

Antibacterial Activity of 2-[(2-Chloro-4-Methylbenzylidene) Amino] Pyridin-4-Ol and Its Some Transitional Metal Ion Complexes

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Abstract: A new Schiff bases containing 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol with some transition metal ions with general formula of the complexes $[M(L_2)_nH_2O]$ [where $M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Pt(II)$ and $L = 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol$] have been synthesized and characterized by elemental analysis, molar conductance, magnetic moment and spectral techniques like Infrared spectra, Electronic Spectra, Mass Spectra, Thermal Analysis, Electron spin Resonance & X-ray powder diffraction. The complexes have six co-ordination numbers with octahedral geometry. The mass spectral data confirms the monomeric structure of the metal complexes, while Thermal studies confirm that presence of two co-ordinate water molecules in the complexes. The covalency factor (β), bonding parameter ($b^{1/2}$) suggest that complexes have covalent nature. The Schiff base and complexes have been tested against some bacteria, it shows that Pt (II) complexes are more active towards all bacteria.

Keywords: 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol, ESR, TGA/DTA, Electronic spectra and Antibacterial activity.

I. Introduction

Schiff's bases bearing heterocyclic compounds have excellent biological activities, which have attracted many researchers' in recent years [1-3]. Pyrimidine ring play an important role in biological system, their heterocyclic derivatives have been used as drugs and to have considerable biological activities like analgesic[4], anthelmintic[5], antitubercular [6], antiviral[7], antifungal[8] and anticancer[9] properties. Heteronuclear compound schiff base complexes have found application as magnetic material, biological engineering & catalyst [10-12]. In view of these facts we come to show that, Schiff base is important not only in medical chemistry, but also in organic synthetic chemistry and catalysis. Schiff base perhaps are synthesized in various method. In this paper, we will research which the simple way to synthesize Schiff base and complexes with its antimicrobial activities.

II. Experimental

2.1 Material, Method and Instrumental Techniques: All reagents and chemicals are used analytical grade, without any further purification. All solvents are purified & distilled by distillation before using. The C, H, N of the schiff base and complexes were determined by using micro analytical methods at Institute of Chemical Technology. Infrared spectra of the schiff base and complexes were recorded by KBr pellets by using Perkin Elmer spectrophotometer. The electronic spin resonances were recorded at RSIC-IIT, Mumbai, Electronic spectra recorded by using DMF and water as solvent. Thermal analysis were carried on Mettler Toledo Star system in the temperature range of 20-900 °C. The Mass spectra were recorded by ESI technique at IPCA laboratories. The Magnetic susceptibilities of complexes were determined on Gouy balance using Hg $[Co(SCN)_4]$ as a calibrate. The Molar conductance measurements were carried out in DMF and water (10^{-3} M) using Electronic Digital conductivity meter and cell is calibrated with KCl. Melting points of the schiff base and decomposition point of complexes were taken.

2.2 Preparation method of schiff base and complex: The schiff base was prepared by mixing ethanolic solutions of 2-aminopyridin-4-ol (1.10 g) and 2-chloro-4-methylbenzaldehyde (1.54g) in 1: 2 ratios. This solution will kept near about 25-30 minutes in microwave using few drops of acetic acid. The solution was cooled, solid separates, kept for drying in oven at 60 °C. The aqueous solution of $MnCl_2, CoCl_2, NiCl_2, CuCl_2, ZnCl_2$ and $PtCl_2$ salts (0.01M) was prepared. The solutions schiff base prepared by dissolving (2.46g) in methanol. The solution of schiff base and aqueous solution of metal chlorides was mix in 2:3 ratios & refluxed for two hours using water condenser. Few drops of alcoholic ammonia solution were added to adjust the pH of

the solution in between 8.0 – 9.0. After two hours. The solution was cooled, solid separates, filtered the complexes, washed with methanol and dried at 60°C in oven. The purity of the products were confirmed by TLC. The yield of the complexes was obtained in range between 59-74 %.

