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Flexible covalent tripods in nonadentate podands: synthesis of tris[3-(6-diethylcarbamoylpyridine-2-carboxamido)propyl]amine and its complexing properties with trivalent lanthanides †

Fabien Renaud,[a] Carole Decurnex,[a] Claude Piguet *[a] and Gérard Hopfgartner[b]

[a] *Department of Inorganic, Analytical and Applied Chemistry, University of Geneva, 30 quai E. Ansermet, CH-1211 Geneva 4, Switzerland. E-mail: Claude.Piguet@chiam.unige.ch*
[b] *F. Hoffmann-La Roche Ltd, Pharmaceuticals Division, PRNS 68/142, CH-4070 Basle, Switzerland*

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The nonadentate podand tris[3-(6-diethylcarbamoylpyridine-2-carboxamido)propyl]amine (L^{14}) is prepared according to a multistep strategy using the flexible tris(3-(*N*-methylamino)propyl)amine (Me-TRPN) covalent tripod. L^{14} exists as a statistical mixture of four conformers in solution whose distribution is slightly affected by protonation of the apical nitrogen atom in $[L^{14} + H]^+$. The pK_a value depends on the length of the spacer separating the apical nitrogen and the appended electron-withdrawing tertiary amide groups, and increases by three orders of magnitude when going from the Me-TREN tripod in $[L^{13} + H]^+$ (ethylene spacer) to Me-TRPN in $[L^{14} + H]^+$ (trimethylene spacer). Reactions of L^{14} and $[L^{14} + H]^+$ with $Ln(ClO_4)_3$ (Ln = La–Lu) produce flexible and poorly stable 1:1 podates $[Ln(L^{14})]^{3+}$ and $[Ln(L^{14} + H)]^{4+}$ in which the terdentate chelating binding units exhibit partial dynamic on–off complexation equilibria. Comparisons of structural and thermodynamic data for $[Ln(L^n)]^{3+}$ (n = 13 or 14) in solution point to a drastic decrease of the molecular organisation of the podand when the constrained Me-TREN tripod is replaced by the elongated Me-TRPN tripod in nine-co-ordinate lanthanide podates, a crucial limiting factor for the design of supramolecular lanthanide complexes with predetermined properties.

Introduction

The recent developments of functional molecular or supramolecular devices based on lanthanide metal ions for light-conversion,[1] magnetic resonance imaging[2] and signaling and labeling technologies[3] require a high degree of structural organisation combined with tunable electronic and magnetic properties. A significant control of the lanthanide co-ordination spheres may be achieved by the wrapping of three semi-rigid symmetrical terdentate binding units to give D_3-symmetrical complexes $[Ln(L^1 - 2H)_3]^{3-}$ and $[Ln(L^n)_3]^{3+}$ (n = 2–5) in which Ln^{III} is nine-co-ordinated in pseudo-tricapped trigonal prismatic sites (Scheme 1).[4] The fine structural tuning of the final molecular architectures results from subtle interstrand interactions,[5] but the simultaneous programming of electronic properties requires the design of unsymmetrical terdentate binding units possessing two different side arms connected to the 2 and 6 positions of the central pyridine ring. The abrupt increase of the absolute emission quantum yields in acetonitrile when going from D_3-symmetrical complexes $[Eu(L^5)_3]^{3+}$ ($\Phi = 8.2 \times 10^{-7}$)[6] and $[Eu(L^2)_3]^{3+}$ ($\Phi = 8.6 \times 10^{-5}$)[4b] to facial C_3-symmetrical building blocks $[Eu(L^6)_3]^{3+}$ ($\Phi = 3.8 \times 10^{-3}$)[7] and $[Eu(L^7 - H)_3]$ ($\Phi = 1.3 \times 10^{-2}$)[8] justifies the design of unsymmetrical terdentate binding units for tuning electronic properties in which the facial arrangement around Ln^{III} is provided by a non-covalent[7,8] or a covalent tripod.[9] Although the latter approach has extensively been used for the facial organisation of three unsymmetrical semi-rigid bidentate binding units around d-block[10] and f-block[11] metal ions, only few attempts have been made to arrange related terdentate units around nine-co-ordinate Ln^{III}. Molecular models suggest that the regular wrapping of three bent semi-rigid terdentate binding units around a spherical ion induces severe structural constraints which are responsible for the only two-co-ordination of potentially terdentate chelating side arms to the same Ln^{III} in $[La(L^8 - 3H)(DMF)_2]$,[12] $[YbLa(L^9 - 3H)(NO_3)_2]^+$[13] and $[Y(L^{10} - 3H)]$.[14] The replacement of the central substituted phenol ring in L^{8-10} by a pyridine ring in L^{11-13} provides stable five-membered chelates upon complexation with large cations such as Ln^{III},[15] thus leading to nine-co-ordinated podates $[Ln(L^{11} - 3H)]$,[16] $[Ln(L^{12})]^{3+}$[17] and $[Ln(L^{13})]^{3+}$.[9] The triazacyclononane, tris(2-aminoethyl)-amine (TREN) and tris(2-(*N*-methylamino)ethyl)amine (Me-TREN) covalent tripods respectively involved in ligands L^{11-13} are rigid enough to organise the tridentate chelating side arms for their facial complexation to Ln^{III}, but are flexible enough to tolerate the helical wrapping and the structural changes associated with the complexation of Ln^{III}. However, the computed pEu values ($[Eu]_t = 10^{-6}$ M and $[L^n]_t = 10^{-5}$ M)[18] for L^{12} (7.6)[17] and for L^{13} (8.0)[9] are significantly smaller than that calculated for the acyclic ligand L^2 (pEu = 12.8)[4b] which points to limited thermodynamic stabilities for the podates $[Ln(L^{12})]^{3+}$ and $[Ln(L^{13})]^{3+}$. This observation suggests that the expected entropic stabilisation of the podates[15] might be balanced by (i) steric constraints within the short TREN tripods of L^{12} and L^{13} and (ii) the irregular wrapping of the co-ordinated terdentate chelating units. The replacement of the ethylene spacers of the Me-TREN tripod in L^{13} by trimethylene units to give the tris-(3-(*N*-methylamino)propyl)amine (Me-TRPN) tripod in L^{14} is expected (i) to increase the degrees of freedom and the flexibility of the podand and (ii) to reduce the steric constraints within the tripod thus favouring a regular wrapping of the binding side arms. However, the considerable flexibility associated with L^{14} will strongly limit crystallisation processes[9] and subsequent investigations in the solid state.

This paper reports the synthesis of L^{14} together with an exploration of the pH-dependent assembly processes leading to the podates $[Ln(L^{14})]^{3+}$ and $[Ln(L^{14}+H)]^{4+}$ in acetonitrile.

† Electronic supplementary information (ESI) available: ESI–MS titration data for L^{14} and $[L^{14} + H]^+$ with $Ln(ClO_4)_3$. See http://www.rsc.org/suppdata/dt/b1/b101118i/

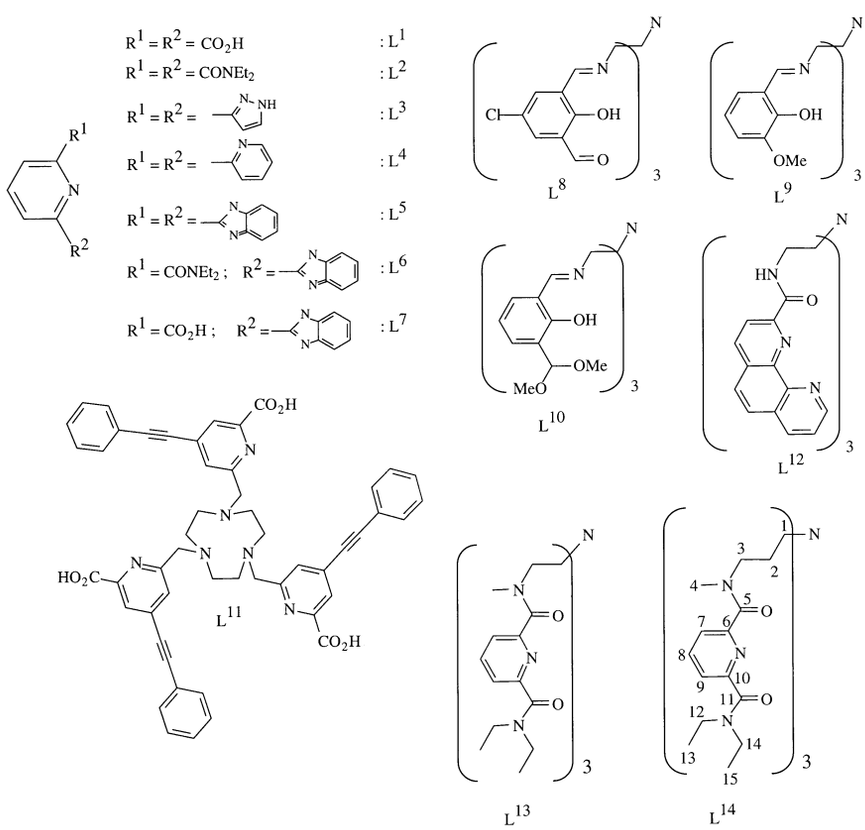
Particular attention has been focused on the thermodynamic and structural consequences of the extension of the spacers within the covalent tripod when going from L^{13} to L^{14}.

