

Lanthanide Chelates Based on Diethylenetriamine Fitted with *O*-Benzoic Acid Pendant Arms

Daniel Imbert,^[a] Nicolas Fatin-Rouge,^[a] and Jean-Claude G. Bünzli*^[a]

Keywords: Carboxylate ligands / Lanthanides / Luminescence / Podand / Stability constant

A new polycarboxylate ligand H_5L has been synthesized by the attachment of five benzoate subunits onto a diethylenetriamine framework. Seven pK_a values have been determined by potentiometry, spectrophotometry and NMR spectroscopy as 1.9(2), 2.8(2), 3.87(5), 4.58(6), 4.87(6), 9.19(6) and 11.68(5), the first four corresponding to the carboxylic functions and the last three to amine sites. The interaction between H_5L and Ln^{III} ions in dilute aqueous solution has been examined by UV/Vis absorption and emission spectrometries, and has been found to result in monometallic complexes that are moderately stable in the pH range 3.7–7.5. Conditional stability constants at pH 5.3 are $\log K_{11} = 5.3(2)$, $6.6(1)$, $6.5(1)$ and $7.2(3)$ for La, Eu, Tb and Lu, respectively. In the case of Tb^{III} , the stability constants for $[Tb(HL)]^-$ and $[Tb(H_2L)]$ are

$\log \beta_{111} = 22.0(2)$ and $\log \beta_{121} = 29.8(1)$, giving a pTb of 10.0. In the pH range 4–7, more than 90% of the Tb^{III} ions are in the form of the neutral species $[Tb(H_2L)]$. Lifetime determinations of the $Eu(^5D_0)$ and $Tb(^5D_4)$ excited levels in both H_2O and D_2O at pH 5.3 indicate 4.8 ± 0.5 (Eu) and 4.5 ± 0.5 (Tb) water molecules being bound in the inner coordination sphere of the Ln^{III} . The triplet state of the ligand in water lies at around 26000 cm^{-1} , resulting in a sizeable sensitisation of the Tb-centred luminescence (absolute quantum yield: $\phi_{abs} = 10.3\%$), while the luminescence of Eu^{III} is only poorly sensitised ($\phi_{abs} = 1.5\%$).

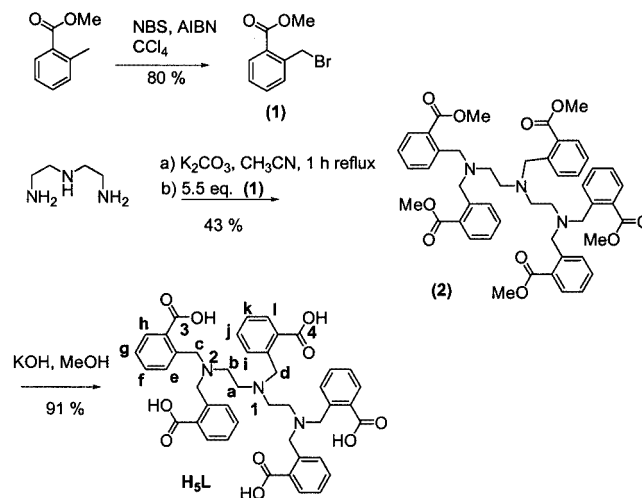
(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2003)

Introduction

Stable chelates of trivalent lanthanide ions are of interest as contrast enhancement agents in magnetic resonance imaging,^[1] as catalysts for the cleavage of phosphodiester bonds in DNA and RNA,^[2] as precursors for various functional materials,^[3] including doped polymers for optical amplifiers,^[4] or as luminescent probes for biomedical analysis,^[5–7] for responsive analytical sensors^[8] or for imaging of cancerous cells.^[9] The main difficulty associated with the design of luminescent probes and sensors lies in overcoming the very low molar absorption coefficients of the Ln^{III} ions, due to the forbidden nature of the f-f transitions. To sensitise the metal ion efficiently, there are specific requirements for ligand molecules i.e. that they should be strong complexation agents, have large absorption coefficients and offer a series of photophysical properties allowing efficient energy transfer from the ligand onto the metal ion and minimization of quenching processes.^[5]

