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Synthesis, Characterization and Antimicrobial Studies of 2-{(E)-[(4-Chlorophenyl)Imino]Methyl}Phenol Schiff Base Ligand and its Cu(II) Complex

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Research Article

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Abstract

A Schiff base ligand (84% yield) was prepared by the condensation of 4-chloroaniline and salicylaldehyde in their ethanolic solutions. The corresponding Cu(II) complex (64% yield) of the prepared Schiff base was obtained by refluxing the ethanolic solution of the Schiff base. The melting point temperature of the Schiff base was found to be 138°C, while the decomposition temperature of the Cu(II) complex was found to be 209°C. Both the Schiff base and the corresponding Cu(II) complex were found to be soluble in some organic solvents but Cu(II) was insoluble in diethylether and n-hexane. The formation of the Schiff base and its Cu(II) complex was confirmed using FTIR spectroscopy. Both the Schiff base and its Cu(II) complex were found to be stable at room temperature. The antimicrobial activity of the Schiff base and its complex were tested against human pathogenic bacteria as well as fungi and the zones of inhibition were recorded. A comparative study of zone of inhibition (ZOI) values of Schiff base and its Cu(II) complex show that, the complex display higher antibacterial activity than the free ligand and this is probably due to the greater lipophilic nature of the complex, which showed 16 mm, 20 mm, 21 mm, 17 mm, 16 mm and 15 mm against Escherichia coli, Staphylococcus aureus, Streptococcus pyogenes, Aspergillus niger, Candida albicans and Mucus indicus respectively. In addition, the results showed that, the complex Cu(II) exhibited potent antibacterial activity with the reference standard ciprofloxacin and Clotrimazole.

Keywords: Schiff base; Metal complexes; Decomposition temperature; Melting point

Introduction

Schiff bases, named after Hugo Schiff (1864) are formed when any 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known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group (C=O) has been replaced by an imine or azomethine group. Schiff bases are some of the most widely used organic compounds. They are used as pigments, dyes, catalysts, intermediates in organic synthesis, and as polymer stabilisers [1]. Schiff bases have also been shown to exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties [2]. Due to the excellent selectivity, sensitivity and stability of Schiff bases for specific metal ions such as Ag(II), Al(III), Co(II), Cu(II), Gd(III), Hg(II), Ni(II), Pb(II), Y(III) and Zn(II), many different Schiff base ligands have been used as cation carriers in potentiometric sensors [1].

The interest in metal complexes in which the Schiff bases play a role as the ligands are increasing as evidenced by the number of publications appearing annually (approximately 500) [3]. So much interest in imines can be explained by the fact that they are widely distributed in many biological systems and they are used in organic synthesis and chemical catalysis, medicine, pharmacy and chemical analysis, as well as new technologies [4]. Schiff base compounds have been shown to be promising leads for the design of efficient antimicrobial agents as a result of the broad range of biological activities exhibited by these compounds.

Schiff bases offer a versatile and flexible series of ligands able to bind with various metal ions to give complexes with suitable properties for theoretical and/or practical applications. Many poly-dentate Schiff's base compounds have been structurally characterized and extensively investigated [5]. Schiff's base ligands and their metal complexes have been extensively studied over past few decades.

Metal complexes containing synthetic macrocyclic ligands have attracted a great deal of attention because they can be used as models for more intricate biological macrocyclic systems like metalloporphyrins (hemoglobin, myoglobin, cytochromes, chlorophylls), corrins (vitamin B_{12}) and antibiotics (valinomycin, nonactin). So it attracted the attention of both inorganic and bioinorganic chemists [6]. Metal complexes of the Schiff bases are generally prepared by treating metal salts with Schiff base ligands under suitable experimental conditions. However, for some catalytic application the Schiff base metal complexes are prepared in situ in the reaction system.

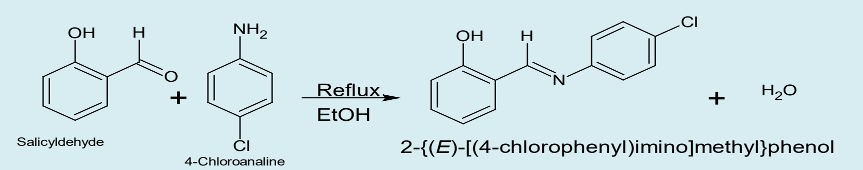
This work aimed to synthesise, characterize and study the antimicrobial potentials of 2-{(*E*)-[(4-chlorophenyl) imino]methyl}phenol Schiff base and its Cu(II) complex.

