Synthesis, spectral studies, thermal decomposition kinetics, reactivity and antibacterial activity of some lanthanide(III) nitrate complexes of 2-(N-indole-2-one)amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene

M Thankamony & K Mohanan*
Department of Chemistry, University of Kerala, Kariavattom, Trivandrum 695 581, Kerala, India
Email: drkmohanran@rediffmail.com

Received 2 March 2006; revised 2 January 2007

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 formed by the condensation of isatin and 2-amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene have been synthesized and characterized on the basis of elemental analysis, molar conductance measurements, magnetic susceptibility data and UV-vis, IR and NMR spectral studies. The spectral data reveal that the ligand acts as neutral tridentate coordinating to the metal ion through the azomethine nitrogen, ester carbonyl and carbonyl oxygen of the isatin moiety. Coordination number nine has been proposed for the complexes. The XRD pattern of the lanthanum(III) complex shows that the metal complex possesses tetragonal crystal lattice. The lanthanum(III) complex undergoes facile transesterification reaction when refluxed in methanol for a long period. Studies on antibacterial activity show that the complexes are more potent bactericides than the ligand.

IPC Code: Int. Cl.8 C07F17/00

Metal chelates of Schiff bases form an interesting class of compounds which find extensive applications in various fields\textsuperscript{1-3}. Among the prodigious number and variety of transition, inner transition and main group metal complexes of Schiff bases, those formed from trivalent lanthanides are of particular interest, because of their synthetic flexibility, structural diversities, bonding interactions, biological significance and other multiple applications\textsuperscript{4-6}. Although several lanthanide complexes of Schiff bases have been reported, those derived from hetrocyclic systems, particularly those containing thiophene ring system have received comparatively less attention\textsuperscript{7}. A deep survey of literature reveals that a few lanthanide complexes of Schiff bases derived from thiophene-2-aldehyde and its derivatives with primary amines have been reported, but those derived from aminothiophenes have been less studied\textsuperscript{8}. This has been mainly due to the instability of aminothiophenes. However, 2-aminothiophene has been made stable by suitable substitution at 3-position and fusion with a cyclohexane ring by Gewald synthesis\textsuperscript{9}. The resulting benzothiophene derivative has been condensed with isatin to form a potentially tridentate Schiff base, namely, 2-(N-indole-2-one)amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene (I) containing the ONO donor sequence. Herein, we describe the synthesis, characterization, thermal decomposition kinetics, reactivity, X-ray diffraction studies and antibacterial activity of some lanthanide(III) nitrate complexes with the title ligand.

Materials and Methods

Carbon, hydrogen, nitrogen and sulphur analyses were performed using Elementar Systeme Vario EL III-CHNS analyzer. The electronic spectra of the
complexes were recorded on a Hitachi 320 UV-vis spectrophotometer. Infrared spectra were recorded on a Shimadzu FTIR 8000 spectrophotometer. Proton NMR spectra were recorded in DMSO-$d_6$ on a JEOL GSX 400 NB 400 MHz FT NMR spectrometer. Far IR spectra were recorded on a Polytec FIR 30 Fourier spectrometer using CsI discs. Molar conductance measurements were conducted using $10^{-3}$ M solutions of the complexes in appropriate solvents at room temperature using a Systronics conductivity meter type 304. Magnetic susceptibility values of the complexes were measured at room temperature with a Gouy type magnetic balance. Thermogravimetric analysis were carried out in dynamic air at a heating rate of $10^°$C/min using a Mettler Toledo SR system. X-ray diffraction pattern was recorded on Siemens (D 5005 model) X-ray spectrometer. Molecular masses of the complexes were determined by camphor method.

The lanthanide nitrates were prepared by dissolving the corresponding oxide in 50% nitric acid, followed by crystallization. 2-Amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene was prepared according to the method suggested by Gewald and co-workers$^9$. Preparation of the ligand
To a hot solution of the amine (0.01 mol) in ethanol (30 mL), was added isatin (0.01 mol) in ethanol (20 mL). The resulting mixture was refluxed on a water-bath for 5 h. The deep coloured solution obtained was concentrated to about half its initial volume. Orange red crystals obtained on cooling were filtered and dried. It was further purified by recrystallization from ethanol. [Yield: 90%, m. pt.: 102°C].