III. Result And Discussion

The physical and analytical data of both schiff base and complexes are given in table No.1. All these complexes are coloured except Zn (II) metal ion, stable at room temperature e.g. Over anhydrous calcium chloride in a desiccators for reasonably long period of time. The complexes are insoluble in organic solvents like toluene, methanol, ethanol, acetonitrile & chloroform. Complexes are soluble in dimethyl sulfoxide and dimethyl formamide. They are decomposed in the range 195-222°C. The melting point & decomposition point reported in open capillary are uncorrected. The molar conductivity values are commensurate with electrolytic behavior of the complexes. The conductivity values of the complexes are observed in dimethyl sulfoxide in 10⁻³ molar solution. They are non-electrolytic in nature [13]. The metals contents were estimated by volumetric titration by using different type's indicators with (0.01M) ethylene diamine tetra acetate solution. The metal-ligand ratio of the complexes is 1:2.

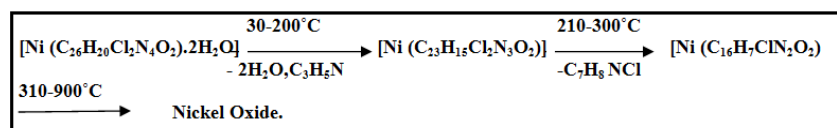
3.1 Infrared spectra: An infrared spectrum provides considerable structural evidence for the formation of schiff base and their complexes. The infrared spectra of complexes were compared with schiff base and their substituted moieties [14]. The schiff base shows prominent bands at 1670 cm⁻¹ and 3358 cm⁻¹ for azomethine (-HC=N-) and -OH absorption. In the complexes band due to the azomethine (-HC=N-) group shifted to lower frequencies in the range 1625-1640 cm⁻¹ and no bands observed for hydroxy group in the complexes. Hence the complexes with 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol indicates that, the coordination take place through azomethine (-HC=N-) and -OH of oxygen. The two new bands were observed at 3510-3528 and 3445-3459 cm⁻¹ are due to two coordinated water molecules. The bands observed far infrared region at 522-545 cm⁻¹ due to (M←N) linkage and 430-448 cm⁻¹ for (M←O)[15-16]. The central metal ions have six co-ordinated number and schiff base behaves as bidentate ligand.

3.2 Electronic spectra: The electronic spectra of the Mn²⁺, Co²⁺ & Ni²⁺ schiff base complexes have been recorded in DMF and water in the wavelength range 250-900 nm⁻¹. The electronic d-d transition bands normally show weak perturbation due to complexation an increase in the intensity, shift to the red region and also splitting of some bands are observed on complex formation. The position shapes and of Mn²⁺, Co²⁺ & Ni²⁺ are observed in solution phase using ethanol and dimethyl sulfoxide. The Mn²⁺, Co²⁺ & Ni²⁺ complexes have lower energies as compared to those of aqua complex. The magnitude of the bath chromic shift of the bands in each case meager Nephelauxetic effect (β)[17], the bonding parameter (b^{1/2})[18] and Sinha's parameter (δ%) [19] have been calculated. The bonding parameter reflects the participation of 3d orbital. The b^{1/2} value obtained for the present complexes indicates a decreasing order of 3d- orbital participation in the Mn²⁺, Co²⁺ & Ni²⁺ complexes. The average value of Sinha's parameter (δ%) & η obtained in each case is positive and smaller[20], indicating the presence of weak covalent bonding character in the complexes.

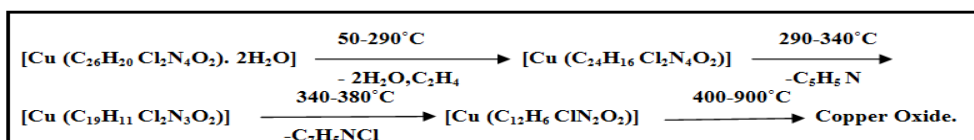
3.3 Magnetic Moment: The corrected magnetic moment (μ_{eff}) in Bohr magneton units [21] of the schiff base complexes are given in Table 1. The magnetic moments of the complexes room temperature except that of zinc (II) complex are diamagnetic in nature and other complexes are paramagnetic in nature[22]. This indicates slight participation of the 3d electron in bond formation.

