

# Lanthanide complexes of iminocarboxylate ligands derived from 1,4,7-triazacyclononane: structural characterisation and relaxivity of the Gd<sup>III</sup> and luminescence of the Eu<sup>III</sup> complexes †

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A new asymmetric derivative of 1,4,7-triazacyclononane with two iminocarboxylic pendant arms attached to the macrocyclic ring has been designed and prepared. Lanthanide complexes of L<sup>1</sup> and of its previously reported symmetric analogue L, containing three pendant arms, are described. The complexes [Ln(L)] (Ln = Gd, Eu, Dy) and [Ln(L<sup>1</sup>)X] (Ln = Y, Gd, Eu, Dy) (X = Cl<sup>-</sup> or CH<sub>3</sub>COO<sup>-</sup>) have been synthesised by Schiff-base condensation of 1,4,7-tris(2-aminoethyl)-1,4,7-triazacyclononane (**1**) or 1,4-bis(2-aminoethyl)-1,4,7-triazacyclononane (**2**), respectively, with sodium pyruvate on a lanthanide ion template. The complexes [Gd(L)] and [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)] have been structurally characterised by X-ray crystallography. <sup>1</sup>H NMR spectroscopic investigation of diamagnetic [La(L)] and [Y(L<sup>1</sup>)] in D<sub>2</sub>O reveals that these complexes show a different pH dependence for hydrolysis of the C=N bonds in L and L<sup>1</sup>. Hydrolysis occurs within several hours for [Y(L<sup>1</sup>)] at neutral pH, while acidic media are required to achieve the same rate of hydrolysis of [La(L)]. A similar value for the number of water molecules (*q*) directly bound to the metal centre for lanthanide complexes of L (*q* = 0) and L<sup>1</sup> (*q* = 1) has been estimated by three different approaches: NMR relaxivity studies for Gd<sup>III</sup> complexes, luminescence spectroscopy for Eu<sup>III</sup> complexes and Dy<sup>III</sup>-induced <sup>17</sup>O NMR water shift experiments for Dy<sup>III</sup> complexes.

## Introduction

The unique spectroscopic and magnetic properties of lanthanides make them very useful for a wide range of biochemical and medical applications.<sup>1–10</sup> For example, their high paramagnetism has been exploited in the design of contrast agents for magnetic resonance imaging (MRI).<sup>2,3</sup> The strong luminescence of Eu<sup>III</sup> and Tb<sup>III</sup> complexes has been applied for fluorescent labelling of immunoassay<sup>4–6</sup> and DNA,<sup>8</sup> while lanthanide complexes have also been used for photodynamic therapy,<sup>7</sup> as radiopharmaceuticals<sup>9</sup> and as chemical shift reagents for determining Na<sup>+</sup> or K<sup>+</sup> ions in cells and tissues.<sup>10</sup> In recent years numerous functionalised macrocycles have been prepared for complexation to lanthanide ions because of the extended stability and diversity these ligands offer. Among these, poly(amino)-carboxylate ligands have been widely studied due to their high selectivity towards lanthanide ions, resulting in highly thermodynamically stable and kinetically inert complexes.<sup>2</sup>

Recently, we have been studying the coordination properties of a symmetric poly(imino)carboxylate derivative of 1,4,7-triazacyclononane ([9]aneN<sub>3</sub>), L, towards lanthanide ions.<sup>11</sup> The structural characterisation of the Y<sup>III</sup>, Sm<sup>III</sup> and La<sup>III</sup> complexes along with NMR spectroscopic studies confirmed the high rigidity of the lanthanide complexes generated by this nine-coordinate ligand.<sup>11</sup> However, reagents for MRI and ion recognition often require one or more vacant coordination site to allow interaction of anions or water molecules with the lanthanide centre. Therefore, the ligand L<sup>1</sup>, which is an asymmetric derivative of [9]aneN<sub>3</sub> with only two iminocarboxylate pendant arms, has been designed. Ligand L has nine donor atoms, namely three amine, three imine N-atoms and three carboxylate O-atoms which fulfil the coordination sphere of the Ln<sup>III</sup> centre to afford the complexes [Ln(L)]. In contrast, L<sup>1</sup> has only seven

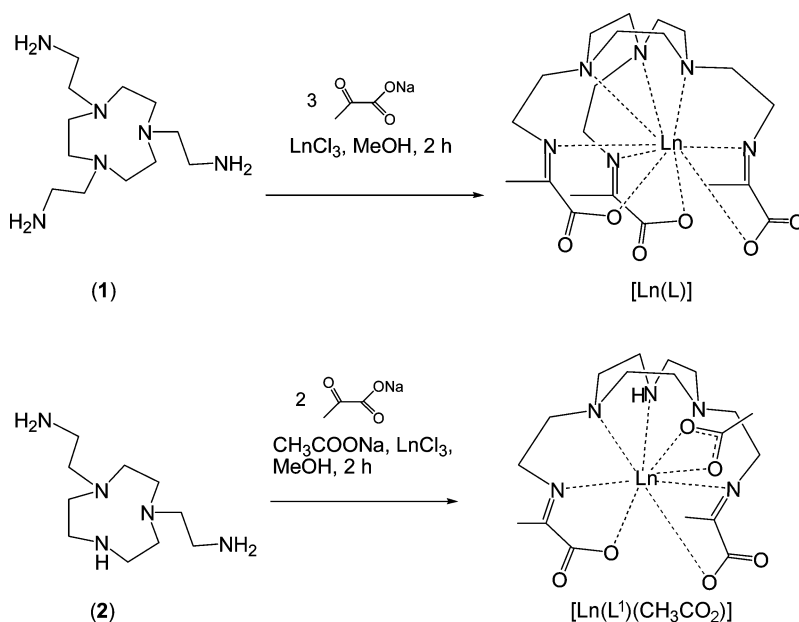
donor atoms thus providing an opportunity for coordination of anions or water molecules to the metal centre. Therefore, the complexes [Ln(L<sup>1</sup>)] are potentially active as MRI or ion recognition agents, while at the same time maintaining elements of the stability of their [Ln(L)] analogues. This paper extends our previous investigations and describes a comparison between the lanthanide complexes of L and L<sup>1</sup>. We report the crystal structures and the relaxivity data for [Gd(L)] and [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)], the <sup>1</sup>H and <sup>13</sup>C NMR spectra of [Y(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)] and we detail the hydrolysis of the imine bonds for the latter complex and for [La(L)]. The number of water molecules bound to the metal centre has been estimated using NMR relaxivity measurements for Gd<sup>III</sup> complexes, dysprosium induced shift (DIS) measurements for Dy<sup>III</sup> complexes, and emission lifetime measurements for Eu<sup>III</sup> complexes. These confirm the number of water molecules bound to the metal centre to be close to zero for the complexes of L and to one for the complexes of L<sup>1</sup>.

