

**AMINO ACID-LANTHANIDE INTERACTIONS. CRYSTAL  
STRUCTURES OF LANTHANIDE COMPLEXES OF  $\alpha$ -  
AMINO ISOBUTYRIC ACID (Aib),  $[\text{La}_2(\text{Aib})_4(\text{H}_2\text{O})_8](\text{ClO}_4)_6$   
AND  $[\text{Pr}_2(\text{Aib})_4(\text{H}_2\text{O})_8]\text{Cl}_6 \cdot \text{H}_2\text{O}$**

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**Abstract**—The structures of  $[\text{La}_2(\text{Aib})_4(\text{H}_2\text{O})_8](\text{ClO}_4)_6$  (**1**) and  $[\text{Pr}_2(\text{Aib})_4(\text{H}_2\text{O})_8]\text{Cl}_6 \cdot \text{H}_2\text{O}$  (**2**) have been determined by X-ray crystallography and show that the two lanthanide cations are bridged by carboxyl groups of four Aib molecules and are surrounded by four oxygen atoms from water molecules thus making the coordination number 8. The geometry around the lanthanum ion in **1** is a distorted bicapped trigonal prism whereas the praseodymium ion in **2** exhibits a square antiprismatic arrangement of the ligands. Coordination mode of Aib is compared with that in other metal complexes.

Lanthanide ions are often used as spectroscopic probes in studies of biological systems.<sup>1,2</sup> Substitution of Ca(II) by Ln(III) allows the investigation of the interaction of metal ions with peptides and proteins. Studies on the interaction of lanthanides with biological systems acquire particular importance in view of the similarities in the sizes of Ca(II) and Ln(III) ions and their preference for oxygen donors in complex formation.<sup>3</sup> In this context, it is necessary to understand the bonding modes of lanthanide ions with amino acids and peptides. Recently crystal structures and spectroscopic studies of lanthanide complexes of a few amino acids and dipeptides have been reported.<sup>4</sup> These studies are expected to provide answers to the following questions:

(a) How does the coordination mode depend on the side chain functionality of the amino acids?

(b) How does the coordination mode change with a change in the ionic radii of the lanthanide ions?

(c) What influence does the counter anion exert on the coordination number and geometry?

As a part of our research programme on structural studies of lanthanide complexes of peptides,<sup>5</sup> we have investigated the crystal structures of two lanthanide complexes of Aib, namely  $[\text{La}_2(\text{Aib})_4(\text{H}_2\text{O})_8](\text{ClO}_4)_6$  (**1**) and  $[\text{Pr}_2(\text{Aib})_4(\text{H}_2\text{O})_8]\text{Cl}_6 \cdot \text{H}_2\text{O}$  (**2**) and the results are reported in this paper. The amino acid Aib is chosen in view of its importance in stabilizing helical conformations when incorporated into peptides.<sup>6</sup> Several metal complexes of the amino acid Aib have been structurally characterized.<sup>7-11</sup> Interestingly, the sole example of an Aib-peptide complex, namely  $\text{Cu(III)}(\text{H}_2\text{Aib}_3)_2\text{H}_2\text{O} \cdot 1.5\text{NaClO}_4$  shows an unusual oxidation state of the metal.<sup>12</sup> The results reported in this paper show that the structures of lanthanide complexes of Aib differ significantly

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from those of the Cu(II), Zn(II), Ni(II) and Pt(II) complexes.

## EXPERIMENTAL

The complexes were prepared by dissolving lanthanide salts (obtained from the appropriate lanthanide oxide) in an aqueous solution of Aib. Crystals were grown at room temperature by slow evaporation of the aqueous solutions. Lanthanum perchlorate hexahydrate (0.1 g;  $1.83 \times 10^{-3}$  mol) and Aib (0.01 g;  $1.83 \times 10^{-3}$  mol) were dissolved in 5 cm<sup>3</sup> of distilled water. On slow evaporation of the solution at room temperature, crystals of [La<sub>2</sub>(Aib)<sub>4</sub>(H<sub>2</sub>O)<sub>8</sub>](ClO<sub>4</sub>)<sub>6</sub> (**1**) were obtained. Important bands (cm<sup>-1</sup>) in the IR spectrum of the complex are: 3466 br, 3202 br, 1671 s, 1629 s. <sup>1</sup>H NMR (D<sub>2</sub>O): 1.25 CH<sub>3</sub>. <sup>13</sup>C NMR (methanol): 23.44 (CH<sub>3</sub>); 57.96 (C); 182.14 (—CO<sub>2</sub>—).

