

Synthesis, Characterization and Antimicrobial Studies of Schiff Base Derived from 2-Amino Phenol and O-Anisaldehyde and Its Co (II), Cu (II) and Zn (II) Complexes

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Abstract

Schiff base was synthesized by refluxing 2-aminophenol and o-anisaldehyde, In similar manner, its corresponding Co(II), Cu(II) and Zn(II) complexes were also synthesized and characterized by Solubility Test, Decomposition Temperature, Molar Conductivity Measurement, Infrared Spectroscopy and UV-Visible Analysis. The melting point of the Schiff base was 110 °C and Decomposition Temperature of the complexes were found to be in the range 124 – 136 °C. The IR spectral analysis of the Schiff base showed a band at 1600cm⁻¹, which was assigned to $\nu(\text{C}=\text{N})$. The band observed in complexes were in the range 1585-1609 cm⁻¹. The shift in absorption band indicated coordination of the Schiff base to the metal ion through azomethine group. Magnetic susceptibility revealed that Co (II) and Cu (II) complexes are paramagnetic whereas Zn complex is diamagnetic. The molar conductance values of the complexes were in the range 6.28-22.37 $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$ which are low indicating that the complexes are non-electrolytes. Job's method revealed 1:2 metal to ligand ratio. The ligand and the complexes were tested for antibacterial and antifungal activities against some pathogenic bacteria which are *Salmonella typhi*, *Staphylococcus aureus* and *Escheria coli* and some fungi species which are *Mucor spp* and *Aspergillus fumigatus* by disc diffusion method. The results show that the complexes have higher activity than the free Schiff base. The activity increases with increase in concentrations. All the complexes are more potent antibacterial than antifungal.

Key words: Schiff base, Complexes, Molar Conductance, Antibacterial and Antifungal

Introduction

Schiff base compound was invented by Hugo Schiff and was named after him. Basically there are compounds with a functional group those possess a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group, not with hydrogen (Bader, 2011). In general a Schiff base could be represented by the general formula $\text{R}^1\text{R}^2\text{C}=\text{NR}^3$, where R is an organic side chain, some of them are restricted to the secondary aldimine (line azomethines as the carbon is attached to the hydrogen atom) with the general formula $\text{RCH}=\text{NR}$ (Yang and Sun, 2006). Generally, Schiff base ligands are able to coordinate through imine nitrogen and another group, usually associated with aldehyde or ketones. Nowadays, Chemists still

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prepare Schiff bases and well-designed Schiff base ligands are considered “privileged ligands”. In fact, Schiff bases are able to stabilize many different metals in a large variety of successful catalytic transformations. It is pertinent to know that, Schiff bases as ligands are of great importance in coordination chemistry due to their synthetic flexibility, selectivity and sensitivity towards the central metal atom, structural similarities with natural biological substances and also due to presence of imine group (-N=CH-) which imports in elucidating the mechanism of transformation and racemization reaction in biological systems (Yang and Sun, 2006). Schiff base complexes have also been used as redox catalysts in organic reactions. Similarly, Schiff base have been found to possess interesting biological properties, such as antibacterial and in some cases antitumor activity (Bader, 2011). Schiff bases have the potentials to be used in areas such as electrochemistry, bioinorganic, catalysis, separation processes, metallic deactivators and environmental chemistry (Ziyad *et al.*, 2011). Several Schiff bases were reported to possess remarkable antibacterial, antifungal and anticancer activities. This class of compounds, containing the C=N moiety is important for biological activity. The number of transition metal complexes that were reported by using variety of Schiff base ligands and studied their different biological activities such as antimicrobial, anticancer, antifungal have an esteemed place in medicinal chemistry (El-Barasi *et al.*, 2023) many drugs possess modified pharmacological and toxicological properties when administered in the form of metallic complexes (More *et al.*, 2019; Ibrahim *et al.*, 2021). The persistent resistance of micro-organisms against certain antimicrobial drugs is becoming a global concern due to rapid increase in multidrug-resistant bacteria. Some previously treatable pathogens are now becoming untreatable. For example, *Staphylococcus aureus* and *enterococcus* are resistant to methicillin, vancomycin, ampicillin, cephalosporins, all beta lactams and occasionally gentamicin, erythromycin and trimethoprim/sulfamethoxazole. So also, Multidrug-Resistant *M. tuberculosis* (MDRTB) Transition metals have initiated the development of metal-based drugs with promising pharmacological application and may offer unique therapeutic opportunities. (Sadi *et al.*, 2017). This research was aimed to synthesized and characterized a novel bioactive Schiff base and its corresponding transition complexes.

