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Synthesis and Spectral Characterization Studies of Bio-Active Cobalt(II) Complexes with Clomipramine Ligand

R.S. Raveendra[1, 2], P.A. Prashanth[1,*], B.M. Nagabhushana[3]

[1]Research Centre, Department of Chemistry, Sai Vidya Institute of Technology, Bengaluru – 560 064, India.
[2]Research & Development Centre, Bharathiar University, Coimbatore – 641 046, India.
[3]Department of Chemistry, M.S. Ramaiah Institute of Technology, Bengaluru – 560 054, India.

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ABSTRACT

In the current article, we report on the synthesis of cobalt(II) complexes with Clomipramie (Cp) ligand. The yield of the product obtained is 73-80%. The complex is characterized by infrared and electronic spectroscopic methods. Elemental analysis of the complexes was measured by analytical techniques on Vario ELIII CHN and S elemental analyzer. Melting point of the complexes were measured using Thomas Hoover apparatus at the heating rate of 1°C/min. The molar conductivity of the metal complexes was measured in DMF of $1x10^{-3}$ M concentration using Digisum electrons DI-9091/9009 direct reading digital conductivity meter and the values are lying in the range 25-39 ohm^{-1} cm^2 mol^{-1}, which reveals the non-electrolytic nature of the complexes. Magnetic susceptibility measurements were done using *Gouy balance.* The observed magnetic moments at room temperature for cobalt(II) complexes are in the range 4.65 - 5.02 BM. Results reveal that the synthesized complexes are non-electronic in nature having high spin octahedral geometry.

1. Introduction

In the previous two decades, considerable awareness has been paid to the chemistry of the metal complexes of multi donor ligands containing N_2 atoms [1]. Multi donor atom containing ligands are capable to combine with transition metal ions to give stable complexes, which have a variety of industrial and biological applications [2]. Transition metal complexes of multi donor atom containing bio-ligands exhibit potential biological activity are of focus of extensive investigations. These multi donor ligands are a class of important compounds in medicinal and pharmaceutical field. They exhibit biological activities including antibacterial [3], antifungal [4-6] and anticancer [7, 8]. In recent days, transition metal complexes of Schiff base ligands have attracted considerable attention, not only due to their spectroscopic properties and applications [9] but also due to their significant antifungal, antibacterial and antitumor activities [10].

Clomipramine (Fig. 1) is a 3- (9-chloro-5, 6-dihydrobenzobenzazepin-11- yl)-N, N-dimethyl propan-1-amine. Clomipramine is a typical antidepressant drug; it is widely used in the treatment of mood disorders, particularly depression and anxiety disorders [11]. It is readily absorbed from the gastrointestinal tract and demethylated in the liver to form its primary active metabolite, desmethylclomipramine [12]. It is a cyclic antidepressant which is used to treat several psychiatric disorders, generalized anxiety disorder, depression, panic disorder, obsessive–compulsive disorder, eating disorders and attention deficit hyperactivity disorder [13, 14].

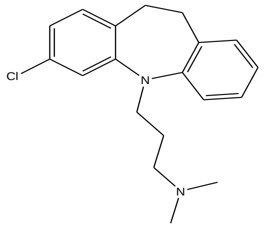

Fig. 1 Structure of Clomipramine

Further there is a large number of literatures are available on metal complexes of Schiff bases and their biological and catalytic applications, but a little attention is paid towards the chemistry of the complexes of transition metals with Cp. This creates interest in our mind to synthesize Co(II) complexes with Cp and to study their spectral characteristics. As part of our interest in this paper, we report the synthesis, spectral characterization and magnetic properties of cobalt(II) complexes with Cp.

