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Synthesis, Characterization and Antibacterial Activity of Some Lanthanide(III) Chloride Complexes of 2-(N-indole-2-one)amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene

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Complexes of La(III) ,Ce(III), Pr(III) ,Nd(III),Sm(III), Eu(III), Gd(III), Dy(III), Yb(III) and Lu(III) with 2-(N-indole-2-one)amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo [b]thiophene (ISAT) formed by the condensation of isatin and 2-amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b] thiophene, were synthesized and characterized on the basis of elemental analysis, molar conductance measurements, magnetic susceptibility data, UV-vis, IR and NMR spectral studies. The spectral data reveal that the ligand acted as neutral tridentate coordinating to the metal ion through the azomethine nitrogen, ester carbonyl and carbonyl oxygen of the isatin moiety. A coordination number of six has been proposed for the complexes. The lanthanum(III) complex was subjected to X-ray diffraction studies. The ligand and the complexes were screened for their antibacterial activity and it has been observed that the complexes are more potent bactericides than the ligand.

Key Words: Lanthanide(III) complexes, Spectral studies, Antibacterial activity, XRD.

INTRODUCTION

The prominent place held in coordination chemistry by metal complexes of schiff base ligands has been witnessed over many years by the large number of publications and by the comprehensive reviews[1-3]. The reasons for this sustained interest in these compounds are undoubtedly many, but important among them must be their general ease of preparation, diverse property and use as biological models[4,5]. Although several lanthanide complexes of Schiff bases have been reported, those derived from hetrocy-clic ring systems, particularly those containing thiophene ring system have received comparatively less attention[6]. Schiff bases derived from thiophene derivatives show considerable antibacterial activity[7]. The chemical versatility of isatin derivatives led their extensive use as synthones for the preparation of many biologically active compounds[8]. Antibacterial and antifungal activities of Schiff bases show significant increase on coordination with metal ion, but are invariably dependant on the structure and orientation of various moieties of the chelates. Because of such significant biological activities, it is worthwhile to incorporate the chemistry of isatin with 2-amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene and to prepare novel ligand and its lanthanide complexes. In this communication the synthesis, characterization, thermal stability and antibacterial activity of some lanthanide (III) chloride complexes with the title ligand have been described.

EXPERIMENTAL

Solvents used were of analytical grade. All lanthanides were used as chlorides derived from their oxides by a reported method[9]. 2-Amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene was prepared by a reported method[10].

Preparation of the ligand

To a hot solution of the amine (0.01 mol) in ethanol (30 mL), add isatin (0.01 mol) solution in ethanol (20 mL). The resulting mixture was refluxed on a water-bath for 5 h. The deeply coloured solution obtained was concentrated to about half of its initial volume. Orange red crystals obtained on cooling were filtered and dried. It was further purified by recrystallization from ethanol. Yield: 90%, melting point: 102°C.

Preparation of the complexes

Lanthanide(III) complexes were prepared by the following general method. Ethanolic solution of the lanthanide(III) chloride (0.005 mol) was added to a hot solution of the ligand (0.005 mol) in ethanol (30 mL) and refluxed on a water-bath for about 10 h and pH was adjusted to 6.5-7.0 and again refluxed for about 6 h. The resulting solution was concentrated and kept overnight. The complex separated was filtered, washed successively with ethanol and ether and dried in vacuum.

The complexes were analyzed for their metal content by oxalate-oxide method[11]. The chloride content of the complexes was determined gravimetrically by Volhard's method[12]. Molecular masses of the complexes were determined by camphor method[13]. The ligand and metal complexes have been screened for their antibacterial activity by agar diffusion method[14].

RESULTS AND DISCUSSION

The formation of the complexes can be represented by the following general equation.

$$LnCl_3 + ISAT \rightarrow [Ln(ISAT)Cl_3]$$

Attempts to prepare 1:2 complex were not successful presumably due to steric factors. The complexes obtained are listed in Table-1. The complexes are deeply coloured, soluble in DMSO, DMF and nitrobenzene, fairly stable at room temperature and possess good keeping qualities. Formulation of these complexes has been made on the basis of their molecular weight, elemental analytical data, molar conductance and magnetic susceptibility measurements. Molar conductance values in DMSO, DMF and nitrobenzene adequately confirm the non-electrolytic nature of the complexes (Table-2). Molecular mass values obtained have been close to monomeric nature of the compounds.