Results and discussion

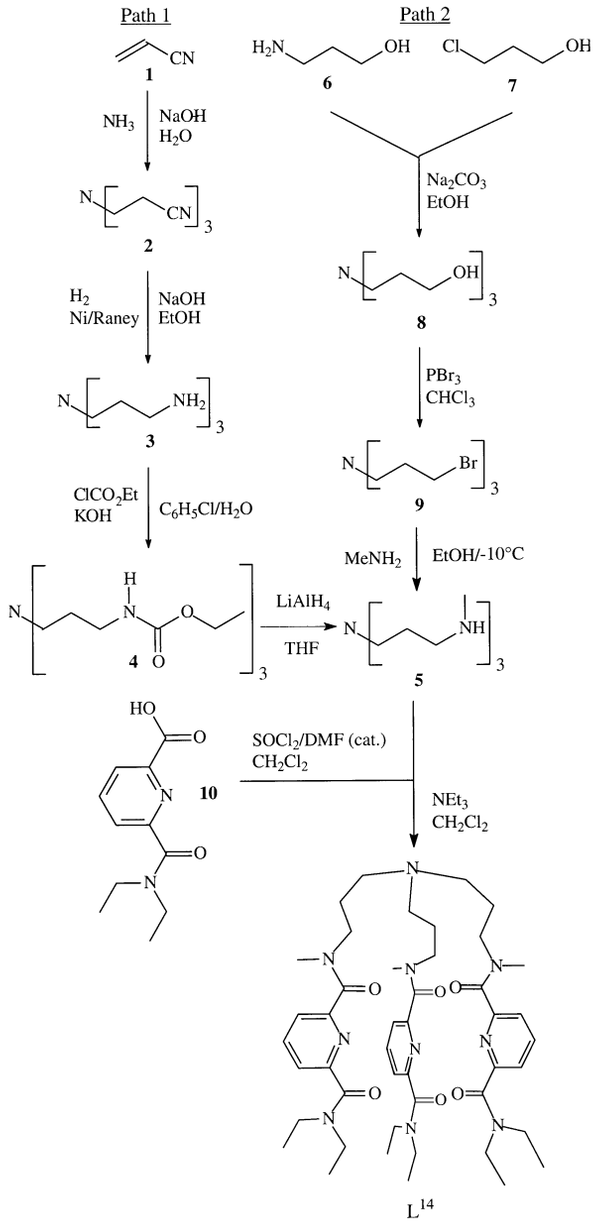
Synthesis and structure of the podand L^{14}

The nonadentate podand tris[3-(6-diethylcarbamoylpyridine-2-carboxamido)propyl]amine (L^{14}) is prepared according to the multistep strategy shown in Scheme 2. In order to limit the quenching of luminescent Ln^{III} (Ln = Eu or Tb) by high-frequency N–H oscillators in the final lanthanide podates,[19] three secondary amines have been introduced into the target covalent tripod Me-TRPN **5** which are then transformed into tertiary amide connectors in L^{14}. In our original strategy (path 1, Scheme 2), acrylonitrile **1** reacts with ammonia (stepwise Michael additions) to give the synthon **2** which is reduced by catalytic hydrogenation into the tetramine **3**. Although the two-step acylation/reductive cleavage procedure leading to the selective trialkylation of TREN to give Me-TREN is straightforward,[9,20] we encounter major difficulties for adapting this synthetic strategy for the extended TRPN **3** ⟶ Me-TRPN **5**. Contrary to TREN, TRPN is poorly soluble in benzene and intricate mixtures of polyacylated compounds are obtained upon reaction of **3** with ethyl chloroformate under standard conditions (benzene/water).[9,20] The selective monoacylation of each side arm requires the replacement of benzene with chlorobenzene together with strict sub-stoichiometric conditions which afford the triacylated compound **4** in moderate yield (49%). The subsequent reduction with $LiAlH_4$ produces **5** (yield: 65%). The purification of the poorly volatile tetramines **3** and **5** requires ultra-high vacuum distillations on small scale samples in order to limit polymerisation and we thus use 'crude' products with 86% (**3**) and 90% (**5**) purity (checked by NMR) for large scale syntheses. In order to overcome these limitations, an alternative strategy (path 2, Scheme 2) uses nucleophilic displacement of **7** by **6** to give the tripod **8** in good yield (85%). Halogenation with PBr_3 produces the expected tris-halide **9** (yield: 85%), and nucleophilic displacement with an excess of methylamine at low temperature gives the crude tetramine **5** (86% purity, yield: 75%). Reaction with an excess (4.0 equivalents) of the acyl chloride[9] of **10** eventually provides L^{14} in moderate yield (48%).

As a result of hindered rotations about the C–N bonds of the three unsymmetrical tertiary amide connectors in L^{14}, we expect the formation of a mixture of four conformers which are dynamically inert on the NMR timescale at room temperature.[9] According to IUPAC nomenclature, a *cis* orientation of the methyl group C^4 with respect to the oxygen atom of the adjacent carbonyl group corresponds to an *E* conformation when we formally consider a double bond between the nitrogen and the C^5 atom of the amide group. A *trans* orientation is thus related to a *Z* conformation and L^{14} exists as four conformers *EEE*, *EEZ*, *EZZ* and *ZZZ*. Each C_{3v}-symmetrical conformer (*EEE* and *ZZZ*) amounts to 12.5% of the statistical distribution and the protons of the C^4 methyl group provide one singlet in the ^1H NMR spectrum. The C_s-symmetrical *EEZ* and *EZZ* conformers complete the statistical distribution (37.5% each) and the protons of the C^4 methyl group provide two sets of two singlets (1:2 ratio). We therefore expect a total of six singlets in the ^1H NMR spectrum of L^{14} with ratios of 1 (*EEE*) : 1(*ZZZ*):1:2 (*EEZ*) and 1:2 (*EZZ*). Such a pattern is indeed observed at δ 2.95, 2.90, 2.86, 2.83, 278 and 2.74 in an approximate 1:2:1:1:2:1 intensity ratio (Fig. 1a) leading to the conclusion that no specific stereoelectronic intramolecular constraints occur for L^{14} in solution. The remaining part of the ^1H NMR spectrum is very complicated since we expect 24 triplets, 12 quartets and 6 quintets in the aliphatic domain (δ 1.0–3.6) and 12 doublets and 6 triplets in the aromatic range (δ 7.4–8.0). No detailed interpretation of these signals is accessible at 300–600 MHz. Finally, as the protons of the C^4 methyl group do not exhibit Nuclear Overhauser Effects (NOEs) with H^7, no reliable assignment of the singlets depicted in Fig. 1a to specific conformers is accessible.[9]



Scheme 1



Scheme 2

Heating a solution of L^{14} in CD_3CN at the highest accessible temperature (343 K) severely broadens the ^1H NMR resonances, but coalescence of the singlets is only observed at 353 K in d^6-DMSO leading to a dynamically averaged C_{3v}-symmetrical structure. A detailed analysis of the coalescence process shows that all possible interconversions *EEE*↔*ZZZ*↔*EEZ*↔*EZZ* occur within a small temperature range (348–353 K in d^6-DMSO) which leads to a rough energy barrier $\Delta G^{\neq} = 70(4)$ kJ mol^{-1} according to the simplified Eyring equation[21] $\Delta G^{\neq} = 19.14T_c(9.97 + \log(T_c/\delta\nu))$ (J mol^{-1}) in which T_c and $\delta\nu$ stand respectively for the coalescence temperature and the frequency difference between the exchangeable singlets of the methyl groups in the blocked conformation. Fig. 2 summarises the stereochemical course of the exchange process for L^{14} which closely matches that reported for L^{13}.[9] The minor stabilization of *EEZ* (*EZZ*) with respect to *EEE* (*ZZZ*) ($\Delta = 2.7$ kJ mol^{-1}) has a pure entropic origin and no enthalpic effect arising from a specific arrangement of the side arms has been detected.