2. Experimental Methods

2.1 Materials

Clomipramine, cobalt(II)chloride hexahydrate ($CoCl_2.6H_2O$), cobalt(II) bromide ($CoBr_2$), cobalt(II) acetate tetrahydrate ($Co(CH_3COO)_2.4H_2O$), cobalt(II) nitrate hexahydrate ($Co(NO_3)_2.6H_2O$), cobalt(II) sulphate heptahydrate ($CoSO_4.7H_2O$), dimethyl formamide, dimethyl sulphoxide, dilute hydrochloric acid, sulphuric acid, nitric acid. All the chemicals are of AR grade and used as such. The chemicals are from S.D. Fine chem. LTD. Indian drug and pharmaceuticals, SISCO chem. industries, Nice laboratories, Sarabhais, Qualigens, Fischer, BDH, Merck and Aldrich.

2.2 Synthesis of Co(II) Complexes with Cp

5 milli moles of hot ethanolic solution of Cp was slowly added to 5 milli moles of $CoX_{2n}H_2O$ salt solution (where X = Cl, Br, NO_3, CH_3COO and ½ SO_4) and n = 0, 1, 2 …) with continuous stirring. The solution was heated on a water bath at 70-80 °C to about 45 min. On cooling, the solid cobalt(II) complexes formed were removed by filtration, washed with cold ethanol, then with ether and dried over fused calcium chloride.

3. Results and Discussion

3.1 Stoichiometry (CHN and S Data Analysis)

Carbon, hydrogen, nitrogen and suphur contents of the complexes were determined by microanalytical techniques on Heracus CHN and S Rapid analyzer. The elemental analysis data of complexes presented in the Table 1, suggesting that the metal: ligand ratio was 1:3 and they can be represented by the general formulae ($CoLX_2$) $2H_2O$ or CoX_2: L: $2H_2O$, where, L = Cp, X= Cl, Br, NO_3, CH_3COO and ½ SO_4.

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*Corresponding Author
Email Address: prsnthmysore@gmail.com (P.A. Prashanth)

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All cobalt(II) complexes are amorphous, blueish green in colour and are stable to air and moisture. Except cobalt(II) sulphate complex, all other complexes are insoluble in water and common organic solvents like ethanol, ether, acetone, benzene, carbon tetrachloride, toluene, and xylene and moderately soluble in methanol, but freely soluble in DMSO and DMF.

Table 1 Elemental analysis data colour and yield of cobalt(II) complexes

Complexes	Found (Calculated) (%)					
	C	H	N	S	Colour	Yield(%)
$[Co(Cp)_2Cl].2H_2O$	60.519	6.203	8.794	-	Blueish green	80
$[Co(Cp)_2Br].2H_2O$	58.151	6.197	8.786	-	Blueish green	76
$[Co(Cp)_2(NO_3)].2H_2O$	61.392	6.465	8.778	-	Blueish green	79
$[Co(Cp)_2(AC)].2H_2O$	59.081	6.186	10.03	-	Blueish green	73
$[Co(Cp)_2½SO_4].2H_2O$	59.829	6.181	8.763	2.17	Blueish green	75

3.2 Molecular Weight Determination

Molecular weight of the complexes was determined by Rast's method using biphenyl as a solvent. The melting point of pure biphenyl was determined using a sensitive thermometer. A known weight of the complex (~0.05 g) was then mixed with a known weight of biphenyl (~0.5 g) and the mixture allowed solidifying. A small portion of the cooled melt was finely powdered and its melting point was determined using a sensitive thermometer. The difference between the two melting points gave the depression in freezing point (ΔT_f). Molecular weight (M) of the complex was then calculated using the relation.

$$M = \frac{1000\,K_f\,w}{W\Delta\,T_f}$$

where 'w' is the weight of the complex (in g); 'W' is the weight of biphenyl (in g) K_f is the molar depression constant of biphenyl, which has been determined by the above method, using camphor (known molecular weight) as the solute, instead of the complex. The data are presented in Table 2.