TABLE-1
ANALYTICAL DATA OF THE Ln(III)Cl$_3$ CHELATES OF ISAT

Chelates	Elemental analysis (%) Found (Calcd.)					
	Ln	C	H	N	S	Cl
[La(ISAT)Cl$_3$]	23.08 (23.18)	37.97 (38.03)	3.63 (3.67)	4.61 (4.67)	5.28 (5.33)	17.89 (17.76)
[Ce(ISAT)Cl$_3$]	23.22 (23.32)	37.96 (38.01)	3.64 (3.66)	4.63 (4.66)	5.29 (5.32)	17.69 (17.73)
[Pr(ISAT)Cl$_3$]	23.30 (23.42)	37.86 (37.91)	3.61 (3.66)	4.63 (4.65)	5.28 (5.32)	17.58 (17.71)
[Nd(ISAT)Cl$_3$]	23.78 (23.84)	37.66 (37.70)	3.59 (3.64)	4.58 (4.63)	5.25 (5.29)	17.63 (17.61)
[Sm(ISAT)Cl$_3$]	24.56 (24.62)	37.21 (37.32)	3.58 (3.60)	4.54 (4.58)	5.21 (5.24)	17.39 (17.43)
[Eu(ISAT)Cl$_3$]	24.71 (24.82)	37.13 (37.22)	3.51 (3.59)	4.51 (4.57)	5.15 (5.22)	17.44 (17.39)
[Gd(ISAT)Cl$_3$]	25.42 (25.45)	36.89 (36.91)	3.53 (3.56)	4.51 (4.53)	5.15 (5.18)	17.38 (17.24)
[Dy(ISAT)Cl$_3$]	26.01 (26.08)	36.55 (36.59)	3.49 (3.53)	4.46 (4.49)	5.11 (5.14)	17.21 (17.09)
[Yb(ISAT)Cl$_3$]	27.20 (27.30)	35.97 (35.99)	3.43 (3.47)	4.40 (4.42)	5.01 (5.05)	16.51 (16.81)
[Lu(ISAT)Cl$_3$]	27.49 (27.53)	35.86 (35.88)	3.43 (3.46)	4.38 (4.41)	5.02 (5.14)	16.46 (16.76)

TABLE-2
MAGNETIC MOMENT AND MOLAR CONDUCTANCE DATA OF THE LANTHANIDE(III) CHELATES OF ISAT

Complex	μ_{eff} B.M.	Molar conductance in Ohm $^{-1}$ cm^2 mol^{-1}		
		DMSO	DMF	Nitrobenzene
$[La(ISAT)Cl_3]$	Diamag.	6.5	12.5	3.6
$[Ce(ISAT)Cl_3]$	2.43	6.1	13.3	2.8
$[Pr(ISAT)Cl_3]$	3.54	5.7	13.5	2.4
$[Nd(ISAT)Cl_3]$	3.60	6.8	11.3	2.9
$[Sm(ISAT)Cl_3]$	1.50	7.3	11.8	3.9
$[Eu(ISAT)Cl_3]$	3.39	6.5	12.8	3.1
$[Gd(ISAT)Cl_3]$	7.82	6.1	13.1	2.7
$[Dy(ISAT)Cl_3]$	10.50	6.3	11.4	3.0
$[Yb(ISAT)Cl_3]$	4.35	7.4	13.2	2.9
$[Lu(ISAT)Cl_3]$	Diamag.	5.6	14.1	2.5