The addition of trifluoromethanesulfonic acid (CF_3SO_3H = TfOH, 1.0 eqivalent) slightly affects the chemical shifts of the protons in $[L^{14} + H]^+$, but the six signals of the C^4 methyl groups are still observed consistent with the existence of a

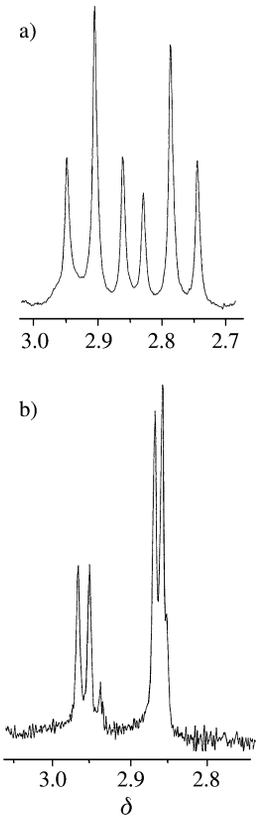


Fig. 1 Part of the 300 MHz ^1H NMR spectra of (a) L^{14} and (b) $[L^{14} + H]^+$ in CD_3CN (298 K).

mixture of the four conformers in the ratio 15% *ZZZ*, 45% *ZZE*, 35% *EEZ* and 5% *EEE* (Fig. 1b). As there is no means to differentiate the conformers within the *ZZZ*/*EEE* and *ZZE*/*EZZ* pairs by NMR spectroscopy, the proportion of conformers within each pair can be interconverted. Protonation of L^{14} induces only a minor change in the distribution of the four conformers which strongly contrasts with the exclusive formation of *ZZZ* and *EZZ* in $[L^{13} + H]^+$ which had been assigned to the formation of trifurcated (*ZZZ*) and bifurcated (*EZZ*) hydrogen bonds between the apical protonated nitrogen atom and the oxygen atoms of the carboxamide units belonging to the side arms displaying *Z* configuration.[9] The increased separation of the apical nitrogen atom in the Me-TRPN tripod prevents the formation of efficient intramolecular hydrogen bonds in $[L^{14} + H]^+$ and leads to a distribution close to the statistics. Potentiometric titrations of L^{14} (1 mM) by TfOH (50 mM) in acetonitrile–water mixtures demonstrate the fixation of a single proton in the pH range 8.0–2.0 with $pK_a([L^{14} + H]^+) = 7.43(2)$ (water–CH_3CN = 95:5, 0.1 M $NaClO_4$) and 7.3(1) (water–CH_3CN = 5:95, 0.1 M NBu_4ClO_4). Compared to $[L^{13} + H]^+$ under the same conditions ($pK_a = 4.66(2)$ and 4.3(2)),[9] the basicity of the apical nitrogen is increased by three orders of magnitude in line with the reduced hyperconjugation involving the carboxamide units when ethylene spacers (L^{13}) are replaced with trimethylene spacers (L^{14}).[22] Simple calculations[23] show that the tertiary amides in $[L^{13} + H]^+$ are strong electron-withdrawing substituents comparable with the nitro group ($pK_a([HN(CH_2CH_2NO_2)_3]^+) = 4.66$, Taft σ^* constant = 0.5).[23] The introduction of an extra methylene group in $[L^{14} + H]^+$ reduces the accepting properties of the tertiary carboxamide units to $\sigma^* = 0.22$ which still corresponds to respectable electron-withdrawing substituents.[23]

We conclude that the replacement of the Me-TREN tripod in L^{13} by the elongated Me-TRPN tripod in L^{14} increases the basicity of the apical nitrogen atom and prevents the formation of strong intramolecular hydrogen bonds in $[L^{14} + H]^+$. This strongly contrasts with the intramolecular trifurcated

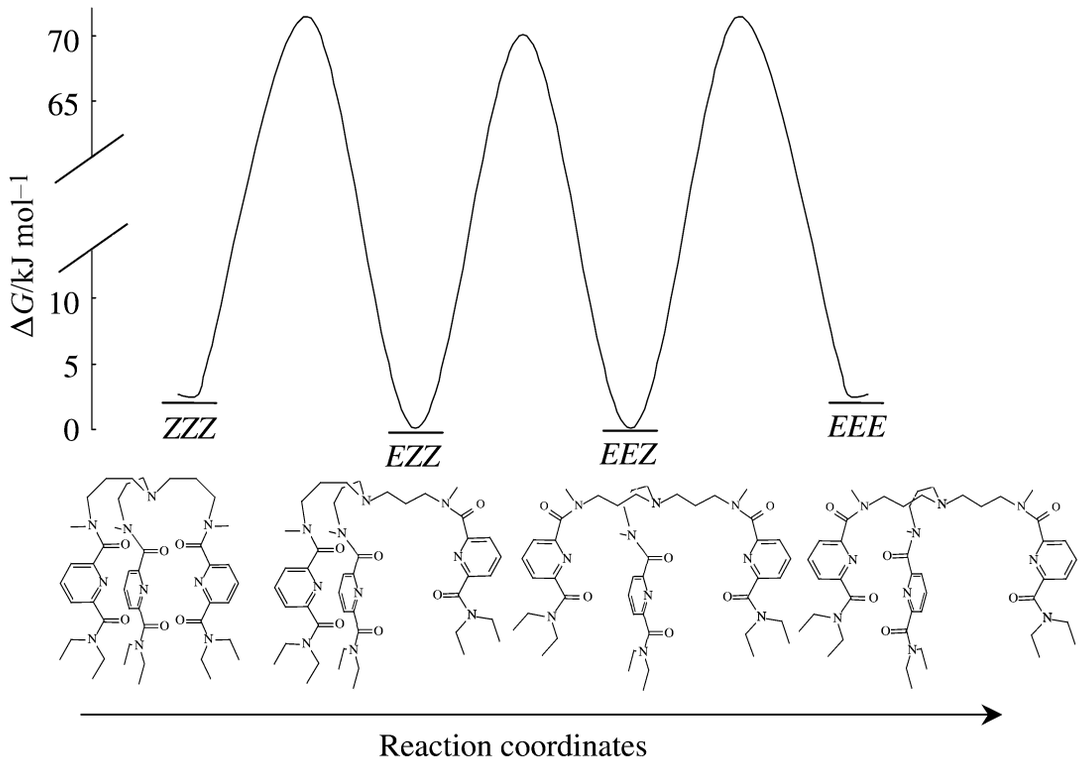


Fig. 2 Potential energy diagram for the intramolecular conversion between the four conformers (*EEE*, *EEZ*, *EZZ* and *ZZZ*) of L^{14} in solution.

hydrogen bonds which preorganise $[L^{13} + H]^+$ in a clipped conformation.[9]

Synthesis and characterisation of the podates $[Ln(L^{14})]^{3+}$ and $[Ln(L^{14} + H)]^{4+}$ (Ln = La–Lu or Y)

Qualitative speciation is obtained by using ESI-MS titrations, while quantitative investigations rely on spectrophotometric titrations leading to thermodynamic stability constants. The structure of the complexes in solution results from NMR studies under specific external conditions (temperature, stoichiometries, concentration) which ensure the quantitative (> 95%) formation of the desired complex in solution. This three-step process has previously and successfully been applied to the characterisation of lanthanide-containing polymetallic helicates[24] and podates[9] in solution.