Table 2 Melting point data and molecular weight of cobalt(II) complexes

Complexes	Melting Point °C	Molecular Weight
$[Co(Cp)_2Cl].2H_2O$	245-247	1091.5732
$[Co(Cp)_2Br].2H_2O$	251-253	1136.0232
$[Co(Cp)_2\ (NO_3)].2H_2O$	260-262	1115.1677
$[Co(Cp)_2(AC)].2H_2O$	258-260	1118.1281
$[Co(Cp)_2½SO_4].2H_2O$	262-264	1104.1482

3.3 Electrical Conductance Measurements

Electrical conductivity measurements are widely helpful to know whether the anions of the metal salts remain inside or outside the coordination sphere in the central metal atom. The use of conductivity measurements in organic solvents for the characterization of coordination compounds have been discussed in detail in a review by William J. Geary [15]. Molar conductance values of different electrolytic systems in different solvents are available as standard references. The following data are useful for interpreting the observed conductance. The molar conductance data presented in the Table 3 suggested that all the cobalt(II) complexes in 10^{-3}M DMF were found to be non-electrolytic in nature and indicate, anions are coordinated to the cobalt ion. Thus it may be concluded that the anions are present inside the coordination sphere.

Table 3 Electrical conductivity of cobalt(II) complexes

Complexes	Conductivity ($ohm^{-1}cm^2mol^{-1}$)
$[Co(Cp)_2Cl].2H_2O$	25
$[Co(Cp)_2Br].2H_2O$	34
$[Co(Cp)_2\ (NO_3)].2H_2O$	39
$[Co(Cp)_2(AC)].2H_2O$	36
$[Co(Cp)_2½SO_4].2H_2O$	27

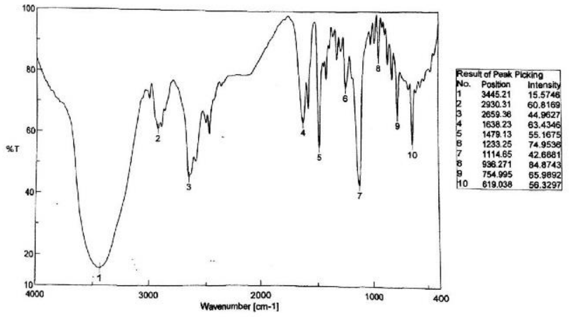
3.4 IR Spectral Measurements

Infrared spectra of the new cobalt complexes with Cp ligand were recorded in KBr discs/Nujol mulls and the relevant data presented in Fig. 2 and Table 4. Generally a comparison of the infrared spectrum of the ligand and its complex will be of much help to find out the atom or atoms through which the ligand is attached to the metal atom. Attention has been focused on a limited number of bands, providing considerable structural information about the most probable manner of coordination of the ligands with the metal atom. When the anions of the metals are polyatomic like perchlorate, sulphate, acetate, nitrate the infrared spectral measurements are useful in determining whether the anionic groups are coordinated or not and if coordinated, to determine the particular atom involved in coordination.

The IR spectra of the Cp indicate the presence of broad, strong band in the region of 2930-3060 cm^{-1} attributable to the heterocyclic nitrogen atom attached to alkyl group [16]. In addition to this, a strong band in the region of 2300-2700 cm^{-1} can be attributed to the heterocyclic nitrogen atom attached to alkyl group combined with halogen and the R_3N^+H combined with halogen present in the molecule of phenothiazine can also give rise to broad band generally 2300-2500 cm^{-1}. The IR spectra of cobalt(II) complex indicates a broad sharp band in the 3150-3600 cm-1 region, be assigned γ O-H thus indicating the presence of coordinated water. The presence of coordinated water is also confirmed from thermogravimetric studies. The peaks in the region of 1380-1320 cm^{-1} in the ligands and complexes are due to C-N stretching vibrations. Two sharp peaks in the region 1610-1560 cm^{-1} are characteristics of aromatic ring system and the sharp peak in the region 950-755cm^{-1} is assignable to 2-substituted phenothiozines. The absorption band at 1653 cm^{-1} in the spectra is assigned to carbonyl stretching vibration. The band in the region of 1410-1310 cm^{-1} is assigned to phenol [17].