## Results and discussion

### Synthesis of the complexes [Ln(L)] and [Ln(L<sup>1</sup>)X] (X = Cl<sup>-</sup> or CH<sub>3</sub>COO<sup>-</sup>)

The lanthanide complexes of the ligands L and L<sup>1</sup> were obtained by Schiff-base condensation of the polyamines 1,4,7-tris(2-aminoethyl)-1,4,7-triazacyclononane (**1**)<sup>11</sup> and 1,4-bis(2-aminoethyl)-1,4,7-triazacyclononane (**2**)<sup>12</sup> with sodium pyruvate using the Ln<sup>III</sup> ion as templating agent (Scheme 1). The synthesis of the complexes [Ln(L)] (Ln = Gd, Dy, Eu) was achieved by refluxing one equivalent of **1** and LnCl<sub>3</sub> with three equivalents of sodium pyruvate in MeOH for 2 h followed by addition of Et<sub>2</sub>O to allow the desired complexes [Ln(L)] to precipitate as white solids. All the complexes of L<sup>1</sup> (except for [Eu(L<sup>1</sup>)Cl]·2NaCl·2H<sub>2</sub>O and [Y(L<sup>1</sup>)Cl]·2NaCl·H<sub>2</sub>O) were synthesised *via* reaction of one molar equivalent of **2** with one of CH<sub>3</sub>COONa, one of LnCl<sub>3</sub> and two of sodium pyruvate in MeOH under reflux for 2 h.

† Electronic supplementary information (ESI) available: <sup>1</sup>H NMR spectra of [Y(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)] (**6**) in D<sub>2</sub>O at 298 K and <sup>1</sup>H NMR data on acid-catalysed hydrolysis of [La(L)] (**5**) in D<sub>2</sub>O (pD = 4.4). See <http://www.rsc.org/suppdata/dt/b2/b209090m/>



**Scheme 1** Synthetic scheme for the preparation of complexes [Ln(L)] and [Ln(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]. i: 3 MeCOCOONa, LnCl<sub>3</sub>, MeOH, 2 h; ii: 2 MeCOCOONa, LnCl<sub>3</sub>, CH<sub>3</sub>COONa, MeOH, 2 h.

### Single-crystal X-ray diffraction analyses of [Gd(L)]·2.75CH<sub>3</sub>OH·0.75H<sub>2</sub>O (**3**) and of [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·CH<sub>3</sub>OH (**4**)

The crystal structures of the complexes [Ln(L)] (Ln = Y, Sm and La) have already been discussed in a previous publication.<sup>11</sup> The single crystal X-ray structure determination confirms that the complex [Gd(L)]·2.75CH<sub>3</sub>OH·0.75H<sub>2</sub>O (**3**) (Fig. 1) is isostructural with the lanthanide complexes [Ln(L)] already reported.<sup>11</sup> The Gd<sup>III</sup> ion is nine-coordinate, using all nine donor atoms of the ligand, namely the three amino N-donors of the macrocycle, the three imino N-donors and the three carboxylate O-donors. Bond lengths (Table 1) are in the range 2.641(5)–2.668(5) Å for the bonds between the Gd<sup>III</sup> and the macrocyclic N-donors, 2.561(5)–2.574(5) Å for the bonds to the N-donors of the imine moieties and 2.373(4)–2.388(4) Å for those to the carboxylate O-donors. A comparison of these bond lengths with those reported for the Y<sup>III</sup>, Sm<sup>III</sup> and La<sup>III</sup> complexes,<sup>11</sup> shows a general shortening due to the lanthanide contraction on moving from La<sup>III</sup> to Y<sup>III</sup>.

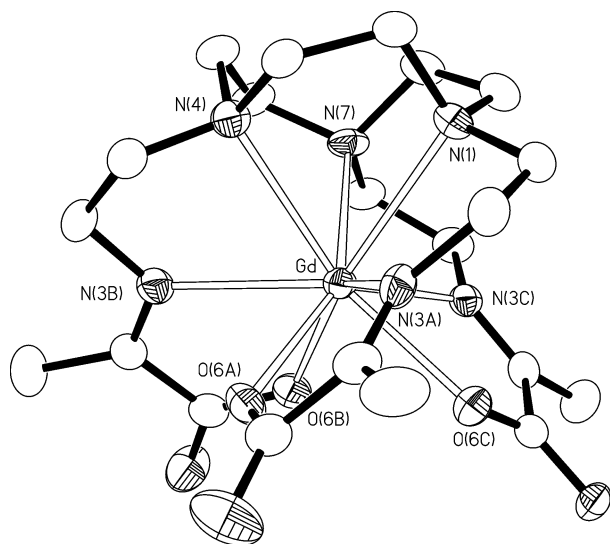
A single-crystal X-ray determination confirms the Gd<sup>III</sup> centre in [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·CH<sub>3</sub>OH (**4**) to be nine-coordinate

**Table 1** Selected bond lengths (Å) in [Gd(L)]·2.75CH<sub>3</sub>OH·0.75H<sub>2</sub>O (**3**) and in [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·CH<sub>3</sub>OH (**4**)

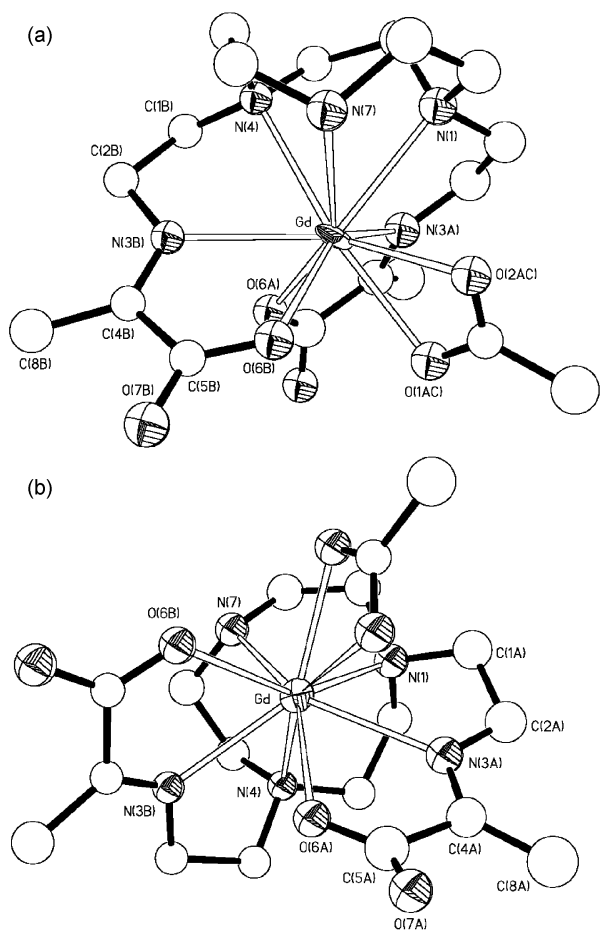
	[Gd(L)]	[Gd(L <sup>1</sup> )(CH <sub>3</sub> CO <sub>2</sub> )]·CH <sub>3</sub> OH
Gd–N(1)	2.668(5)	2.667(8)
Gd–N(4)	2.648(5)	2.664(7)
Gd–N(7)	2.641(5)	2.625(9)
Gd–N(3A)	2.561(5)	2.593(9)
Gd–N(3B)	2.565(5)	2.591(8)
Gd–N(3C)	2.574(5)	—
Gd–O(6A)	2.373(4)	2.401(7)
Gd–O(6B)	2.378(4)	2.382(7)
Gd–O(6C)	2.388(4)	—
Gd–O(1AC)	—	2.496(7)
Gd–O(2AC)	—	2.492(7)

using seven donor atoms of the ligand, namely the three amino N-donors of the macrocycle, the two imino N-donors and the two carboxylate O-donors, (Fig. 2). The Gd<sup>III</sup> centre is further coordinated to a bidentate acetate anion thereby achieving a coordination number of nine. Bond lengths (Table 1) are in the range 2.667(8)–2.625(9) Å for the bonds between the metal and the macrocyclic N-donors, 2.593(9) and 2.591(8) Å for the bonds to the N-donors of the imine moieties [Gd–N(3A) and Gd–N(3B)], 2.382(7), 2.401(7) Å for the carboxylate O-donors [Gd–O(6A) and Gd–O(6B)], while the acetate anion is bound with bond lengths of 2.496(7) and 2.492(7) Å [Gd–O(1AC) and Gd–O(2AC), respectively].