The electronic spectrum of the ligand in DMSO exhibited two absorption bands at 264 nm and 300 nm due to $\pi \rightarrow \pi^*$ transition and to $n \rightarrow \pi^*$ transition, respectively. The IR spectra of the ligand is characterized by the presence of a strong band at 3170 cm^{-1} which is assignable to ν(NH) of the indole ring of isatin moiety. Strong bands observed at 1730 and 1650 cm^{-1} correspond to ν(C=O) of ester and ν(C=O) of isatin moiety. A medium intensity band at 1596 cm^{-1} is due to ν(C=N) of azomethine group. The proton NMR data of the ligand recorded in DMSO-d_6 reveals peaks in five regions. One of them between 1.3 and 1.8 nm characteristic of CH_3 protons. The signals appearing between 2.4 and 2.6 ppm and *ca.* 3.4 ppm are due to CH_2 protons and protons of cyclohexane moiety. The signal observed between 6.9 and 7.5 ppm is of aromatic proton and the signal at 11 ppm is characteristic of NH proton[15]. Thus the proton NMR spectral studies reinforce the conclusion drawn from the IR and UV spectral data.The above spectral data adequately support the formation of the ligand as in Fig. 1.

In the electronic spectra of the complexes the bands corresponding to that observed in the ligand are identifiable but they are slightly red shifted to *ca.* 272 nm and 305 nm, respectively. There is an additional band in the spectra of the complexes *ca.* 430 nm due to L → M charge transfer transition. There is a weak band in the spectra of the complexes *ca.* 536 nm due to weak *f - f* transition[16]. IR spectra of the complexes exhibit a strong band *ca.* 3170 cm^{-1} indicating the non-coordination of NH of the isatin moiety. Considerable negative shift is observed in ν(C=O) of ester by *ca.* 70 cm^{-1}, ν(C=O) of isatin moiety by *ca.* 40 cm^{-1} and ν(C=N) of azomethine by *ca.* 25 cm^{-1} indicating the coordination of ester carbonyl group, carbonyl oxygen of isatin moiety and nitrogen of azomethine group, respectively[16]. Far infrared spectra of the complexes gave added evidence to coordination by nitrogen, oxygen and chlorine. The non-ligand bands of medium intensity appearing *ca.* 430, 360 and 324 cm^{-1} can be assigned to ν(Ln-N), ν(Ln-O) and ν(Ln-Cl) modes, respectively[17] (Table-3). The proton NMR spectral data of lanthanum (III) chloride complex recorded in DMSO-d_6 further substantiate the mode of coordination suggested by IR spectral studies. In the complexes the signals have been shifted to down field about 0.1-0.2 ppm. This confirms non-coordination of NH and acting of the ligand in a tridentate fashion. From the spectral data it is evident that the ligand acted as neutral tridentate bonding to the lanthanide ion through the ester carbonyl, carbonyl oxygen of the isatin moiety and nitrogen of the azomethine group (Fig. 2).

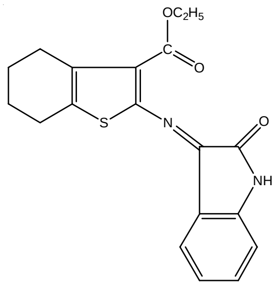

Fig. 1

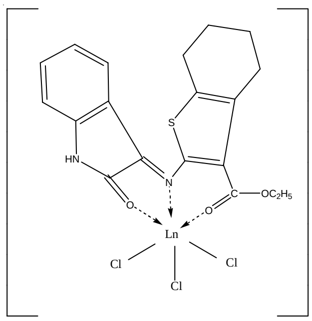

Fig. 2

TABLE-3
IMPORTANT IR SPECTRAL DATA OF THE LIGAND AND ITS LANTHANIDE(III) CHELATES

Assignment	ν(N-H)	ν(C=O) ester	ν(C=O) ring	ν(C=N)	ν(Ln-N)	N(Ln-O)	ν(Ln-Cl)
ISAT	3170	1730	1650	1596	-	-	-
[La(ISAT)Cl_3]	3170	1659	1614	1571	430	361	324
[Ce(ISAT)Cl_3]	3170	1660	1615	1570	430	360	324
[Pr(ISAT)Cl_3]	3170	1658	1616	1570	429	360	324
[Nd(ISAT)Cl_3]	3170	1660	1615	1571	431	359	324
[Sm(ISAT)Cl_3]	3170	1659	1614	1571	431	361	323
[Eu(ISAT)Cl_3]	3170	1659	1616	1571	430	360	323
[Gd(ISAT)Cl_3]	3170	1660	1614	1570	430	359	324
[Dy(ISAT)Cl_3]	3170	1660	1614	1570	430	360	324
[Yb(ISAT)Cl_3]	3170	1660	1614	1570	430	359	324
[Lu(ISAT)Cl_3]	3170	1659	1615	1571	429	360	324

