

Preparation, Characterization and Antimicrobial Studies of Some Divalent Metal Complexes with Schiff Base Ligand Derived from 2-aminophenol and 3-formyl-2-hydroxy-6-methoxyquinoline

*Abubakar Muhammad JABBI, Habu Nuhu ALIYU and Abdullahi Muhammad KABIR

Department of Pure and Industrial Chemistry, Faculty of Physical Sciences,
Bayero University Kano, (BUK) P.M.B. 3011, Kano, Nigeria

*Corresponding Authors Email: abubakarmuhammadjabbi@gmail.com

Abstract; Schiff base ligand was prepared by refluxing a mixture of 3-formyl-2-hydroxy-6-methoxyquinoline with 2-aminophenol. The transition metal(II) complexes, were prepared by the reaction of the prepared Schiff base ligand and the respective metal(II) chlorides. The ligand and the metal(II) complexes were characterized by melting point and decomposition temperature, elemental analysis, molar conductivity, IR spectral analysis, AAS analysis, solubility test, and magnetic susceptibility. The FTIR spectral data of the Schiff base determined showed a band at 1622cm^{-1} which was assigned to the $\nu(\text{C}=\text{N})$, a feature of azomethine group. The same band was observed to shift to lower frequencies 1573 and 1614cm^{-1} in the complexes suggesting coordination of the Schiff base with the respective metal(II) ions. Molar conductance values 14.89 and $10.76\ \Omega^{-1}\text{cm}^2\text{mol}^{-1}$ show that the metal complexes were non-electrolytic in nature. The magnetic susceptibility of the complexes were determined and the gram magnetic susceptibility of the complexes were found to be positive, revealing that they are paramagnetic, except cadmium which has negative value. The elemental analysis of the complexes for C, N and H determined suggested 1;1 metal to ligand ratio. The result of the antimicrobial studies showed that, the metal(II) complexes exhibited better antibacterial and antifungal activity than the Schiff base.

1.0 Introduction

Schiff base ligand is a compound containing an imine or azomithine group, ($-\text{N}=\text{CH}-$). It is condensation product of aldehyde (or) ketone with primary amine and was first reported in 1864 by a German chemist Hugo Schiff [Aliyu, 2018; 38, 2 18]. Schiff base ligand is a very important structure for synthetic organic chemistry. These compounds are usually characterized by an imine functional group ($-\text{N}=\text{CH}-$), that helps us to clarify the mechanism, racemization and transamination interaction in biological system. Azomethine nitrogen in the Schiff base, is of considerable chemical and biological importance, not only provides binding sites for metal ions but also makes attachments with various substrate of bio-molecules like proteins and amino acids in biological systems and that of diseases-causing germs [Chaudary, 2012; 3]. These compounds play an important role in medicinal fields because of their wide spectrum of biological activities. Many of them have antimicrobial and anticancer effect as biologically important compounds. A part from their biological effect, they are used in many fields such as pigments, dyes, fungicidal, corrosion inhibitors, analytical chemistry, polymer stabilizers, agrochemical, ion exchange, electrical conductivity catalysis, nonlinear optics and magnetism [3, Zoubi, (2013); Emriye, 2016; & Arulmurugan, *et l.*, 2010]. Schiff base is changeable molecule and can be bi- or tridentate ligands capable of producing very stable complexes with transition metals like manganese, iron, cobalt, copper, vanadium etc. Most of the metal chelates have higher antibacterial and antifungal activities than the individual ligands [Emriye, 2016]. The biological implementations and chelating ability of metal complexes have attracted a significant concern. Transition metal complexes have been widely studied due to their various biological applications in pharmacological areas. These complexes were reported to have antitumor, anti-inflammatory, antioxidan, antimalarial, and antimicrobial activities [Savithra and Revanasiddappa, 2018; Qin, *et l.*, 2013 and Wang, *et al.*, 2012]. Metal complexes with N, O as their donor atoms are very noticeable because of their important biological activities like anticancer, and herbicidal activity.

In this study the schiff base of 3-[(2-hydroxy-phenylimino)-methyl]-6-methoxy -quinolin-2-ol was synthesized from 2-aminophenol and 3-formyl-2-hydroxy-6-methoxyquinoline and its divalent metal complexes were prepared. The schiff base ligand and metal complexes were further characterized and their antibacterial and antifungal activity was also determined.