There is a high degree of planarity in the C(2)–C(8) units of the pendant arms in both structures, due to conjugation between the imine and carboxylate groups, with mean deviations of only 0.003–0.068 Å from the least-squares mean plane through these seven atoms. It is interesting to note the difference in the pitch angles between the plane of the macrocycle and the plane of each pyruvate. The average of the three pitch angles for **3** is 50.6°, which is intermediate between the values of 52.2° observed for [La(L)] and 49.6° for [Y(L)].<sup>11</sup> The differences in the pitch angles observed for the complexes [Ln(L)] can be attributed to the different effective ionic radius for the metal ions,<sup>11</sup> therefore, taking the effective ionic radii for the three nine-coordinate metal ions as 1.22 Å for La<sup>3+</sup>, 1.11 Å for Gd<sup>3+</sup> and 1.07 Å for Y<sup>3+</sup>,<sup>13</sup> the intermediate value for the averaged pitch angle in **3** was expected. In contrast to what is observed for complexes [Ln(L)], in [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·CH<sub>3</sub>OH the pitch angles formed by the plane of the macrocycle and the plane of

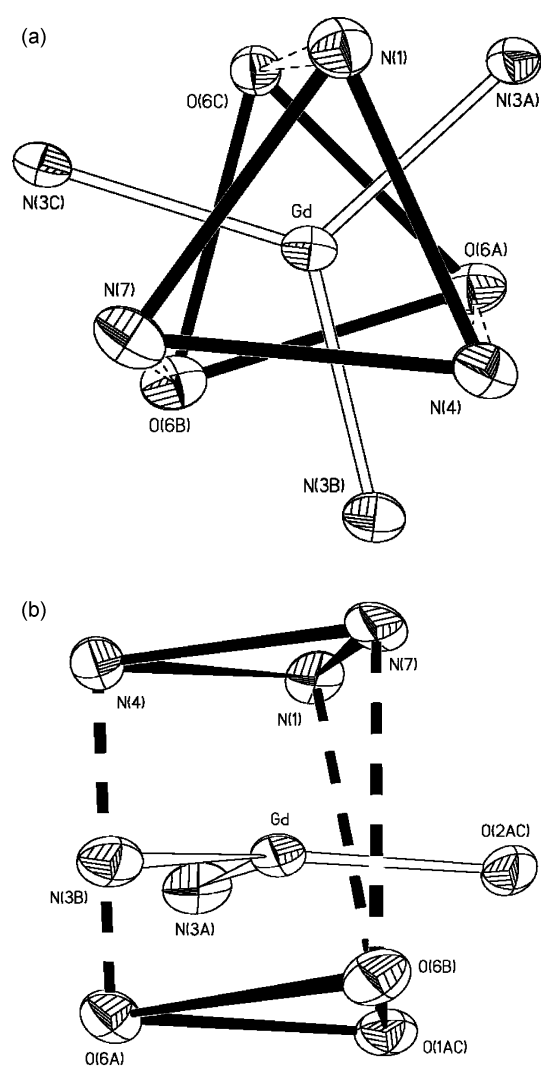


**Fig. 1** Ellipsoid plot of [Gd(L)]·2.75CH<sub>3</sub>OH·0.75H<sub>2</sub>O (**3**) with numbering scheme adopted. Hydrogen atoms and solvent molecules have been omitted for clarity. Displacement ellipsoids are drawn at 50% probability.



**Fig. 2** (a) Structure of  $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot\text{CH}_3\text{OH}$  (**4**) with numbering scheme adopted. Hydrogen atoms and solvent MeOH molecules have been omitted for clarity. (b) Complementary view of the crystal structure of  $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot\text{CH}_3\text{OH}$  (**4**).

each pyruvate group are dissimilar [ $51.4^\circ$  for C(2A)–C(8A) and  $44.0^\circ$  for C(2B)–C(8B)], with the plane containing the acetate anion oriented at an angle of  $57.1^\circ$  with respect to the macrocyclic plane. The coordination geometries at the  $\text{Gd}^{\text{III}}$  centres in both **3** and **4** are slightly distorted tricapped trigonal prismatic (Fig. 3(a) and (b)). The two most common geometries for nine-coordinate complexes are capped square antiprismatic and tricapped trigonal prismatic;<sup>14</sup> the presence of 1,4,7-triazacyclononane as the capping system forces the  $\text{Gd}^{\text{III}}$  ion to assume a trigonal prismatic structure as the macrocyclic nitrogen donors impose a triangular face. While in **3** the second triangular face of the prism is formed by the carboxylate oxygens with the imine nitrogens capping the three rectangular faces of the prism, in **4** it is formed by the two carboxylate oxygens and one acetate oxygen [O(1AC)], with the imine nitrogens and the other acetate oxygen capping the rectangular faces of the prism. The trigonal prismatic geometry in **4** is more distorted than in **3** with a face formed by the three oxygens that is less equilateral [angle range  $55.2$ – $67.1^\circ$  ( $58.2$ – $61.6^\circ$  in **3**)]. Furthermore, the angle between the plane defined by the triangle of three oxygen donors and that defined by the three nitrogen donors shows a greater distortion in **4** ( $12.2^\circ$ ) than in **3** ( $3.3^\circ$ ). The oxygen triangular faces are slightly twisted about the three-fold axis compared to the nitrogen triangular faces with the average of the three torsion angles formed by the four atoms of every rectangular face of the prism being  $21.4^\circ$  in **3** and  $19.4^\circ$  in **4**. It can be seen that the twist angle in  $[\text{Gd}(\text{L})]$  is intermediate between the values observed for  $[\text{La}(\text{L})]$  and for  $[\text{Y}(\text{L})]$  (*i.e.*  $27.0^\circ$  and  $20.2^\circ$ , respectively)<sup>11</sup> and that the twist between the two triangular faces of the prism is more evident in the tris(imino)carboxylate complexes  $[\text{Ln}(\text{L})]$  than in  $[\text{Gd}(\text{L}^1)]$ ,



**Fig. 3** (a) View of the coordination geometry in  $[\text{Gd}(\text{L}^1)\cdot 2.75\text{CH}_3\text{OH}\cdot 0.75\text{H}_2\text{O}]$  (**3**) down the non-crystallographic three-fold axis. (b) Coordination geometry about the metal centre in  $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot\text{CH}_3\text{OH}$  (**4**).

probably due to greater flexibility of  $\text{L}^1$  which has only two amines of the [9]ane $\text{N}_3$  ring functionalised and does not encapsulate the lanthanide ion as rigidly as does  $\text{L}$ . However, although  $\text{L}^1$  has only seven donor atoms and, therefore, leaves an empty site at the coordinated lanthanide ion, it prefers the coordination of an acetate anion to the formation of a polymeric complex as observed in the complexes formed by Schiff-base condensation of tris(2-aminoethyl)amine (tren) and sodium pyruvate with the  $\text{Ln}^{\text{III}}$  ion as templating agent.<sup>15,16</sup>

