



Synthesis, characterization and antimicrobial studies of Cu (II) and Zn (II) complexes of Schiff base derived from 2-Amino-2-hydroxybenzoic acid and 2-hydroxybenzaldehyde



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ABSTRACT

Schiff base derived from condensation reaction of 4-amino-2-hydroxybenzoic acid and 2-hydroxybenzaldehyde was synthesized. The aim of this work is to synthesize, characterize and study the antimicrobial activities of Schiff base and their Cu (II) Zn (II) complexes. It was refluxed with metals (II) chlorides which results in the formation of the corresponding metal (II) complexes in good yield. The compounds were characterized on the basis of their melting point, decomposition temperature, Fourier transform infrared spectroscopy, magnetic susceptibility, conductivity measurement and determination of metal - ligand ratio. The IR spectral data revealed azomethine peak of the Schiff base at 1591 cm^{-1} while for the complexes, the peak was found within $1538 - 1588\text{ cm}^{-1}$. The molar conductance of the Cu (II) and Zn(II) complexes were found to be 24.8 and $6.2\ \Omega^{-1}\text{cm}^2\text{ Mol}^{-1}$ respectively which indicated that, the complexes were non- electrolytes. The decomposition temperature of Cu (II) and Zn (II) complexes were found to be $292\text{ }^\circ\text{C}$ and $255\text{ }^\circ\text{C}$ respectively, showed that the complexes are stable. Cu (II) complexes exhibit Magnetic moment values of 1.72 which suggested that the complexes, is paramagnetic while Zn (II) to be diamagnetic. Determination of metal: ligand ratio was 1:2. The biological screening of the compound were studied against three bacterial and two fungal isolates; *S. aureus*, *E. coli* and *P. aeruginosa*, *M. indicus* and *A. flavus*. *Seprtin* and *Nystatin* were used as control for the bacteria and fungi respectively. The result revealed that the complexes exhibit higher activities than the Schiff base but lower than the control.

Keywords:

4-amino-2-hydroxybenzoic acid,
2-hydroxybenzaldehyde,
Schiff's base,
Characterization,
Antimicrobial activity

INTRODUCTION

Schiff bases (also known as imine or azomethine), a chemical compound containing carbon and nitrogen double bond ($-\text{HC}=\text{N}-$). They are nitrogen analog of an aldehyde or ketone in which the $\text{C}=\text{O}$ group is replaced by a compound containing $\text{C}=\text{N}-\text{R}$ group (Ghosh *et al.*, 2020). Schiff bases that occur as natural and non-natural origin, have shown different range of applications such as antibacterial, antitubercular, antifungal, antiparasitic, antiviral, antioxidant, anticancer, analgesic, catalytic and anti-inflammatory properties (Ghosh *et al.*, 2020, Noor *et al.*, 2020). Hence, their continuous to show great interest in field in medicine (Muhammad *et al.*, 2020, Mohkles *et al.*, 2019). In general the Schiff bases which have been derived from aldehydes are called aldimine and from ketones as ketamine and the stability of the final product depend on the nature of aldehyde, ketone and amine (Yaseer, 2017).

Several spectroscopic methods have been used in the analysis of Schiff bases and their metal complexes. These include infrared (IR), nuclear magnetic resonance (NMR) and electronic absorption spectroscopy. The thermal analysis methods include thermo gravimetric analysis (TGA) and differential scanning calorimetry (DSC). Magnetic moment measurements have also been used in assigning geometries to Schiff base metal complexes. Siraj and Rabi, (2020) reported the preparation of the Mn (II) and Ni (II) complexes with the Schiff base derived from the salicylaldehyde and 2-aminobenzoic acid. The complexes were characterized by gravimetric, molar conductance and infrared spectral analysis. The Schiff base and its Ni (II) complex were found to be soluble in most organic solvents, except ether, acetonitrile and tetra chloromethane. The molar conductances values obtained from the complexes measured were low,

indicating their non - electrolytic nature. Siraj and Rabi, (2024) reported on synthesis, characterization and antimicrobial studies of salicylic acid complexes of some transition metals (II) Co (II), Mn (II) and Zn (II). The preliminary investigation of antimicrobial activities of the metal complexes revealed that the inhibitory ability of the metal complexes is notably higher than the ligand, though less than the control. The appearance of resistant bacteria was found to reduce the efficiency of antimicrobial therapies with the current antibiotics, thereby increasing the need for more efficient drugs for the treatment of infections