3.4 Thermal analysis: Thermogravimetric and differential thermal analysis results of [Ni(C₁₃H₁₀ClN₂O)₂.2H₂O] and [Cu(C₁₃H₁₀ClN₂O)₂.2H₂O] are reported. Complexes losses weight due to exothermic [23] and endothermic process [24]. These complexes are thermally stable at room temperature and decompose in four steps [25].

3.4.1 [Ni(C₁₃H₁₀ClN₂O)₂.2H₂O] complex: Thermal analysis study of Ni²⁺ complex shows loss weight in the temperature range 30-200°C, which is corresponds to loss of two coordinated water molecules and some part of chelate. The experimental percentage loss is calculated from TGA analysis curve is 15.52. This value is comparable with theoretical percentage loss value. The differential thermal analysis peak at this range is endothermic. In the temperature range 210-300°C, the major part of complex is lost. The experimental percentage loss is 24.01, which is obtained from Thermo gravimetric analysis curve. The experimental percentage loss value is comparable with theoretical percentage loss values. The differential thermal analysis peak is exothermic (refer figure 5). The probable leaving part of complex in this temperature range is C₇H₈N Cl. The temperature range 340-900°C leading to the formation of nickel oxide. The decomposition of complex represented as below.



3.4.2 [Cu (C₁₃H₁₀ClN₂O)₂.2H₂O] complex: Thermal analysis study of Cu²⁺ complex shows that the complex weight loss in four stages(see figure 6). In the first stage at temperature range 50-290°C, which is corresponds to loss of coordinated two water molecules and some part of complex. The experimental percentage loss is calculated from TG curve is 15.52. This is comparable with theoretical percentage loss value and DT peak at this range is endothermic. In the second stage at temperature range 290-340°C, the some part of complex is lost and probable leaving groups are C₅H₅NCl. In the third stage, major part of chelating agent is lost in the temperature range of 340- 390°C. The experimental percentage loss 21.40 is obtained from TG curve. The experimental percentage loss value is comparable with theoretical percentage loss value i.e. 22.10. The differential thermal analysis peak is exothermic. The probable possible leaving part of complex in this temperature range is C₇H₅NCl. In the final stage at temperature range 400-900°C leading to the formation of Copper oxide. The decomposition of complex represented as below.



3.5 Mass Spectra of Schiff Base and Its Complexes: The mass spectra of the metal complexes and ligand recorded at room temperature. Their composition and are listed in table 4 .The theoretical mass of Co (II) complex is m/z =586.32. Similarly Zn (II) complex is m/z =592.80 which corresponds to molecular weight of the respective compounds while that of Co (II) & Zn (II) complexes molecular peaks shows at m/z=587.28, & m/z= 593.72 respectively, which corresponds to [M+1]. These peaks support to the structure of the complexes. The different molecular ion peaks appeared in the mass spectra of complexes are attributed to the fragmentation of the metal complex molecule obtained from the rupture of different bonds inside the molecule [26] by successive degradation leading to many more important peaks due to formation of various radicals[27]. The spectra of complexes show molecular ion peaks in good agreement with the structure suggested by elemental analysis, spectral and magnetic studies. The spectra of the complex shows characteristic molecular ion peak at their expected m/z values confirming their monomeric form [28].

3.6 Antimicrobial Activity: The Preparation of Schiff Base and its metal (II) complexes were screened in vitro for its antibacterial activity against four Gram-negative bacteria like E coli, S flexenari, P aeruginosa and S typhi and two Gram-positive bacteria like B subtilis and S aureus strains using agar gel diffusion method [29] The plates were incubated immediately at 37°C for 24 hours. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). Growth inhibitions were compared [30] with the standard drug. In order to clarify any participating role of DMF in the biological screening, separate studies were carried out with the solutions alone of DMF and they showed no activity against any bacterial strains.