#### NMR spectroscopic studies on $[\text{La}(\text{L})]$ (**5**) and $[\text{Y}(\text{L}^1)(\text{CH}_3\text{CO}_2)]$ (**6**)

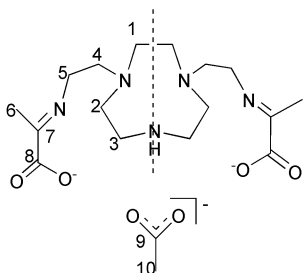
The  $^1\text{H}$  NMR spectra of  $[\text{La}(\text{L})]$  (**5**) and of other complexes  $[\text{Ln}(\text{L})]$  ( $\text{Ln} = \text{Y}, \text{Sm}, \text{Yb}$ ) have been reported.<sup>11</sup> The 2D COSY experiments on  $[\text{Y}(\text{L}^1)(\text{CH}_3\text{CO}_2)]$  (**6**) in  $\text{D}_2\text{O}$  at 298 K recorded at 300 MHz allowed the assignment reported in Table 2 (see Fig. 4 for labelling scheme). The flexibility of these asymmetric complexes does not allow discrimination between axial and equatorial protons, but allows the detection of triplets due to coupling between  $\text{CH}_2$  groups. In contrast to **6**, the  $^1\text{H}$  NMR spectrum of  $[\text{Y}(\text{L}^1)\text{Cl}]$  in  $\text{D}_2\text{O}$  shows a broad multiplet with only the peaks of the pyruvate and of the  $\text{CH}_2$  adjacent to the imine nitrogen distinguishable at 2.14 and 3.77 ppm, respectively. These features of the  $^1\text{H}$  NMR spectrum of  $[\text{Y}(\text{L}^1)\text{Cl}]$  could arise because the vacant coordination site is occupied by a water molecule, while the presence of the coordinated acetate

**Table 2**  $^1\text{H}$  NMR chemical shifts (ppm) for diamagnetic  $[\text{Y}(\text{L}^1)(\text{CH}_3\text{CO}_2)]$  (**6**)

Atom	Multiplicity	Chemical shift
H <sup>1</sup>	s	2.61
H <sup>2</sup>	t	2.89 ( $J = 6.8$ Hz)
H <sup>3</sup>	t	3.05 ( $J = 6.8$ Hz)
H <sup>4</sup>	t	2.80 ( $J = 5.9$ Hz)
H <sup>5</sup>	broad	3.70
H <sup>6</sup>	s	2.08
H <sup>12</sup>	s	1.82

**Table 3**  $^{13}\text{C}$  NMR chemical shifts (ppm) for  $[\text{Y}(\text{L}^1)\text{Cl}]$

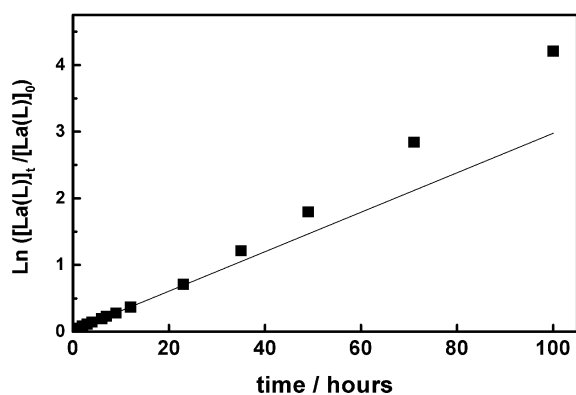
Atom	Chemical shift
C <sup>1</sup>	51.4
C <sup>2</sup>	50.0
C <sup>3</sup>	48.9
C <sup>4</sup>	57.6
C <sup>5</sup>	45.1
C <sup>6</sup>	14.6
C <sup>7</sup>	170.1
C <sup>8</sup>	171.0



**Fig. 4** Labelling scheme for the macrocycle and the acetate.

ion might lead to an increase in rigidity for **6**. The  $^{13}\text{C}$  NMR data for  $[\text{Y}(\text{L}^1)\text{Cl}]$  are reported in Table 3.

Recent work in Nottingham has involved the synthesis and the study of lipophilic, water soluble complexes of the lanthanides that undergo partial ligand hydrolysis and/or irreversible demetallation at acidic pH.<sup>16</sup> The complex  $[\text{La}(\text{L})]$  (**5**) is very stable in water at neutral pH. To test the stability of **5** in acidic media,  $^1\text{H}$  NMR kinetic studies were performed in  $\text{D}_2\text{O}$  in acetate buffer at pH 4.0 (Fig. 5). The  $^1\text{H}$  NMR spectra of the hydrolysis products show a multiplet (3.06–3.14 ppm) due to the ethylenic moiety of the arms and a singlet at 2.92 ppm due to the macrocyclic protons. The final products of the hydrolysis are likely to be the metal ion coordinated to water molecules and the protonated hexamine ligand. The hydrolysis of the



**Fig. 5** Acid-catalysed hydrolysis of  $[\text{La}(\text{L})]$  (**5**) in  $\text{D}_2\text{O}$  (pD = 4.4). The solid line represents a pseudo-first order approximation for initial 25% conversion.

three pyruvate groups leads to the formation of  $\alpha$ -ketobutyric acid where the protons of the methyl group have been exchanged with deuterium and are not detected in the  $^1\text{H}$  NMR spectrum. A first order approximation at small conversion rates (Fig. 5) gives a value of  $8.2 \times 10^{-6} \text{ s}^{-1}$  for the pseudo first order rate constant of hydrolysis process.

In contrast to what was observed for **5**, complex **6** undergoes partial ligand hydrolysis even at neutral pH. The  $^1\text{H}$  NMR spectrum of **6** after complete hydrolysis (more than 4 days) shows that none of the triplets due to the  $\text{CH}_2$  groups of the macrocycle (Table 2) has been considerably shifted. The observed decrease in intensity of the peaks assigned to the methylene group adjacent to the imine bond (3.70 ppm) and to the methyl group of the pyruvate (2.08 ppm) is accompanied by the concomitant growth of a new triplet at 3.09 ppm due to the  $\text{CH}_2$  adjacent to the primary amines of **2**. The fact that the signals assigned to the methylene groups of the macrocycle do not shift during the hydrolysis might suggest either that the ligand **2** remains coordinated to the metal ion or that the amines are partly protonated. The other hydrolysis products are likely to be  $\alpha$ -ketobutyric acid with the methyl group deuterated and the metal ion complexed partly by the ligand **2** and partly by water molecules.