Several synthetic strategies intended to meet all these requirements have been examined,^[3] including the use of pre-

organised (macrocyclic)^[10] or predisposed receptors,^[11,12] leading to induced cavities; these receptors can also be obtained by self-assembly processes^[13] or by the use of flexible podands.^[14] These latter are readily available, cheap and are easy to derivatize. In this paper we attempt to combine the stability of Ln^{III} complexes with ligands derived from polyaminocarboxylates, such as $dtpa$,^[15] with the large



Scheme 1

^[a] Swiss Federal Institute of Technology Lausanne, Institute of Molecular and Biological Chemistry
1015 Lausanne, Switzerland
Fax: (internat.) +41-21/693-9825
E-mail: jean-claude.bunzli@epfl.ch

Supporting information for this article is available on the WWW under <http://www.eurjic.org> or from the author.

sensitisation of Tb^{III} ion luminescence (and also other Ln^{III} ions) achieved by incorporation of the benzoate chromophore,^[5,16] absolute quantum yields of 100 and 20% having been reported for Tb^{III} and Eu^{III}, respectively, in the solid state.^[17] We have therefore synthesized the polydentate ligand H₅L [1,4,7-heptanetriamine-*N,N,N',N',N''*-pentakis-(2-methylbenzoic acid), Scheme 1] and investigated its complexation and sensitisation properties towards trivalent lanthanide ions.

Results and Discussion

Acidity Constants of the Ligand

The ligand H₅L was prepared in three steps (Scheme 1) in an overall yield of 31%. Its acidity constants were determined separately by potentiometry (Figure 1) and spectrophotometry (Figure 2) and further confirmed by ¹H NMR spectroscopy. The extracted p*K_a* values, defined by the following equations and obtained by titration in the 2–12 pH range, are summarized in Table 1.

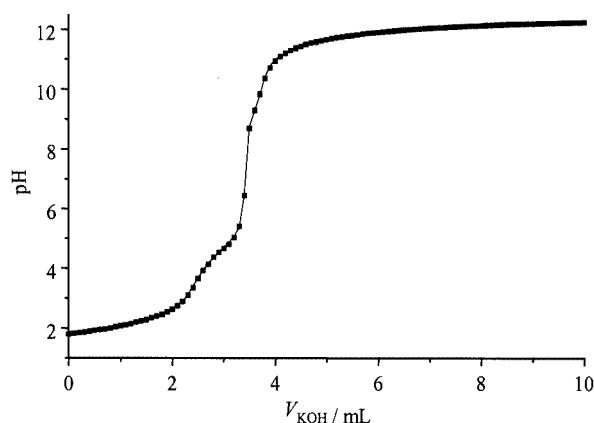


Figure 1. Potentiometric titration of H₇L²⁺ with OH[−] in H₂O/CH₃OH (98:2 v/v); *T* = 20.0 ± 0.2 °C; μ = 0.1 M (KCl)

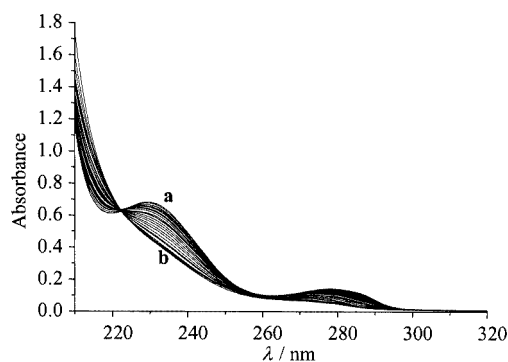
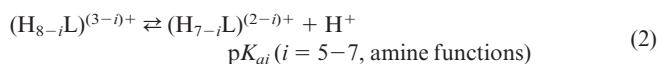
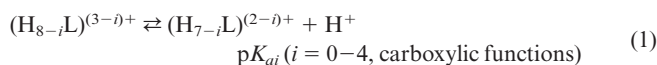


Figure 2. UV/Visible absorption spectra of H₇L²⁺ as a function of pH in H₂O/CH₃OH (98:2 v/v); *T* = 20.0 ± 0.2 °C; μ = 1 M (KCl): curve a (pH = 1.37), curve b (pH = 12.04)