Antifungal activities of schiff base and its metal complexes were studied against three fungal cultures like C. albicans, F. solani and C. glaberata. Sabouraud’s dextrose agars seeded with 10⁵ (cfu) mL⁻¹ fungal spore suspensions and were transferred to Petri-dishes. Discs soaked in 20mL (10 µg/mL in DMF) of schiff base and complexes were kept in different positions on the agar surface. The plates were incubated at 37 °C for five days. The results were recorded as zones of inhibition in mm and were compared with standard drugs.

The antibacterial activity and antifungal activity results presented in Table 5 show that the prepared Schiff base and its metal ion complexes possess biological activity. These schiff bases were obtained from condensation of the 2-amino pyridine-4-ol of amino with 2-chloro-4-methyl benzaldehyde were screened for their antibacterial activity against E coli, B. subtilis, S. flexenari, S. aureus, P. aeruginosa and S. typhi. Antifungal activity against C. albicans, F. solani and C. glaberata and results exhibited markedly an enhancement in activity on co-ordination.

IV. Figures And Tables

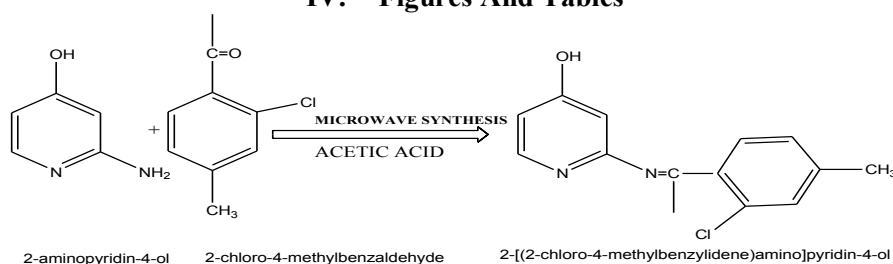


Fig.1. Synthesis of Schiff base

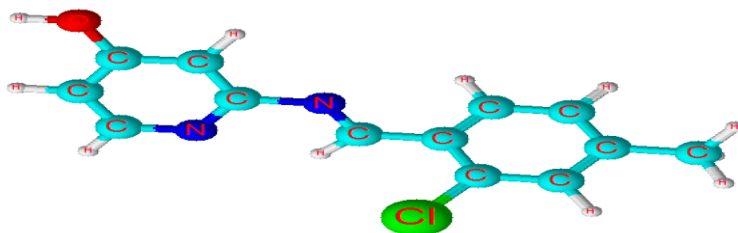


Fig.2. 3D Synthesis of Schiff base

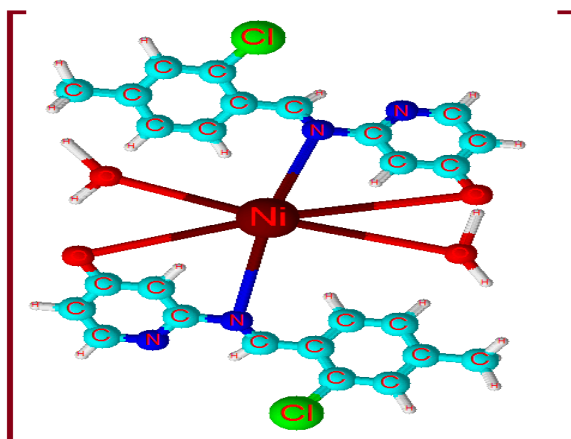