### Relaxivity of $[\text{Gd}(\text{L})]\cdot 3\text{NaCl}\cdot 3\text{H}_2\text{O}$ and $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot 3\text{NaCl}\cdot \text{H}_2\text{O}$

One of the most important parameters used to evaluate the efficiency of a compound as a contrast agent is its relaxivity  $r_{1p}$  ( $\text{mM}^{-1} \text{ s}^{-1}$ ). This represents the net increment in the water proton longitudinal relaxation rate per millimolar concentration of the paramagnetic compound.<sup>2,3</sup> The overall relaxivity of a  $\text{Gd}^{\text{III}}$  ion is typically described as a superposition of contributions from water molecules in the inner, outer, and second coordination spheres of a complex,<sup>3</sup> with the outer sphere term being determined at 20 MHz as *ca.*  $2.0\text{--}2.5 \text{ mM}^{-1} \text{ s}^{-1}$ .<sup>3</sup>

The relaxivity values for  $[\text{Gd}(\text{L})]\cdot 3\text{NaCl}\cdot 3\text{H}_2\text{O}$  and  $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot 3\text{NaCl}\cdot \text{H}_2\text{O}$  at 300 MHz and  $37^\circ\text{C}$  were determined as  $1.26 (\pm 0.05) \text{ mM}^{-1} \text{ s}^{-1}$  and  $3.02 (\pm 0.13) \text{ mM}^{-1} \text{ s}^{-1}$ , respectively. For  $[\text{Gd}(\text{L})]$ , this suggests that no water molecules are coordinated to the metal centre in solution, which is consistent with the results of X-ray crystallography. For  $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot 3\text{NaCl}\cdot \text{H}_2\text{O}$ , the X-ray crystal structure shows that the acetate anion acts as a bidentate ligand, thus completing nine coordination of  $\text{Gd}^{\text{III}}$ . However, the relaxivity value of  $3.02(13) \text{ mM}^{-1} \text{ s}^{-1}$  is considerably lower than the value of  $4.7(4) \text{ mM}^{-1} \text{ s}^{-1}$  determined for the  $\text{Gd}^{\text{III}}$  complex of the ligand obtained by Schiff-base condensation of tris(2-aminoethyl)amine (tren) with three equivalents of sodium pyruvate,<sup>15,16</sup> which contains two water molecules coordinated to the  $\text{Gd}^{\text{III}}$ . This suggests a lability of the acetate ion in  $[\text{Gd}(\text{L}^1)(\text{CH}_3\text{CO}_2)]$  in solution, allowing the possibility of an equilibrium<sup>17</sup> between the species containing bidentate acetate, monodentate acetate and no coordinated acetate ion, with a water molecule occupying any vacant coordination site.

### $\text{Dy}^{\text{III}}$ -induced $^{17}\text{O}$ NMR water shift experiments on $[\text{Dy}(\text{L})]\cdot 3\text{NaCl}\cdot 2\text{H}_2\text{O}$ and $[\text{Dy}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot 3\text{NaCl}\cdot \text{H}_2\text{O}$

The dysprosium induced shift (DIS) has been exploited to estimate quantitatively the number of bound water molecules in various lanthanide complexes.<sup>18</sup> A gradient of  $387 (\pm 1) \text{ ppm M}^{-1}$  for DIS as a function of concentration of  $\text{DyCl}_3$  [Fig. 6(c)] gives a value of 48 ppm per each bound water molecule, if a hydration number of eight for  $\text{Dy}^{\text{III}}$  in  $\text{DyCl}_3$ <sup>19</sup> is assumed. The plots of DIS versus the concentration of  $[\text{Dy}(\text{L})]\cdot 3\text{NaCl}\cdot 2\text{H}_2\text{O}$  [Fig. 6(a)] and  $[\text{Dy}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot 3\text{NaCl}\cdot \text{H}_2\text{O}$  [Fig. 6(b)] have gradients of  $14.3 (\pm 0.3) \text{ ppm M}^{-1}$  and  $63 (\pm 4) \text{ ppm M}^{-1}$ , respectively. These values give an estimate of 0.3 water molecules coordinated to the metal centre in  $[\text{Dy}(\text{L})]$  and 1.3 water molecules in  $[\text{Dy}(\text{L}^1)]$ . Fractional values of  $q$  are normally

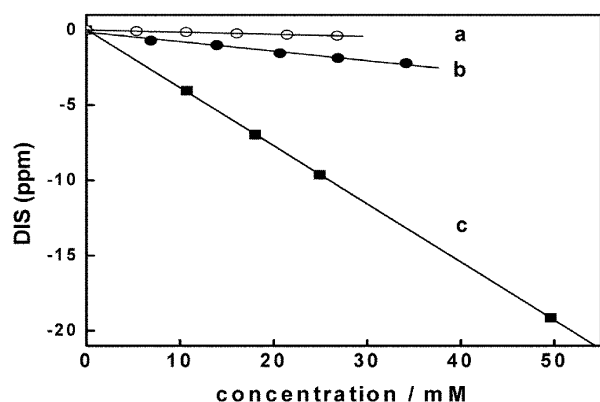


Fig. 6 Dysprosium induced shift (DIS,  $\Delta\delta$ ) as a function of concentration of:  $[\text{Dy}(\text{L})]\cdot 3\text{NaCl}\cdot 2\text{H}_2\text{O}$  (a),  $[\text{Dy}(\text{L}^1)(\text{CH}_3\text{CO}_2)]\cdot 3\text{NaCl}\cdot \text{H}_2\text{O}$  (b) and  $\text{DyCl}_3$  (c).

found by the DIS method,<sup>18</sup> due to outer and/or second-sphere contribution. It can be assumed that in  $[\text{Dy}(\text{L})]$  no water molecules are directly bound to the  $\text{Dy}^{\text{III}}$  centre and that the 0.3 number obtained expresses therefore the outer and/or second-sphere contribution for this type of complexes. This suggests that there is one water molecule directly bound to  $\text{Dy}^{\text{III}}$  in  $[\text{Dy}(\text{L}^1)(\text{CH}_3\text{CO}_2)]$ , and therefore the acetate anion is likely to be bound to the metal centre in a monodentate fashion. It is also possible that in solution there is equilibrium between different modes of acetate ion binding, as discussed above for the  $\text{Gd}^{\text{III}}$  complex of  $\text{L}^1$  on the basis of the relaxivity data.

#### Emission of $[\text{Eu}(\text{L})]\cdot 3\text{NaCl}\cdot 3\text{H}_2\text{O}$ (7) and $[\text{Eu}(\text{L}^1)\text{Cl}]\cdot 2\text{NaCl}\cdot 2\text{H}_2\text{O}$ (8)

Many lanthanide complexes exhibit characteristic luminescence with a long emission lifetime, which can provide an extremely sensitive probe of different quenching process occurring at the metal centre. Energy transfer to O–H oscillators of water molecules bound to the lanthanide is an efficient non-radiative quenching mechanism,<sup>20</sup> while a replacement of an O–H oscillator with O–D leads to a significant decrease in the rate constant for vibronic quenching.<sup>20</sup> The number of water molecules directly bound to the lanthanide centre can be estimated from the difference between the excited state lifetimes in water and  $\text{D}_2\text{O}$  (eqn. (1),  $A = 1.2$  ms and  $C = 0.25$  for  $\text{Eu}^{\text{III}}$ ):<sup>21,22</sup>

$$q = A(1/\tau_{\text{H}_2\text{O}} - 1/\tau_{\text{D}_2\text{O}} - C) \quad (1)$$

where  $\tau_{\text{H}_2\text{O}}$  and  $\tau_{\text{D}_2\text{O}}$  represent emission lifetimes in ms in water and  $\text{D}_2\text{O}$ , respectively, and parameter  $C$  in the equation represents the *second-sphere* contribution in the non-radiative quenching.<sup>21–23</sup>

