

## Synthesis, Spectral and Thermal Studies of Biologically Active Complexes of Lanthanum(III) with N-alkylphenothiazines

B. KESHAVAN\* and RAMALINGAIAH

Department of Studies in Chemistry  
University of Mysore, Mysore-570 006, India

Six N-alkylphenothiazines have been used to synthesize the complexes of lanthanum(III) of the general formula  $[La(L)_2(NO_3)_2]NO_3$ , (where L = N-alkylphenothiazine). The complexes have been characterized on the basis of analytical, spectral, conductometric and thermogravimetric studies. Spectroscopic studies indicate that two N-alkylphenothiazine ligands and two nitrate groups are coordinated to the metal in a bidentate fashion suggesting a coordination number eight around lanthanum. The antibacterial screenings of all compounds were carried against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis sp.* and *Salmonella sp. bacteriae*.

### INTRODUCTION

N-alkylphenothiazines (NAP) have been reported to be biologically versatile compounds, possessing anticholinergic, antihistaminic and antiemetic activities<sup>1</sup>. It is well-known that NAP find extensive applications in industry<sup>2</sup> and chemical analysis<sup>3</sup>. N-alkylphenothiazines are capable of causing wide variety of adverse effects in patients including cardiovascular and hematological behavioral problems<sup>4</sup>. Biologically active complexes of dioxouranium(VI) with N-alkylphenothiazines have been reported<sup>5</sup>. The present paper describes the synthesis, spectral, thermal and antibacterial studies of lanthanum(III)-NAP complexes.

### EXPERIMENTAL

Lanthanum nitrate (A.R.), distilled ethanol and methanol and all other solvents viz., ether, DMF and DMSO used were of reagent grade. Chlorpromazine hydrochloride (CPH), promethazine hydrochloride (PMH), trifluoperazine hydrochloride (TFPH), butaperazine dimaleinate (BPD), perazine (PZ) and propericiazine (PPC) were used as received without further purification.

#### Preparation of complexes

Methanolic solution of lanthanum nitrate (0.025 mole) was added slowly to the methanolic solutions (0.06 mole) of CPH or PMH or PZ with constant stirring. The solid complexes formed immediately were filtered, washed with methanol and dried *in vacuo* over fused  $CaCl_2$ .

In a similar way, complexes of La(III)-TFP and La(III)-PPC in ethanolic medium were prepared.

La(III)-BP complex was prepared by refluxing aqueous solutions of lanthanum nitrate and BPD in 1 : 2 molar ratio with equal volume of benzene. The excess

of benzene was removed by evaporation and the complex was separated as stated earlier.

## RESULTS AND DISCUSSION

The complexes were analysed for lanthanum by conventional method<sup>6</sup> and nitrate (ionic) was estimated as nitron nitrate<sup>7</sup>. The analytical data obtained for carbon, hydrogen and nitrogen for the synthesized complexes were listed in Table -1 suggest the stoichiometry  $[\text{La}(\text{L})_2(\text{NO}_3)_2]\text{NO}_3$ . The complexes are stable at room temperature, non-hygroscopic and do not possess sharp melting points. They are soluble in DMF and DMSO but insoluble in water and common organic solvents. The molar conductivity values fall in the range  $70\text{--}90 \text{ ohm}^{-1} \text{ mole}^{-1} \text{ cm}^2$  at  $10^{-3} \text{ M}$  concentration suggesting that these complexes show 1 : 1 electrolytic behaviour.