Fig.3. 3D Structure of Ni complex

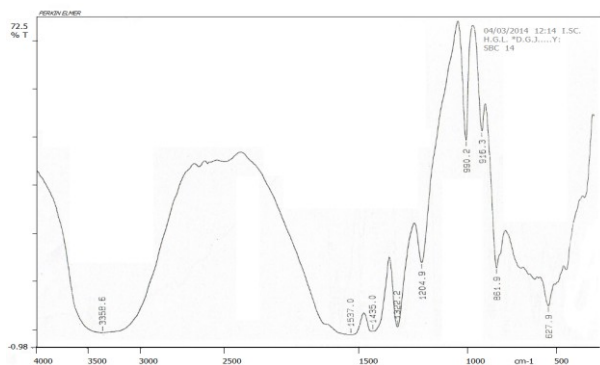


Fig. 4: IR of Schiff base

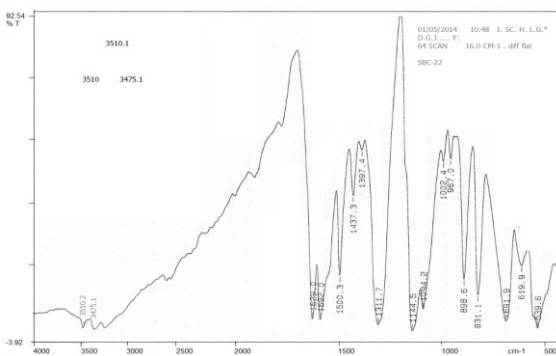


Fig. 5: IR Of [Co (C₁₃H₁₀ClN₂O)₂.2H₂O] complex

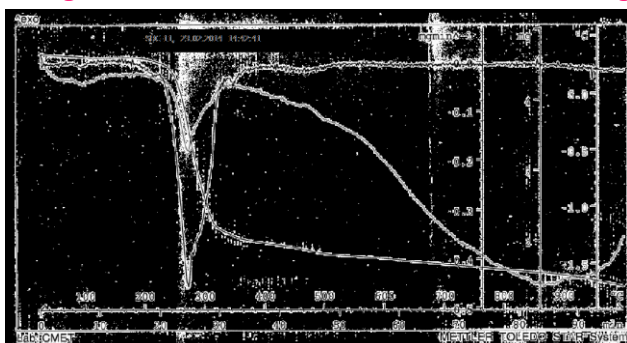


Fig. 6. TGA/DTA of [Ni (C₁₃H₁₀ClN₂O)₂.2H₂O] complex

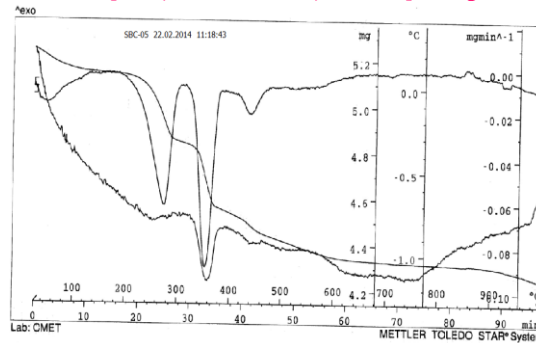


Fig. 7. TGA/DTA [Cu (C₁₃H₁₀ClN₂O)₂.2H₂O] complex

Schiff base/ Complexes	% Yield	MP/DP °C	C%	N%	M%	$\Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$	BM μeff
(C ₁₃ H ₁₁ ClN ₂ O)	82	245-247	63.29	11.36		17	
			62.82	10.95			
[Mn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O] Light gray	64	220-222	53.62	9.62	9.43*	22	5.47
			53.22	9.33	9.11		
[Co(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O] Light brown pinkish	59	217-219	53.26	9.56	10.05	24	4.42
			52.81	9.07	9.65		
[Ni(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O] Light greenish yellow	67	211-213	53.28	9.55	10.01	16	3.28
			52.74	9.02	9.57		
[Cu(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O] Light buff	74	207-209	52.84	9.48	10.75	20	1.85
			52.37	9.01	10.27		
[Zn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O] colourless	68	201-203	52.68	9.45	11.03	18	Dimag
			52.14	8.97	10.64		
[Pt(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O] Light reddish brown	65	195-197	43.22	9.81	27.0	21	
			42.77	9.34	26.57		