ESI-MS titrations. Titrations of L^{14} (2×10^{-4} M, CH_3CN) with $Ln(ClO_4)_3 \cdot xH_2O$ (Ln = La, Sm, Lu or Y; x = 6–8) in the range L^{14}:Ln = 0.1–1.0:1 show exclusive formation of the podates $[Ln(L^{14})]^{3+}$ together with their gas-phase adducts[24,25] with perchlorate counter anions $[Ln(L^{14})(ClO_4)_i]^{(3-i)+}$ (i = 1 or 2; Table S1 in the ESI supporting information). Traces of protonated podates $[Ln(L^{14} + H)]^{4+}$ also detected under these conditions, are removed upon the addition of an excess of podand L^{14} consistent with complete deprotonation in excess of base. For a ratio L^{14}:Ln = 2.0:1, we observe detectable amounts of 1:2 complexes $[Ln(L^{14})_2]^{3+}$ in the gas phase along the complete lanthanide series, which contrasts with the exclusive detection of related complexes $[Ln(L^{13})_2]^{3+}$ for large Ln^{III} (Ln = La–Pr).[9] The addition of 1.0 equivalent of TfOH per L^{14} to give $[L^{14} + H]^+$ has three consequences on the ESI-MS titrations with Ln^{III}: (i) the intensity ratio of the peaks corresponding to $[Ln(L^{14} + H)]^{4+}$:$[Ln(L^{14})]^{3+}$ dramatically increases as a result of protonation of the apical nitrogen atom of the tripod, (ii) adducts with trifluoromethanesulfonate anions complicate the ESI-MS spectra (Table S1) and (iii) electrostatic repulsion between $[Ln(L^{14} + H)]^{4+}$ and $[L^{14} + H]^+$ precludes the formation of 1:2 complexes $[Ln(L^{14} + H)_2]^{5+}$ in the gas phase, even in large excess of protonated ligand.[9]

Table 1 Cumulative thermodynamic formation constants $\log(\beta_{ijk}^{Ln})^a$ for the podates $[Ln_i(L^{14})_j(H)_k]^{(3+k)+}$ in acetonitrile and acetonitrile–water (95: 5, v/v) at 298 K

Metal	Ionic radius[b]/Å	Solvent	$\log(\beta_{110}^{Ln})$	$\log(\beta_{111}^{Ln})$
La^{III}	1.216	CH_3CN	6.4(2)	6.4(2)
		CH_3CN–water	4.1(2)	4.3(2)
Sm^{III}	1.132	CH_3CN	6.6(2)	6.3(2)
		CH_3CN–water	5.1(2)	5.4(2)
Y^{III}	1.075	CH_3CN	7.1(3)	6.5(2)
		CH_3CN–water	4.9(2)	5.1(2)
Er^{III}	1.062	CH_3CN	6.9(2)	n.d.[c]
Yb^{III}	1.042	CH_3CN	6.8(2)	n.d.[c]
Lu^{III}	1.032	CH_3CN	6.5(2)	6.8(3)
		CH_3CN–water	5.6(2)	5.6(2)

[a] i represents the number of metal ions, j the number of ligands and k the number of additional protons in the final podate. [b] Effective ionic radius for nine-co-ordinate Ln^{III}.[38] [c] Not determined.

Although gas-phase speciations do not strictly correspond to speciations in solutions,[24,25] the ESI-MS results point to simple models including $[Ln(L^{14})_i]^{4+}$ (i = 1 or 2) and $[Ln(L^{14} + H)]^{4+}$ as good candidates for rationalising solution species.

Spectrophotometric titrations. Titrations of L^{14} (10^{-4} M, CH_3CN) with $Ln(ClO_4)_3 \cdot xH_2O$ (Ln = La, Sm, Er, Yb Lu or Y; x = 6–8) in the range L^{14}:Ln = 0.1–2.5:1 show a single sharp end-point for L^{14}:Ln = 1.0:1 consistent with the formation of the podates $[Ln(L^{14})]^{3+}$ (Fig. 3a,b). Factor analysis[26] indicates the existence of only two absorbing species and the data can be fitted with equilibrium (1) and thermodynamic stability constants $\log(\beta_{110}^{Ln})$ collected in Table 1. Attempts to fit the spectrophotometric data with equilibria (1) and (2) led to divergence for all Ln^{III} and required the use of constraints on $\log(\beta_{110}^{Ln})$ to

$$Ln^{3+} + L^{14} \rightleftharpoons [Ln(L^{14})]^{3+} \quad \log(\beta_{110}^{Ln}) \qquad (1)$$

$$Ln^{3+} + 2\,L^{14} \rightleftharpoons [Ln(L^{14})_2]^{3+} \quad \log(\beta_{120}^{Ln}) \qquad (2)$$

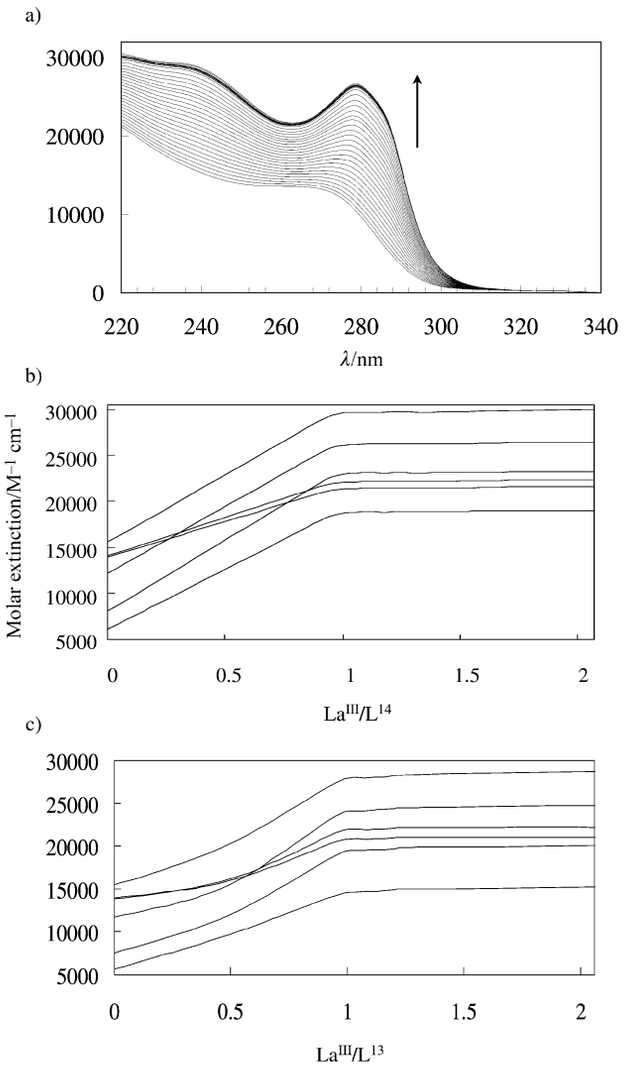


Fig. 3 Variations of (a) UV absorption spectra and (b) molar absorptions at 6 different wavelengths for the spectrophotometric titrations of L^{14} (10^{-4} M) with $La(ClO_4)_3$ in acetonitrile at 298 K. (c) Variation of molar absorptions at 6 different wavelengths for the spectrophotometric titrations of L^{13} (10^{-4} M) with $La(ClO_4)_3$ in acetonitrile at 293 K (adapted from ref. 9).