Materials and Methods

All the reagents and solvents purchased were of analytical grade and used without further purification. The melting point/decomposition temperature for the Schiff base and its corresponding Cu(II) complex were determined using melting point apparatus SMP1. The FTIR spectra of the prepared Schiff base and its corresponding Cu(II) complex were carried out in a range of 4000 – 400cm^{-1} on Shimadzu FTIR – 8400S.

Preparation of the Schiff Base

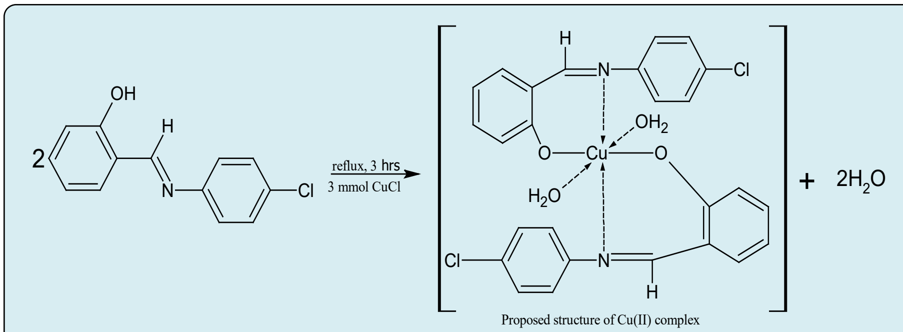
To a stirred solution of chloroaniline (0.01mol) in ethanol, a solution of salicylaldehyde (0.01mol) in ethanol 50 cm^3 was added. The resulting mixture were refluxed for a period of 3 Hours, the resulting mixture was then left to cool at room temperature. After cooling, it was filtered, washed and dried in a desiccator over anhydrous $CaCl_2$ [7] (Scheme 1).



Scheme 1: Preparation of Schiff Base.

Preparation of the Metal Complex

To a 6 mmol Ethanolic solution of the Schiff base, 3 mmol of Copper (II) chloride solution was added in ratio of 2:1. The mixture was refluxed for 3 hours. 10 cm^3 of ethanol was added and the mixture was refluxed for 3 hours using a hot plate magnetic stirrer. The reaction mixture was allowed to cool at room temperature, filtered, washed with ethanol and stored in a desiccator containing phosphorus pentaoxide for 3 hours [7] (Scheme 2).



Scheme 2: Preparation of Cu(II) complex from Schiff base loigand.

Solubility Test

The solubility of the Schiff base and the corresponding Cu(II) complex were studied from ethanol, chloroform, distilled water, DMSO, DMF, methanol, n-hexane, diethylether.

Schiff Base Solubility Test

0.2g of the Schiff base was measured and transferred into the solvents, stirred and allowed for about 3 min, the resulting mixture was filtered, allowed to dry and weighed.

Metal Complex Solubility Test

0.2g of the metal complex was measured and transferred into the respective solvents, it was stirred for 2-3 minutes, and the resulting mixture was filtered, allowed to dry then weighed.

Antimicrobial Activity

The synthesized ligand and its complexes were tested for their in-vitro antimicrobial activity against the bacteria *Staphylococcus aureus, Escherichia coli* and *Streptococcus pyogenes* as well as against the fungi *Candida albicans, Aspergillus niger* and *Mucus indicus* using agar well diffusion method. The stock solutions (102 mol L^{-1}) of the compounds were prepared in DMSO and the zone of inhibition values of the compound were determined by serial dilution method. For determination of zone of inhibition, the respective medium was poured into the petriplates and allowed to solidify at room temperature. Wells were made on the solidified medium and the serially diluted solutions were added on to the wells and allowed to diffuse into the wells. The indicator organisms were overlaid on to the agar medium and the plates were incubated for 37°C for 48 h. After incubation the zone of inhibition by the compound were measured and zone of inhibition was determined.

Results and Discussion

The Schiff base ligand and its metal complex were characterized by FT-IR (Figure 1). The results in Table 1 indicate that, the Schiff base and its corresponding Cu(II) complex are colored. The color orange is for the Schiff base as reported by Archana, et al. & Hassan, et al. [8,9] while the brown colour is for Cu(II) complex. The change in color of the Schiff base from orange to the brown color of the Cu(II) complex was due to complexation which resulted into the formation of coordination compound. The melting point for the Schiff base and its corresponding Cu(II) complex range between 130°C – 210°C (Table 1). The results showed some similarities in physical properties of both Schiff base and its corresponding Cu(II) complex. There were similarities with a report by Mustapha, et al. [10] and it indicated the high stability of the compounds.