Table 1. Acidity constants of H₇L²⁺ (± σ) and dtpa (see text for the definition of *K_{ai}*)

	L ^[a]	L ^[b]	L ^[c]	dtpa ^[d]
p <i>K_{a1}</i>	—	1.9(2)	1.7(4)	1.45
p <i>K_{a2}</i>	—	2.8(2)	2.9(3)	1.75
p <i>K_{a1}</i> + p <i>K_{a2}</i>	4.20(8)	4.7(4)	4.6(7)	3.20
p <i>K_{a3}</i>	3.87(5)	—	—	2.06
p <i>K_{a4}</i>	4.58(6)	4.5(2)	4.7(1)	2.73
p <i>K_{a5}</i>	4.87(6)	—	—	4.28
p <i>K_{a6}</i>	9.19(6)	9.4(3)	9.0(4)	8.65
p <i>K_{a7}</i>	11.68(5)	11.6(3)	11.6(4)	10.59

^[a] Potentiometric data. [L]₀ = 1.0·10^{−3} M; *I* = 0.1 M (KCl); *T* = 20.0 °C. ^[b] Spectrophotometric data. [L]₀ = 2.0·10^{−5} M; *I* = 1 M (KCl); *T* = 20.0 °C. ^[c] ¹H NMR spectroscopic data. [L]₀ = 1.0·10^{−3} M; *T* = 20 °C. ^[d] ¹H NMR spectroscopic data. *I* = 0.1 M (KNO₃); *T* = 25.0 °C.^[34]



The agreement between the values from various experimental techniques is quite good, and the dissociation constants display behaviour similar to that reported for dtpa: five p*K_a* values are in the 2 to 5 range while the last two are between 9 and 12. A fit of the data with eight p*K_a* values did not converge, indicating that p*K_{a0}*, corresponding to the deprotonation of a carboxylic group (see below, NMR spectra), probably lies below pH 2. However, the protolytic groups of H₅L are less acidic than those of dtpa. The first is only slightly less acidic (Δlog*K_a* = 0.35), but the difference increases up to Δlog*K_a* = 1.9 for p*K_{a4}*. The electron-donor ability of the benzene moieties and the larger number of bonds separating the nitrogen atoms from the carboxylate groups explain this trend.

¹H NMR spectra were measured from pH 12.2 to 1.1 in D₂O/CD₃OD (95:5) solutions (Figure 3), and the resonances were attributed on the basis of their chemical shifts, signal intensities and ¹H-¹H COSY experiments. In the aromatic region, because of superimposed signals, only the protons labelled (i) and (h) could be unambiguously assigned. The eight protons labelled (c) and the two protons labelled (d) appear to be equivalent, pointing to an averaged structure of the molecule on the NMR timescale. The (a) and (b) protons are nonequivalent and appear as two broad peaks because of spin coupling and conformational motions.

The variation of the chemical shifts with pH is shown at the bottom of Figure 3. At pH 12.2, corresponding to a solution containing mainly the totally deprotonated ligand L^{5−}, the resonances for the (c) and (d) protons have very similar chemical shifts, and this is also true for protons (a) and (b). A decrease in the pH to 10.4 by the addition of one equivalent of acid causes only slight variations in the