Table 4 IR Spectral data of cobalt(II) complexes

Compounds	Frequencies (cm^{-1})						
	-OH	$N-CH_3$	CN	CH_2-O	$C-O-CH_3$	M-N	M-Cl
Clomipramine(Cp)	3346	2377- 2674	-	-	1168, 1243	-	-
$[Co(Cp)_2Cl].2H_2O$	3323	2270- 2679	-	-	1179, 1241	-	-
$[Co(Cp)_2Br].2H_2O$	3220- 3500, 1623	-	2468	1336	-	460	270
$[Co(Cp)_2\ (NO_3)].2H_2O$	3220- 3450, 1621		2475	1337	-	470	269
$[Co(Cp)_2(AC)].2H_2O$	3220- 3500, 1624	-	2475	1342	-	466	-
$[Co(Cp)_2½SO_4].2H_2O$	3050- 3550, 1617	-	2473	1340	-	467	-



Result of Peak Picking

No.	Position	Intensity
1	3445.21	15.5746
2	2930.31	60.8169
3	2659.36	44.9627
4	1638.23	63.4346
5	1479.13	55.1675
6	1233.25	74.9536
7	1114.65	42.6681
8	936.271	84.8743
9	754.995	65.9892
10	619.038	56.3297

Fig. 2 IR spectrum of cobalt(II) chloride complex

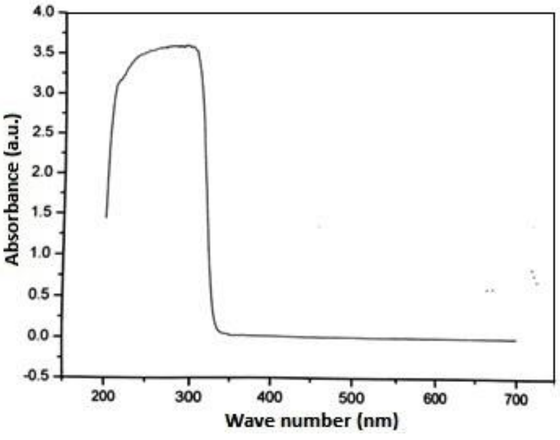


Fig. 3 UV-Vis spectrum of cobalt(II) chloride complex

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3.5 Electronic Spectral and Magnetic Susceptibility Measurements

Electronic spectra of these complexes were recorded as described earlier and the corresponding data are presented in Table 5. The UV-Vis spectrum (Fig. 3) of cobalt(II) chloride complex exhibit strong absorption bands at 282 nm and 300 nm, which were attributed to π-π* and n-π* transitions respectively [18].

Cobalt(II) ion which has seven d electrons is best known in four coordinated tetrahedral and six coordinated octahedral geometry. The spectrum of tetrahedral cobalt(II) is more intense than that of octahedral cobalt(II) and is characterized by a strongly structured peak in a visible region. Both the environments give rise to bands in the same region 15850-17000 cm^{-1} although tetrahedral compounds more frequently, exhibit maxima near 15000 cm^{-1}. The ground term arising from the $t^5_{2g}\,e_g^2$ configuration in an octahedral field is $^4T_{1g}$. An octahedral coordinated cobalt(II) ion should have the following three spin allowed d-d transitions.

$^4T_{1g} \rightarrow {}^4T_{2g}$ $^4T_{1g} \rightarrow {}^4A_{2g}$ (F) and $^4T_{1g} \rightarrow {}^4T_{1g}$ (P)

In general the band in the near infrared is assigned to lowest energy transition $^4T_{1g} \rightarrow {}^4T_{2g}$ and the band in visible region near 16000 – 17000 cm^{-1} is assigned to the $^4T_{1g} \rightarrow {}^4T_{1g}$ (P) transition. $^4T_{1g} \rightarrow {}^4A_{2g}$ transition due to a band near 15000 cm^{-1} [19]. The $^4A_{2g}$ state is derived from a $t^3_{2g}\,e_g^4$ configuration. The $^4T_{1g} \rightarrow {}^4A_{2g}$ (F) transition is essentially a two electron process and for this region it should be weaker than the other transition. This weakness combined with closeness of the $^4T_{1g} \rightarrow {}^4T_{2g}$ (P) band results in the $^4T_{1g} \rightarrow {}^4A_{2g}$ transition being unobserved. The band located in the region 14450 - 15600 cm^{-1} and 15650-16550 cm^{-1} are assigned to $^4T_{1g} \rightarrow {}^4A_{2g}$(F) and $^4T_{1g} \rightarrow A_g$(P) transitions respectively. These bands characterize octahedral ligand field around the cobalt(II) ion. The more intense bands beyond 31500 cm^{-1} are charge transfer bands [20].