Materials and Methods

All the chemicals were of analytical grade (Analar) and were used without further purification. The metal (II) chlorides of Copper, Nickel and Iron were obtained from PSPARK Scientific Limited, UK. All glass wares were washed with detergent, rinsed with distilled water and dried in the oven at 110°C. All weighing were carried out on electrical meter balance Toledo BI54. Melting point and decomposition temperatures were recorded using Gallenkamp melting point apparatus. Conductivity measurement was done using Jenmway conductivity meter mode 4010. Infrared spectral analysis was recorded using FTIR 8400-S. Magnetic susceptibility measurements were conducted and recorded using MKT Sherewood magnetic susceptibility meter. The *in vitro* antibacterial and antifungal screening was performed by disc diffusion on three bacteria species namely: *typhi*, *Staphylococcus aureus* and *Escheria coli* and two fungal species namely: *Mucor spp* and *Aspergillus fumigitus* at the Department of Microbiology, Bayero University Kano.

Synthesis of Schiff Base

An ethanolic solution of 2-amino phenol (0.01mol) was mixed gently and refluxed for 3hrs. The volume of the resulting solution was reduced to half by evaporation and cooled to room temperature. The product obtained was filtered, washed with ethanol, dried and preserved in a desiccator over CaCl₂ for a week (Fugu *et al.*, 2013).

Synthesis of Metal (II) Complexes

An ethanolic solution of ligand (0.002 mol) and metal (II) chlorides (0.001mol) were mixed gently and refluxed for 3hrs. The volume of the resulting solution was reduced to half by evaporation and cooled to room temperature. The solid obtained was filtered, washed thoroughly with ethanol and dried in a desiccator over CaCl₂ for a week (Fugu *et al.*, 2013).

Solubility Test

The Schiff base and its metal complexes were subjected to solubility test in some common solvents which are acetone, deionize water, methanol, ethanol, nitrobenzene, carbontetrachloride, chloroform, Dimethyl sulfoxide (DMSO), Dimethylformamide (DMF) and benzene. The result is shown in (Table 2).

Conductivity Measurement

Three millimole of each metal complex was dissolved in 10 mL of DMSO and the corresponding conductance values recorded, molar conductance of each metal complex was then evaluated. (Aliyu and Abdullahi,2009). The result is shown in table 3.

Magnetic Susceptibility Measurement

The metal complex was introduced into a capillary tube and the reading recorded using the magnetic susceptibility balance. The magnetic moment calculated using the relation reported by (Idris *et al.*, 2020)

Determination of Melting Point and Decomposition Temperature.

The melting point of the Schiff base as well as the decomposition temperatures of the metal complexes were determined by introducing a pinch of each into a capillary tube and then inserted into the Gallenkamp apparatus, the temperature at which the ligand melt and that which the complexes decompose were recorded. The result is shown in table 1.

Determination of the Metal to Ligand Ratio in the Complex Compounds Using Job's Method of Continuous Variation

The number of coordinated ligands in the metal ion were determined using Job's method in which 3 millimolar solution of the ligand and the metal(II) chloride were separately prepared. By mixing this solution to make a total volume of 16cm³ in which the mole fraction of the ligand, x_i is $0.06 \leq x_i \leq 1.0$ were also prepared. The absorbance of each solution mixture was measured at the wave length of maximum absorbance of the metal (II) chloride solutions.

