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Solution properties of trivalent lanthanide trinuclear complexes with ligand 1,3,5-triamino-1,3,5-trideoxy-*cis*-inositol

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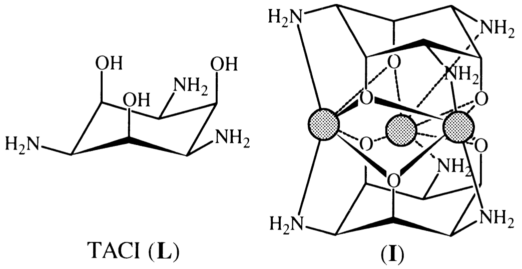
Abstract

The aqueous complexation reactions of trivalent lanthanide cations with the ligand 1,3,5-triamino-1,3,5-trideoxy-*cis*-inositol (TACI) have been characterised using potentiometry, electrospray ionisation mass spectrometry and solution NMR. Isostructural trinuclear complexes, $[Ln_3(TACIH_{-3})_2]^{3+}$, are formed all along the series and their stability constants are extremely dependent on the cation radius.

Keywords: Lanthanides; Trinuclear complexes; Cyclohexanic ligands; Stability constants; ES-MS; NMR

1. Introduction

Lanthanide (III) coordination chemistry has recently received growing interest because of the numerous applications of rare-earth compounds as for example relaxation agents in nuclear magnetic resonance imaging [1], luminescent probes in biology and medicine [2] or catalysts for the cleavage of RNA and DNA [3,4]. Trivalent lanthanide ions are also present in the nuclear fuel and thus separation of lanthanide from actinide by liquid–liquid extraction remains still a challenge because of the great chemical similarity of those two cation families. We are studying rare-earth complexation in solution with some synthetic ligands based on cyclohexanic platforms [5], which possess the specific sites present in sugars and derivatives like *cis*-inositol [6]. The ligand TACI (1,3,5-triamino-1,3,5-trideoxy-*cis*-inositol) is especially attractive because it displays a great selectivity along the lanthanide series. This ligand is able to form complexes with many metal ions of the periodic table, and a great number of X-ray structures have been analysed [7]. In 1998, Hedinger et al. demonstrated that TACI gives some trinuclear lanthanoid complexes with a sandwich-type structure **I** (Scheme 1) [8]. The $[Gd_3(TACIH_{-3})_2(H_2O)_6]^{3+}$ complex has been especially studied as a model compound from the point of view of MRI [9].



Scheme 1.

This contribution deals with the characterisation of all lanthanide complexes with TACI in aqueous solution. Selectivity has been evaluated by thermodynamic formation constant measurements all along the 4f series. It has been demonstrated by electrospray ionisation mass spectrometry that only one type of complex is formed from lanthanum to lutetium: $[Ln_3(LH_{-3})_2]^{3+}$. Furthermore, the proton NMR analysis has shown that the complexes are isostructural from praseodymium to ytterbium. Finally, some heterotrinuclear complexes have been identified in water solution containing a mixture of lanthanide cations.

2. Experimental

The ligand TACI was synthesised according to published procedures [10]. Lanthanide chlorides and triflates were commercially available materials.

The mass spectra were acquired on an LCQ-ion trap (Finnigan-Thermoquest, San Jose, USA) equipped with an

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electrospray source. Electrospray full scan spectra in the range *m*/*z* 100–1300 were obtained by infusion through a fused silica tubing at 2–10 μl/min. The solutions were analysed in the positive mode. The LCQ calibration (*m*/*z* 50–2000) was achieved according to the standard calibration procedure from the manufacturer (mixture of caffeine, MRFA and Ultramark 1621). The temperature of the heated capillary for the LCQ was set to 170°C, the ion-spray voltage was in the range of 1–6 kV and the injection time of 5–200 ms. Samples for ES-MS were prepared by dissolving the ligand (10^{-3} mol l^{-1}) and the lanthanide triflate salt in water. pH was then adjusted with triethylamine (pH = 8).