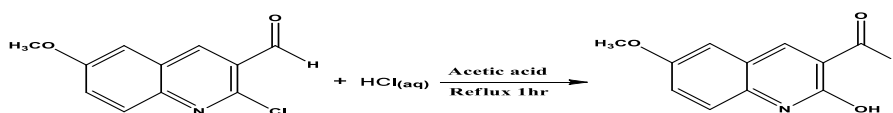
2.0 Material and Methods

2.1 Chemicals, Reagents and Apparatus

All the reagents and chemicals used in this research work were of analytical grade and used without further purification. All weighing were carried out using an electric balance model AB54. The IR spectral analysis was recorded using Cary 630 FTIR Agilent Technologies. Conductivity measurement was carried out in DMSO solvent using Jenway 4010 conductivity meter. Melting point and decomposition temperature measurements were obtained with a SMP10 STUART melting point apparatus. The *in vitro* antimicrobial screening was performed by using disc diffusion method.

2.2 Synthesis of the 3-formyl-2-hydroxy-6-methoxyquinoline

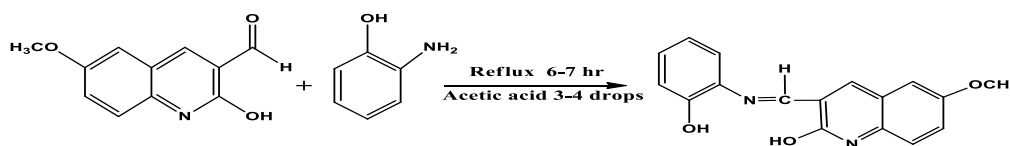
2-chloro-6-methoxy-3-quinolinecarboxaldehyde (2.4g, 0.01mol) was added to aqueous hydrochloric acid (35ml, 4mol) and the resulting solution was heated under reflux on water bath for about 1 hour. Then resulting mixture cooled to room temperature. 3-formyl-2-hydroxy-6-methoxyquinoline was filtered, washed thoroughly with cold ethanol followed by diethylether into yellow cotton-like (Siddappa and Chandrakant, 2012).



Scheme 1: Synthesis of 3-formyl-2-hydroxy-6-methoxyquinoline

2.3 Synthesis of the Schiff base Ligand

The Schiff base ligand was prepared by condensation of 3-formyl-2-hydroxy-6-methoxyquinoline (0.01mol) with 2-aminophenol (0.01mol) in ethanol and refluxing on water bath for six to seven (6 – 7) hours in the presence of a few drops of acetic acid. The reaction mixture was cooled to room temperature and then the ligand was filtered, washed thoroughly with cold ethanol followed by diethylether to get a pure sample. (Siddappa and Reddy, 2012).



Scheme : Formation of 3-[(2-Hydroxy-phenylimino)-methyl]-6-methoxy -quinolin-2- ol

2.4 Preparation of the metal (II) Schiff Base Complexes

To the hot solution of 3-[(2-Hydroxy-phenylimino)-methyl]-6-methoxy -quinolin-2- ol (0.001mol) in ethanol (35ml), a hot ethanolic solution of respective metal(II) chlorides (0.001mol) in ethanol (15ml) was added. The resulting solution was refluxed on a water bath for 4 - 5 hours to get a clear solution. 0.5g of excess sodium acetate, was added to the reaction mixture to adjust the pH (7 to 8) of the solution and the refluxing was continued further for 2 hours. The resulting reaction mixture was then decomposed by pouring into distilled water (100ml) with constant stirring. The yellow complex obtained was allowed to settle and separated

out by filtration, washed with distilled water, then with hot ethanol and cold diethylether and dried in vacuum over phosphorus pentoxide (Siddappa and Reddy, 2012).

2.5 Physical measurements

The IR spectroscopy of the Schiff base and its metal(II) complexes were recorded using FTIR Carry Agilent 630 spectrophotometer at 4000 - 650 cm^{-1} region in KBr pellets. Carbon, Hydrogen and Nitrogen were estimated using elemental analyzer Perkin-Elmer model 240c. Jenway 4010 conductivity meter was used in conductivity measurement using DMSO as solvent. Melting point and decomposition temperature were obtained by using SMP10 STUART melting point apparatus. Magnetic susceptibilities of the complexes were measured on Gouy's balance at room temperature.