A plot of absorbance against mole fractions was made and by extrapolation, mole fraction (x_i) at maximum absorbance was recorded, which was the point where the metal ion and the ligand are in stoichiometric ratio. The number of coordinated Schiff base ligand to metal ion was calculated using the relation;

$$\bar{n} = \frac{x_i}{1 - x_i}$$

Where \bar{n} = the number of coordinated ligands

x_i = corresponding mole fraction of the ligand at maximum absorbance

Antibacterial and Antifungal Test

The antibacterial and antifungal tests of the Schiff base and metal complexes were carried out by disc diffusion method. The bacteria species used in the screening were *Staphylococcus aureus*, *Escheria coli* and *Salmonella typhi* and the fungi species used were *Mucor spp* and *Aspergillus fumigatus*. Three different concentrations 60 µg/disc, 30 µg/disc and 15 µg/disc of each complex and ligand were prepared using Dimethyl sulfoxide (DMSO). 0.06 g of each of

the complexes and the ligand was dissolved in 1 mL of the solvent separately. 0.5 mL of each solution were introduced into 50 sterile discs in the bijou bottles respectively to make 60 $\mu\text{g}/\text{disc}$ concentrations. 0.5 mL of DMSO was added into the remaining stock solution; making 1 mL, 0.5 mL was taken and placed into other bottles containing 50 discs to make the 30 $\mu\text{g}/\text{disc}$ concentrations. 0.5 mL of DMSO was added to the stock solution and another 0.5 mL was taken and added to 50 discs in the bottles to make the 15 $\mu\text{g}/\text{disc}$ concentration (Yusha'u and Salisu, 2011). Standard inocula of the isolates were swabbed onto to the surface of the prepared and solidified nutrient Agar in separate petri-dishes. The prepared discs of the complexes and standard antibiotic discs were placed on the surface of the inoculated media at interval. the standard used for the bacteria tests were Gentamycin and Ciprofloxacin and standard used for the fungi test was Ketoconazole. The plates were incubated at 37 °C for 24 hours before observation and measurement of inhibition zone. The same procedure was used for the fungal isolates using potato dextrose agar and the plates were incubated at room temperature for 48 hours.

Results

Result of the characterization, antimicrobial activity of the Schiff base and its metal(II) complexes are presented in the table below:

Table 1: Physical properties of the ligand and its metal (II) complexes

Compound	Colour	B.M (μ_{eff})	Decomposition Temperature(°C)	Melting Point (°C)	Percentage yield%
Ligand	Light Brown	-	-	110	82.57
[Co L ₂]	Dark Grey	4.34	127	-	71.43
[Cu L ₂]	Black	2.19	136	-	82.35
[Zn L ₂]	Black	Dia	124	-	74.52

L = Ligand

Table 2: Solubility tests of the Ligand and its metal (II) complexes

Compound	Deionize H ₂ O	MeOH	EtOH	Chloroform	Acetone	Nitro Benzene	CCl ₄	Benzene	DMF	DMSO
Ligand	IS	S	S	SS	SS	S	IS	SS	S	S
[Co L ₂]	IS	SS	SS	SS	SS	S	IS	SS	S	S
[Cu L ₂]	IS	SS	SS	S	SS	S	IS	SS	S	S
[Zn L ₂]	IS	SS	S	S	IS	SS	IS	S	S	S

KEY: S = Soluble, SS = Slightly Soluble, IS = Insoluble

Table 3: Conductivity Measurement of Complexes in 3×10^{-3} DMSO

Complex	Concentration Moldm ⁻³	Specific Conductance Ohm ⁻¹ cm ⁻¹	Molar conductance Ohm ⁻¹ cm ² mol ⁻¹
[Co L ₂]	3×10^{-3}	67.1×10^{-6}	22.37
[Cu L ₂]	3×10^{-3}	38.1×10^{-6}	12.70
[Zn L ₂]	3×10^{-3}	18.65×10^{-6}	6.28