Potentiometric titrations were performed in 0.1 mol l^{-1} aqueous KCl under an argon atmosphere, the temperature was controlled to ±0.1°C with a circulating water bath. The p[H] (p[H] = $-\log H^+$, concentration in molarity) was measured in each titration with a combination glass electrode (Metrohm) and the titrant addition was automated by use of a 751 GPD titrino (Metrohm). The electrode was calibrated by titration of HCl with KOH in 0.1 mol l^{-1} KCl [11]. A plot of meter reading versus p[H] allows the determination of the electrode standard potential ($E°$) and the slope factor (f). Continuous potentiometric titrations with KOH 0.1 mol l^{-1} were conducted on 20 ml of aqueous solutions containing 10^{-3} mol l^{-1} TACI.$(HCl)_3$, 1.5×10^{-3} mol l^{-1} $LnCl_3$ and 0.1 mol l^{-1} KCl. The ligand's concentration was determined by potentiometric titration, and the metal concentrations by EDTA titrations using xylenol orange indicator. Back titration with 0.1 mol l^{-1} HCl was performed after each experiment to check whether equilibration had been achieved. At the beginning of the series (from La to Gd) 200 points were measured with 5 min waiting between two points, whereas at the end (from Tb to Lu) the kinetic was much slower and only 38 points were measured with 90 min waiting. Experimental data were refined using the computer program Hyperquad 2000 [12,13]. All equilibrium constants are concentration quotients rather than activities. The ionic product of water at 25°C and 0.1 mol l^{-1} ionic strength is $pK_w = 13.78$ [14]. The acidity constants of TACI were measured by titration and are comparable to values found in the literature [8]: $pK_{a_1} = 6.01$, $pK_{a_2} = 7.43$, $pK_{a_3} = 8.84$. Fixed values were used for pK_w, ligand's acidity constants and total concentrations of metal ligand and acid.

Samples for NMR spectroscopy were prepared by dissolving the ligand (10^{-2} mol l^{-1}) and the lanthanide triflate salt in 700 μl of deuterium oxide (euriso-top, 99.9 at.% D). pD was adjusted with a sodium deuteroxide solution, pD = 8 ($pD = pH_{read} + 0.41$) [15]. NMR spectra were recorded using a Varian Unity 400 spectrometer, and calibrated by assigning the residual solvent signal a shift from DSS of 4.7 ppm. Longitudinal relaxation rates were measured using a non selective inversion recovery pulse sequence, and T_1 values were obtained from a three-parameter fit of the data to an exponential recovery function.

3. Results and discussion

3.1. Potentiometric titrations

The protonation constants of TACI and the stability constants of the lanthanide–TACI complexes were calculated from the potentiometric titration curves using the program Hyperquad 2000. Multiple speciation models which included $[LnL]^{3+}$, $[LnL_2]^{3+}$, $[Ln_3LH_{-3}]^{6+}$ and $[Ln_3L_2H_{-6}]^{3+}$ were tested. Of these, only $[Ln_3L_2H_{-6}]^{3+}$ was the major complex as it was demonstrated by Hedinger et al. for europium cation [8]. At high pH (above 9), further deprotonation of the complex occurs to form the $[Ln_3L_2H_{-6}(OH)]^{2+}$ species. This potentiometric analysis along the 4f-series shows that the three hydroxyl groups of the ligand are deprotonated upon lanthanide complexation. The refinement of experimental data allows the determination of complex formation constants ($\beta_{32\text{-}6}$) according to the equilibrium:

$$3Ln^{3+} + 2TACI \rightarrow [Ln_3(TACI)_2(H)_{-6}]^{3+} + 6H^+$$

In most cases, refinement was better when deprotonated species $[Ln_3L_2H_{-6}(OH)]^{2+}$ were considered and the constants $\beta_{32\text{-}7}$ could be evaluated (Table 1). The calculated constants are slightly different than those reported by Hedinger et al. in similar conditions ($\beta_{32\text{-}6}$ Eu, Gd, Dy, Lu: −18.5, −18.2, −14.6, −11.3): they are a little higher for Eu and Gd, and lower for Dy and Lu. But in the main they are in good agreement. There is an increase of Ln–TACI complex stability with increasing atomic number, which is more effective at the beginning of the series (from La to Sm). TACI thus displays an amazing selectivity along the 4f series. Comparison with EDTA and DTPA [16], well-known aminopolycarboxylate ligands that form LnL com-

Table 1
Logarithmic stability constants of lanthanide TACI complexes in 0.1 mol l^{-1} KCl at 25°C in water

	log $\beta_{32\text{-}6}$	log $\beta_{32\text{-}7}$
La^{III}	−33.83±0.02	−44.73±0.04
Pr^{III}	−25.45±0.03	−35.74±0.03
Nd^{III}	−24.09±0.01	−34.36±0.02
Sm^{III}	−19.29±0.02	−29.13±0.02
Eu^{III}	−17.93±0.01	−28.34±0.02
Gd^{III}	−17.25±0.10	−27.54±0.11
Tb^{III}	−16.59±0.09	
Dy^{III}	−15.54±0.05	
Ho^{III}	−14.59±0.08	−25.48±0.13
Er^{III}	−14.43±0.06	
Tm^{III}	−13.84±0.07	−24.11±0.09
Yb^{III}	−13.01±0.06	−24.07±0.11
Lu^{III}	−12.5±0.08	−22.51±0.1

plexes with trivalent lanthanide cations, shows that the thermodynamic constants for lanthanide complex formation with TACI are much more sensitive to cation size (Fig. 1).