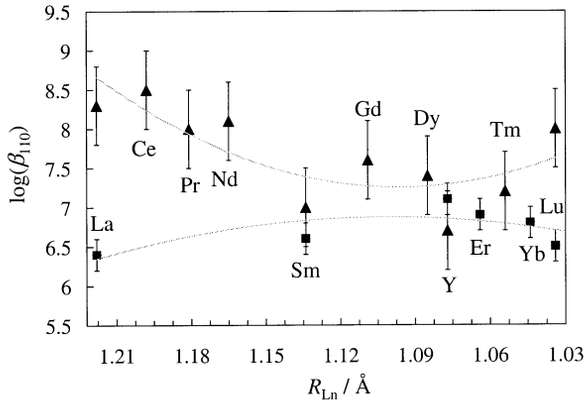


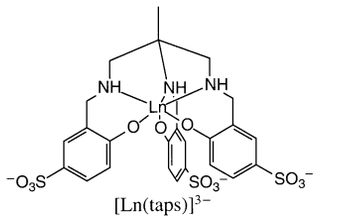
Fig. 4 Thermodynamic formation constants $\log(\beta_{110}^{Ln})$ for $[Ln(L^{13})]^{3+}$ (▲)[9] and $[Ln(L^{14})]^{3+}$ (■) *vs.* the ionic radii of nine-co-ordinate Ln^{III} (R_{Ln})[42] in acetonitrile at 298 K. Standard deviations for each data point are represented by vertical lines. The dotted trendlines are only guides for the eyes.

restore convergence which strongly suggests that $[Ln(L^{14})_2]^{3+}$ is not formed in significant amount in solution under these conditions. This is supported by the calculated UV spectra of $[Ln(L^{14})_2]^{3+}$ which correspond to linear combinations of those of L^{14} and $[Ln(L^{14})]^{3+}$ and by the calculated amounts of $[Ln(L^{14})_2]^{3+}$ which never exceed 10% of the ligand speciation during the titration. Moreover, a careful consideration of the spectrophotometric data previously obtained for L^{13} with La^{III} under the same conditions (Fig. 3c)[9] demonstrates that the 1:2 complex $[La(L^{13})_2]^{3+}$ possesses a characteristic UV spectrum which affects the evolution of the molar absorption in the range $La:L^{13} = 0.1–1.0:1$, a behaviour which is not observed for the related podand L^{14} (Fig. 3b). We thus conclude that $[Ln(L^{14})_2]^{3+}$ are not formed in significant amount during the spectrophotometric titrations and equilibrium (1) holds for a reliable quantitative speciation in solution. The small amounts of $[Ln(L^{14})_2]^{3+}$ detected by ESI-MS can tentatively be assigned to gas-phase processes and/or to specific relative cationisation efficiencies[27] which favour the detection of traces of 1:2 complexes.[28]

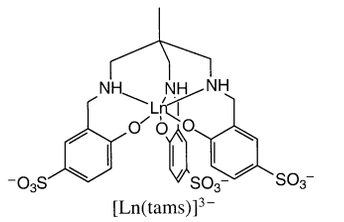
$\log(\beta_{110}^{Ln})$ for $[Ln(L^{14})]^{3+}$ slightly vary along the lanthanide series and are 1–2 orders of magnitude smaller than those reported for $[Ln(L^{13})]^{3+}$ under the same conditions (Fig. 4). No straightforward correlation with the ionic radii of the metal ions can be deduced and, in order to compare the efficiency of the podands L^{13} and L^{14} for complexing Ln^{III}, we have resorted to the calculation of pLn values (= $-\log[Ln]$ with $[Ln]_t = 10^{-6}$ M and $[Ligand]_t = 10^{-5}$ M).[18] We obtain $pSm(L^{13}) = 8.0$,[9] $pSm(L^{14}) = 7.6$, and $pSm(L^2) = 12.5$ [4b] for the medium-size samarium complexes taken as a reference. The large decrease of pSm when going from L^2 to L^{13} has tentatively been ascribed to steric constraints in the compact Me-TREN tripod which force the apical nitrogen atom to adopt the *endo* conformation in $[Ln(L^{13})]^{3+}$,[9] but the further reduction of pSm with L^{14} rules out this hypothesis and suggests that the regular wrapping of the tridentate binding units around Ln^{III} is affected by the tripods in both podates $[Ln(L^n)]^{3+}$ ($n = 13$ or 14). Moreover, the significant stability decrease observed when going from L^{13} to L^{14} can be traced back to unfavourable entropic and enthalpic contributions associated with 14-membered chelate rings involving the Me-TRPN tripod in $[Ln(L^{14})]^{3+}$ compared with only 12-membered chelate rings in $[Ln(L^{13})]^{3+}$.[15] Related stereochemical effects affecting the binding mode and the stability of lanthanide podates have been investigated by Orvig and co-workers[29] who demonstrated that Ln^{III} was encapsulated by podands possessing short and rigid tripods to give $[Ln(taps)]^{3-}$ and $[Ln(tams)]^{3-}$, while the more flexible TREN spacer in H_6trns prevented regular wrapping of the chelating side arms around Ln^{III}, thus leading to monocapped $[Ln(H_3trns)(H_2O)_x]$ and bicapped $[Ln(H_3trns)_2]^{3-}$ podates (Scheme 3). The formation of 16-membered chelate rings in the latter complexes was stabilised by the formation of a network of hydrogen bonds involving the protonated nitrogen atoms of the tripod.[29] The systematic observation of a 1:2 complex for lanthanide podates including a TREN tripod ($[Ln(H_3trns)_2]^{3-}$,[29] $[Ln(L^{12})_2]^{3+}$ [17] and $[Ln(L^{13})_2]^{3+}$)[9] strongly suggests that Ln^{III} is not efficiently protected by the wrapped podand in the 1:1 podates and remains accessible for further complexation, a behaviour which is removed when the more flexible Me-TRPN tripod is used in L^{14}.

The addition of 5% water in acetonitrile (vol./vol.) reduces $\log(\beta_{110}^{Ln})$ for $[Ln(L^{14})]^{3+}$ by one to two orders of magnitude and restores the well established enthalpy-driven electrostatic effect (*i.e.* a monotonous increase of $\log(\beta_{110}^{Ln})$ with decreasing ionic radii, Table 1)[30] as previously discussed for $[Ln(L^{13})]^{3+}$.[9] Finally, spectrophotometric titrations of the protonated podand $[L^{14} + H]^+$ (10^{-4} M) with $Ln(ClO_4)_3 \cdot xH_2O$ (Ln = La, Sm Lu or Y; $x = 6–8$) in acetonitrile or acetonitrile–water (95:5) can satisfactorily be fitted with equilibrium (3) to give $\log(\beta_{111}^{Ln})$ collected in Table 1.

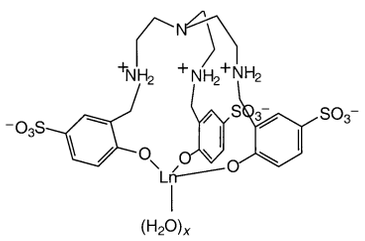
$$Ln^{3+} + [L^{14} + H]^+ \rightleftharpoons [Ln(L^{14} + H)]^{4+} \quad \log(\beta_{111}^{Ln}) \quad (3)$$



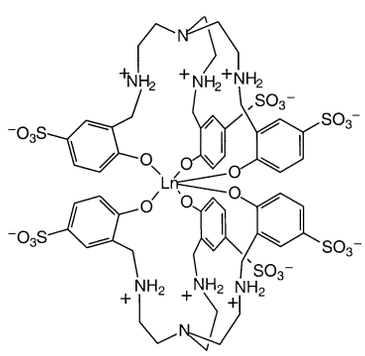
$[Ln(taps)]^{3-}$



$[Ln(tams)]^{3-}$



$[Ln(H_3trns)(H_2O)_x]$



$[Ln(H_3trns)_2]^{3-}$

Scheme 3

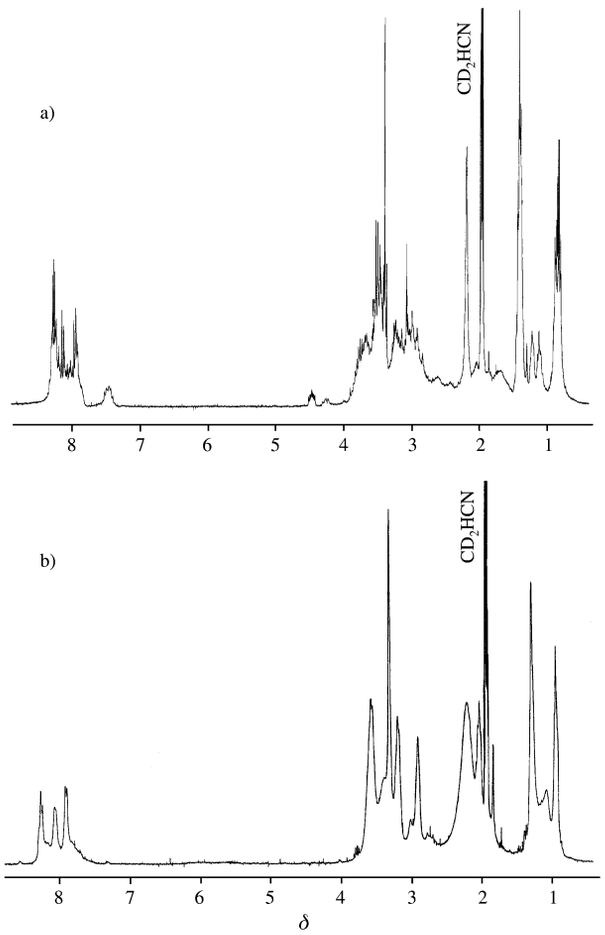


Fig. 5 ^{1}H NMR spectra of (a) $[Y(L^{14})]^{3+}$ at 298 K and (b) $[La(L^{14})]^{3+}$ at 343 K in CD_3CN.