TABLE-1  
ANALYTICAL AND MOLAR CONDUCTANCE DATA OF LANTHANUM(III)-NAP COMPLEXES

Complexes Colour	% Analysis Found (Calcd.)				<sup>a</sup> NO <sub>3</sub> (ionic)	<sup>b</sup> Λ <sub>M</sub>
	C	H	N	La		
[La(CP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ] Light blue	42.96 (42.43)	3.98 (3.94)	10.26 (10.18)	14.60 (14.43)	0.0636 (0.0644)	75
[La(PM) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ] Blue	45.12 (45.70)	4.52 (4.47)	10.86 (10.97)	15.38 (15.54)	0.0701 (0.0693)	82
[La(TFP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ] Grey	44.62 (44.27)	4.18 (4.21)	10.92 (11.05)	12.32 (12.19)	0.0538 (0.0543)	70
[La(BP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ] Yellow	50.96 (50.41)	5.38 (5.42)	11.12 (11.01)	12.27 (12.14)	0.0536 (0.0541)	85
[La(PZ) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ] Light pink	48.31 (47.88)	5.03 (4.98)	12.64 (12.55)	13.96 (13.84)	0.0624 (0.0617)	80
[La(PPC) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ] Light yellow	47.40 (47.88)	4.21 (4.17)	11.83 (11.96)	13.02 (13.18)	0.0595 (0.0588)	90

<sup>a</sup>Sample taken for the estimation of nitrate = 1.0 g

<sup>b</sup> $\text{ohm}^{-1} \text{ mole}^{-1} \text{ cm}^2$

The electronic spectra of N-alkylphenothiazines show two absorption maxima, a sharp peak at 260–273 nm and a broad peak at 306–312 nm region due to  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions respectively. The two peaks observed in the spectra of lanthanum(III)–NAP complexes at 266–280 and 304–320 nm region due to  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions respectively may be attributed to coordinating effect.

The selected IR frequencies of the lanthanum(III)–NAP complexes are given in Table-2. Broad bands in the region  $2600\text{--}2350 \text{ cm}^{-1}$  in the IR spectra of the NAP ligands correspond to the interaction of  $\text{—CH}_2\text{NR}_2\text{H}^+$  (R = methyl or pentyl)<sup>1</sup> is found to be disappeared or shifted towards higher frequency in the spectra of

the corresponding complexes indicating that the tertiary nitrogen atom of the side chain is a site of coordination. Broad bands in the region 2860–2826  $\text{cm}^{-1}$  observed in the spectra of NAP due to heterocyclic nitrogen atom carrying the alkyl side chain is found to be absent or shifted to higher frequency suggesting that the heterocyclic nitrogen atom is also another site of coordination.

TABLE-2  
SELECTED IR SPECTRAL BANDS ( $\text{cm}^{-1}$ ) OF LANTHANUM(III)-NAP COMPLEXES

Complex	$\nu(\text{NO}_3^-)$ (coordinated)			$\nu(\text{NO}_3^-)$ (ionic)	$\nu(\text{La-N})$	
[La(CP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1494	1290	1045	820	1380	460
[La(PM) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1488	1284	1036	825	1374	470
[La(TFP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1490	1280	1040	822	1386	465
[La(BP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1496	1288	1038	825	1382	450
[La(PZ) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1492	1286	1045	820	1372	460
[La(PPC) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1490	1285	1040	822	1384	470

The sharp band around 750  $\text{cm}^{-1}$  in the spectra of NAP assignable to  $\nu(\text{CSC})$  stretching frequency<sup>8</sup> remains unaffected in the spectra of La(III)-NAP complexes supporting non-coordination of heterocyclic sulphur atoms. Thus IR spectra have shown that NAP act as bidentate ligands. It can be seen that IR spectra of nitrate complexes exhibit four bands at about 1494, 1290, 1040 and 825  $\text{cm}^{-1}$  which can be assigned to the vibrational modes of the coordinated ( $\text{C}_{2v}$ ) nitrate groups. The magnitude of splitting of the two bands at higher energies *ca.* 204  $\text{cm}^{-1}$  suggest that the nitrate groups are present as bidentate ligands<sup>9</sup>. The bands observed at 1386  $\text{cm}^{-1}$  are due to ionic nitrate groups present in the complexes. This shows that these complexes have both ionic and covalent nitrate groups. The far IR spectra of the complexes exhibit new bands in the region 470–450  $\text{cm}^{-1}$  assigned to  $\nu(\text{La-N})$  modes<sup>10</sup>.