MATERIALS AND METHODS

All the reagents used in this work were of analytical grade and used without further purification. All glass wares used were washed with detergent, rinsed with distilled water and dried in the oven at 110 °C before used. The weighing was carried out on electrical Metler balance Toledo B154. The infrared (IR) spectra were recorded

using Fourier Transformed Infrared Spectroscopy (FTIR CARY 630 Agilent technologist). The melting point and decomposition temperature were determined using Gallekemp melting point apparatus. Magnetic susceptibility was determined using Sharwood MK1 balance. The molar conductance measurement was carried out using Jenway 4010 model conductivity meter. The antimicrobial screening was conducted by disc diffusion method at Department of Microbiology, Bayero University Kano.

Preparation of the Schiff Base

Schiff base were prepared as described by Siraj and Ado, (2018), Metholic solution of 4-aminosalicylic acid (1.531 g, 0.01 mol) was added to metholic solution of 4-aminosalicylic acid (1.531 g, 0.01 mol) with constant stirring and the mixture was refluxed for 2 h. The solution was cooled and the yellow solid product formed was separated by filtration, washed with cold ethanol, and dried in a vacuum over anhydrous calcium chloride.

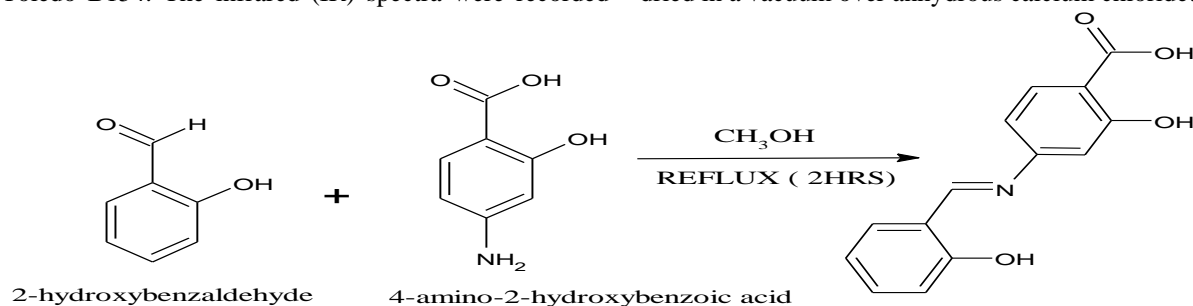


Fig 1. Reaction pathway for preparation of Schiff base

Preparation of Metal (II) Complexes

Complexes were prepared as described by Siraj and Ado, (2018), Schiff base (5.14 g, 0.02 mol) in hot methanol and aqueous solution of the metal (II) chloride (0.01 mol),

was mixed and refluxed for 2 h. The precipitate formed was filtered off, washed with ethanol and dried in a desiccator over anhydrous calcium chloride for a week.