$\log(\beta_{111}^{Ln})$ are close to $\log(\beta_{110}^{Ln})$ found for the non-protonated podand which indicates that protonation of the remote apical nitrogen atom of the Me-TRPN tripod has negligible influence on the complexation of Ln^{III} by the tridentate chelating side arms in $[Ln(L^{14})]^{3+}$. As $\log(\beta_{111}^{Ln}) = \log(\beta_{110}^{Ln}) + pK_a[Ln(L^{14} + H)]^{4+} - pK_a[L^{14} + H]^+$,[9] we deduce that $pK_a[Ln(L^{14} + H)]^{4+} \approx pK_a[L^{14} + H]^+ = 7.4(1)$ which can be compared to $pK_a[Ln(L^{13} + H)]^{4+} \approx pK_a[L^{13} + H]^+ - 0.8$.[9] We thus conclude that the electrostatic repulsion between the co-ordinated Ln^{3+} and the protonated apical nitrogen atom of the Me-TREN tripod in $[Ln(L^{13} + H)]^{4+}$ which is responsible for the increased acidity of the podate, is removed by the extension of the spacer in the Me-TRPN tripod of $[Ln(L^{14} + H)]^{4+}$.

^{1}H NMR titrations. The addition of 1.0 equivalent of $Ln(ClO_4)_3 \cdot xH_2O$ (Ln = La, Sm, Lu or Y; x = 6–8) to a 17.5 mM solution of L^{14} in CD_3CN produces quantitatively (> 98% of the ligand speciation) the podate $[Ln(L^{14})]^{3+}$ according to $\log(\beta_{110}^{Ln})$ reported in Table 1. The very complicated ^{1}H NMR spectra of $[Ln(L^{14})]^{3+}$ (Ln = Sm, Lu or Y) at 298 K correspond to intricate mixtures of dynamically inert conformers on the NMR timescale (Fig. 5). This strongly contrasts with the simple ^{1}H NMR spectra previously reported for $[Ln(L^{12})]^{3+}$ and $[Ln(L^{13})]^{3+}$ corresponding to rigid nine-co-ordinated C_3-symmetrical podates in solution.[9,17] Although the resolution and the complexity of the ^{1}H NMR signals of $[Ln(L^{14})]^{3+}$ escape a detailed analysis even at 600 MHz, careful consideration of the δ 0.5–1.5 domain allows some valuable discussions. According to the analogous podates $[Ln(L^{13})]^{3+}$ (Ln = Sm, Lu or Y), only two triplets originating from the methyl groups H^{13} and H^{15} are observed in the δ 0.5–1.5 range. Moreover, the H^{13} and H^{15} signals occur at δ 1.10–1.20 for L^{13} and are split into two separated triplets at δ 0.55 (H^{15}) and 1.35 (H^{13}) for $[Ln(L^{13})]^{3+}$ (Ln = Sm, Lu or Y).[9] A closely related trend is observed for H^{13} and H^{15} in L^{14} which display a mixture of triplets in the range δ 1.02–1.22 (corresponding to the mixture of *EEE*, *EEZ*, *EZZ* and *ZZZ* conformers). Co-ordination to the metal in $[Ln(L^{14})]^{3+}$ (Ln = Sm, Lu or Y) splits this signal into two intense motives of interpenetrated triplets at δ 0.6–0.8 (H^{15}) and at 1.3–1.4 (H^{13}) (Fig. 5a). Interestingly, two weaker signals reminiscent of H^{13} and H^{15} in the free ligand are observed in the ^{1}H NMR spectra of $[Ln(L^{14})]^{3+}$ at δ 1.02–1.22 (Fig. 5a), thus implying partial decomplexation of the terminal carboxamide units and/or of the side arms in the final podates. Integration of the two sets of signal observed for H^{13} and H^{15} at δ 1.02–1.22 (unco-ordinated side arms) and 0.6–0.8 and 1.3–1.4 (co-ordinated side arms) gives a rough estimation of the ratios of co-ordinated *vs.* unco-ordinated side arms which amount to 3:1 for Ln = Sm, Lu and Y. Increasing the temperature up to 343 K slightly broadens the ^{1}H NMR signals, but coalescence is not observed.

Since the lability of the side arms is expected to increase with increasing ionic radii,[9] we have recorded the ^{1}H NMR spectrum of $[La(L^{14})]^{3+}$ at 298 K which is similar to those described for Ln = Sm, Lu and Y except for significantly broadened signals. Coalescence almost occurs at 343 K leading a dynamically averaged C_{3v} symmetry for $[La(L^{14})]^{3+}$ on the NMR timescale

assigned to a fast exchange between co-ordinated and partially co-ordinated side arms (Fig. 5b).[31] This behaviour reminds one of similar dynamic on–off equilibria characterised by NMR for terminal side arms co-ordinated to Ln^{III} in monometallic triple helical complexes $[Ln(L^4)_3]^{3+}$,[32] [tris(diethyl pyridine-2,6-dicarboxylate)lanthanum(III)]$^{3+}$ [33] and [tris(oxydiacetato)-lanthanum(III)].[34] In the latter case[34] the chemical exchange rate increases with the increasing size of Ln^{III} and complexes with the smaller lanthanides (Ln = Dy–Lu) provide separated ^{1}H NMR signals for free and co-ordinated side arms at room temperature as similarly observed for $[Ln(L^{14})]^{3+}$. For ester side arms in [tris(diethyl pyridine-2,6-dicarboxylate)lutetium(III)]$^{3+}$ the exchange rate is faster and resolution only occurs below 253 K.[33] However, on–off equilibria of carboxamide side arms on the NMR timescale has no precedent in $[Ln(L^2)_3]^{3+}$ [4b] or $[Ln(L^{13})]^{3+}$,[9] thus pointing to specific steric constraints induced by the Me-TRPN tripod in $[Ln(L^{14})]^{3+}$ which prevent a regular helical wrapping of the side arms compatible with their strong co-ordination to Ln^{III}.

The addition of an excess of ligand to 17.5 mM solutions of $[Ln(L^{14})]^{3+}$ induces variable changes in the ^{1}H NMR spectra according to the size of Ln^{III}. For the small Ln^{III} (Ln = Sm, Lu or Y) the observation of separated signals corresponding to L^{14} and $[Ln(L^{14})]^{3+}$ at 298 K points (i) to slow chemical exchange between bound and "free" ligand on the NMR timescale and (ii) to the absence of 1:2 complexes in solution. For Ln = La we observe a broadening of the original spectrum at 298 K which resolves into two sets of signals corresponding to L^{14} and $[La(L^{14})]^{3+}$ at 243 K. A similar larger kinetic lability for large Ln^{III} has previously been noticed for $[Ln(L^{13})]^{3+}$ under the same conditions.[9] Finally, the protonation of $[Ln(L^{14})]^{3+}$ to give $[Ln(L^{14} + H)]^{4+}$ has minor effects on the ^{1}H NMR spectra except for some downfield shifts of the multiplets corresponding to $H^{1,1'}$ and $H^{2,2'}$ which lie close to the protonated apical nitrogen atom of the tripod. No extra rigidification or specific intramolecular organisation of the backbone is detected upon protonation of the remote apical nitrogen atom.