Compound	Melting point (°C)	Decomposition Temperature (°C)	Percentage Yield (%)	Colour	Molecular Formula
Schiff base	138	-	84	Orange	$C_{13}H_{10}ClNO$
Cu(II)	-	209	64	Brown	$C_{26}H_{22}Cl_2CuN_2O_4$

Table 1: Physical data of Schiff base ligand and its Cu(II) Complex.

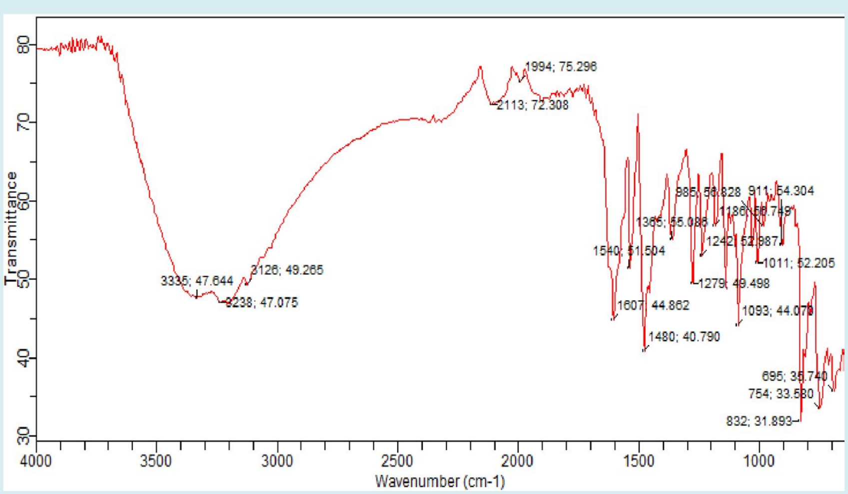


Figure 1: the FTIR Spectrum of the Schiff base.

Functional Groups	Schiff Base (cm^{-1})	Cu(II) Complex (cm^{-1})
V(C-Cl)	590	-
v(OH)	3339	3238
v(M-N)	-	562
v(C=N)	1611	1614
H2O	-	3335
v(C-H)	3095.7	-

Table 2: FTIR data of the Schiff base and its Cu(II) complex.

The FTIR results were reported in Table 2, and showed The appearance of absorption band at the region of 1611cm^{-1} assigned to υ(C=N) stretching vibration which is an important feature of Schiff base and it was supported by the literature [9,11]. Absorption band also appeared in the free ligand at 3095.70cm^{-1} can be assigned to υ (C-H) stretching vibration and is within the range of 3100-3000cm^{-1} for C-H aromatic. A weak absorption band appeared at 590^{-1} can be assigned to υ (C-Cl) because it was within the range of 590 – 700 cm^{-1} [12]. In the Cu(II) complex (Figure 2), there were a little shift in υ (C=N) from 1614.60 to 1615.90 – 1614.80 cm^{-1} this indicate stretching vibration of the azomethine group and possible formation of the complex [13]. The appearance of weak absorption band in the C(II) complex at the range of 562.33 – 557.15 cm^{-1} can be attributed to the stretching vibration of Metal –Nitrogen (M–N) and it was similar to what was confirmed in the literatures (Deoghoria, Bagihalli, Shahabadi [14]).

