Synthesis and antibacterial activity of rare earth perchlorate complexes of 4-(2'-hydroxynaphthylazo)antipyrine

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Abstract. Rare earth perchlorate complexes of 4-(2'-hydroxynaphthylazo) antipyrine (H-NAP) of the composition $[\text{Ln}(\text{NAP})_2]\text{ClO}_4$ (where Ln = La, Pr, Nd, Sm, Gd, Dy and Y) have been prepared and characterised. In these complexes NAP^- acts as a tridentate ligand and ClO_4^- is uncoordinated. These complexes were screened for their anti-staphylococcal activity by turbidimetric assay method and were found to be more antibacterial than the ligand.

Keywords. Rare earths, complexes; antibacterial activity; 4-(2'-hydroxynaphthylazo) antipyrine.

1. Introduction

Metal complexes of biologically active organic compounds and their derivatives are of great importance owing to their effectiveness as antibacterial drugs. However, there have not been many studies on the antibacterial activity of the complexes of rare earths. As a continuation of our earlier investigation on rare earth complexes (Alaudeen and Radhakrishnan 1990), we report here the synthesis and antibacterial studies of a few rare earth complexes of the ligand 4-(2'-hydroxynaphthylazo)antipyrine.

2. Experimental

2.1 Reagents

The perchlorates of La, Pr, Nd, Sm, Gd, Dy and Y were prepared by dissolving the respective oxides in 50% perchloric acid and crystallising the salts by evaporating the solution on a steam bath. The ligand was prepared as reported earlier (Alaudeen and Radhakrishnan 1990).

2.2 Preparation of the complexes

Four mmol of H-NAP in ethylacetate was refluxed for 30 min. To this suspension 2 mmol of a hot solution of the rare earth perchlorate in acetonitrile was added to get a clear brown solution. It was refluxed for 1 h. The precipitated complex was filtered,

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washed with hot acetonitrile–ethyl acetate mixture and dried in vacuum over phosphorus (V) oxide (yield: 65%).

2.3 Physical methods and analysis

The complexes were analysed for metal (Nair *et al* 1981) and perchlorate (Kurz *et al* 1958) contents by conventional methods. The physical methods used in the present investigation were the same as reported earlier (Alaudeen and Radhakrishnan 1990).

The antibacterial activity of the test compounds was assayed as follows. The bacteria, *Staphylococcus aureus* (strain-H), obtained from National Chemical Laboratory, Pune was transferred to sterilised enrichment medium (Schmidt and Mayer 1944) and incubated for 34 h at 35°C. This culture medium (0.5 ml) was then applied to each sample of basal medium made from difcobaconutrient broth (Schmidt and Mayer 1944; Sharpe 1955), yeast extract, glucose and the test compound, in varying concentrations (mg/ml). It was then incubated for 4 h at 37°C and the resultant turbidity was measured at 530 nm. Controls were run under the same conditions without the test compounds. Antimicrobial activity of each compound was tested at five different concentrations from 0.01 to 0.05 mg ml⁻¹. Students *t* test was employed to assess the statistical significance of the results.

3. Results and discussion

Analytical data (table 1) of the complexes indicate 1:2:1 (metal:ligand:anion) stoichiometry. All the complexes are dark brown non-hygroscopic solids. They are soluble in acetone, acetonitrile, nitrobenzene, chloroform, methanol and ethanol but insoluble in benzene, carbon tetrachloride and diethylether. The molar conductivity of the complexes in nitrobenzene (25–35 ohm⁻¹ cm² mol⁻¹) and acetonitrile (121–168 ohm⁻¹ cm² mol⁻¹) are

Table 1. Analytical* and magnetic moment data of rare earth perchlorate complexes of H-NAP.

Complex	Ln%	C%	H%	N%	ClO ₄ %	μ_{eff} (BM)
[La(NAP) ₂]ClO ₄	14.66 (14.59)	53.01 (52.92)	3.60 (3.57)	11.61 (11.76)	10.40 (10.44)	—
[Pr(NAP) ₂]ClO ₄	14.53 (14.76)	52.50 (52.81)	3.55 (3.56)	11.78 (11.73)	10.43 (10.42)	3.32
[Nd(NAP) ₂]ClO ₄	15.10 (15.06)	52.13 (52.63)	3.50 (3.55)	11.81 (11.69)	10.50 (10.38)	3.57
[Sm(NAP) ₂]ClO ₄	15.49 (15.60)	51.92 (52.29)	3.55 (3.53)	11.49 (11.62)	10.14 (10.32)	1.53
[Gd(NAP) ₂]ClO ₄	16.29 (16.20)	50.95 (51.92)	3.53 (3.50)	11.65 (11.54)	10.31 (10.25)	9.79
[Dy(NAP) ₂]ClO ₄	16.47 (16.65)	51.97 (51.64)	3.45 (3.48)	11.47 (11.48)	10.21 (10.19)	10.38
[Y(NAP) ₂]ClO ₄	9.91 (9.85)	56.01 (55.85)	3.76 (3.77)	12.45 (12.41)	10.97 (11.02)	—

*Calculated values in parentheses

in the range expected for 1:1 electrolytes (Geary 1971). Thus the complexes may be formulated as $[\text{Ln}(\text{NAP})_2]\text{ClO}_4$, where $\text{Ln} = \text{La}, \text{Pr}, \text{Nd}, \text{Sm}, \text{Gd}, \text{Dy}$ and Y .