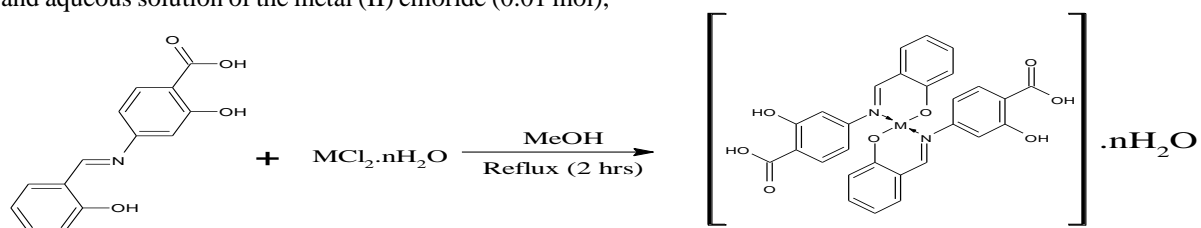


Fig 2: Reaction pathway for preparation of metal (II) complexes

Antibacterial and Antifungal Activities Test

The Schiff base and complexes were screened for their activity against clinically isolated bacteria and fungi (*S. aureus*, *E. coli* and *P. aeruginosa*, *M. indicus* and *A. flavus*). The Schiff base and the complexes were dissolved separately in DMSO to produced three different concentrations (15µg, 30 µg, and 60 µg) per disc. The prepared disc of the ligand and complexes together with standard antibiotic disc were placed on to the surface of the incubated media at an interval and incubated at 37 °C

for 24 h. The diameter of the zone of inhibition produced by the ligand and the complexes were measured and compared with the standard antibiotics while DMSO wetted disc was used as negative control (Habla *et al.*, 2020)

RESULTS AND DISCUSSION

The results of the characterization, antibacterial and antifungal activities of the Schiff base and its metal (II) complexes are presented in the Tables 1 and 2

Table 1: Physical Properties of the ligand and its Metal (II) complexes

Compound	Colour	Melting point (°C)	Decomposition Temperature (°C)	Percentage yield (%)
L	Yellow	-	185	76.3
[CuL ₂]. 2H ₂ O	Green	292	-	70.5
[ZnL ₂]. 3H ₂ O	Pale yellow	255	-	71.6

L = C₁₄H₁₁NO₄**Table 2:** Solubility test of the compounds in water some common organic solvent

Compounds	Water	MeOH	Ethanol	Acetone	Chloroform	Benzene	DMSO	DMF
L	IS	S	IS	IS	SS	SS	S	S
[CuL ₂]. 2H ₂ O	IS	S	SS	IS	SS	IS	S	S
[ZnL ₂]. 3H ₂ O	IS	IS	SS	IS	SS	SS	S	S

L = C₁₄H₁₁NO₄

Where; S = Soluble, SS = Slightly Soluble, IS = Insoluble

Table 3: Conductivity Measurement of Complexes in (1 x 10⁻³) DMSO Solution

Complexes	Concentration (Mol dm ⁻³)	Specific conductance (Ohm ⁻¹ cm ⁻¹)	Molar conductance (Ohm ⁻¹ cm ⁻² mol ⁻¹)
[CuL ₂]. 2H ₂ O	1 x 10 ⁻³	24.8 x 10 ⁻⁶	24.8
[ZnL ₂]. 3H ₂ O	1 x 10 ⁻³	6.2 x 10 ⁻⁶	6.2

L = C₁₄H₁₁NO₄**Table 4:** Magnetic susceptibility value of the metal (II) complexes

Complexes	Magnetics Susceptibility (cm ³ g ⁻¹)	Molar Magnetics Susceptibility (cm ³ mol ⁻¹)	B.M (μ _{eff})
[CuL ₂]. 2H ₂ O	2.0084 x 10 ⁻⁶	1.24 x 10 ⁻³	1.72
[ZnL ₂]. 3H ₂ O	-3.9433 x 10 ⁻⁷	-2.442 x 10 ⁻⁴	Diamagnetic

L = C₁₄H₁₁NO₄**Table 5:** Infrared Spectral data of the ligand its Metal (II) Complexes

Compounds	V(C=N) cm ⁻¹	V(M-N) cm ⁻¹	V(M-O) cm ⁻¹
L	1574	-	-
[CuL ₂]. 2H ₂ O	1538	606	486
[ZnL ₂]. 3H ₂ O	1588	609	412

L = C₁₄H₁₁NO₄

Table 6: Percentage composition by weight of metal in the complexes

Complexes	Percentage composition of metal in the complex	
	Calculated	Observed
[CuL ₂]. 2H ₂ O	11.03	10.91
[ZnL ₂]. 3H ₂ O	11.32	11.48