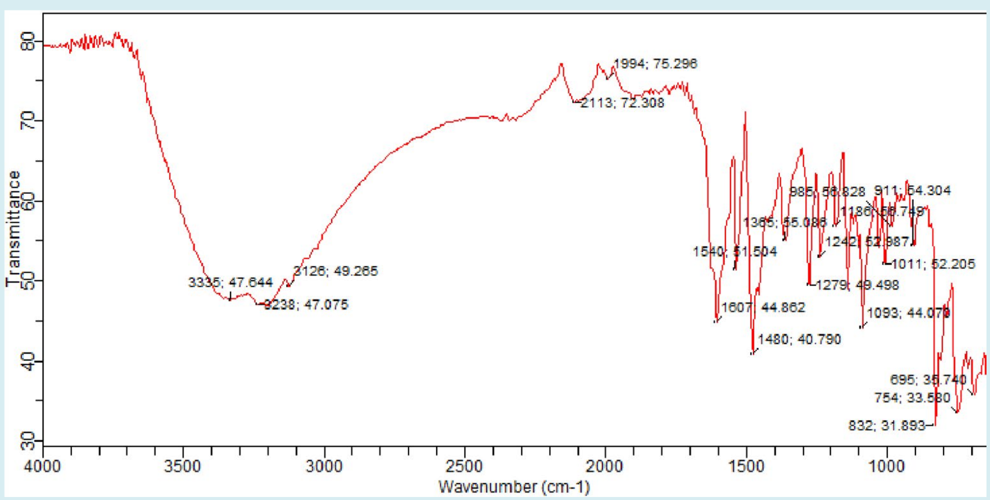


Figure 2: FTIR Spectrum of the Cu(II) complex.

Solvents	Schiff Base	Cu(II) Complex
n-hexane	S	IS
DMSO	S	S
Ethanol	S	SS
Methanol	S	S
DMF	S	S
Chloroform	SS	SS
Distilled water	SS	SS
Diethyl ether	SS	IS

Table 3: Solubility of the Schiff base and Cu(II) Complex.
KEY: IS = Insoluble, S = Soluble, SS = Slightly Soluble.

Chandra Mohan, et al. [15] reported the Infrared spectra of the ligands which showed strong bands at 3407 cm^{-1} and 3146 cm^{-1} and were assigned to symmetric or asymmetric ν(NH_2) stretching and ν(N–H) vibration of free NH_2 groups. The spectrum also shows bands at 1588, 1294 and 838 cm^{-1} due to the ν(C=N), ν (C=S) & δ(C=S) groups respectively (Table 3).

The solubility test was also carried out and the results obtained from the Schiff base and its corresponding Cu(II) complex showed that both were soluble in DMSO, Methanol and DMF. The table also showed that, the Cu(II) complex is insoluble in n-hexane and Diethyl-ether while the Schiff base is soluble in n-hexane and slightly soluble in Diethyl ether.

Both the Schiff base and the corresponding Cu(II) complex are slightly soluble in chloroform and distilled water. However, the solubility of the Schiff base and the Cu(II) complex in different organic solvents can be attributed to the covalent nature of the of the compounds (Table 4).

Test Microbes	Ligand(mm)	Cu(II) complex(mm)	Ciprofalxacin
Escherichia coli	13	16	20
Staphylococcus aureus	10	20	24
Streptococcus pyogenes	11	21	23
			Clotrimazole
Aspergillus niger	13	17	21
Candida albicans	14	16	22
Mucus indicus	14	15	19

Table 4: Results of zone of inhibition (mm) of Schiff base ligand and its Cu(II) complex.

The Schiff base ligand and its Cu(II) complex have been monitored for their antibacterial activity against various pathogenic bacteria such as *Staphylococcus aureus, Streptococcus pyogenes* and *Escherichia coli* and *antifungal activity* against *Candida albicans, Aspergillus niger* and *Mucus indicus*. Ciprofloxacin and Amphotericin-B were used as the standard for bacterial and fungal studies respectively. The antimicrobial activity of the Schiff base and its complexes were tested against human pathogenic bacteria as well as fungi and the zones of inhibition were recorded. A comparative study of the growth inhibition zone values of Schiff base and its Cu(II) complex show that complex display higher antibacterial activity than the free ligand and this is probably due to the greater lipophilic nature of the complex. Metal complexes activity can be explained on the basis of Overtone's concept and Tweedy's chelation theory [16,17]. According to the overtone concept of cell permeability, the lipid membrane surrounding the cell favours the passage of only lipid-soluble materials, which means that liposolubility is an important factor controlling antimicrobial activity. On chelation, the polarity of metal ion is reduced to a greater extent due to overlap of the ligand orbital and partial sharing of its positive charge with the donor groups. In addition, it is also due to delocalization of the π-electrons over whole chelate ring, enhancing the penetration of the complexes into the lipid membranes and the blocking of the metal binding sites of the enzymes of the microorganisms.

Conclusion

The Schiff base and its corresponding copper(II) complex were successfully synthesized and characterized by FTIR spectroscopic technique, FT-IR spectra confirm the functional groups present in the ligand and its complex. The solubilities of the ligand and its corresponding Cu(II) complex were determined from solvents of different polarities, and were found to be soluble in most organic solvents. A comparative study of zone of inhibition (ZOI) values of Schiff base and its Cu(II) complex show that, the complex display higher antibacterial activity than the free ligand and this is probably due to the greater lipophilic nature of the complex.

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