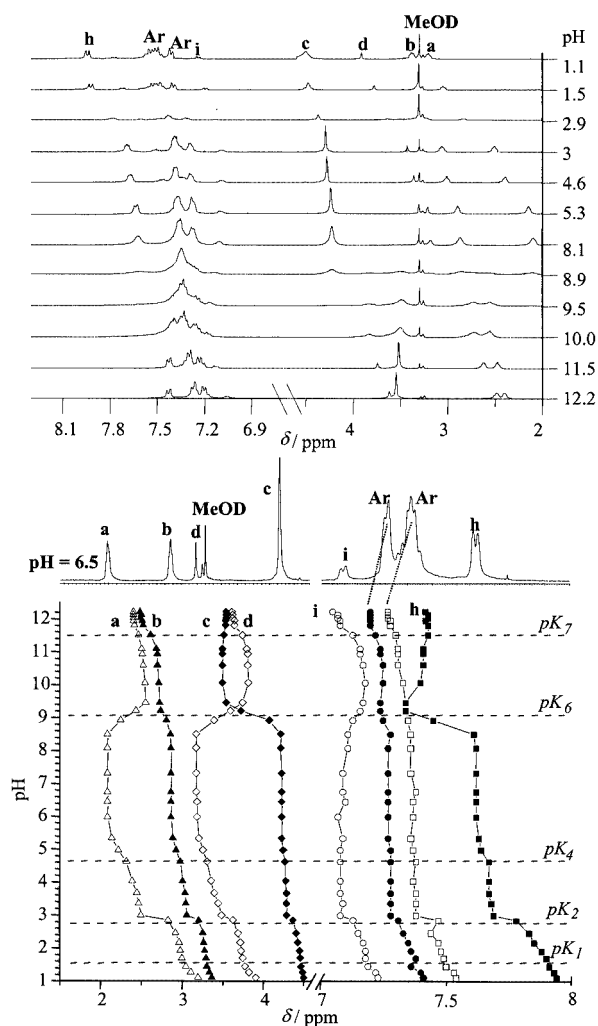


Figure 3. (Top) ^1H NMR spectra of $\text{H}_n\text{L}^{(5-n)-}$ vs. pH in $\text{D}_2\text{O}/\text{CD}_3\text{OD}$ (95:5 v/v) at $T = 20^\circ\text{C}$, and (bottom) variation of the ^1H NMR chemical shifts vs. pH

shifts of the methylene protons, which become more shielded, except for protons (d), which become deshielded. Similarly, the aromatic protons undergo small positive shifts, except for protons (h), which become deshielded. Further addition of acid again results in relatively small changes until around pH 9, except that the shift tendency inverts for protons (d) and (i), which become more shielded. In the pH range 9 to 3, dramatic changes occur for the methylene protons and for protons (h); in particular, the resonances of protons (a) and (b) on one hand and (c) and (d) on the other become clearly separated. After a discontinuity at pH 3, all the protons, particularly protons (h), become more shielded upon further addition of acid.

The observed shift of the methylene protons is in fact an average value reflecting the mean time that each proton spends in a given chemical environment.^[18] Quantitative analysis of the pH dependence of these chemical shifts can therefore be performed by assuming that the contributions to the shift of a given proton i (δ_i) are additive and linearly related to the fraction of time spent in each environment.

As a result, the preferred protonation sites and the extent of protonation can be estimated from a simple model taking into account only the two closest protonation sites, where f is the fractional population of a given protonation site, C is the chemical shift increment caused by the presence of the proton in this site, and the indices α and β refer to the position of the protonated nitrogen atom relative to the resonant proton.

$$\delta_a = \delta_a^0 + f_1 \times C_{N\alpha} + f_2 \times C_{N\beta} \quad (3)$$

$$\delta_b = \delta_b^0 + f_2 \times C_{N\alpha} + f_1 \times C_{N\beta} \quad (4)$$

$$\delta_c = \delta_c^0 + f_2 \times C_{N\alpha} + f_3 \times C_{O3} \quad (5)$$

$$\delta_d = \delta_d^0 + f_1 \times C_{N\alpha} + f_4 \times C_{O4} \quad (6)$$

We have set C_{O3} , C_{O4} , C_O to be equal. The δ_i^0 values were taken as equal to the chemical shifts measured at pH 12.2. Finally, the f_i values were normalised by the following relationship, where n is the number of equivalents of acid added to the fully deprotonated ligand L^{5-} .