Praseodymium chloride hexahydrate (0.1 g;  $3.63 \times 10^{-4}$  mol) and Aib (0.037 g;  $3.63 \times 10^{-4}$  mol) were dissolved in 5 cm<sup>3</sup> of water. On slow evaporation of the solution at room temperature, crystals of [Pr<sub>2</sub>(Aib)<sub>4</sub>(H<sub>2</sub>O)<sub>8</sub>]Cl<sub>6</sub>·H<sub>2</sub>O (**2**) were obtained. IR spectrum (cm<sup>-1</sup>): 3360 br, 1664 s, 1630 s, 1584 s, 1506 s. <sup>1</sup>H NMR (D<sub>2</sub>O): 5.57 br. <sup>13</sup>C NMR (methanol): 28.5 (CH<sub>3</sub>), 89.3 (C), 184.0 (CO<sub>2</sub>). The lanthanide metal contents in both the complexes were determined by titration with EDTA, using xylenol orange as the indicator and corresponded to the empirical formulae noted above.

### *X-Ray data collection*

A suitable single crystal of the lanthanum perchlorate complex (dimensions 0.35 × 0.40 × 0.73 mm) or the praseodymium chloride complex (dimensions 0.40 × 0.30 × 0.35 mm) was mounted on a glass fibre and coated with paraffin oil for X-ray diffraction measurements. Intensity data were collected by using Enraf-Nonius CAD-4 automated diffractometer at room temperature with a graphite monochromated Mo-*K*<sub>α</sub> radiation ( $\lambda = 0.7107$  Å). The unit cell parameters were refined by the least-squares method using 25 reflections in the 2 $\theta$  range 24–34°. Intensity data were corrected for Lorentz and polarization effects. The data for the praseodymium complex were corrected for extinction and absorption.<sup>13</sup>

### *Structure solution and refinement*

The structures were solved by the heavy atom method and refined by using the full matrix least-squares refinement program.<sup>14,15</sup> For both the

complexes, all the non-hydrogen atoms were refined anisotropically. For the lanthanum perchlorate complex **1** the hydrogen atoms were located from the difference map and refined isotropically. For the praseodymium complex **2** no attempt was made to locate the hydrogen atoms. The crystal data and relevant details of structure solution and refinement are given in Table 1.

## RESULTS AND DISCUSSION

### *Metal coordination*

The lanthanum perchlorate complex of Aib (**1**) as well as the praseodymium chloride complex (**2**) form binuclear units in which the coordination number of the metal is 8. The bonding mode of the amino acid is the same in both the complexes; the two lanthanide metals are bridged by the carboxylate groups of four Aib molecules, each of which exists in its zwitterionic form. In the lanthanum complex (**1**) several hydrogen bonds involving the Aib unit, water molecules and the perchlorate ions have been identified. The coordination polyhedron around the lanthanum ion is a distorted bicapped trigonal prism. In the praseodymium chloride complex, the coordination polyhedron around the metal is square antiprism. Perspective views of the crystal structures of the complexes are shown in Figs 1 and 2. Selected bond lengths and bond angles are listed in Table 2.

### *Comparisons with related structures*

The glycine complex of neodymium perchlorate Nd<sub>2</sub>(Gly)<sub>6</sub>(ClO<sub>4</sub>)<sub>6</sub>·9H<sub>2</sub>O<sup>16</sup> is polymeric; the coordination polyhedron around neodymium comprises seven oxygen atoms from glycine and two from water molecules. Of the six glycine molecules, two of them are coordinated to the metal in a tridentate fashion and the other four in a bidentate mode bridging the two Nd ions. In contrast to the glycine neodymium complex, L-alanine complexes of lanthanides show a different coordination mode.<sup>17</sup> In these complexes the two lanthanide ions are bridged by four L-alanine groups. Unlike the Nd-glycine structure, the L-alanine complexes are dimeric.

Aib-lanthanide complexes are similar to the L-alanine complexes. In the Aib complexes, changing the counter ion from perchlorate to chloride results in the incorporation of one more water molecule in the lattice which is not coordinated to the metal.