L = C₁₄H₁₁NO₄**Table 7:** Job's Methods of continuous Variation Results of the Metal (II) Complexes

S/N	Cu (II) Complexes (λ _{max} = 540nm)		Zn (II) Complexes (λ _{max} = 465nm)	
	X _L	Abs	X _L	Abs
1	0.083	0.7485	0.083	0.0213
2	0.167	0.8925	0.167	0.052
3	0.250	1.1023	0.250	0.0875
4	0.333	1.3253	0.333	0.1196
5	0.417	1.5023	0.417	0.1323

6	0.500	1.6785	0.500	0.1576
7	0.583	1.7954	0.583	0.1964
8	0.667	1.9547	0.667	0.2249
9	0.750	1.7412	0.750	0.1769
10	0.833	1.3008	0.833	0.1332
11	0.917	0.9888	0.917	0.1138

Table 8: Determination of Water of Crystallization in the Complexes

Complex	Initial Mass (g)	Final Mass (g)	Loss Mass (g)	% of Water
[CuL ₂]. 2H ₂ O	0.2003	0.1874	0.0129	6.44
[ZnL ₂]. 3H ₂ O	0.2004	0.1820	0.0184	9.18

L = C₁₄H₁₁NO₄**Table 9:** Determination of Empirical Formulae of the Complexes

Sample	Cu (II)	L	H ₂ O	Zn (II)	L	H ₂ O
% by Mass	11.03	82.53	6.44	11.32	79.49	9.19
Moles	0.1736	0.3211	0.3578	0.1731	0.3093	0.5106
Mole ratio	1	2	2	1	2	3
Empirical Formula	[CuL ₂].2H ₂ O			[ZnL ₂].3H ₂ O		

L = C₁₄H₁₁NO₄**Table 10:** Result of antibacterial activities of Schiff base and metal (II) complexes

Test Organisms	<i>Staphylococcus aureus</i>			<i>Escherichia coli</i>			<i>Pseudomonas aeruginosa</i>		
	60	30	15	60	30	15	60	30	15
L	6	6	6	6	6	6	9	6	6
[CuL ₂]. 2H ₂ O	6	6	6	12	10	8	14	11	9
[ZnL ₂]. 3H ₂ O	6	6	6	10	7	6	6	6	6
Septtrin	27	27	27	38	38	38	39	39	39

L = C₁₄H₁₁NO₄

Table 11: Result of antifungal activities of Schiff base and metal (II) complexes

Test Organisms	<i>Mucor species</i>			<i>Aspergillus flavus</i>		
	60	30	15	60	30	15
Compounds/ Conc.(µg/disc)	60	30	15	60	30	15
L	6	6	6	6	6	6
[CuL ₂]. 2H ₂ O	6	6	6	12	10	8
[ZnL ₂]. 3H ₂ O	6	6	6	10	7	6
Nystatin	31	31	31	39	39	39



The Schiff base appeared yellow crystalline solids. The percentage yield recorded was 73.6% with the decomposition temperature of 185 °C as shown in Table 1.

The metal complexes of Cu (II) and Zn (II) were found to be green and pale-yellow crystalline products with a yield of 70%, and 71.6% respectively. The decomposition temperature of both Cu (II) and Zn (II) complexes were found to be 292 and 255 °C respectively, this suggests a good thermal stability.

Solubility test carried out on Schiff base and corresponding metal complexes were determined in different solvents showed that, the Schiff base was found to be insoluble in water, ethanol and acetone but soluble in dimethylsulfoxide (DMSO) and dimethylformamide (DMF). Likewise, all the complexes are insoluble in water but soluble in DMSO and DMF. Both Schiff base and the complexes were found to behave differently in other solvents as presented in Table 2.

The molar conductance measurement of the complexes were carried out in 10⁻³ M of DMSO and the values were found to be in the range of 24.5 and 6.2 Ω⁻¹cm² Mol⁻¹ in Table 3.