We have probed the number of water molecules coordinated to the metal centre in  $[\text{Eu}(\text{L})]\cdot 3\text{NaCl}\cdot 3\text{H}_2\text{O}$  (7) and  $[\text{Eu}(\text{L}^1)\text{Cl}]\cdot 2\text{NaCl}\cdot 2\text{H}_2\text{O}$  (8) by performing emission measurements in water and  $\text{D}_2\text{O}$  solutions. The emission spectra of 7 and 8 obtained under direct f–f excitation (395 nm) in deaerated  $\text{H}_2\text{O}$  at 298 K (Fig. 7) show a characteristic metal-centred emission of  $\text{Eu}^{\text{III}}$ , originating from  $\{^5\text{D}_0 \rightarrow ^7\text{F}\}$  transitions with  $\Delta J$  ranging from 0 to 4. 7 displays emission bands at 580 ( $J = 0$ ); 592 and 595 ( $J = 1$ ); 614.5 and 619 ( $J = 2$ ); 649.5 and 653 ( $J = 3$ ); 685 and 694 ( $J = 4$ ) nm. 8 displays emission bands at 581 ( $J = 0$ ); 591.5 and 593.5 ( $J = 1$ ); 614, 616.5 and 619.5 ( $J = 2$ ); 650 ( $J = 3$ ); 685 and 696 ( $J = 4$ ) nm. The difference between relative intensity of the bands and the shape of the hypersensitive emission band ( $J = 2$ ) between 7 [Fig. 7(a)] and 8 [Fig. 7(b)] reflects the difference in the local surroundings of the metal centre.<sup>24</sup>

The emission lifetime is 0.87 ms in  $\text{H}_2\text{O}$  and 1.25 ms in  $\text{D}_2\text{O}$  for 7; 0.36 ms in  $\text{H}_2\text{O}$  and 0.50 ms in  $\text{D}_2\text{O}$  for 8. Application of eqn. (1) and of 0.075 additional correction for the non-radiative

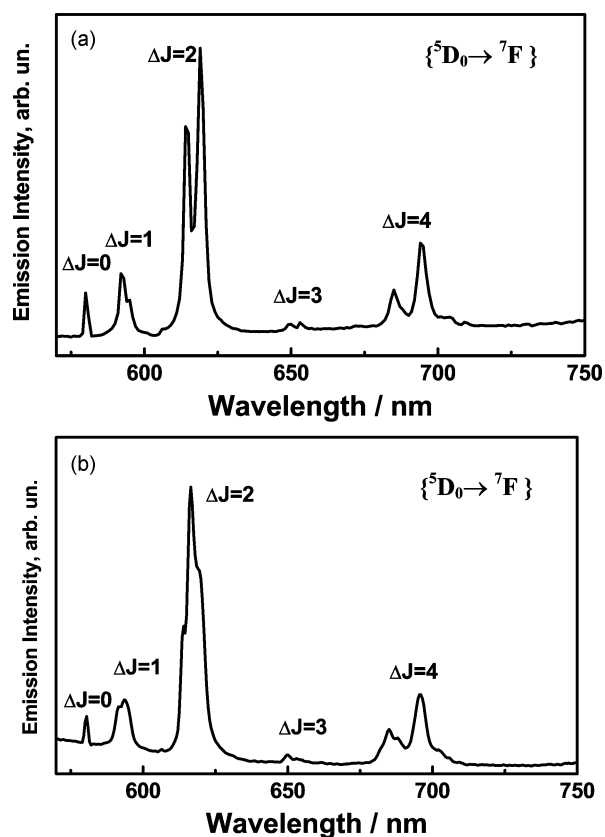


Fig. 7 Corrected emission spectra of (a)  $[\text{Eu}(\text{L})]\cdot 3\text{NaCl}\cdot 3\text{H}_2\text{O}$  (7) and (b)  $[\text{Eu}(\text{L}^1)\text{Cl}]\cdot 2\text{NaCl}\cdot 2\text{H}_2\text{O}$  (8) obtained under 395 nm excitation in deaerated  $\text{H}_2\text{O}$  at 298 K. The excitation and emission monochromator slits were set to bandwidths of 1 and 0.5 nm, respectively.

quenching *via* N–H oscillator<sup>21</sup> in 8, gives the number of water molecules directly bound to the metal centre equal to 0.10 and 0.9 for 7 and 8, respectively. Bearing in mind 10% error in lifetime measurements,<sup>21</sup> this corresponds to appropriate values for  $q$  of zero and one. Thus, the values obtained from luminescence spectroscopy for the L and  $\text{L}^1$  complexes of  $\text{Eu}^{\text{III}}$  are consistent with those obtained for the  $\text{Gd}^{\text{III}}$  complexes by relaxivity measurements and for  $\text{Dy}^{\text{III}}$  complexes by DIS, particularly if the correction for outer sphere contribution is applied to all the experimental data.

#### Conclusions

The new asymmetric bis-iminocarboxylate derivative of [9]ane $\text{N}_3$  forms lanthanide complexes where the metal ion is coordinated by the seven donor atoms of  $\text{L}^1$  and by the acetate anion. The number of water molecules directly bound to the metal centres ( $q$ ) for lanthanide complexes of L and  $\text{L}^1$  has been found to be similar using three different approaches: relaxivities of the  $\text{Gd}^{\text{III}}$  complexes, luminescence spectroscopy for the  $\text{Eu}^{\text{III}}$  complexes and  $\text{Dy}^{\text{III}}$ -induced  $^{17}\text{O}$  NMR water shift experiments for  $\text{Dy}^{\text{III}}$  complexes. Given that the complexes  $[\text{Ln}(\text{L})]$  are nine-coordinate and no water molecule is directly bound to the  $\text{Ln}^{\text{III}}$  centre, the relaxivity value obtained for the complex  $[\text{Gd}(\text{L})]$  and the  $q$  number determined by DIS (for the  $\text{Dy}^{\text{III}}$  complex) and by luminescence spectroscopy (on the  $\text{Eu}^{\text{III}}$  complex) can be considered to be due to the outer and/or second-sphere contribution. The studies on the hydrolysis of the imine bonds for the complexes  $[\text{La}(\text{L})]$  and  $[\text{Y}(\text{L}^1)(\text{CH}_3\text{CO}_2)]$  have shown different stability in  $\text{H}_2\text{O}$  with the former being very stable at neutral pH while undergoing a slow irreversible hydrolysis at low pH.

#### Experimental

Spectra were recorded on a Bruker DPX 300 spectrometer ( $^1\text{H}$  and  $^{13}\text{C}$  NMR), and on a Perkin-Elmer 1600 spectrometer

(FTIR, KBr disks). Elemental analytical data were obtained by the Microanalytical Service (Perkin-Elmer 240B analyser) at the University of Nottingham. Emission measurements of deaerated solutions were performed on Edinburgh Instrument FLS 920. The steady-state emission spectra were collected with a Xe lamp as an excitation source, and lifetimes were determined in single photon counting mode with microsecond flash lamp excitation. FAB (fast atom bombardment) mass spectra were obtained by the EPSRC National Mass Spectrometry Service at the University of Swansea. 1,4,7-Tris(2-aminoethyl)-1,4,7-triazacyclononane (**1**)<sup>11</sup> and 1,4-bis(2-aminoethyl)-1,4,7-triazacyclononane (**2**)<sup>12</sup> were prepared as described in the literature. All starting materials were obtained from Aldrich Chemical Co. and were used without further purification.

#### Synthesis of Gd<sup>III</sup>, Eu<sup>III</sup> and Dy<sup>III</sup> complexes of L

1,4,7-Tris(aminoethyl)-1,4,7-triazacyclononane (**1**) (0.20 mmol), sodium pyruvate (0.60 mmol) and the appropriate Ln<sup>III</sup> chloride were heated under reflux in MeOH (30 cm<sup>3</sup>) for 2 h. After cooling, the solvent volume was reduced, Et<sub>2</sub>O was added and the resulting pale yellow solid was filtered off and dried *in vacuo*.