Magnetic susceptibility measurements of the complexes were done in order to find out the effective magnetic moment of each metal atom in the complexes. Magnetic susceptibility data are given in the Table-5. The number of unpaired electrons 'n' possessed by the metal ion can be determined from the effective magnetic moment of the metal ion. From the knowledge of the number of unpaired electrons, it is possible to infer the valence state of the metal ion $\mu_{eff} = [n(n+1)]^{1/2}$ BM in a complex and further, if there are more than three d electrons, the complex is of octahedral stereochemistry.

Cp complexes of cobalt(II) have magnetic moment in the range of 4.65 - 5.02 BM, characteristic of octahedral geometry. The magnetic properties of high spin octahedral cobalt(II) complexes are governed by the orbitally degenerated ground term $^4T_{1g}$ which provides an orbital contribution to magnetic moment [21]. Thus at room temperature the magnetic moment of cobalt(II) ligand complexes are found to be in the range 4.65 - 5.02 BM as given in the Table 5. Cobalt(II) complexes with low spin octahedral geometry have the ^2E_g ground term arising from the $t^6_{2g}e^1_g$ electronic configuration.

Square planar cobalt(II) complexes are rare and all of them are low-spin type at room temperature with magnetic moment in the range 2.1 - 2.8 BM. None of the cobalt(II) complexes investigated by the author has magnetic moment value in this range. Therefore, these ligand complexes are not assigned square planar geometry.

Theoretically, cobalt(II) can exist in two possible spin states namely (i) low spin with a magnetic moment of 1.8 BM and (ii) high spin with a magnetic moment of 4.3 - 5.2 BM. The observed magnetic moments at room temperature for cobalt(II) complexes are in the range 4.73 - 5.20 BM indicating a high spin nature of the complexes.

Table 5 Electronic spectral and magnetic susceptibility data of cobalt(II) complexes

Complexes	Electronic spectra [cm^{-1}]				Magnetic moment (BM)
$[Co(Cp)_2Cl].2H_2O$	14792	16394	28985	35587	4.82
$[Co(Cp)_2Br].2H_2O$	14814	16286	28901	35460	4.80
$[Co(Cp)_2\ (NO_3)].2H_2O$	14880	16366	28735	35587	4.65
$[Co(Cp)_2(AC)].2H_2O$	14836	16313	28818	35842	4.79
$[Co(Cp)_2½SO_4].2H_2O$	14858	16339	29154	35460	5.02

4. Conclusion

The synthesized cobalt(II) complexes are amorphous, anhydrous in nature and are freely soluble in DMF, DMSO nitrobenzene and nitromethane, but these are insoluble in water, alcohol, acetone, acetonitrile, chloroform, carbon tetrachloride and benzene. The molar conductivity values are lying in the range 25-39 $ohm^{-1}cm^2mol^{-1}$ which reveals the non-electrolytic nature of the complexes. The elemental data supports 1:2 (metal: ligand) stoichiometry. The magnetic moments are lie in the range 4.65-5.02 BM, which supports the high spin octahedral geometry. The electronic spectra of the cobalt(II) complexes show a band in the region 14880-14947 cm^{-1} and 16232-16393 cm^{-1} are assigned to $^4T_{1g} \rightarrow {}^4A_{2g}$(F) and $^4T_{1g} \rightarrow {}^4T_{2g}$(P) transition respectively commensurate with octahedral stereochemistry. The ligand exhibit band at 1343 cm^{-1} and 3282 cm^{-1} can be attributed to C-O-C and N-H, has been fairly considerable shifting in the metal complexes. This indicates the coordination of the metal and ligand through nitrogen atom.

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