The IR spectra (in KBr) of the ligand and complexes are presented in table 2. The medium broad band at 2900cm^{-1} in H-NAP, attributable to the OH stretching vibration of hydrogen-bonded phenolic group, is absent in the complexes. Also the $\nu_a(\text{C}=\text{O})$ band of H-NAP at 1310cm^{-1} is shifted to 1325cm^{-1} in the complexes. These results show that the deprotonated phenolic oxygen is coordinated (Doretto *et al* 1980). The strong IR band at 1660cm^{-1} in H-NAP, assigned to the carbonyl stretching vibration, is shifted to 1605cm^{-1} in the complexes, indicating coordination of carbonyl oxygen (Radhakrishnan *et al* 1984). The medium band at 1460cm^{-1} in H-NAP, assigned to the $\text{N}=\text{N}$ stretching vibration, is intensified with a shift to 1445cm^{-1} showing that the azo nitrogen is coordinated (Radhakrishnan 1985). Thus NAP^- acts as a monovalent tridentate ligand in these complexes coordinating through the oxygens of the carbonyl and the phenolic groups and one of the nitrogens of the azo group, thus forming two chelate rings (one of five-membered and the second six-membered). The IR spectra of the complexes also show a strong unsplit band at 1100cm^{-1} and a medium unsplit band at 620cm^{-1} assignable to the ν_3 and ν_4 vibrations, respectively, of ionic perchlorate, which are not present in the free ligand. Therefore, the perchlorate is not coordinated (Hathway and Underhill 1961) as confirmed by the conductance studies. Hence a coordination number of six may be assigned to the rare earth ions in these complexes.

All the absorptions due to $f-f$ transition of the $\text{Pr}(\text{III})$, $\text{Nd}(\text{III})$ and $\text{Sm}(\text{III})$ ions in the visible region are obscured in these complexes by the strong absorption of the ligand and by the charge transfer band spreading over the whole visible region.

The magnetic data (table 1) show that all the complexes, except those of La and Y , are paramagnetic as expected. The observed magnetic moment of the present complexes shows little deviation from van Vleck values (van Vleck and Frank 1929) which suggests that $4f$ electrons, well shielded by the $5s^2 5p^6$ octet, play only a small role in bonding.

3.1 Antibacterial activity

The results of the antibacterial activity of AAP (4-aminoantipyrine), H-NAP and the complexes are given in table 3. All the test compounds are found to show considerable antibacterial activity at a concentration of 0.05mg ml^{-1} . At this dose the antimicrobial activity of AAP is highly significant. But its azo derivative H-NAP shows rather

Table 2. IR spectral data* (in cm^{-1}) of rare earth complexes of H-NAP.

Compound	$\nu(\text{O}-\text{H})$	$\nu(\text{C}=\text{O})$	$\nu(\text{N}=\text{N})$	$\nu_a(\text{C}-\text{O})$	$\nu_3(\text{ClO}_4)$	$\nu_4(\text{ClO}_4)$
H-NAP	2900 m, br	1660 vs	1460 m	1310 s	—	—
$[\text{La}(\text{NAP})_2]\text{ClO}_4$	—	1605 vs	1445 s	1325 s	1100 vs	620 m
$[\text{Pr}(\text{NAP})_2]\text{ClO}_4$	—	1606 vs	1445 s	1325 s	1100 vs	620 m
$[\text{Nd}(\text{NAP})_2]\text{ClO}_4$	—	1605 vs	1445 s	1325 s	1100 vs	620 m
$[\text{Sm}(\text{NAP})_2]\text{ClO}_4$	—	1605 vs	1445 s	1325 s	1095 vs	620 m
$[\text{Gd}(\text{NAP})_2]\text{ClO}_4$	—	1604 vs	1445 s	1325 s	1100 vs	620 m
$[\text{Dy}(\text{NAP})_2]\text{ClO}_4$	—	1605 vs	1445 s	1325 s	1100 vs	620 m
$[\text{Y}(\text{NAP})_2]\text{ClO}_4$	—	1605 vs	1445 s	1325 s	1100 vs	620 m

*m = medium; br = broad; vs = very strong; s = strong

Table 3. Effect of AAP, H-NAP and rare earth perchlorate complexes of H-NAP on the growth of bacteria at concentration of 0.05 mg ml.

Compound	Mean optical density at 530 mm $\pm$ standard deviation	Effect on bacterial growth	Activity of compound (%)
Control without test compound	0.422 $\pm$ 0.008		
AAP	0.291 $\pm$ 0.008	—	31.1**
H-NAP	0.545 $\pm$ 0.216	+	10.8*
[La(NAP) ₂]ClO ₄	0.327 $\pm$ 0.038	—	22.6**
[Pr(NAP) ₂]ClO ₄	0.324 $\pm$ 0.026	—	23.6**
[Nd(NAP) ₂]ClO ₄	0.367 $\pm$ 0.042	—	13.9**
[Sm(NAP) ₂]ClO ₄	0.387 $\pm$ 0.045	—	8.3*
[Gd(NAP) ₂]ClO ₄	0.320 $\pm$ 0.028	—	24.2**
[Dy(NAP) ₂]ClO ₄	0.315 $\pm$ 0.040	—	25.4*
[Y(NAP) ₂]ClO ₄	0.308 $\pm$ 0.024	—	27.1**

*Significant at 0.05 level

**Significant at 0.01 level

a nutrient effect on the bacterial growth. This may be due to the loss of two hydrogen atoms on the amino group of AAP (Fox and Gibas 1955). Among the complexes the anti-staphylococcal activity with respect to the rare earth ion shows the order Y > Dy > Gd > Pr > La > Nd > Sm. However, the antibacterial activity of the complexes is less than that of AAP but greater than that of H-NAP. This is due to the inhibitory involvement of the metal ion, perchlorate ion, complex ion or the complex as a whole in the growth of *S. aureus* (Fox and Gibas 1955).

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