3.2. ES-MS qualitative speciation

A mass spectrometry study was undertaken to confirm the nature of the species identified during the refinement of potentiometric data. Electrospray ionisation mass spectrometry (ES-MS) has been shown to be a suitable technique to characterise qualitatively preformed ions in solution [17] and has moreover been used for identification of supramolecular coordination complexes [18–20]. Most of the lanthanides possess several isotopes and the MS peak patterns are thus characteristic of the number of cations present in the complex. Solutions of europium (III) triflate and ligand TACI in the presence of triethylamine at constant pH have been analysed for the following stoichiometric conditions: EuL_3, EuL_2, EuL, Eu_3L_2 and Eu_2L. The molecular ion in every spectra corresponds to the monocharged cation $[Eu_3L_2H_{-6}(OTf)_2]^+$, the ions $[Eu_3L_2H_{-6}(OTf)(OH)]^+$ and $[Eu_3L_2H_{-6}(OH)_2]^+$ are also observed. Every signal corresponds to $[Eu_3L_2H_{-6}]^{3+}$ complexes. The same behaviour is observed for the other 4f cations, for which Ln/TACI (3/2) samples were analysed. Some characteristic features are shown in Fig. 2.

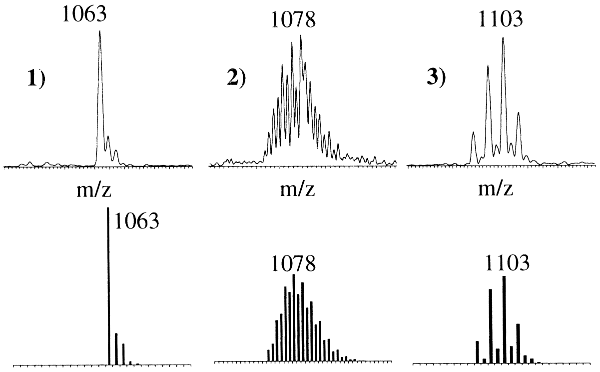

Fig. 2. ES-MS spectra and calculated isotopic patterns of Ln_3TACI_2 samples at pH 8 in water solution (1) La, (2) Nd, (3) Eu.

3.3. Proton NMR studies

$[Ln_3L_2H_{-6}]^{3+}$ complexes were analysed in deuterium oxide at constant pD (pD = 8) by 400 MHz proton NMR at 298 K. Every spectrum displays only two signals that correspond to H^N (H connected to the C–NH_2 group) and H^O (H connected to the C–OH group); this indicates that complexes possess an averaged symmetry D_{3h} in solution. Proton chemical shifts and longitudinal relaxation times are very sensitive to the nature of metal ions (Table 2). Diamagnetic lanthanum and lutetium induce very small chemical shift difference in complexes in comparison to free ligand, whereas paramagnetic lanthanide cations induce large LIS (lanthanide-induced shifts) and LIR (lanthanide-induced relaxation). LIS are between 2.42 ppm (Sm) and 262 ppm (Tb) for H^O and between 2.53 ppm (Sm) and 191 (Tb) for H^N. LIR are very fast in the second part of the 4f series, longitudinal relaxation times are inferior to 1 ms for Tb, Dy and Ho ions. They are smaller for H^O than for H^N in a given complex, because H^O is closer to paramagnetic centres.

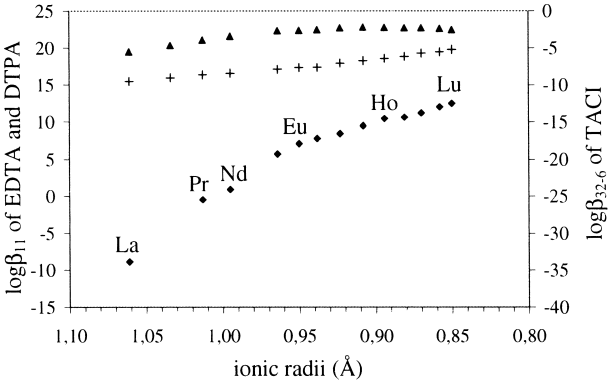

Fig. 1. Formation constants of lanthanide complexes, with TACI ♦ (right scaling), with EDTA + and DTPA ▲ (left scaling).