$$f_1 + 2f_2 + 4f_3 + f_4 = n \quad (7)$$

Values of f_1 , f_2 and $C_{N\alpha}$, $C_{N\beta}$ were obtained only for $n = 1$ and 2, because the data become too imprecise beyond this amount of acid. For $n = 0-2$, f_3 and f_4 were set as equal to zero, which is a reasonable assumption. The best results for $n = 1$ were obtained at pH $1/2(\text{p}K_{a6} + \text{p}K_{a7})$, and Equations (3), (4), (6) and (7) give $f_1 = 0.22$, $f_2 = 0.39$, $C_{N\alpha} = 0.59$ ppm and $C_{N\beta} = 0.05$ ppm. Generally speaking, the C values have large error margins because of the fairly small chemical shift changes. The calculated $C_{N\alpha}$ value is in good agreement with literature data for dtpa (0.75), but the value found for $C_{N\beta}$ is much lower than the reported value of about 0.35 ppm.^[18] At pH $1/2(\text{p}K_{a4} + \text{p}K_{a3})$, different values of n were again tested and $n = 2$ gave the best result, with Equations (3)–(5) and Equation (7) yielding $f_1 = 0.38$, $f_2 = 0.81$, $C_{N\alpha} = 0.82$ ppm, and $C_{N\beta} = 0.77$ ppm. These calculations offer evidence of the drastic change in the charge repartition on the three nitrogen atoms on going from $n = 1$ to $n = 2$, consistent with the data for dtpa.^[18] At $n = 2$, for instance, the protons are mainly bound to the end nitrogen atoms N2, as a result of electrostatic repulsion. Further attempts to determine quantitatively the extent of protonation of the benzoate groups with pH failed. Nevertheless, the similar values of the three largest $\text{p}K_a$ values for dtpa and for H_5L point to the protonation of L^{5-} occurring first on the three nitrogen atoms. However, distribution diagrams show that protonation of the benzoate sites starts while full protonation of the central nitrogen atom is not yet complete.

Interaction with Trivalent Lanthanide Ions

The interaction between Ln^{III} ions ($\text{Ln} = \text{La}, \text{Eu}, \text{Tb}, \text{Lu}$) and H_5L was first monitored in dilute aqueous solu-

tions by UV/Vis spectrophotometry at pH 5.3. The variation of the absorbance versus $R = [\text{Ln}^{\text{III}}]_{\text{tot}}/[\text{H}_5\text{L}]_{\text{tot}}$ (Figure 3) points to the presence of a single 1:1 complex species in the stoichiometry range investigated ($0 < R < 5$). This is in agreement with the ESI-MS spectra. The conditional stability constants extracted from these data amount to $\log K_{11} = 5.3(2)$, $6.6(1)$, $6.5(1)$ and $7.2(3)$, respectively (Figure S1, Supporting Information, see also the footnote on the first page of this article). The linear relationship between the magnitude of the binding constants and the charge density of the cation is a clear indication that there is no steric effect in the coordination of the metal ions. To determine the influence of the pH on the speciation, we titrated the ligand in the presence of one equivalent of Tb^{III} and monitored the experiment both by spectrophotometry (Figure 4) and by luminescence spectroscopy (Figure 5). Potentiometry could not be used because of precipitation of the metal complexes at concentrations greater than 10^{-3} M. The best model used to fit the titration data was fairly complex, with ten different $[\text{Ln}_i(\text{OH})_j\text{H}_k\text{L}_l]^{(3i-j+k-5l)+}$ species: one hydroxide moiety ($i = 1; j = 3; k = l = 0$), six protonated forms of the ligand ($i = j = 0$) determined independently from the potentiometric titration described above, and two protonated 1:1 complexes ($i = 1, j = 0, k = 1$ and $2, l = 1$). The absorption maxima of the different species are given in Table 2. The two proton-dependent stability constants refined amount to $\log \beta_{111} = 22.0(2)$ [Equation (8)] and $\log \beta_{121} = 29.8(1)$ [Equation (9)].