2.6 Antibacterial and Antifungal Test

The method used by Jorgensen [Jorgensen, and Turnidge, 2003] was used in antibacterial test, in which the schiff base ligand and its metal(II) complexes were assayed by ager disc diffusion method using cultures of *Escherichia coli*, *salmonella typhi* and *staphylococcus aureus*. The samples were separately dissolved in dimethylsulfoxide to have three different concentrations (1000, 2000 and 3000) $\mu\text{g}/\text{disc}$. Each of these was separately placed on the surface of the culture media before incubation at 37°C for 24 hrs. The diameter of zone of inhibition produced by the ligand and its metal(II) complexes were taken and recorded. Similar procedure was applied in antifungal by using *Aspergillus flarus*, *Aspergillus niger* and *Mucor indicus* fungal isolates.

3. Results and Discussion

3.1. Physical Properties of the Schiff base and its Metal(II) Complexes

The Schiff base ligand and its metal(II) complexes were prepared in good yield, the physical properties of the synthesized ligand and its complexes were analyzed and presented in table 1. The percentage yield of the Schiff base was 75 % while that of the complexes were 66 and 63 %. The Schiff base ligand was cotton-like yellow whereas the Fe(II), and Mn(II) complexes were light-brown and brown respectively. It was found that the melting point of the Schiff base was 251°C and the decomposition temperature of the metal(II) complexes were 280 and 285°C, this is an indication of their thermal stability.

The molar conductance of the complexes were 14.89 and 10.76 $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$ for Mn(II) and Fe(II) complexes. These low values suggest their non-electrolytic nature as reported by Eman [Eman, 2015]. The effective magnetic moments values of 5.72 and 5.12B.M show the paramagnetic nature of the complexes.

Table 1: Physical Properties of the Schiff base Ligand and its Metal(II) Complexes

Compounds	Color	% yield	M.P. (°C)	D. Temp (°C)	μ_{eff} (B.M.)	Molar Conductance ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$)
L (Ligand)	Yellow	75	251	-	-	-
[MnL(H ₂ O) ₃].H ₂ O	Brown	66	-	280	5.72	14.89
[FeL(H ₂ O) ₃].H ₂ O	Brown	63	-	285	5.12	10.76

Keys: M.P = Melting Point, D. Temp. = Decomposition temperature

3.2 Solubility Test

Some common organic solvents and water were used to determine the solubility of the Schiff base and its metal(II) complexes. From the result of solubility test presented in table 2, the Schiff

base ligand and its metal(II) complexes were found to be soluble in dimethylsulfoxide and dimethylformamide, insoluble in n-hexane and water and slightly soluble in methanol.

Table 2. Solubility test of the Schiff base Ligand and its metal(II) complexes

Compound	Solvents						
	Acetone	n-hexane	CCl ₄	DMF	DMSO	Methanol	water
L (Ligand)	SS	IS	S	S	S	SS	IS
[MnL(H ₂ O) ₃].H ₂ O	SS	IS	SS	S	S	SS	IS
[FeL(H ₂ O) ₃].H ₂ O	SS	IS	SS	S	S	SS	IS

Keys: S = Soluble, SS = Slightly Soluble, and IS = Insoluble

3.3 Elemental Analysis

The elemental analysis values of the Schiff base ligand and its metal (II) complexes for C, N and H determined, indicated that the stoichiometry of the complexes are 1:1 (metal to ligand ratio) and recorded in table 3. The elemental analysis data of the Schiff base ligand suggested the formation of C₁₇H₁₄N₂O₃ while that of the complexes revealed the formation of [MnL(H₂O)₃].H₂O and [FeL(H₂O)₃].H₂O. This is in consistent with similar work done by Abubakar [Abubakar, *et al.*, 2017].