**[Gd(L)]·3NaCl·3H<sub>2</sub>O (3)**. Yield 75.1%. Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 645 (M<sup>+</sup> [C<sub>21</sub>H<sub>33</sub>N<sub>6</sub>O<sub>6</sub>Gd + Na<sup>+</sup>]). Elemental analysis: found (calc. for C<sub>21</sub>H<sub>33</sub>N<sub>6</sub>O<sub>6</sub>Gd·3NaCl·3H<sub>2</sub>O): C, 29.83 (29.60); H, 4.46 (4.61); N, 10.10 (9.86%). IR (KBr disk), cm<sup>-1</sup>: 2925w, 2869w, 1617s (ν<sub>C=N, C=O</sub>), 1388m, 1205s, 1109m, 1032w, 939w. Single crystals suitable for X-ray structural analysis were obtained by diffusion of Et<sub>2</sub>O vapour into a MeOH solution at room temperature.

**[Dy(L)]·3NaCl·2H<sub>2</sub>O**. Yield 72.5%. Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 652 (M<sup>+</sup> [C<sub>21</sub>H<sub>33</sub>N<sub>6</sub>O<sub>6</sub>Dy + Na<sup>+</sup>]). Elemental analysis: found (calc. for C<sub>21</sub>H<sub>33</sub>N<sub>6</sub>O<sub>6</sub>Dy·3NaCl·2H<sub>2</sub>O): C, 29.93 (30.05); H, 4.34 (4.44); N, 9.89 (10.01%). IR (KBr disk), cm<sup>-1</sup>: 2991w, 2966w, 2878w, 1617s (ν<sub>C=N, C=O</sub>), 1387m, 1206s, 1110m, 1033w, 941w.

#### [Eu(L)]·3NaCl·3H<sub>2</sub>O (7)

Yield 68.7%. Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 641 (M<sup>+</sup> [C<sub>21</sub>H<sub>33</sub>N<sub>6</sub>O<sub>6</sub>Eu + Na<sup>+</sup>]). Elemental analysis: found (calc. for C<sub>21</sub>H<sub>33</sub>N<sub>6</sub>O<sub>6</sub>Eu·3NaCl·3H<sub>2</sub>O): C, 29.91 (29.78); H, 4.47 (4.64); N, 10.11 (9.92%). IR (KBr disk), cm<sup>-1</sup>: 2962w, 2916w, 2848w, 1614s (ν<sub>C=N, C=O</sub>), 1383m, 1229s, 1173m, 1024w, 809w.

#### Synthesis of [Ln(L')Cl]·2NaCl·xH<sub>2</sub>O (Ln<sup>III</sup> = Eu<sup>III</sup> and Y<sup>III</sup>)

4,7-bis(2-Aminoethyl)-1,4,7-triazacyclononane (**2**) (30.0 mg, 0.128 mmol) dissolved in MeOH (5 cm<sup>3</sup>) was added to a solution of sodium pyruvate (28.2 mg, 0.256 mmol) and LnCl<sub>3</sub>·6H<sub>2</sub>O (1 molar equivalent) in MeOH (30 cm<sup>3</sup>). The resulting solution was heated under reflux for 2h. After cooling, the solvent volume was reduced, Et<sub>2</sub>O was added and the resulting white solid was filtered off and dried *in vacuo*.

**[Y(L')Cl]·2NaCl·H<sub>2</sub>O**. (44.1 mg, 0.072 mmol, yield 84.7%). Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 442 (M<sup>+</sup> [C<sub>16</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>Y]<sup>+</sup>). Elemental analysis: found (calc. for C<sub>16</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>YCl·2NaCl·H<sub>2</sub>O): C, 31.81 (31.37); H, 4.96 (4.77); N, 11.68 % (11.43 %) (KBr disk), cm<sup>-1</sup>: 2964w, 1636s (ν<sub>C=N, C=O</sub>), 1384m, 1262m, 1207w, 1098m, 1026m, 803m.

**[Eu(L')Cl]·2NaCl·2H<sub>2</sub>O (8)**. (71.5 mg, 0.103 mmol, yield 80.5%). Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 506 (M<sup>+</sup> [C<sub>16</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>Eu]<sup>+</sup>). Elemental analysis: found (calc. for C<sub>16</sub>H<sub>30</sub>N<sub>5</sub>O<sub>6</sub>Eu·2NaCl·2H<sub>2</sub>O): C, 28.06 (27.70); H, 4.76 (4.50);

N, 10.41 (10.09%). IR (KBr disk), cm<sup>-1</sup>: 2919w, 2858w, 1637s (ν<sub>C=N, C=O</sub>), 1383m, 1263w, 1204m, 1109m, 963w, 805m, 666m.

#### Synthesis of [Ln(L')(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O (Ln<sup>III</sup> = Y<sup>III</sup>, Gd<sup>III</sup> and Dy<sup>III</sup>)

4,7-Bis(2-aminoethyl)-1,4,7-triazacyclononane (**2**) (30.0 mg, 0.128 mmol) dissolved in MeOH (5 cm<sup>3</sup>) was added to a solution of sodium pyruvate (28.2 mg, 0.256 mmol), LnCl<sub>3</sub>·6H<sub>2</sub>O (1 molar equivalent) and CH<sub>3</sub>COONa (10.5 mg, 0.128 mmol) in MeOH (30 cm<sup>3</sup>). The resulting colourless solution was heated under reflux for 2 h. After cooling, the solvent volume was reduced, and addition of Et<sub>2</sub>O led to the precipitation of white solid, which was filtered off and dried *in vacuo*.

**[Gd(L')(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O (4)**. (76.3 mg, 0.10 mmol, yield 78.3%). Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 511 (M<sup>+</sup> [C<sub>16</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>Gd]<sup>+</sup>). Elemental analysis: found (calc. for C<sub>18</sub>H<sub>30</sub>N<sub>5</sub>O<sub>6</sub>Gd·3NaCl·H<sub>2</sub>O): C, 28.58 (28.33); H, 4.11 (4.23); N, 9.04 (9.18%). IR (KBr disk), cm<sup>-1</sup>: 2963w, 2922w, 2852w, 1635s (ν<sub>C=N, C=O</sub>), 1384m, 1261m, 1205s, 1039m, 802m. Single crystals suitable for X-ray structural analysis were obtained from an Et<sub>2</sub>O–MeOH (10:1) solution of the complex at room temperature.

**[Y(L')(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O (6)**. (49.3 mg, 0.071 mmol, yield 83.5%). Mass spectrum (FAB, 3-NOBA matrix): *m/z* = 524 (M<sup>+</sup> [C<sub>18</sub>H<sub>30</sub>N<sub>5</sub>O<sub>6</sub>Y + Na<sup>+</sup>], 501 [M<sup>+</sup> – Na<sup>+</sup>] and 442 [M<sup>+</sup> – CH<sub>3</sub>COONa]). Elemental analysis: found (calc. for C<sub>18</sub>H<sub>30</sub>N<sub>5</sub>O<sub>6</sub>Y·3NaCl·H<sub>2</sub>O): C, 31.52 (31.12); H, 4.37 (4.64); N, 10.33 (10.08%). IR (KBr disk), cm<sup>-1</sup>: 2958w, 2925m, 2853w, 1634s (ν<sub>C=N, C=O</sub>), 1558m, 1456m, 1262m, 1206w, 1041m, 803m.