Preparation of the complexes
Lanthanide(III) complexes were prepared by the following general method. Ethanolic solution of the lanthanide(III) nitrate (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. The 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 thus separated was filtered, washed successively with ethanol and ether and dried in vacuum. The complexes were analysed for their metal content by oxalate-oxide method.

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

\[
\text{Ln (NO}_3\text{)}_3 + \text{ISAT} \rightarrow [\text{Ln (ISAT) (NO}_3\text{)}_3]
\]

(II)

Attempts to prepare 1:2 complex were not successful presumably due to steric factors. The analytically pure complexes obtained are listed in Table 1. Formulation of these complexes has been made on the basis of their elemental analytical data, molar conductance and magnetic susceptibility measurements. Molar conductance values in DMSO, DMF and nitrobenzene adequately confirm the nonelectrolytic nature of the complexes$^{10}$ (Table 2). Molecular masses of the complexes were determined by camphor method and the values obtained were close to monomeric values.

Infrared spectral studies
The spectra of the ligand and complexes exhibit a strong band ~ 3170 cm$^{-1}$ which is assignable to $\nu$(NH) of the indole ring of isatin moiety. This band remains almost unaffected in the metal chelates indicating that NH of isatin moiety is not involved in coordination. A strong band observed at 1730 cm$^{-1}$ in the ligand, characteristic of $\nu$(C=O) of ester is shifted by ~ 70 cm$^{-1}$ to a lower frequency upon complexation, indicating coordination of ester carbonyl with lanthanide ion. This type of bonding by ester carbonyl group has already been reported by several investigators$^{11}$. A strong band observed at 1650 cm$^{-1}$
in the ligand, corresponding to \(\nu(C=O)\) of isatin moiety is shifted downwards by \(\sim 40\) cm\(^{-1}\) indicating the coordination of carbonyl oxygen with lanthanide ion. A medium intensity band at \(1596\) cm\(^{-1}\) in the ligand, due to \(\nu(C=N)\) of azomethine group, is shifted to lower frequencies by \(\sim 25\) cm\(^{-1}\) upon complexation\(^{10}\).

In the spectra of the metal complexes there are two additional bands observed at \(\sim 1473\) cm\(^{-1}\) and \(\sim 1246\) cm\(^{-1}\) and these bands are assigned to the \(\nu_3\) and \(\nu_1\) modes of the nitrate ion respectively. Since the magnitude of the splitting of \(\nu_1\) \((NO_3)\) i.e., \((\nu_3 - \nu_1)\) is \(\sim 220\) cm\(^{-1}\), it is concluded that the nitrate ion is coordinated to the lanthanide ion in a bidentate fashion\(^{12}\).

Far infrared spectra of the metal complexes show several absorption bands which are not observed in the ligand spectrum. These are due to \(\nu(M-N)\) and \(\nu(M-O)\) vibrations of the coordinated ligand. The non-ligand bands of low intensity appearing in the regions 420-430 and 360-370 cm\(^{-1}\) may be assigned to \(\nu(Ln-N)\) and \(\nu(Ln-O)\) respectively\(^{13}\). Thus from the infrared spectra, it is evident that in all the complexes the ligand acts as neutral tridentate bonding to the lanthanide ion through the ester carbonyl, carbonyl group of the isatin moiety and azomethine nitrogen, while the nitrate ion is coordinated invariably as bidentate.