Table 3. Elemental Analysis Data of the Schiff base and its Metal(II) Complexes

Compound	Found /(Calculated) %			
	% N	% C	% H	% M
L (Ligand)	8.90	64.39	4.18	-
[MnL(H ₂ O) ₃].H ₂ O	6.34 (6.68)	49.02 (48.70)	4.73 (4.81)	13.10
[FeL(H ₂ O) ₃].H ₂ O	7.02 (6.67)	48.09 (48.59)	5.10 (4.81)	13.29

3.4 FTIR Analysis

- The infrared spectral analysis of the Schiff base ligand and its metal(II) complexes were determined. The band observed at 3339cm⁻¹ in the Schiff base is assigned to ν(OH), and it disappeared in the metal(II) complexes, which indicate the involvement of phenolic oxygen atom in bonding with the respective metal(II) ions. Similar result was reported by Abdullahi and Gareth [Abdullahi and Gareth, 2013]. The broad band at 3387 and 3337cm⁻¹ in the spectra of the complexes are assigned to water of hydration as reported in the work of El-ajaily *et al* [El-ajaily, *et al.*, 2006 and Siddappa and Chandrakant, 2012]. The FTIR spectral data of the Schiff base determined showed a band at 1622cm⁻¹ and it was assigned to ν(C=N), a feature of azomethine group. The same band was observed to shift to lower frequencies 1573 and 1614cm⁻¹ in the complexes suggesting coordination of the Schiff base to the respective metal(II) ions [Mounika, *et al.*, 2010; Rasha, S and Farah, 2012]. New bands in the metal(II) complexes appeared and they are attributed to ν(M-N), stretching frequencies (Table 4).

Table 4. Infrared spectral data of the Schiff base and its metal(II) complexes

Compound	νOH (cm ⁻¹)	νH ₂ O (cm ⁻¹)	νC=N (cm ⁻¹)	νC-O (cm ⁻¹)	νM-N (cm ⁻¹)	νM-O (cm ⁻¹)
L (Ligand)	3339	-	1622	1383	-	-
[MnL(H ₂ O) ₃].H ₂ O	-	3387	1614	1235	562	687

[FeL(H ₂ O) ₃].H ₂ O	-	3335	1573	1231	581	762
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3.5 Antimicrobial and antifungal Activity

The antimicrobial activity results of the screened ligand and its metal(II) complexes are given in the table 5. The Schiff base and its complexes were screened for their antibacterial activities against the selected bacteria isolates of *Eschirichia coli*, *Salmonella typhi* and *Staphylococcus aureus*, by disc diffusion method. It was discovered that the metal(II) complexes possess more effect in inhibiting the microbial growth. This is possibly because of the interaction of the metal(II) complexes with lipoproteins of the cell. Therefore the metal(II) complexes can restrict the usual functioning of the microbial cell. Similar result was reported by Yahyazadeh and Azimi [Yahyazadeh, 2013]. Furthermore, higher stability of the complexes at higher temperature can also allow them to be used as a potential antimicrobial agent. Similar result was also recorded in table 6 for antifungal activity shown by selected fungi isolates of *Aspergillus flarus*, *Aspergillus niger* and *Mucor iudicus* respectively.

Table 5. Antibacterial activity on the schiff base Ligand and its metal(II) complexes

Compound	Concentration (µgcm ⁻³)	Bacterial inhibition zones in mm		
		Staphylococcus aureus	Eschirichia coli	Salmonella typhi
L (Ligand)	1000	07	09	08
	2000	06	08	10
	3000	09	07	09
[CdL(H ₂ O) ₃].H ₂ O	1000	09	10	11
	2000	11	13	13
	3000	13	18	16
[CuL(H ₂ O) ₃].H ₂ O	1000	11	11	10
	2000	12	15	15
	3000	16	18	14

Table 6. Antifungal activity on the schiff base Ligand and its metal(II) complexes

Compound	Concentration (µgcm ⁻³)	Fungal inhibition zones (mm)		
		Aspergillus flarus	Mucor iudicus	Aspergillus niger
L (Ligand)	1000	06	03	04
	2000	08	05	06
	3000	09	07	07
[CdL(H ₂ O) ₃].H ₂ O	1000	10	11	12
	2000	12	16	15
	3000	20	20	19
[CuL(H ₂ O) ₃].H ₂ O	1000	11	09	11
	2000	15	12	14
	3000	18	17	17

4 Conclusion

Schiff base ligand with its metal(II) complexes were synthesized and characterized. The molar conductance values of the metal(II) complexes obtained were low, this indicated the non

electrolytic behavior of the metal(II) complexes. The elemental analysis data suggested 1:1 (metal to ligand ratio). The infrared data indicated that the ligand was coordinated to the central metal(II) ion in a tridentate manner via the azomethine nitrogen and phenolic oxygen atoms after deprotonation. The result of the solubility tests showed that the Schiff base ligand and both of its metal(II) complexes were soluble in dimethylsulphoxide (DMSO) and dimethylformamide (DMF), slightly soluble in acetone and ethanol and insoluble in water and n-hexane. The ligand and its metal(II) complexes were also screened for antimicrobial activity against three selected fungi and bacteria isolates using disc diffusion method respectively. The metal(II) complexes were found to be more active than the ligand but less than the reference drugs *Amoxicillin* and *Ketoconazole* used respectively.