**[Dy(L')(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O**. (74.5 mg, 0.097 mmol, yield 75.6%). Mass spectrum (FAB, 3-NOBA matrix) *m/z* = 517 (M<sup>+</sup> [C<sub>16</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>Dy]<sup>+</sup>). Elemental analysis: found (calc. for C<sub>18</sub>H<sub>30</sub>N<sub>5</sub>O<sub>6</sub>Dy·3NaCl·H<sub>2</sub>O): C, 28.01 (28.14); H, 4.40 (4.20); N, 9.34 (9.12%). IR (KBr disk), cm<sup>-1</sup>: 2923w, 2861w, 1636s (ν<sub>C=N, C=O</sub>), 1384s, 1263s, 1207w, 1162m, 935s, 808m, 651m.

#### Hydrolysis experiments

Acidic (pH = 4) buffer: Potassium acetate (0.10 g) and acetic acid (0.32 cm<sup>3</sup>) were dissolved in D<sub>2</sub>O (5 cm<sup>3</sup>). The pH of the buffer solution was measured, and the pD was calculated using the formula pD = pH<sub>measured</sub> + 0.4. The complex [La(L)]·2CH<sub>3</sub>OH (0.01 g) was dissolved in the acidic buffer solution (0.6 cm<sup>3</sup>). The resulting clear solution was transferred to an NMR tube and the <sup>1</sup>H NMR spectra were acquired at time intervals. The proportion of [La(L)]·2CH<sub>3</sub>OH remaining unhydrolysed ([La(L)]<sub>t</sub>/[La(L)]<sub>t=0</sub>) was calculated by: [La(L)]<sub>t</sub>/[La(L)]<sub>t=0</sub> = I/[La(L)]/(I/[La(L)] + I[I]), where I/[La(L)] is the sum of the integrals of peaks corresponding to the protons on [La(L)], and I[I] is the sum of the integrals of peaks corresponding to the protons of **1**.

#### Relaxivity of [Gd(L)]·3NaCl·3H<sub>2</sub>O and of [Gd(L')(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O

Samples of [Gd(L)]·3NaCl·3H<sub>2</sub>O and of [Gd(L')(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O were weighed and dissolved in D<sub>2</sub>O (0.70 cm<sup>3</sup>) before being transferred to an NMR tube. The transverse relaxation times (*T*<sub>1</sub>) of the HDO peak at 4.707 ppm were measured using a 180–τ–90 pulse sequence at 37 °C on a Bruker 300 MHz NMR spectrometer. Plots of *T*<sub>1</sub><sup>-1</sup> (s<sup>-1</sup>) against concentration of [Gd(L)] or [Gd(L')(CH<sub>3</sub>CO<sub>2</sub>)] (mM) give appropriate straight lines (the correlation coefficient is 0.996 for both linear plots). The intercept with the y-axis gives the relaxation rate (*T*<sub>1</sub><sup>-1</sup> = 0.058 s<sup>-1</sup>) of the HDO peak without the presence of the paramagnetic metal complex (concentration = 0).

**Table 4** Details of single crystal structure determinations on [Gd(L)]·2.75CH<sub>3</sub>OH·0.75H<sub>2</sub>O and [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·CH<sub>3</sub>OH

Compound	[Gd(L)]·2.75CH <sub>3</sub> OH·0.75H <sub>2</sub> O	[Gd(L <sup>1</sup> )(CH <sub>3</sub> CO <sub>2</sub> )]·CH <sub>3</sub> OH
Formula	C <sub>21</sub> H <sub>32</sub> N <sub>6</sub> O <sub>6</sub> Gd·2.75CH <sub>3</sub> OH·0.75H <sub>2</sub> O	C <sub>18</sub> H <sub>29</sub> N <sub>5</sub> O <sub>6</sub> Gd·CH <sub>3</sub> OH
<i>M</i> /g mol <sup>-1</sup>	723.40	600.75
Crystal system	Rhombohedral	Monoclinic
Space group	<i>R</i> 3̄	<i>P</i> 2 <sub>1</sub> / <i>c</i>
<i>a</i> /Å	28.0190(12)	11.213(2)
<i>b</i> /Å	28.0190(12)	15.138(3)
<i>c</i> /Å	23.1774(13)	15.278(3)
<i>β</i> /°	—	111.476(4)
<i>V</i> /Å <sup>3</sup>	15758.0(13)	2413(2)
<i>T</i> /K	150(2)	150(2)
<i>Z</i>	18	4
<i>D<sub>c</sub></i> /g cm <sup>-3</sup>	1.372	1.654
<i>μ</i> /mm <sup>-1</sup>	1.945	2.795
Unique reflections, <i>R</i> <sub>int</sub>	8371, 0.090	4229, 0.099
Observed reflections	5400 [ <i>F</i> <sub>o</sub> ≥ 4σ( <i>F</i> <sub>o</sub> )]	2665 [ <i>F</i> <sub>o</sub> ≥ 4σ( <i>F</i> <sub>o</sub> )]
<i>R</i> <sub>1</sub> , <i>wR</i> <sub>2</sub> <sup>a</sup>	0.0548, 0.1203	0.0628, 0.1212

<sup>a</sup> Following absorption corrections.**<sup>17</sup>O NMR measurements on [Dy(L)]·3NaCl·2H<sub>2</sub>O and [Dy(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O**

The natural abundance <sup>17</sup>O NMR experiments were run at 40.686 MHz on a Bruker DPX 300 spectrometer, using a 10 mm sample tube. Five samples of [Dy(L)]·3NaCl·2H<sub>2</sub>O and of [Dy(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O were weighed and the first dissolved in deionised water containing 20% D<sub>2</sub>O (1.6 cm<sup>3</sup> of H<sub>2</sub>O and 0.4 cm<sup>3</sup> of D<sub>2</sub>O). The successive samples were dissolved in the same solution, thereby increasing the concentration of the complexes. The complexes with L<sup>1</sup> were found to hydrolyse slowly in D<sub>2</sub>O, but the delay between dissolving the sample in D<sub>2</sub>O and completing the <sup>17</sup>O measurement was less than 15 min, a time interval over which hydrolysis of the complex is thought to be minimal. The <sup>17</sup>O shifts were measured using the <sup>17</sup>O shift of the water/D<sub>2</sub>O as external reference (*δ* = -28.81). Plots of DIS (ppm) against concentration of DyCl<sub>3</sub>, [Dy(L)]·3NaCl·2H<sub>2</sub>O and [Dy(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·3NaCl·H<sub>2</sub>O (mM) give appropriate straight lines (correlation coefficients = 0.999, 0.996 and 0.992, respectively, Fig. 6).

**Crystal structure determinations**

Crystal data, data collection and refinement parameters for [Gd(L)]·2.75CH<sub>3</sub>OH·0.75H<sub>2</sub>O (**3**) and [Gd(L<sup>1</sup>)(CH<sub>3</sub>CO<sub>2</sub>)]·CH<sub>3</sub>OH (**4**) are given in Table 4. In **4** only the Gd could be refined anisotropically. Disorder was modelled in one MeOH and two H<sub>2</sub>O molecules in **3**. In **4** O(7A) was found to be unequally disordered over two sites. H atoms on water and disordered methanol molecules were not located.

CCDC reference numbers 195031 (**3**) and 193873 (**4**).

See <http://www.rsc.org/suppdata/> for crystallographic data in CIF or other electronic format.

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