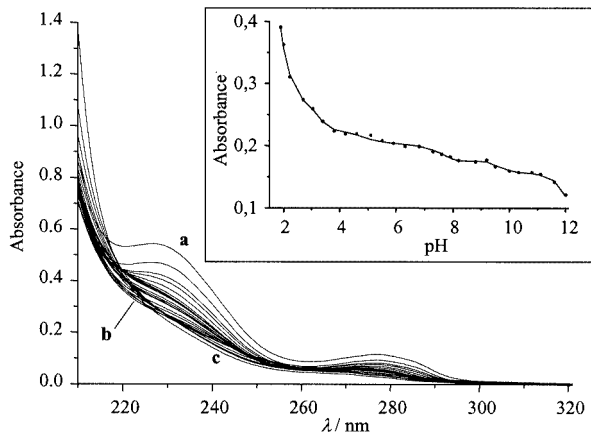


Figure 4. UV/Visible absorption spectra of $\text{H}_7\text{L}^{2+} \cdot 2 \cdot 10^{-5}$ M in $\text{H}_2\text{O}/\text{CH}_3\text{OH}$ (98:2 v/v), $\mu = 0.1$ M (KCl) in the presence of one equivalent of Tb^{III} , at $T = 20.0 \pm 0.2$ °C at various pH; curve a, b, and c: pH = 1.92, 9.22, and 12.0; the inset shows the absorbance variation at 240 nm



The calculated distribution curves from these stability constants are presented in Figure 6. In the pH range 3.5–7.5, the neutral species $[\text{Tb}(\text{H}_2\text{L})]$ is clearly dominant,

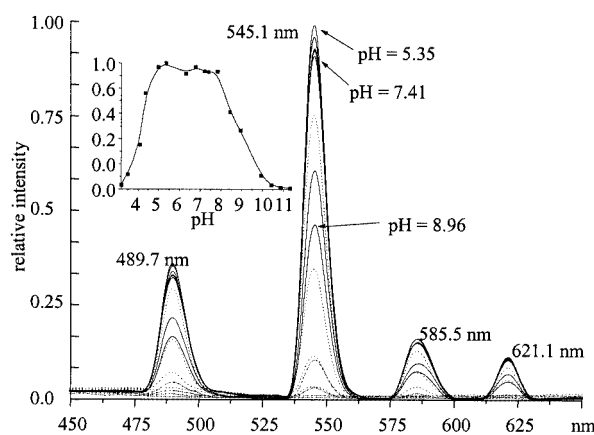


Figure 5. Emission spectra of $\text{H}_7\text{L}^{2+} \cdot 2 \cdot 10^{-5}$ M in $\text{H}_2\text{O}/\text{CH}_3\text{OH}$ (98:2 v/v), $\mu = 0.1$ M (KCl) in the presence of one equivalent of Tb^{III} , at $T = 20.0 \pm 0.2$ °C as a function of pH; inset: phosphorescence intensity at 545 nm vs. pH

Table 2. Absorption maxima of the ligand species at $T = 20$ °C

Species	λ_{max} (nm) ^[a]	ϵ_{max} ($\text{M}^{-1} \cdot \text{cm}^{-1}$) ^[b]	Species	λ_{max} (nm) ^[a]	ϵ_{max} ($\text{M}^{-1} \cdot \text{cm}^{-1}$) ^[b]
$[\text{L}]^{5-}$	268 sh	3300	$[\text{H}_5\text{L}]$	230	33800
				278	7200
$[\text{HL}]^{4-}$	268 sh	3600	$[\text{H}_7\text{L}]^{2+}$	277	6700
$[\text{H}_2\text{L}]^{3-}$	272	4300	$[\text{TbHL}]^-$	272 sh	3600
$[\text{H}_3\text{L}]^{2-}$	228sh	30000	$[\text{TbH}_2\text{L}]$	272	3700
	275	5600			
$[\text{H}_4\text{L}]^-$	229	33900			
	278	6600			

^[a] ± 2 nm. ^[b] $\pm 10\%$.

which explains the difficulty in solubilising the metal complexes after their isolation as solid-state samples. At lower pH, competition with protons dissociates the complex, while very stable hydroxides are the major species at pH values higher than 8.5. Altogether, the metal complexes are moderately stable, as shown by the pTb value of 10.0,^[19] calculated with $[\text{Tb}]_{\text{tot}} = 10^{-6}$ M, $[\text{H}_5\text{L}]_{\text{tot}} = 10^{-5}$ M and pH 7.4, in comparison with 19.2 for $[\text{Tb}(\text{dtpa})]^-$ ^[20] and with 6.7 for terbium benzoate. This result is a clear indication that the nitrogen atoms of the H_5L ligand are most probably nonbonding and remain protonated in the metal complexes, as indicated by the unchanged values of the two highest apparent $\text{p}K_a$ values upon addition of Ln^{III} ions.