\(^{1}H\) NMR Spectra

The proton NMR spectral data of lanthanum(III) nitrate complex recorded in DMSO-\(d_6\) further substantiate the mode of coordination suggested by IR spectral studies. The ligand exhibits signals at \(1.3-1.8\) ppm due to \(CH_3\) protons, at \(2.4-2.6\) ppm due to \(CH_2\) protons, at \(\sim 3.4\) due to protons of cyclohexane moiety, at \(6.9-7.5\) ppm due to aromatic proton and at \(11\) ppm due to NH proton\(^{11}\). In the complexes the signals shift downfield by about 0.1-0.2 ppm. This confirms non-coordination of NH group and also that the ligand coordinates in a tridentate manner. Thus, proton NMR spectral studies reinforce the conclusion drawn from the IR spectral data.

Electronic spectral data

The electronic spectra of the ligand in DMSO exhibit two absorption bands at \(264\) nm and \(300\) nm due to \(\pi\rightarrow\pi^*\) transition and to \(n\rightarrow\pi^*\) transition respectively. These bands are present in the spectra of all the complexes, although these are slightly red shifted to \(\sim 272\) nm and \(311\) nm respectively. There is an additional band in the spectra of the complexes at \(\sim 340\) nm due to \(L\rightarrow M\) charge transfer transition. There is a weak band in the spectra of the complexes \(\sim 536\) nm due to weak \(f-f\) transition\(^{10}\).

Thermogravimetric studies

The lanthanum(III) nitrate complex was subjected to thermogravimetric analysis and the kinetic parameters have been evaluated. The complex decomposes in three stages, being stable up to \(120^\circ C\). At this temperature, the first stage of decomposition starts and is completed at \(200^\circ C\) with DTG peak at \(188^\circ C\). The corresponding mass loss is equivalent to isatin moiety (Mass loss: Found=19.20%; Calc.=19.29%). The second stage of decomposition takes place in the temperature range \(220-430^\circ C\) with a
DTG peak at 428°C, and mass loss equivalent to the loss of benzothiophene moiety (Mass loss: Found=33.81%; Calc.=33.14%). The next stage of decomposition occurs in the range 480-620°C corresponding to the decomposition of nitrate and oxidation of lanthanum to its oxide. The final decomposition product was analysed to be La2O3 and the DTG profile shows a peak at 619°C. The mass loss agrees fairly well with the mass loss in independent pyrolysis experiments. The thermal analysis was carried out up to 900°C and no further change was observed after 620°C.

The kinetic parameters of the thermal decomposition of [La(ISAT)(NO3)3] were evaluated using the Coats-Redfern equation. The values of energy of activation (E), Arrhenius factor (A), entropy of activation (ΔS) and order (n) obtained for different decomposition stages are given in Table 3. The values obtained using the Coats-Redfern equation are comparable to those reported for similar type of complexes. The negative values of ΔS show that the complex was more ordered in the activated state than the reactants and that the reactions were slower than normal15. The thermogravimetric profiles and their corresponding kinetic data are in agreement with a multistage decomposition/oxidation of the metal complex. The variation in the activation energies of the different stages of decomposition can be attributed to the different types of decomposition mechanisms operating in different temperature ranges16.

The deduction of the mechanism of the reaction by the use of non-isothermal kinetic methods has been discussed15. The kinetic equations, which govern the reaction mechanism, are based on the form of g(α). Among the nine forms of g(α), the form representing the best experimental data is considered as the mechanism of the reaction15. In the case of the first and third stages of decomposition, the highest value of correlation coefficient was for g(α)=[-ln(1-α)]1/3 representing random nucleation-Avrami equation II.

**X-ray diffraction studies**

The X-ray diffraction pattern of [La(ISAT)(NO3)3] complex showed 12 reflections between 2θ ranging from 11 to 58° with maxima at 2θ=12.3832°, which corresponds to interplanar distance, d=7.1418 Å. The main peaks have been indexed by trial and error method. The sin2θ and 2θ values obtained have been compared with the calculated values and the sin2θ values are in agreement with the tetragonal crystal lattice17. On the basis of the above observations, it can be concluded that the complex belongs to a tetragonal crystal system with the lattice constants a=7.1521Å and c=10.9817 Å.

**Transesterification**

Transesterification reactions are considered to be those which effect interchange of ester fragment on the substituent group attached to the coordinated azomethine nitrogen. It has been observed that metal complexes of carboxylic esters undergo transesterification on refluxing with alcohol. Transesterification of the metal chelate was carried out by a reported method18.