Conclusion

The replacement of ethylene spacers in the Me-TREN tripod of L^{13} by trimethylene units to give the elongated Me-TRPN tripod in L^{14} has only minor effects on the solution structure of the free podands. The only remarkable differences concern (i) the increasing basicity of the apical nitrogen atom (three orders of magnitude) when going from L^{13} to L^{14} and (ii) the absence of intramolecular hydrogen bonding within the tripod in $[L^{14} + H]^+$ which can be assigned to the larger separation between the tertiary amide connectors and the protonated nitrogen atom. Complexation with Ln^{III} provides 1:1 podates $[Ln(L^n)]^{3+}$ (n = 13 or 14) in acetonitrile, but 1:2 complexes are restricted to L^{13} with large Ln^{III} because the increased flexibility of L^{14} is not compatible with the efficient co-ordination of a second podand to $[Ln(L^{14})]^{3+}$. The reduced thermodynamic stability of $[Ln(L^{14})]^{3+}$ compared with $[Ln(L^{13})]^{3+}$ also results from specific steric constraints within the tripod which prevent a regular helical wrapping of the chelating strands around Ln^{III} in solution. This statement is supported by our NMR investigations which establish that the terdentate side arms of L^{14} act as hemi-labile ligands displaying on–off equilibria leading to blocked conformations on the NMR timescale at room temperature.[31] A detailed quantitative analysis of the distribution of the different conformers occurring in solution for $[Ln(L^{14})]^{3+}$ is precluded by the complexity of the ^{1}H NMR spectra since on–off equilibria of the side arms produce intricate mixtures of podates possessing variable denticities and symmetries lower than C_3. Protonation of the remote apical nitrogen atom of the Me-TRPN tripod has negligible effects on the organisation of the podates and any attempts to isolate $[Ln(L^{14})]X_3$ or $[Ln(L^{14} + H)]X_4$ (X = Cl^-, ClO_4^-, PF_6^-, $CF_3SO_3^-$ or NO_3^-) in the solid state only give non-crystalline gelatinous materials. We eventually conclude that the minimal rigidity compatible with the facial organisation of three helically wrapped terdentate pyridine-2,6-dicarboxylate derivatives around Ln^{III} is restricted to three links (CH_2 units, O or N atoms) between the carbon atom of the co-ordinated carbonyl group and the apical atom of the tripod as found in L^{12} and L^{13}. Larger separations can only be envisaged if additional structural constraints and organisation are provided by rigid aromatic groups as found in non-covalent d–f podates in which the co-ordinated imine group and the apical atom of the tripod are separated by eight carbon atoms.[35]

Experimental

Solvents and starting materials

These were purchased from Fluka AG (Buchs, Switzerland), Aldrich or Merck and used without further purification unless otherwise stated. Dichloromethane, acetonitrile, *N,N*-dimethylformamide and chloroform were distilled from CaH_2, THF from sodium. Silica gel (Merck 60, 0.040–0.060 mm) was used for preparative column chromatography. The synthon 6-*N,N*-diethylcarbamoylpyridine-2-carboxylic acid **10** was prepared according to a literature procedure.[7] The syntheses of the intermediate compounds **2**[36] and **8**[37] were reported for crude products, but further purifications were required for our multistep strategy. The perchlorate salts $Ln(ClO_4)_3 \cdot nH_2O$ (Ln = La to Lu) were prepared from the corresponding oxides (Rhodia, 99.99%) and dried according to published procedures.[38] The lanthanide content of solid salts was determined by complexometric titrations with Titriplex III (Merck) in the presence of urotropine and xylene orange.[39]

CAUTION: dry perchlorates may explode and should be handled in small quantities and with the necessary precautions.[40]

Preparation

Tris(2-cyanoethyl)amine 2. Acrylonitrile **1** (56.6 cm^3, 2.39 mol) and ammonia (25%, 37.5 cm^3, 0.53 mol) were dissolved in water (175 cm^3), stirred at room temperature for 1 hour. A second crop of acrylonitrile (50 cm^3, 2.13 mol) was added and the resulting mixture refluxed for 6 h. A third crop (50 cm^3, 2.13 mol) was then added and the mixture further refluxed for 17 h. Water and excess of acrylonitrile were distilled and the residue was dissolved in dichloromethane (200 cm^3). The organic phase was washed with aq. NaOH (2.5 M, 20 cm^3), dried with Na_2SO_4 and evaporated to dryness. The intermediate bis(2-cyanoethyl)amine was separated by distillation (160 °C, 0.04 Torr) and the residue triturated with ethanol in an ultrasonic bath. The resulting clear solution was cooled at −20 °C for 12 h to give 39.6 g (0.23 mol, yield 43%) of tris(2-cyanoethyl)amine **2** as white crystals. mp = 48–49 °C. ^{1}H NMR in $CDCl_3$: δ 2.53 (6 H, t, ^3J = 7), 2.99 (6 H, t, ^3J = 7 Hz). ^{13}C NMR in $CDCl_3$: δ 17.73, 49.95 (secondary C), 118.32 (quaternary C). EI-MS (70 eV): *m*/*z* 176 (M^+).

Tris(3-aminopropyl)amine 3. Tris(2-cyanoethyl)amine **2** (4 g, 22.7 mmol) and Raney nickel (2.2 g, Fluka no. 72240, 38.6 mmol) were dissolved in ethanol (83 cm^3) containing NaOH (2.33 g, 58.3 mmol). The resulting mixture was heated at 45 °C in an autoclave under hydrogen pressure (500 psi) for 6 days. Raney nickel was filtered off, the solvent evaporated and the residue extracted with dichloromethane (2 × 100 cm^3). The combined organic phase was dried with NaOH, filtered over aluminium oxide (activity III) and evaporated to dryness to give 2.94 g (15.6 mmol, crude yield 69%) of tris(3-aminopropyl)amine **3** as a pale yellow oil with an estimated purity of 86%. ^{1}H NMR in $CDCl_3$: δ 1.54 (6 H, quint, ^3J = 7.0), 2.40 (6 H, t, ^3J = 7), 2.68 (6 H, t, ^3J = 7 Hz). ^{13}C NMR in $CDCl_3$:

δ 31.15, 40.93, 52.07 (secondary C). EI-MS (70 eV): *m*/*z* 188 (M^+).

Tris[3-(ethoxycarbonylamino)propyl]amine 4. Tris(3-aminopropyl)amine **3** (1.25 g, 86% purity, 5.7 mmol) was dissolved in chlorobenzene–water (12 cm^3/5 cm^3). Ethyl chloroformate (0.63 cm^3, 5.7 mmol) was added dropwise and then KOH (6 M, 1.25 cm^3). After 1 h stirring at room temperature, the organic phase was separated, ethyl chloroformate (0.19 cm^3, 1.7 mmol), KOH (6 M, 0.38 cm^3) and fresh chlorobenzene (8 cm^3) were added to the aqueous phase. This procedure was successively repeated six times. The final aqueous phase was extracted with chloroform (50 cm^3) and the combined organic phases were dried (Na_2SO_4), evaporated to dryness and the crude product purified by column chromatography (silica gel; CH_2Cl_2–MeOH 96:4 ⟶ 90:10) to give 1.13 g (2.8 mmol, yield 49%) of **4** as a white powder. ^{1}H NMR in $CDCl_3$: δ 1.2 (9 H, t, $^3J = 7$), 1.61 (6 H, quint, $^3J = 7$), 2.4 (6 H, t, $^3J = 7$), 3.18 (6 H, q, $^3J = 7$), 4.06 (6 H, q, $^3J = 7$ Hz). ^{13}C NMR in $CDCl_3$: δ 14.86 (primary C), 27.12, 39.72, 51.95, 60.87 (secondary C), 160.0 (tertiary C). EI-MS (70 eV): *m*/*z* 404 (M^+).

Tris(3-hydroxypropyl)amine 8. 3-Amino-1-propanol **6** (10 cm^3, 131.6 mmol), 3-chloro-1-propanol **7** (25.3 cm^3, 302.6 mmol) and sodium carbonate (33.5 g, 316 mmol) were dissolved in absolute ethanol (75 cm^3) and refluxed for 24 h. Chloroform (100 cm^3) was added to the cooled solution which was filtered and the solvent evaporated to dryness. The crude yellow oil was distilled under vacuum to give a first fraction of bis(3-hydroxypropyl)amine (8.23 g, 110–115 °C/0.02 Torr) followed by 16.31 g (85.4 mmol, yield 85%) of tris(3-hydroxypropyl)amine **8** (155–170 °C/0.02 Torr) as a colorless liquid. ^{1}H NMR in $CDCl_3$: δ 1.73 (6 H, quint, $^3J = 7$), 2.59 (6 H, t, $^3J = 7$), 3.70 (6 H, t, $^3J = 7$ Hz), 4.60 (3 H, s, broad). ^{13}C NMR in $CDCl_3$: δ 28.98, 52.32, 61.95 (secondary C). EI-MS (70 eV): *m*/*z* 191 (M^+).