Photophysical Properties of the Ligand and the $[\text{LnH}_2\text{L}]$ Complexes

In water, the ligand displays two main adsorption bands around 46080 (shoulder at 42370 cm^{-1}) and 39370 cm^{-1} . The high-energy band is slightly blue-shifted (ca. 400–500 cm^{-1}) in the Ln^{III} complexes. The photophysical properties of the ligand and of its 1:1 complexes with La, Lu, Eu and Tb in water (pH 5.3) and in frozen glycerol/water mixtures are summarized in Table 3. UV excitation in the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ absorption bands of the ligand results in a

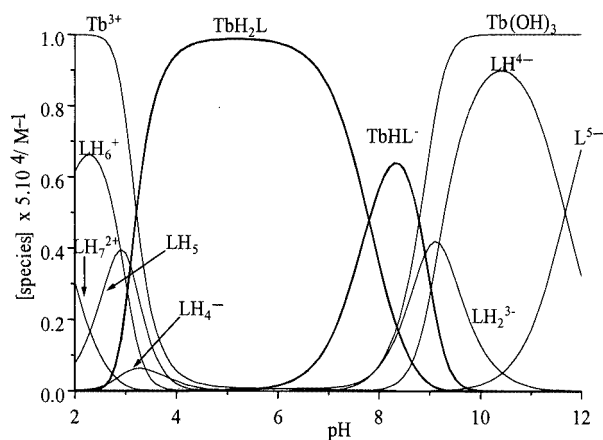


Figure 6. Corresponding formation curves of proton and terbium complexes, computed from the stability constants given in the text; $[L]_{\text{tot}} = [Tb^{III}]_{\text{tot}} = 2.0 \cdot 10^{-5} \text{ M}$; $\lambda_{\text{exc}} = 274 \text{ nm}$; $T = 20^\circ \text{C}$

ligand-centred emission displaying two overlapping bands assigned to emission from the $^1\pi\pi^*$ (33110 cm^{-1}) and $^3\pi\pi^*$ states (Figure 7). The absolute fluorescence quantum yield of the fully deprotonated ligand (L^{5-}) is small at 0.3%, a value that increases slightly for the $[Ln(H_2L)]$ complexes: 0.4 and 0.5% for La and Lu, respectively, at pH 5.3. At 77 K, the $^3\pi\pi^*$ state emission is structured with a vibrational progression of $1350 \pm 30 \text{ cm}^{-1}$, corresponding to a ring breathing mode and its 0-phonon transition is located at 26520 cm^{-1} . The gap between the $^3\pi\pi^*$ and $^1\pi\pi^*$ states (ca. 6320 cm^{-1}) is favourable for a relatively efficient intersystem crossing process.^[5] The emission spectra of the ligand and its complexes at room temperature are consistent with this finding, since they display emission from both the singlet and triplet states, although very weakly for Eu and Tb. The $^3\pi\pi^*$ lifetime amounts to 1.88 s, a value close to that obtained for benzoic acid ($\tau = 2 \text{ s}$).^[21] As would be expected from the relatively high energy of the $^3\pi\pi^*$ 0-phonon component, both the Eu^{III} ions, with $\Delta E(^3\pi\pi^* - ^5D_0) \approx 9700 \text{ cm}^{-1}$, and the Tb^{III} ions, with $\Delta E(^3\pi\pi^* - ^5D_4) \approx 6500 \text{ cm}^{-1}$, are reasonably well sensitised (Figure 7). This is in agreement with what has been observed for Tb^{III} poly(aminocarboxylates), for which the best antenna effect was observed for $^3\pi\pi^*$ states around 26000 cm^{-1} .^[22]

The high-resolution excitation spectrum of a solid-state sample of $[EuH_2L]$ in the $^5D_0 \leftarrow ^7F_0$ spectral range, obtained