Table 1 Analytical and Physical Data

	-CH=N-	-OH	C-O	C-N	M-N	M-O	H ₂ O
(C ₁₃ H ₁₁ ClN ₂ O)	1670	3358	-	-	-	-	-
[Mn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	1630	-	1311	1144	534	442	3522,3475
[Co(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	1633	-	1318	1122	522	433	3515,3468
[Ni(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	1628	-	1315	1134	538	430	3510,3474
[Cu(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	1633	-	1348	1129	545	448	3528,3479
[Zn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	1625	-	1312	1130	538	442	3518,3475
[Pt(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	1630	-	1318	1142	532	437	3512,3470

Table 2 : Infrared spectra of Schiff base and its complexes

Complexes	Band observed in cm ⁻¹	Assignments	Parameters
[Mn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	14500 18550 23875	6A _{1g} → 4T _{1g} (G) 6A _{1g} → 4T _{2g} (G) 6A _{1g} → 4A _{1g} (G)	β=0.95870 b ^{1/2} =0.1016 δ%=2.1800 η=0.02130
[Co(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	9120 19000 21010	4T _{1g} (F) → 4T _{2g} (F) 4T _{1g} (F) → 4A _{2g} (F) 4T _{1g} (F) → T _{1g} (P)	β=0.96010 b ^{1/2} =0.0995 δ%=2.1039 η=0.02070
[Ni(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	9855 17420 24750	3A _{2g} → 3T _{2g} 3A _{2g} → 3T _{1g} (F) 3A _{2g} → 3T _{1g} (P)	β=0.96830 b ^{1/2} =0.0890 δ%=1.6523 η=0.01722

Table: 3 Electronic spectra of complexes and parameters

	Expected m/z	Found m/z	Peak assigned
(C ₁₃ H ₁₁ ClN ₂ O)	246.69	246.73	M
[Mn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	582.33	582.33	M
[Co(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	586.32	587.28	M+1
[Ni(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	586.09	586.09	M
[Cu(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	590.94	590.94	M
[Zn(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	592.80	593.72	M+1
[Pt(C ₁₃ H ₁₀ ClN ₂ O) ₂ .2H ₂ O]	722.47	722.47	M

Table :4 Mass spectra of the Schiff bases and Its complexes

	P. Aeruginosa	S. Typhi	E. Coli	B. Subtilis	S. Flexenari	S. Aureus	C. Albicans	F. Solani	C. Glaberata
Schiff base	12	14	11	15	13	14	15	11	00
Mn Complex	18	16	22	27	15	18	14	14	08
Co Complex	22	16	18	20	17	16	18	19	13
Ni Complex	17	18	18	18	20	20	18	22	10
Cu Complex	15	20	17	22	18	22	20	18	11
Zn Complex	22	17	15	20	21	27	00	09	05
Pt Complex	25	24	21	23	20	24	22	18	13

(10 & less: very weak; 10 & above: weak; 15 & above good; 20 & above: very good)

Table 5: Results of antibacterial and antifungal activity

V. Conclusion

Synthesis of schiff base and its metal complexes of Mn (II), Co (II), Ni (II), Cu(II) , Zn(II) and Pt(II) have been prepared . The complexes were characterized and found that, the metal ligand stoichiometry in all these complexes is 1:2. All the complexes are non-electrolytes in nature due to chloride ion are absent in the coordination sphere. The spectral data show that, the ligand act as neutral and bidentate coordinating through nitrogen atom of the anilino and oxygen atoms of hydroxyl group of the 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol . Based on Analytical, Molar Conductance, Magnetic and Spectral data all these complexes are assigned to be in octahedral geometry. The antimicrobial results also indicate that, the metal complexes are better Antimicrobial agents as compared to the Schiff bases.

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