The values obtained were low – suggesting that, the complexes are non-ionic, therefore non-electrolytes.

The bonding formation between the Schiff base and metal (II) ions were studied by comparing the IR spectrum of free Schiff's base with that of the complexes. The infrared spectral result of the Schiff base showed vibrational peak at 1574 cm⁻¹ in the spectrum of the ligand which was absent in the spectrum of the starting aldehyde and amine materials. This new band at 1574 cm⁻¹ can be assigned to the azomethine band (-C=N-). However, it was observed to shift in the spectra of the metal complexes of Cu(II) and Zn (II) to 1538 and 1588 cm⁻¹ respectively. The shift in the frequency might suggest that azomethine nitrogen have been involved in the coordination with the metal ion. Furthermore, two new peaks were observed in the spectrum of the complexes, one in the range of 606 – 609 cm⁻¹ and the other within the 694 to 764 cm⁻¹ range, the

new peaks were assigned to the corresponding metal–oxygen and metal–nitrogen bonds respectively.

The results are presented in Table 5. The magnetic moment values of the complexes obtained are in the range of 1.72 BM, (Table 4).

The values suggested that the complexes are paramagnetic in nature. Metal ions in the complexes exhibit paramagnetic and diamagnetic properties due to the presence of unpaired electron(s) or absence of it respectively in the orbital of the metals (Housecraft and Sharp, 2018).

The percentage composition of the metal was found in the complexes gravimetrically. The result obtained was in good agreement with calculated values. The percentage of the ligand was determined by difference and the results obtained were within the calculated values as presented in Table 6.

The percentage of water of crystallization in the complexes was determined and the result showed that Cu (II) and Zn(II), complexes contained 6.44% and 9.18% water respectively (Table 9).

The empirical formulae of the metal (II) complexes were determined from the % compositions of the metal (II) ions, water of crystallization and the ligand. The results obtained suggested the general formula [ML₂].nH₂O. Where M = Cu²⁺ and Zn²⁺, as presented in Table 10

Determination of metal: ligand ratio was done using Job's method of continuous variations, the result showed a metal: ligand ratio of 1:2 as presented in Table 7.

The biological screening of the Schiff base and its metal (II) complexes were studied against three bacterial and two fungal isolates using disc diffusion method. The bacteria isolated used were *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* while the fungi are *Mucor indicus* and *Aspergillus Flavus*. Septrin and Nystatin were used as control for the bacteria and fungi respectively. The zones of inhibition (mm) were measured for both the discs. The results of the antibacterial screening of the Schiff base at a concentration of 60mg/ml against all bacteria isolates studied indicated that the Schiff bases showed significant activity against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* while the complexes were

found to be more active against all tested bacterial strains. Antibacterial activity of these compounds increase with increase concentration as presented in Table 10.

The antifungal activity studies of the compound showed that Cu (II) have highest activity in both *Mucor indicus* and *Aspergillus flavus* isolates. Zn (II) showed moderate activity while the Schiff base has minimal activity against the isolates (Table 11).

The antimicrobial data reveals that the complexes and the ligand are bioactive because of their activities against these tested microbes. The results of antimicrobial activities were compared with standard drug as positive control their activities were found to be lower than that of the control.

CONCLUSION

Schiff base derived from 4-amino-2-hydroxybenzoic acid and 2-hydrobenzaldehyde were successfully synthesized. The Schiff base is use as a ligand in the synthesis of Cu (II) and Zn (II) have been demonstrated. Both the ligand and the complexes were successfully characterized by (infrared spectral) Job's method of continuous variations. In addition, its conductivity, magnetic susceptibility and decomposition temperature were determined. The spectral studies indicated that the metal ion coordinated to the Schiff base through the N and O donor atoms indicating that the Schiff base is acting as a bidentate ligand. The Schiff base and the complexes were found to be active against the bacterial and fungal isolates tested in the work. Cu (II) was found to possess some remarkable antibacterial activities, but lower than the control.

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