L = Ligand

Table 4: Infrared spectral data of the Ligand and its metal (II) complexes

Compound	$\nu(\text{OH}) \text{ cm}^{-1}$	$\nu(\text{C}=\text{N}) \text{ cm}^{-1}$	$\nu(\text{M} - \text{N}) \text{ cm}^{-1}$	$\nu(\text{M}-\text{O}) \text{ cm}^{-1}$
Ligand	3304	1600	-	-
[Co L ₂]	-	1586	753	415
[Cu L ₂]	-	1585	754	463
[Zn L ₂]	-	1609	759	410

L = Ligand

Table 5A: Antibacterial activities of the ligand and its metal (II) complexes against some bacterial species

Test organisms used	Concentration of Complexes									Control (mm)
	Co Complex			Cu Complex			Zn Complex			
	60	30	15	60	30	15	60	30	15	
<i>staphylococcus aureus</i>	10	9	-	-	-	-	35	23	18	Gentamycine 35
<i>E. coli</i>	-	-	-	20	11	10	14	9	6	Gentamycine 38
<i>Salmonella typhi</i>	13	11	9	25	20	16	30	30	29	Cyprofloxacin 32

Table 5B: Antifungal activities of the ligand and its metal (II) complexes against some fungi species

Test organisms used	Concentration of Complexes									Control (mm)
	Co Complex			Cu Complex			Zn Complex			
	60	30	15	60	30	15	60	30	15	
<i>Mucor spp.</i>	-	-	-	12	-	-	12	9	8	Ketoconazole 32
<i>Aspergillus fumigatus.</i>	-	-	-	-	-	-	-	-	-	Ketoconazole 25

Discussion

The Schiff base was prepared by condensation of 2-aminophenol and o-anisaldehyde. It was found to be brown in colour with high yield (82.57%). The high yield indicate that the reaction is economically feasible and promising, with a melting point of 110°C. The values of melting point precisely indicate that the Schiff base is thermally stable. The complexes formed from the reaction of the Schiff base and the corresponding metal(II) chlorides were found to be of various colours (Table 1) due to chromophores and electronic transitions in the d-orbitals of the metal ions in the complexes. All the complexes formed have an appreciable percentage yield in the range of 71.43 - 82.35% indicating the feasibility of the process for their synthesis. This is similar to the result reported by (Xingming, *et al.*, 2011) Decomposition temperature of the complexes were found to be in the range 131-149°C, these values indicated that the complexes are stable are more thermally stable than the free Schiff base due to presence of metal ion. This result is in good agreement with the result reported by (Sadi *et al.*, 2017). Solubility test for the Schiff base and its corresponding complexes were carried out in order to identify the best solvent used for the purification and other spectroscopic and analytical measurements as shown in Table 2. The result indicated that the Schiff base and its corresponding complexes were insoluble in water. All the compounds were found to be slightly soluble in moderately polar solvents and soluble in methanol, ethanol and readily soluble in DMSO and DMF due to their high dielectric constant. The solubility in these solvents might be due to the presence of polar ends of the compounds. This agrees with the results reported by (Worku *et al.*, 2002). The molar conductance measurement in DMSO carried out on the metal(II) complexes, and were found to be in the range 6.28 - 22.37 Ohm⁻¹cm²mol⁻¹. The low values of molar conductance suggested the non-electrolytic nature of the complexes (Gupat *et al.*, 2012). The IR spectral data of the Schiff base, showed vibrational peak at 1600cm⁻¹ which may be attributed to the azomethine $\nu(\text{C}=\text{N})$ (Byeong *et al.*, 1996). The band in the range 15.85-16.09cm⁻¹ are all observable in the metal(II) complexes which showed an indication of the participation the metal(II) ions in the formation of the complexes. New absorption bonds at 753 - 759cm⁻¹ and 410 - 463cm⁻¹ in the metal(II) complexes indicate the