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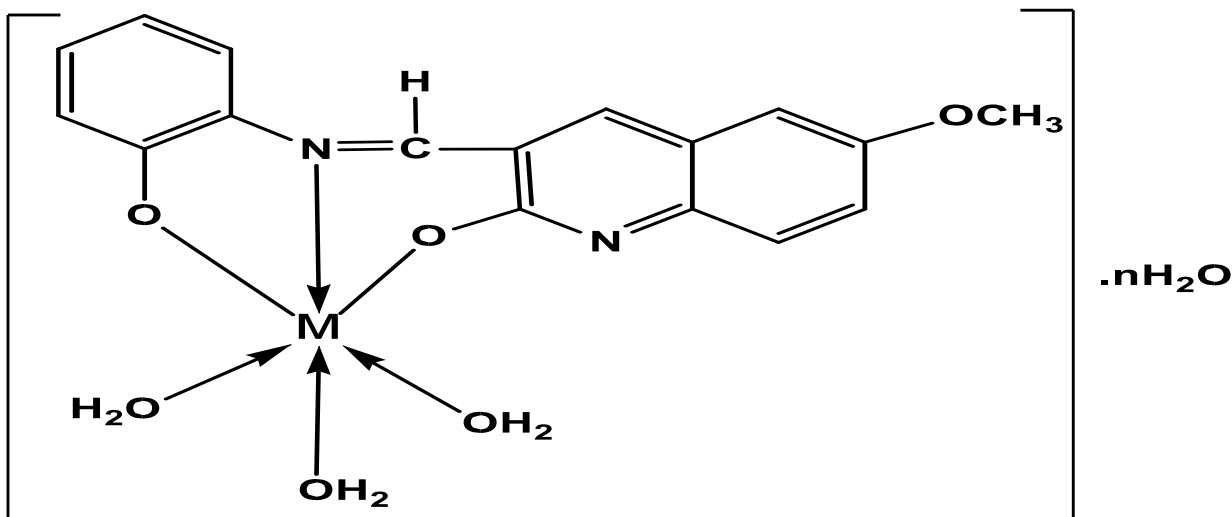