The thermal analysis studies of the complexes show that the complexes are stable up to 230°C which indicate the absence of solvent molecules either in or out of the coordination sphere. The complexes undergo two stage decomposition in the range 265–330°C with the weight loss of 67–74% due to organic moiety and 360–560°C with the weight loss of 15–19% due to nitrate followed by the formation of  $\text{La}_2\text{O}_3$ . The weight loss became constant around 650°C and was in full agreement with the weight loss calculated on the basis of the stoichiometry proposed for the complexes.

N-alkylphenothiazines and their corresponding complexes of lanthanum(III) were screened for their antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Salmonella sp.* by employing paper disc method<sup>11</sup> at 0.1, 0.2 and 0.3% concentration in DMF. Filter paper discs of 4 mm size were used and zones of inhibition (in mm) formed around each paper after incubating for a period of 24 h at 30°C were recorded. The inhibitory activity was found to be enhanced on complexation. Further, it is also observed that the

controls (sterile distilled water and DMF solvent) do not possess inhibitory activities. The screening data is presented in Table 3.

TABLE-3  
ANTIBACTERIAL SCREENING DATA OF LANTHANUM(III)-NAP COMPLEXES

Complex	Average inhibition zone (in mm)											
	<i>E. coli</i>			<i>S. coccus sp.</i>			<i>Bacillus sp.</i>			<i>Salmonella sp.</i>		
	0.1	0.2	0.3	0.1	0.2	0.3	0.1	0.2	0.3	0.1	0.2	0.3
[La(CP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1.5	3.0	4.5	0.5	1.0	2.0	1.0	2.0	3.5	1.5	2.5	4.0
[La(PM) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1.5	2.5	4.0	1.0	2.0	3.0	1.5	2.5	4.0	1.5	2.5	4.0
[La(TFP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1.0	2.5	3.5	1.0	2.0	3.5	1.5	3.0	4.5	1.5	3.0	4.5
[La(BP) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1.5	3.0	4.0	1.5	2.5	3.5	1.5	3.0	4.5	1.0	2.5	4.0
[La(PZ) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1.5	2.5	4.0	1.5	2.5	4.0	1.5	3.0	4.5	1.5	3.0	4.5
[La(PPC) <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> ]NO <sub>3</sub>	1.0	2.0	3.0	1.5	2.5	4.0	1.5	2.5	3.5	1.5	3.0	4.5
NAP	—	—	0.5	—	—	0.5	—	—	0.5	—	—	0.5
La(NO <sub>3</sub> ) <sub>3</sub>	—	—	0.5	—	—	0.5	—	—	0.5	—	—	0.5

### ACKNOWLEDGEMENTS

The authors are thankful to Mr. H.N. Rameshbabu and Miss Sumithra K. Urs, Department of Studies in Applied Botany, University of Mysore for antibacterial activities. One of the authors (RL) is thankful to UGC, New Delhi, for awarding Teacher Fellowship.

### REFERENCES

1. A.R. Katritzky and A.J. Boulton, *Advances in Heterocyclic Chemistry*, Academic Press, New York, 9, 336 (1968).
2. C.M. Murphy, H. Rainer and N.L. Smith, *Analyt. Chem.*, **42**, 2479 (1950).
3. B. Keshavan, *Analyst (London)*, **106**, 465 (1981).
4. O. Bratfos and J.O. Haug, *Acta Psychiat. Scand.*, **1**, 60 (1979).
5. B. Keshavan and J. Seetharamappa, *Inorg. Chim. Acta*, **138**, 135 (1987).
6. I.M. Kolthoff and P.S. Elving, *Treatise on Analytical Chemistry*, Vol. 8, Part II, Interscience, New York (1963).
7. A.I. Vogel, *A Text Book of Quantitative Inorganic Analysis*, 3rd Ed., ELBS, p. 583 (1975).
8. L.J. Bellamy, *Infrared Spectra of Complex Molecules*, Methuen, London, p. 355 (1964).
9. K. Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 3rd Ed., John Wiley and Sons, New York (1978).
10. M.K.M. Nair and P.K. Radhakrishnan, *Synth. React. Inorg. Met-Org. Chem.*, **25**, 1077 (1995).
11. P.C. Fahy and G.J. Persley, *Plant Bacterial Diseases: A Diagnostic Guide*, Academic Press, p. 393 (1983).