial isolates. The Ni (II) complex was found to be more active than Co (II) complex, but less active than the control.

Table 9 shows the antifungal activity of the Schiff base and its metal (II) complexes as carried out against fungal isolates (*Mucor specie* and *Candida albica*) using Ketoconazole (200mg) as control, which indicates that the Schiff base ligand and its metal (II) complexes shows no activity against *Mucor specie* at all concentrations with a control having 35mm inhibition, but are active against *Candida albica* with a control having 37mm inhibition. The Ni (II) complex shows more activity, and the activity increases with increasing concentration. The complexes show better activity than the free Schiff base in both antibacterial and antifungal sensitivity.

**Table 5:** Conductivity Measurement of the complexes

Compound	Electrical conductance (ohm <sup>-1</sup> cm <sup>-1</sup> ) x 10 <sup>-6</sup>	Molar conductance (ohm <sup>-1</sup> cm <sup>2</sup> mol <sup>-1</sup> )
[CoL <sub>2</sub> ]	943	26.19
[NiL <sub>2</sub> ]	110.3	3.06

L = Ligand, C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O

**Table 6:** Percentage compositions of the metals and chlorine

Complex	% composition of metal		% composition of Cl <sup>-</sup>		% composition of Ligand	
	calculated	Experimental	calculated	Experimental	calculated	Experimental
Co (II)	10.67	9.60	12.86	11.90	76.47	75.20
Ni (II)	10.64	10.80	12.86	11.70	76.50	71.70

**Table 7:** Percentage water of crystallization

Compound	Initial weight (g)	Weight loss (g)	% water of crystallization
Co (II) Complex	0.2	0.0066	3.3
Ni (II) Complex	0.2	0.0116	5.8

**Table 8:** Antibacterial activity of the Schiff base and its metal (II) complexes

Compound	Zone of inhibition (mm)/concentration ( $\mu\text{g/ml}$ )					
	<i>Staphylococcus aureus</i>			<i>Escherichia coli</i>		
	60	30	15	60	30	15
Ligand	-	-	-	15	12	11
[CoL <sub>2</sub> ]	14	12	10	16	10	-
[NiL <sub>2</sub> ]	20	19	17	16	15	12
Standard	31			27		

L = Ligand, C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O Standard = Ciprofloxacin (500mg)

**Table 9:** Antifungal sensitivity test of the Schiff base and its metal (II) complexes

Compound	Zone of inhibition (mm)/concentration ( $\mu\text{g/ml}$ )					
	<i>Candida albican</i>			<i>Mucor specie</i>		
	60	30	15l	60	30	15
Ligand	23	20	13	-	-	-
[CoL <sub>2</sub> ]	20	10	-	-	-	-
[NiL <sub>2</sub> ]	36	29	22	-	-	-
Standard	37			35		

L = Ligand, C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O Standard = Ketoconazole (200mg)

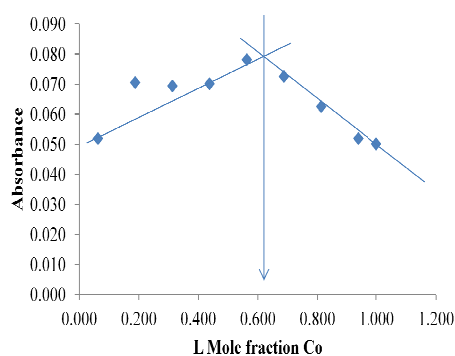


Fig. 1: Plot of absorbance against ligand mole fraction at 620nm for Co(II) complex

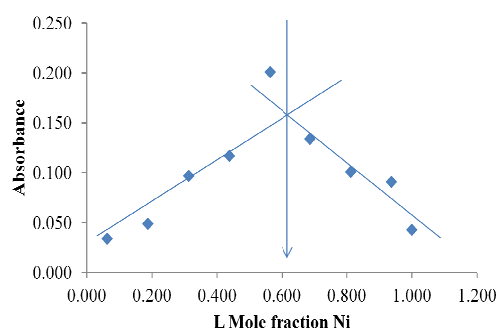


Fig. 2: Plot of absorbance against ligand mole fraction at 700nm for Ni(II) complex

### CONCLUSION

The Schiff base and its metal (II) complexes were synthesized, characterized, and tested for their antimicrobial activity. The Schiff base ligands were found to be bidentate and octahedral geometry was suggested for the two

metal complexes. The complexes were found to be sensitive against the bacterial and fungal isolates used for the antimicrobial test, and the complexes shows better activity than the free ligand.

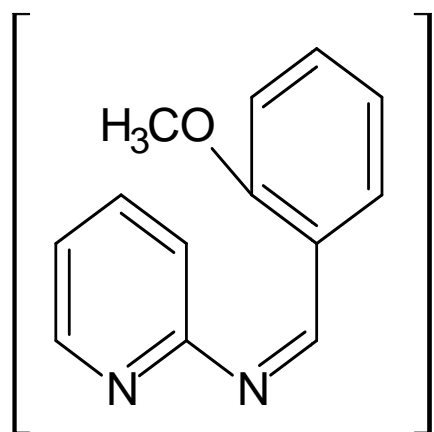
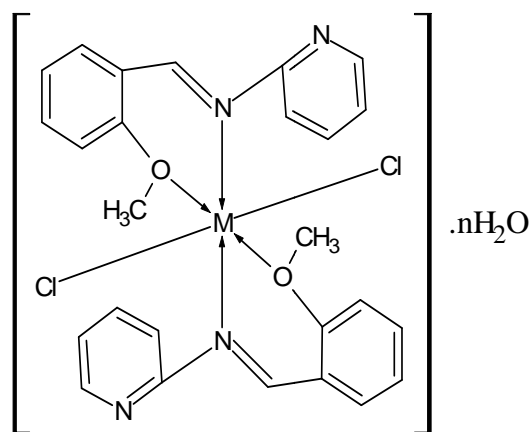


Fig. 3: Proposed structure of the Schiff Base



Where M = Co<sup>2+</sup> or Ni<sup>2+</sup>, n = 1 for Co(II) and n = 2 for Ni(II)  
Fig. 4: Proposed structure of the complexes

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