The lanthanide complexes of glycine, L-alanine and Aib show considerable differences from the analogous Ca(II) complexes. In the Ca(II)-glycine

Table 1. Crystallographic data for  $[\text{La}_2(\text{Aib})_4(\text{H}_2\text{O})_8](\text{ClO}_4)_6$  (1) and  $[\text{Pr}_2(\text{Aib})_4(\text{H}_2\text{O})_8]\text{Cl}_6 \cdot \text{H}_2\text{O}$  (2) complexes

Parameter	1	2
Molecular formula	$\text{C}_{16}\text{H}_{52}\text{Cl}_6\text{La}_2\text{O}_{40}$	$\text{C}_{16}\text{H}_{54}\text{Cl}_6\text{O}_{17}\text{Pr}_2$
Molecular weight	1375.2	1013.2
Crystal system	Triclinic	Tetragonal
Space group	$\text{P}\bar{1}$	$\text{P}4/\text{n}$
Z	1	2
a (Å)	11.125 (2)	14.225 (3)
b (Å)	11.706 (2)	—
c (Å)	11.783 (2)	10.882 (2)
$\alpha$ (°)	62.47 (1)	—
$\beta$ (°)	76.92 (2)	—
$\gamma$ (°)	67.02 (1)	—
V (Å <sup>3</sup> )	1250	2201
Linear abs. coeff. (cm <sup>-1</sup> )	20.83	24.50
Radiation (Å)	Mo-K $\alpha$ ( $\lambda = 0.7107$ )	Mo-K $\alpha$ ( $\lambda = 0.7107$ )
Measured reflections	5784	4419
Unique reflections	5447	1930
Observed reflections (with $F > 5\sigma(F)$ )	5235	1870
Scan technique	$\omega/2\theta$	$\omega$
$\theta$ range (°)	1–25	1–25
R factor	0.052	0.0545
R factor, weighted <sup>a</sup>	0.058	0.0547

<sup>a</sup> $w = 1.0000/(\sigma^2F + 0.025069F^2)$  (for complex 1);  $w = 1.0000/(\sigma^2F + 0.000000F^2)$  (for complex 2).  $R = \sum||F_o| - |F_c||/\sum|F_o|$ ;  $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$ .

complex,<sup>18</sup> only one glycine unit is connected to two Ca ions in a bidentate fashion, while the other glycine molecule is monodentate. This is in contrast to the lanthanide complexes of glycine, L-alanine

and Aib in which the amino acid molecules bridge the two lanthanide metals through their carboxylic groups. On the other hand, in the Cu(II), Zn(II), Ni(II) and Pt(II) complexes of Aib,<sup>7–11</sup> the coordination is through a nitrogen and an oxygen atom. Also in another Pt(II) complex of Aib, namely  $[\text{Cl}_2\text{Pt}(\text{H}-\text{Aib}-\text{OH})_2]$ , the amino acid acts as a monodentate nitrogen donor ligand.<sup>10</sup>

#### Solution studies

The structure of the lanthanide complexes in solution has been investigated by <sup>1</sup>H NMR spectroscopy. For this purpose, the methyl resonance

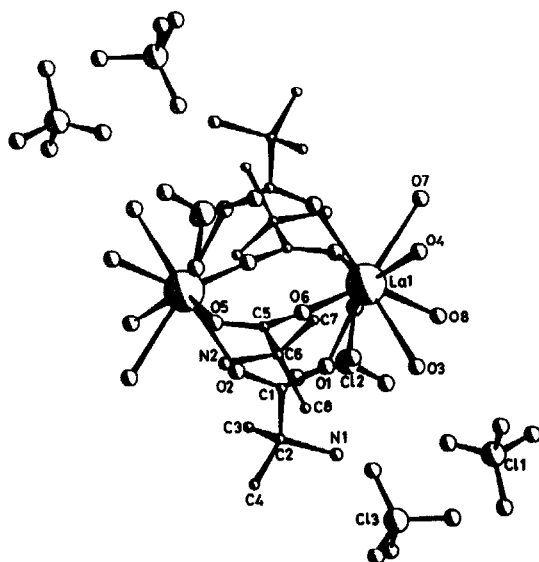


Fig. 1. Perspective view of  $[\text{La}_2(\text{Aib})_4(\text{H}_2\text{O})_8](\text{ClO}_4)_6$  (1).

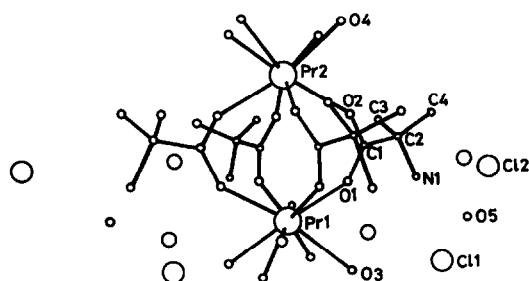


Fig. 2. Perspective view of  $[\text{Pr}_2(\text{Aib})_4(\text{H}_2\text{O})_8]\text{Cl}_6 \cdot \text{H}_2\text{O}$  (2).