The crystallinity, appearance and solubility behaviour of the product obtained after transesterification are distinctly different from those of the ethyl derivative. Ester carbonyl stretching frequency observed for the methyl derivative at 1643 cm^-1 is a direct indication of the occurrence of transesterification. This is further confirmed by proton NMR spectral data of the product.

Several mechanisms have been proposed to explain transesterification reactions. However, it appears that increased nucleophilicity of the acyl carbon atom

<table>
<thead>
<tr>
<th>Decomp. stage</th>
<th>Peak temp. (°C)</th>
<th>Order (n)</th>
<th>Corr. coeff.</th>
<th>Energy of activation, E (kJ mol^-1)</th>
<th>Arrhenius factor, A (S^-1)</th>
<th>Entropy of activation, ΔS (JK^-1mol^-1)</th>
<th>Probable mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>188</td>
<td>1.85</td>
<td>0.9984</td>
<td>184.72</td>
<td>0.5372 × 10^19</td>
<td>182.9835</td>
<td>Random nucleation-one nucleus on each particle</td>
</tr>
<tr>
<td>II</td>
<td>428</td>
<td>1.6</td>
<td>0.9944</td>
<td>121.51</td>
<td>1.0002 × 10^7</td>
<td>-63.5332</td>
<td>Random nucleation-Avrami equation II</td>
</tr>
<tr>
<td>III</td>
<td>619</td>
<td>2.1</td>
<td>0.9956</td>
<td>274.14</td>
<td>3.3099 × 10^15</td>
<td>99.5666</td>
<td>Random nucleation-one nucleus on each particle</td>
</tr>
</tbody>
</table>
induced by the azomethine group is of great importance. The electron withdrawing azomethine group increases the reactivity of the alkoxycarbonyl group. In this connection it may also be noted that alkoxycarbonyl group directly attached to the α-carbon atom can be esterified easily.

Antibacterial study

Biological activities of lanthanide complexes have been well documented in literature. Encouraged by such reports, the ligand and metal complexes were screened for their antibacterial activities against *Vibrio cholerae*, *Salmonella typhi* and *Bacillus megaterium*. It is interesting to observe that in all the cases the ligand is a less potent bactericide than the metal complexes.

The increased activity on metal chelation can be explained on the basis of chelation theory. Chelation reduces the polarity of the metal ion considerably because of the partial sharing of its positive charge with the donor group and also due to π-electron delocalization on the whole chelate ring. The lipids and polysaccharides are some important constituents of the cell wall and membranes which are preferred for metal ion interaction. Apart from this, the cell walls also contain many phosphates, carbonyl and cystenyl ligands which maintain the integrity of the membrane by acting as a diffusion barrier and also provide suitable sites for binding. Furthermore, the reduction in polarity increases the lipophilic character of the chelates and an interaction between the metal ion and the lipid is favoured. This may lead to the breakdown of the permeability barrier of the cell resulting in interference with the normal cell processes. Besides this, the complexes may also indulge in the formation of hydrogen bonded interaction through the coordinated anions and azomethine group with the active centres of the cell constituents. Factors capable of increasing lipophilic nature are expected to enhance the antibacterial property. While chelation is not the only criterion for antibacterial activity, it is an intricate blend of several contributions such as the nature of the metal ion and the ligand, the geometry of the metal complex, the lipophilicity, the presence of co-ligands, the steric and pharmacokinetic factors.

Acknowledgement

We express our sincere thanks to Prof. P. Indrasenan, Department of Chemistry and Prof. K.Dhevendran, Department of Aquatic Biology, University of Kerala, Trivandrum for their valuable help in conducting these studies. Instrumental facilities provided by Sophisticated Analytical Instrument Facility (SAIF), Cochin, IIT, Bombay and RRL, Trivandrum are gratefully acknowledged. One of the authors (MT) is grateful to the University Grants Commission, New Delhi for financial support.

References