formation of M-N and M-O bonds respectively which indicated that the ligand is coordinated to the metal ions through these groups. The result is similar with the one reported by (Zeinab and Ali 2012). Magnetic susceptibility measurement at room temperature showed that the metal(II) complexes are all paramagnetic in nature. All the metal(II) complexes synthesized were found to have effective magnetic moment values between 4.3 - 5.0 BM. The values suggested octahedral geometries for the complexes. (Greenwood and Earnshaw, 1997), for Cu(II) complexes the range is 2.12 - 2.44 BM (Gehad *et al.*, 2006). The result obtained from Jobs method suggest 1:2 metal to ligand ratio. Therefore, the ligand and complexes were established to be as proposed in (Fig. 4 and 5) respectively. The antibacterial and antifungal activity for the Schiff base and its metal(II) complexes were determined using the disc diffusion method. The diameters of zone of inhibition (mm) were measured for each treatment. Co(II) complex showed a minor activity against bacterial species tested with no activity against fungal species. Cu(II) complex showed moderate activity against all bacterial species tested and a little activity on fungal specie (*Mucor spp*) at its highest concentration with no activity on the *Aspergillus fumigatus*. Zn(II) complexes showed good activity against *Escherichia coli* and *Salmonella typhi* and the activity was found to be more at highest concentration (60 µg/ disc). Zn(II) shows moderate activity on fungal species (*Mucor spp*) with the highest activity at 60 µg/ disc. Zn(II) does not show any activity on (*Aspergillus fumigatus*) This is comparable to the results reported by (Tarafder *et al.*, 2000). The Schiff base and the complexes showed significant activity at high concentrations, the activity generally increases with increase in concentrations. Moreover, the all the complexes were more potent antibacterial and antifungal than the free Schiff base, but lower than the standard drugs. This Agrees with the result reported by (Sadi *et al.*, 2017).

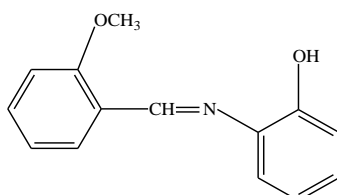


Fig. 4: Proposed structure of the ligand

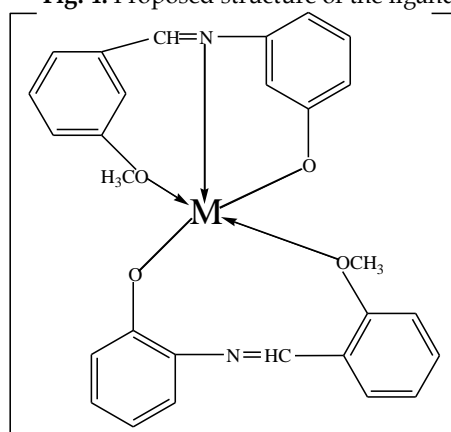
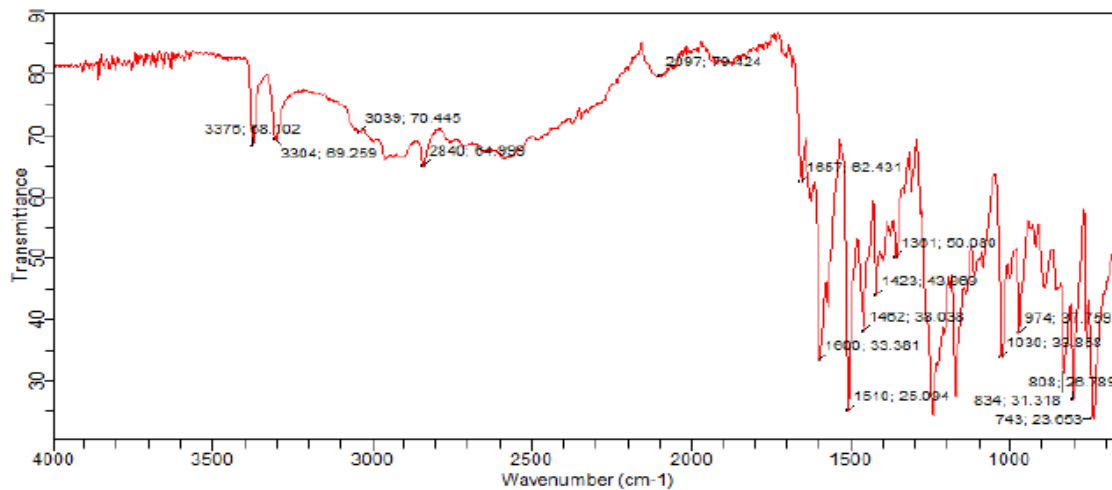