Fig 1. Proposed structure of Metal (II) Complex

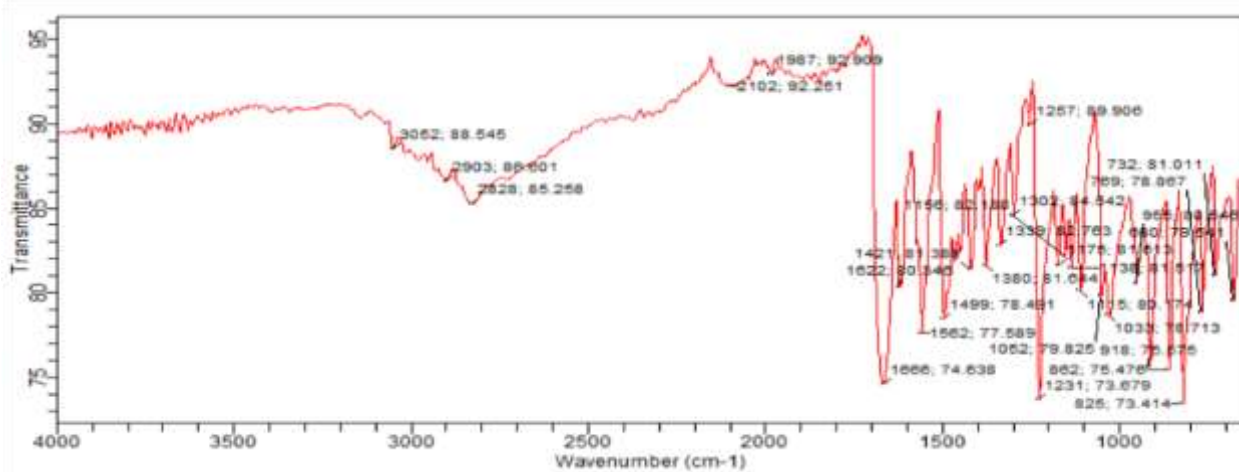


Fig 2. FTIR of the 3-Formyl-2-hydroxy-6-methoxyquinoline

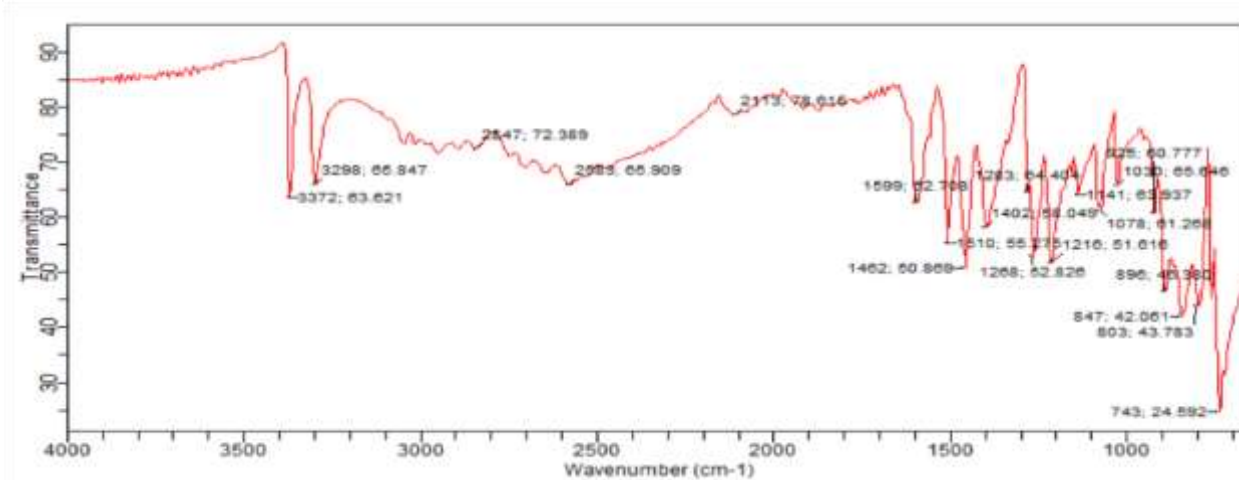


Fig 3. FTIR of 2-Aminophenol