Table 2. Selected bond distances (Å) and bond angles (°) in complexes **1** and **2**

1		2	
<b>Bond distances</b>			
La(1)—O(1)	2.457 (5)	Pr(1)—O(1)	2.427 (4)
La(1)—O(2)	2.439 (3)	Pr(2)—O(2)	2.397 (4)
La(1)—O(3)	2.586 (4)	Pr(1)—O(3)	2.501 (4)
La(1)—O(4)	2.551 (5)	Pr(2)—O(4)	2.526 (4)
La(1)—O(5)	2.448 (3)	O(1)—C(1)	1.285 (7)
La(1)—O(6)	2.399 (5)	O(2)—C(1)	1.254 (7)
La(1)—O(7)	2.636 (7)	N(1)—C(2)	1.516 (8)
La(1)—O(8)	2.521 (4)	C(1)—C(2)	1.525 (8)
O(1)—C(1)	1.251 (8)	C(2)—C(3)	1.526 (10)
O(2)—C(1)	1.252 (5)	C(2)—C(4)	1.479 (10)
O(5)—C(5)	1.266 (6)		
N(1)—C(2)	1.503 (6)		
N(2)—C(6)	1.501 (7)		
C(1)—C(2)	1.534 (7)		
C(2)—C(3)	1.542 (7)		
C(2)—C(4)	1.509 (10)		
C(5)—C(6)	1.554 (6)		
C(6)—C(7)	1.511 (12)		
C(6)—C(8)	1.534 (7)		
C(5)—C(6)	1.252 (7)		
<b>Bond angles</b>			
O(1)—La(1)—O(3)	72.3 (1)	O(1)—Pr(1)—O(3)	76.5 (1)
O(2)—La(1)—O(4)	80.0 (2)	O(2)—Pr(2)—O(4)	77.0 (1)
La(1)—O(1)—C(1)	140.4 (3)	Pr(1)—O(1)—C(1)	138.7 (4)
La(1)—O(2)—C(1)	144.8 (3)	Pr(2)—O(2)—C(1)	141.6 (4)
O(1)—C(1)—O(2)	128.2 (5)	O(1)—C(1)—O(2)	124.4 (5)
O(2)—C(1)—C(2)	114.6 (4)	O(2)—C(1)—C(2)	116.4 (5)
O(1)—C(1)—C(2)	117.2 (4)	O(1)—C(1)—C(2)	119.0 (5)
N(1)—C(2)—C(1)	108.3 (4)	N(1)—C(2)—C(1)	107.7 (5)
C(1)—C(2)—C(4)	112.1 (5)	C(1)—C(2)—C(4)	112.4 (6)
C(1)—C(2)—C(3)	108.6 (4)	C(1)—C(2)—C(3)	107.2 (5)
N(1)—C(2)—C(4)	108.9 (4)	N(1)—C(2)—C(4)	108.2 (5)
N(1)—C(2)—C(3)	108.8 (5)	N(1)—C(2)—C(3)	107.5 (5)
C(3)—C(2)—C(4)	110.2 (5)	C(3)—C(2)—C(4)	113.6 (6)

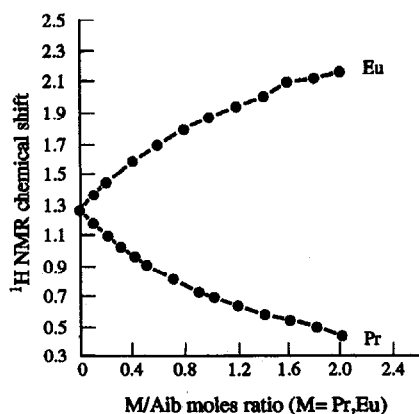


Fig. 3. A plot of  $^1\text{H}$  NMR chemical shift (ppm) vs molar ratio of  $\text{M}^{3+}$  ( $\text{M} = \text{Pr}, \text{Eu}$ ) and Aib concentration.

of Aib is observed upon successive addition of the appropriate lanthanide salt. The resonance is shifted downfield on adding Eu(III) perchlorate whereas it is shifted upfield on addition of Pr(III) perchlorate. The change in the chemical shift with a change in the molar ratio of the metal ion and Aib concentration is shown graphically in Fig. 3. The NMR studies clearly show that in solution Aib is coordinated to lanthanide ion via the carboxylic acid oxygens.

In view of the pronounced differences observed between the solid state structures of lanthanide amino acid complexes and those of Ca(II), the assumption of isomorphism between Ca(II) and La(III) complexes (implicit in the use of the latter as models for bonding of Ca(II) to biological systems) requires a reappraisal.

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