The paramagnetic chemical shift $\delta^{\text{para}}_{i,\text{Ln}}$ for a proton i and a lanthanide Ln in an axial complex is given by Eq. (1), where $\delta^{\text{exp}}_{i,\text{Ln}}$ is the measured chemical shift and $\delta^{\text{dia}}_{i,\text{Ln}}$ is the diamagnetic contribution obtained by measuring chemical shifts for isostructural diamagnetic complexes (La or Lu). The contact term $\delta^{\text{contact}}_{i,\text{Ln}}$ results from through-bond interactions and the pseudo contact term $\delta^{\text{pseudo-contact}}_{i,\text{Ln}}$ results from through-space effects. They are expressed by Eq. (2) where $\langle S_Z\rangle_{\text{Ln}}$ is the spin expectation value of S_Z, D_{Ln} is the anisotropic part of the axial magnetic susceptibility tensor, F_i and G_i are, respectively, the contact and pseudo-contact terms for proton i

$$\delta^{\text{para}}_{i,\text{Ln}} = \delta^{\text{exp}}_{i,\text{Ln}} - \delta^{\text{dia}}_{i,\text{Ln}} = \delta^{\text{contact}}_{i,\text{Ln}} + \delta^{\text{pseudo-contact}}_{i,\text{Ln}} \quad (1)$$

$$\delta^{\text{contact}}_{i,\text{Ln}} = F_i \times \langle S_Z\rangle_{\text{Ln}} \text{ and } \delta^{\text{pseudo-contact}}_{i,\text{Ln}} = G_i \times D_{\text{Ln}}. \quad (2)$$

Table 2
Chemical shifts (ppm) and longitudinal relaxation times (ms) in $[Ln_3L_2H_{-6}]^{3+}$ complexes at 298 K, 400 MHz in D_2O at pD 8

Ln	$\delta(H^N)$	$\delta(H^O)$	$T_1(H^N)$	$T_1(H^O)$
La	2.97	4.12	626	1110
Pr	24.72	24.47	25	14
Nd	21.80	19.28	19	10
Sm	5.46	6.33	270	174
Eu	−21.72	−14.59	50	26
Tb	194	266	0.4	0.2
Dy	176	241	0.3	0.2
Ho	84	122	0.4	0.2
Er	−117	−112	6	3
Tm	−179	−195	2	1
Yb	−46.1	−42.64	11	6
Lu	2.93	3.91	628	940

In a polymetallic system containing several identical paramagnetic centres, these equations can be simply derived if there is no magnetic coupling interactions between the ions (Eq. (3)) [21]. It has been indeed demonstrated by magnetic measurements on $Gd_3(TACIH_{-3})_2$ complex that the three Gd centres were uncoupled at 60 K, although the Gd–Gd distance measured in the solid state structure is inferior to 4 Å. Only a weak antiferromagnetic interaction was evidenced at very low temperature 2.3 K [8]

$$\begin{aligned}\delta^{\mathrm{para}}_{i,\mathrm{Ln}} &= \sum_n F^n_i \times \langle S_Z\rangle^n_{\mathrm{Ln}} + \sum_n G^n_i \times D^n_{\mathrm{Ln}} \\ &= F^{\mathrm{global}}_i \times \langle S_Z\rangle_{\mathrm{Ln}} + G^{\mathrm{global}}_i \times D_{\mathrm{Ln}}\end{aligned} \tag{3}$$

$$\frac{\delta^{\mathrm{para}}_{i,\mathrm{Ln}}}{\langle S_Z\rangle_{\mathrm{Ln}}} = F^{\mathrm{global}}_i + G^{\mathrm{global}}_i \times \frac{D_{\mathrm{Ln}}}{\langle S_Z\rangle_{\mathrm{Ln}}} \tag{4}$$

It is generally assumed that $\langle S_Z\rangle_{\mathrm{Ln}}$ and D_{Ln} values are the same for the complexes and the free ion, for which they have been calculated [22,23]. The isostructurality of a complex series can then be checked by Eq. (4) which is a linearised form of Eq. (3) [24]. The samarium complex was not included in the calculation because Sm(III) induces very small paramagnetic shifts. Plots according to Eq. (4) demonstrate that all the complexes from Pr to Yb are isostructural (Fig. 3). Agreement factors AF_i calculated according to literature are 0.18 and 0.19.