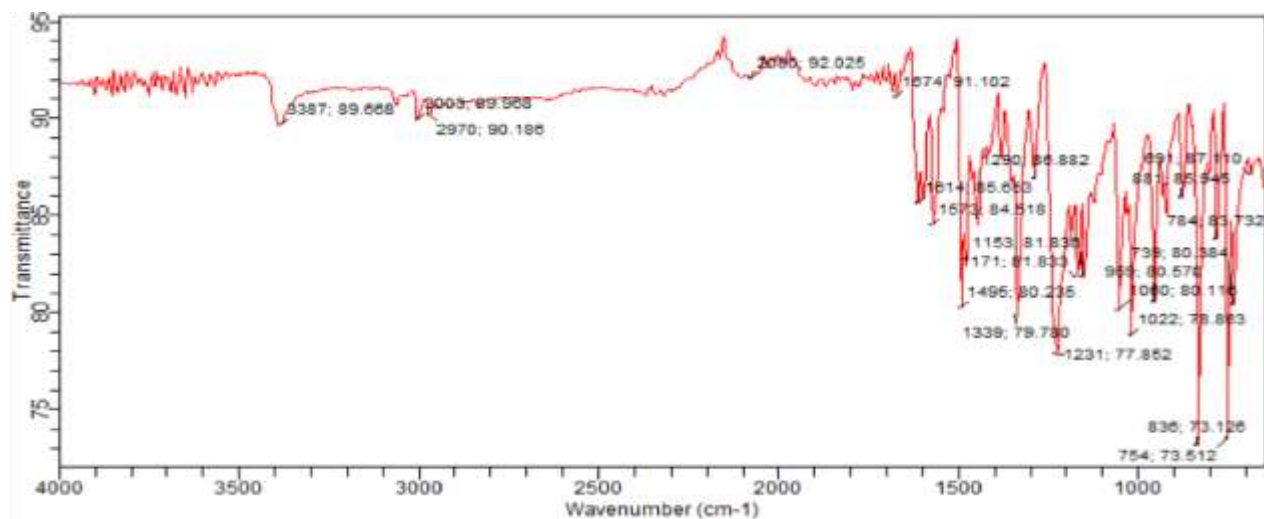


Fig 4. FTIR of Schiff base Ligand

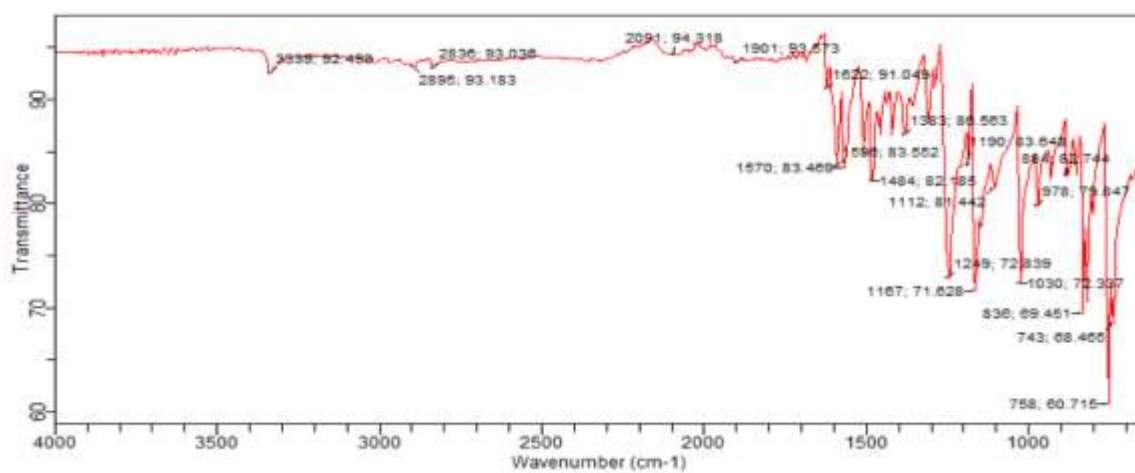


Fig 5. FTIR of Mn(II) complex

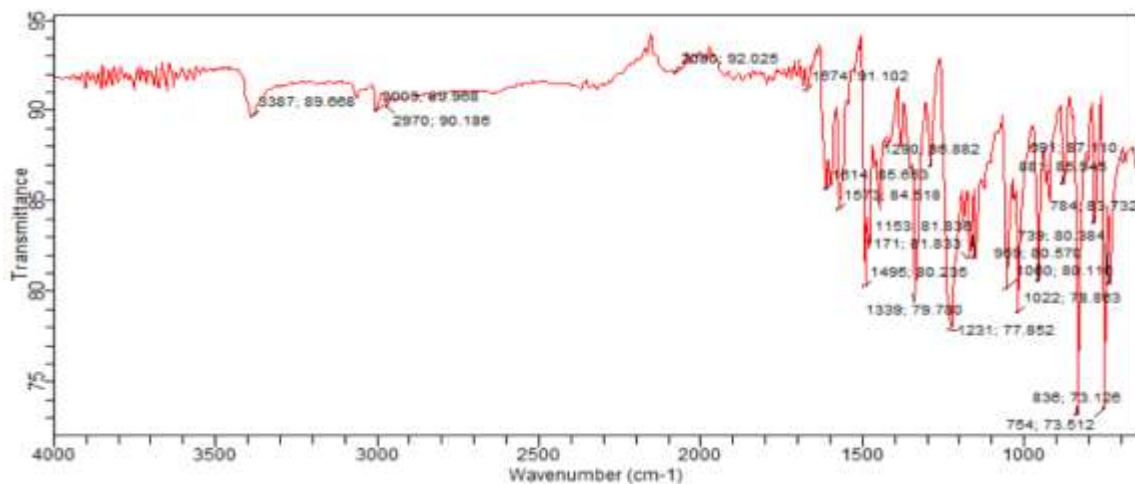


Fig 6. FTIR of Fe(II) complex