Fig 5: Proposed structure of the complex



6: FTIF Spectrum of Schiff Base

Fig

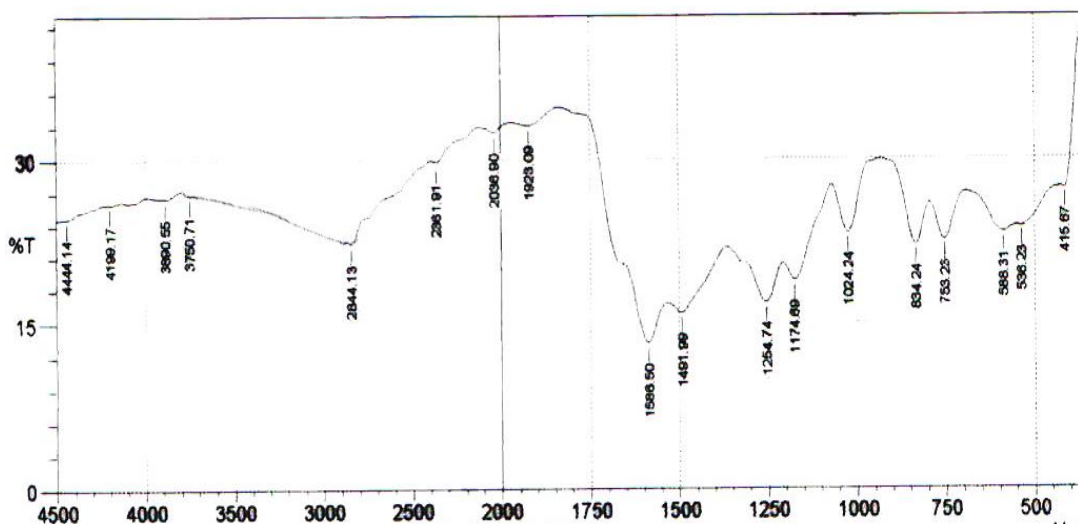


Fig 7: FTIR Spectrum of Co(II) Complex

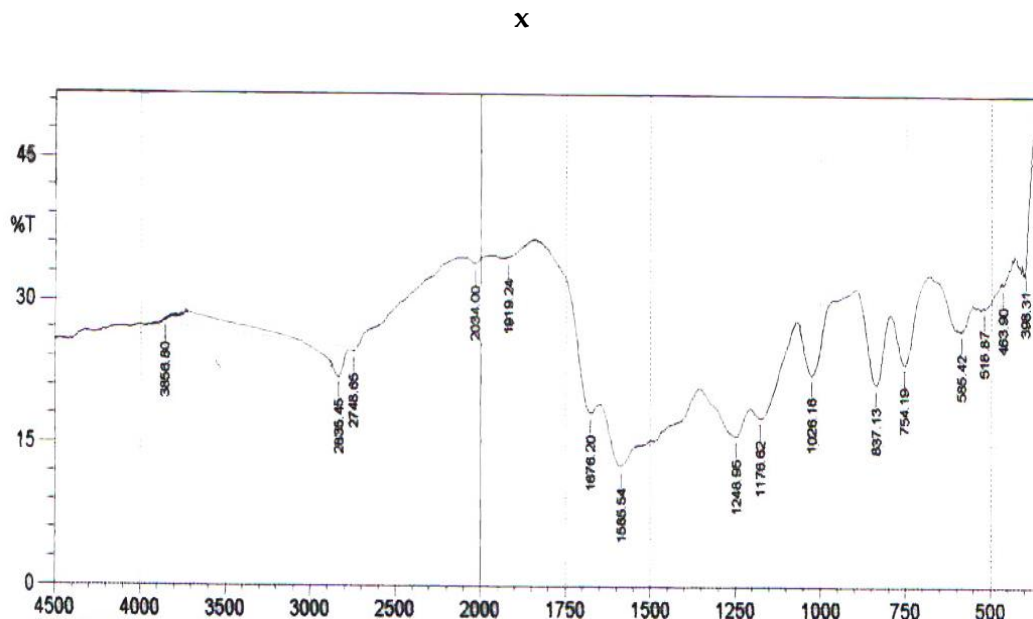


Fig 8: FTIR Spectrum of Cu(II) Complex

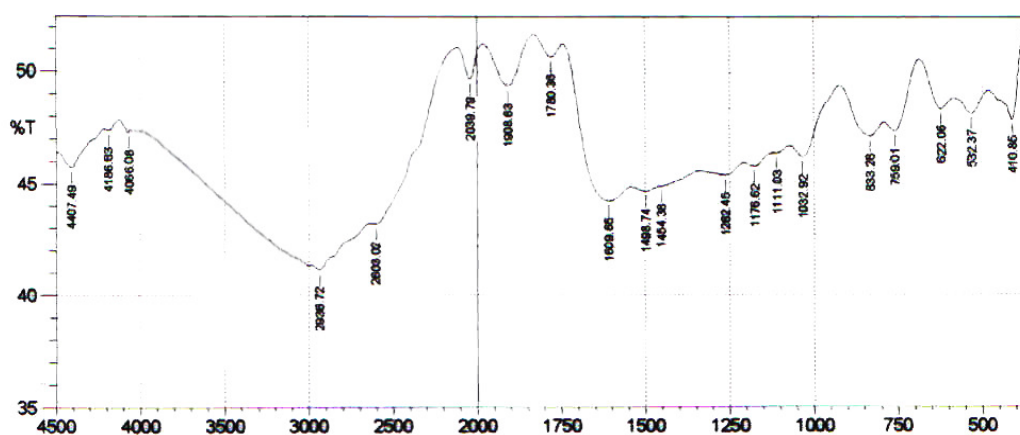


Fig 9: FTIR Spectrum of Zn(II) Complex

Conclusion

The Schiff base was prepared by condensation of 2-aminophenol. The corresponding Co(II), Cu(II) and Zn(II) Complexes were also prepared from the reaction of the ethanolic solution of the Schiff base and metal(II) chlorides. Characterization showed that the complexes are non-electrolyte. The decomposition temperature of the metal complexes showed that they are thermally stable. Magnetic susceptibility show that Co(II) and Cu(II) complexes are paramagnetic in nature while Zn(II) complex is diamagnetic in nature. The solubility test carried out showed that all the complexes and the ligand were soluble in dimethylformamide and dimethyl sulfoxide. IR spectroscopy showed the Schiff base ligand are coordinated to the metal ion in a tridentate manner through the N-atom of the azomethine and two oxygen of the phenol and ether (methoxy group). Job's method showed that the ligand to metal ratio is 2:1. Some of the compounds showed significant antibacterial and antifungal activity at high concentrations.

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