Tris(3-bromopropyl)amine 9. Tris(3-hydroxypropyl)amine **8** (500 mg, 2.6 mmol) and phosphorus tribromide (1.32 cm^3, 13.1 mmol) in dry chloroform (50 cm^3) were refluxed for 8 h. Excess of phosphorus tribromide was destroyed with ethanol (10 cm^3), the solvents were distilled and the residue was dissolved in dichloromethane (50 cm^3). The organic phase was washed with half-sat. aq. Na_2CO_3 (50 cm^3), the solvent evaporated to dryness and the crude solid recrystallised in ethyl acetate to give 850 mg (2.2 mmol, yield 85%) of tris(3-bromopropyl)amine **9** as white crystals. mp 82 °C. ^{1}H NMR in $CDCl_3$: δ 2.51 (12 H, m), 3.49 (6 H, t, $^3J = 7$ Hz). ^{13}C NMR in $CDCl_3$: δ 26.38, 29.48, 52.68 (secondary C). EI-MS (70 eV): *m*/*z* 379/377 (M^+).

Tris[3-(*N*-methylamino)propyl]amine 5. *Method a.* Compound **4** (937 mg, 2.3 mmol) in dry THF (4 cm^3) was added dropwise to a suspension of $LiAlH_4$ (0.5 g, 12.7 mmol) in THF (12 cm^3). The resulting mixture was heated at 50 °C for 24 h, and stirred at room temperature for two days. Excess of $LiAlH_4$ was hydrolysed with aqueous KOH (3 M, 6 cm^3) and the white gel was separated by centrifugation. The clear filtrate was evaporated to dryness to give 343 mg (1.49 mmol, crude yield 65%) of tris(3-methylaminopropyl)amine **5** as a pale yellow oil with an estimated purity of 90%.

Method b. Tris(3-bromopropyl)amine **9** (500 mg, 1.32 mmol) in absolute ethanol (6 cm^3) was added dropwise to 35 cm^3 of methylamine (33% in ethanol, 285 mmol) at −10 °C. The resulting mixture was stirred for two hours at −10 °C and 6 days at room temperature. The solution was dried (NaOH), diluted with dichloromethane (20 cm^3), filtered over aluminium oxide (activity III) and evaporated to dryness to give 263 mg (1.14 mmol, crude yield 87%) of **5** with an estimated purity of 86%. ^{1}H NMR in $CDCl_3$: δ 1.59 (6 H, quint, $^3J = 7$), 2.37 (9 H, s), 2.40 (6 H, t, $^3J = 7$), 2.53 (6 H, t, $^3J = 7$ Hz). ^{13}C NMR in $CDCl_3$: δ 27.46 (primary C), 36.72, 50.88, 52.56 (secondary C). EI-MS (70 eV): *m*/*z* 230 (M^+).

Tris[3-(6-diethylcarbamoylpyridine-2-carboxamide)propyl]-amine (L^{14}). A solution of 6-(*N,N*-diethylcarbamoyl)pyridine-2-carboxylic acid **10** (1.3 g, 6.0 mmol), thionyl chloride (6.6 cm^3, 90 mol) and *N,N*-dimethylformamide (50 µl) in dry dichloromethane (70 cm^3) was refluxed for 1 h. The resulting mixture was evaporated to dryness, coevaporated twice with dichloromethane (2 × 20 cm^3) and dried under vacuum. The residual pale yellow powder was dissolved in dichloromethane (50 cm^3) and tris[3-(*N*-methylamino)propyl]amine **5** (343 mg, 90% purity, 1.34 mmol) and triethylamine (4.2 cm^3, 30 mmol) in dichloromethane (15 cm^3) were added dropwise under an inert atmosphere. The mixture was refluxed for 45 min, evaporated to dryness and partitioned between dichloromethane (100 cm^3) and half-sat. aq. NH_4Cl (100 cm^3). The aqueous phase was extracted with dichloromethane (3 × 50 cm^3) and the combined organic fractions were dried (Na_2SO_4), evaporated to dryness and the crude product was purified by column chromatography (silica gel; CH_2Cl_2–MeOH 94:6 ⟶ 93:7) to give 585 mg (0.64 mmol, yield 48%) of $L^{14}\cdot 1.5CH_3OH\cdot H_2O$ as a pale yellow oil. ^{1}H NMR in CD_3CN: δ 1.02–1.22 (18 H, m), 1.4–1.9 (6 H, m), 1.95–2.6 (6 H, m), 2.8–3.1 (9 H, m), 3.14–3.30 (9 H, m), 3.4–3.6 (9 H, m), 7.47–7.53 (6 H, m), 7.85–8.00 (3 H, m). ^{1}H NMR in d^6-DMSO (413 K): δ 1.08 (18 H, t, $^3J = 7$), 1.60 (6 H, m), 2.29 (6 H, m), 2.90 (9 H, s), 3.34 (18 H, m), 7.48–7.50 (6 H, m), 7.92 (3 H, t, $^3J = 8$ Hz). ESI-MS (CH_2Cl_2 + 0.1% HCO_2H): *m*/*z* 843.7 ($[L^{14} + H]^+$). Calc. for $C_{45}H_{66}N_{10}O_6\cdot 1.5CH_3OH\cdot H_2O$: C, 61.44; N, 15.40; H, 8.20. Found: C, 61.4; N, 15.3; H, 8.0%.

Physical measurements

^{1}H and ^{13}C NMR spectra were recorded at 25 °C on a Broadband Varian Gemini 300 spectrometer. Chemical shifts are given in ppm with respect to TMS. EI-MS (70 eV) spectra were recorded with VG-7000E and Finnigan-4000 instruments. Pneumatically assisted electrospray (ES-MS) mass spectra were recorded from acetonitrile solutions on API III or API 3000 tandem mass spectrometers (PE Sciex) by infusion at 4–10 µl min^{-1}. The spectra were recorded under low up-front declustering or collision induced dissociation (CID) conditions, typically $\Delta V = 0$–30 V between the orifice and the first quadrupole of the spectrometer. Electronic spectra in the UV-visible range were recorded at 298 K from 10^{-3} M acetonitrile solutions with Perkin-Elmer Lambda 5 and 900 spectrometers using quartz cells of 0.1 and 1 cm path length. Spectrophotometric titrations were performed with a Perkin-Elmer Lambda 5 spectrometer connected to an external computer. In a typical experiment, 50 cm^3 of ligand L^{14} (10^{-4} M) in acetonitrile were titrated at 298 K with a solution of $Ln(ClO_4)_3\cdot xH_2O$ (10^{-3} M) in acetonitrile. After each addition of 0.2 cm^3 the absorption spectra were recorded using a 1 cm quartz cell and transferred to the computer. Plots of absorbance as a function of the metal:ligand ratio gave a first indication of the number and stoichiometry of the complexes formed; factor analysis[26] was then applied to the data to confirm the number of different absorbing species and finally a model for the distribution of species was fitted with a non-linear least-squares algorithm to give stability constants using the SPECFIT program.[41] Potentiometric titrations were performed under an inert atmosphere in a thermostatted titration vessel (298 K) equipped with a pH electrode Metrohm 6.0202.000 connected to a pH meter Metrohm 691. In a typical experiment, 50 cm^3 of ligand L^{14} (10^{-3} M) in acetonitrile–water (95:5) containing NBu_4ClO_4 (0.1 M) or acetonitrile–water (5:95) containing $NaClO_4$ (0.1 M) were titrated with a solution of trifluoromethanesulfonic acid 0.05 M in the same solvent. After each addition of 0.05 cm^3 the pH was recorded and transferred to a computer. A model for the distribution of species was fitted with a non-linear least-squares algorithm to give

acid–base constants. Elemental analyses were performed by Dr H. Eder from the Microchemical Laboratory of the University of Geneva.

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