3.4. Heteronuclear complexes

Ligand TACI forms isostructural trinuclear complexes with trivalent lanthanide cations all along the 4f series. We were then wondering if, in the presence of a mixture of those ions, some heteronuclear complexes could be obtained in aqueous solution. We examined some samples containing two distinct lanthanide triflates with Ln/Ln′/TACI ratios of 3/3/2 in deuterium oxide for pD=8. Proton NMR spectra at 298 K were very indicative of the solution composition. When lanthanum and neodymium are mixed, only the proton signals belonging to the $[Nd_3L_2H_{-6}]^{3+}$ species are detected in the NMR spectrum. For neodymium–europium mixture, $[Eu_3L_2H_{-6}]^{3+}$ is the major complex, but some traces of heteronuclear species are also seen in the spectrum. For the samarium–europium couple, a completely different behaviour is observed; $[Eu_3L_2H_{-6}]^{3+}$ is no longer the major species. In that case, four complexes are coexisting in aqueous solution, and their proportions could be evaluated by the integrated intensities in the proton NMR spectrum: $[Eu_3L_2H_{-6}]^{3+}$ 20%, $[SmEu_2L_2H_{-6}]^{3+}$ 49%, $[Sm_2EuL_2H_{-6}]^{3+}$ 27% and $[Sm_3L_2H_{-6}]^{3+}$ 4%. Paramagnetic chemical shifts have been assigned by COSY spectroscopy and longitudinal relaxation times measurements (Fig. 4). The study of a similar ytterbium–lutetium mixture gave the same results; the four complexes, $[Lu_3L_2H_{-6}]^{3+}$, $[YbLu_2L_2H_{-6}]^{3+}$, $[Yb_2LuL_2H_{-6}]^{3+}$ and $[Yb_3L_2H_{-6}]^{3+}$ are present in solution.

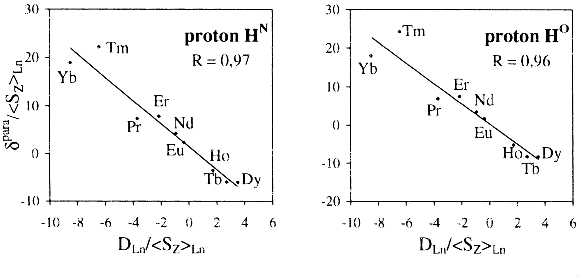

Fig. 3. Plots of $\delta^{\mathrm{para}}_{i,\mathrm{Ln}}/\langle S_Z\rangle_{\mathrm{Ln}}$ vs. $D_{\mathrm{Ln}}/\langle S_Z\rangle_{\mathrm{Ln}}$ for protons H^N and H^O.

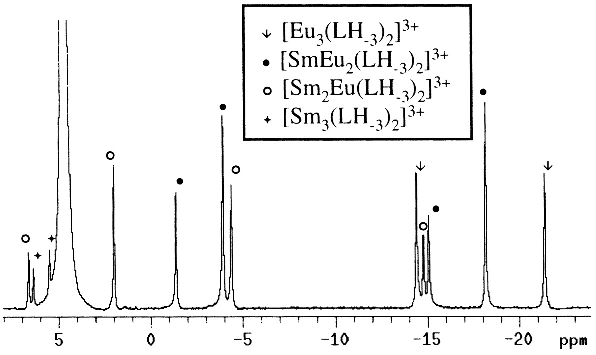

Fig. 4. 400 MHz ^1H NMR spectrum of a 3/3/2 $Sm(OTf)_3/Eu(OTf)_3$/TACI mixture in deuterium oxide at 298 K (pD=8).

4. Conclusion

This work demonstrates that the cyclohexanic ligand TACI forms only trinuclear complexes with all the trivalent lanthanide cations in water solution. These species are isostructural from Pr to Yb and the stability constants are very sensitive to the cation, especially at the beginning of the series. Some triheteronuclear complexes have been characterised when the ligand is mixed with two distinct lanthanide salts. When the difference between the thermodynamic formation constants of the trihomonuclear complexes is high, for example for metals belonging to the beginning of the series, only the most stable trihomonuclear species is formed in solution. For cations having affinities for the ligand of the same order, a great amount of heteronuclear species are obtained in solution. These triheteronuclear complexes are currently under investigation.

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