The lanthanum(III) chloride complex was subjected to thermogravimetric analysis. The weight loss curve of the complex suggests that the complex does not show the presence of water molecules either in or out of the coordination sphere[18].The complex decomposed in three stages. The complex was stable up to 140°C. At this temperature it started the first stage of decomposition and the decomposition was completed at 220ºC with DTG peak at 194°C. The mass loss corresponding to this was equivalent to isatin moiety (mass loss found = 21.75%; calculated mass loss = 21.85%). The second stage of decomposition took place in the temperature range 240-460°C with a DTG peak at 437°C and the mass loss was equivalent to the loss of remaining part of the ligand. (mass loss found = 47.46%; calculated mass loss = 47.58%)The next stage of decomposition occurred in the range 560-690°C corresponding to the loss of chlorine and oxidation of lanthanum to its oxide. The final decomposition product was analysed to be La_2O_3 and the DTG profile showed a peak at 628°C. The mass loss agreed fairly well with the mass loss in independent pyrolysis experiments (Table-4).

TABLE-4
THERMAL DECOMPOSITION DATA OF [La(ISAT)Cl_3]

Decomp. Stage	Temp. range (ºC)	Peak Temp. (ºC)	Mass loss (%)	Probable assignment
I	140-220	194	21.75	Loss of isatin moiety
II	240-460	437	47.46	Loss of benzothiophene moiety
III	560-690	628	32.67	Loss of chlorine and oxidation to La_2O_3

The molecular structure of the lanthanum(III) chloride complex was studied by X-ray diffraction method. The X-ray diffraction pattern of the complex indicates amorphous nature. The diffractogram recorded only one reflection having 2θ = 27.0448° and d spacing = 3.2942 Å with relative intensity 100%.

The ligand and the metal complexes have been screened for their antibacterial activity against *Bacillus megaterium, Vibiro cholerae* and *Salmonella typhi.* It is observed that all the lanthanide(III) complexes are more potent bactericides than the ligand (Table-5). This enhancement in the activity on chelation may be rationalized on the basis of chelation theory[19]. Chelation reduces the polarity of the metal ion mainly because of the partial sharing of its positive charge with the donor groups within the chelate ring system so formed during coordination. This process, in turn, increases the lipophilic nature of the central metal atom, which favours its permeation more efficiently through the lipoid layer of the microorganism thus destroying them more aggressively[20].Apart from this ligands with nitrogen and oxygen donor systems inhibit enzyme activity since the enzymes which require these groups for their activity appear to be especially more susceptible to deactivation by the metal ions on coordination.

TABLE-5
ANTIBACTERIAL ACTIVITY OF THE LIGAND AND ITS METAL COMPLEXES

Complex	Inhibition zone (mm)		
	Vibrio cholerae	*Salmonella typhi*	*Bacillus megaterium*
ISAT	7	8	7
[La(ISAT)Cl$_3$]	12	14	13
[Ce(ISAT)Cl$_3$]	13	15	14
[Pr(ISAT)Cl$_3$]	14	14	13
[Nd(ISAT)Cl$_3$]	15	16	14
[Sm(ISAT)Cl$_3$]	14	15	13
[Eu(ISAT)Cl$_3$]	16	18	15
[Gd(ISAT)Cl$_3$]	15	16	14
[Dy(ISAT)Cl$_3$]	16	17	15
[Yb(ISAT)Cl$_3$]	16	17	14
[Lu(ISAT)Cl$_3$]	15	16	13

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