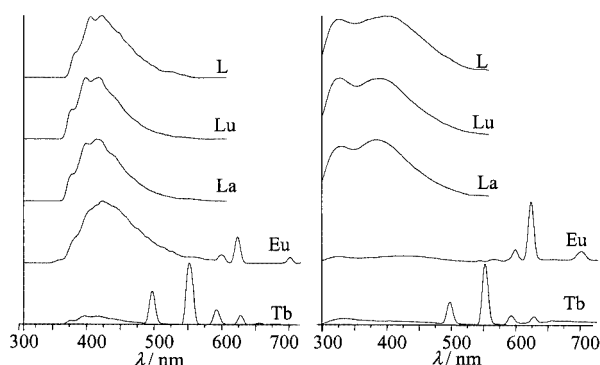


Figure 7. Emission spectra of the $[LnH_2L]$ complexes ($Ln = La, Eu, Tb, Lu$), pH = 5.3; (left) phosphorescence spectra in solutions of glycerol/water, 10:90% at 77 K; (right) fluorescence spectra at 295 K in water

by analysis of the maximum on the $^5D_0 \rightarrow ^7F_2$ transition at 10 K, displays a single broad and symmetrical peak at 17246 cm^{-1} with a full width at half height (fwhh) of 26.9 cm^{-1} , which is consistent with the presence of a single site for the Eu^{III} ion.

The metal-centred luminescence of diluted aqueous solutions is pH dependent, due to the distribution of the various species present in solution. The Tb complex displays emission over a large pH range, from pH 3.5 to 10.5 (Figure 4), with maximum intensity occurring in the pH range 5–8, in which $[TbH_2L]$ is the major species in solution. The average numbers of water molecules bound to the metal ions were determined from the experimental lifetimes at room temperature for solutions of $[LnH_2L]$ ($Ln = Eu, Tb$) in H_2O (pH 5.3) and D_2O (pD 5.7).^[23,24] For the Eu complex, the measured lifetimes ($\tau = 1.41 \pm 0.04 \text{ ms}$ in D_2O and $0.20 \pm 0.01 \text{ ms}$ in H_2O) give $q = 4.8 \pm 0.5$, while $q = 4.5 \pm 0.5$ is obtained for the Tb podate ($\tau = 1.47 \pm 0.01 \text{ ms}$ in D_2O and $0.61 \pm 0.01 \text{ ms}$ in H_2O). The presence of at least eight OH oscillators in the inner coordination sphere is consistent with the reasoning, based on the stability constants, that at least four benzoate units are coordinated to the metal ions (in a monodentate fashion), but the nitrogen atoms are not. The large number of water molecules in the first coordination sphere explains the inability of the ligand to sensitise the luminescence of the Dy^{III} , Er^{III} and Tm^{III} ions. Despite this, the quantum yields of metal-centred luminescence in

Table 3. Ligand-centred absorption and emission properties of the ligand (pH 12) and $[LnH_2L]$ podates at pH 5.3

Compound	$E (\text{cm}^{-1})^{[a]}$	$E (\text{cm}^{-1})^{[a]}$			$\tau(^3\pi\pi^*) (\text{ms})^{[b]}$
		$^1\pi\pi^*^{[c]}$	$^3\pi\pi^*^{[c]}$	$^3\pi\pi^*^{[b]}$	
$[L]^{5-}$	46080, 42370 sh, 39370	33110	25706	26790, 25360, 23980	1879 ± 26
$[LuH_2L]$	46510, 42370 sh, 39275	33005	26140	26920, 25540, 24240, 22910, 21530	789 ± 12
$[LaH_2L]$	46590, 42370 sh, 39525	33445	26040	26880, 25510, 24210, 22940, 21600	809 ± 6
$[EuH_2L]$	46619, 42370 sh, 36490	33655	25445	26920, 25610, 24230	1363 ± 14
$[TbH_2L]$	46619, 42370 sh, 36490	33700	25640	26920, 25610, 24270	456 ± 12

^[a] The most intense component is italicised. ^[b] Luminescence data and lifetimes for frozen solutions in glycerol/water 10:90% (77 K). ^[c] Electronic spectroscopic data at 295 K in water; energies are given for the maximum of the band envelope (sh: shoulder).

water at pH 5.3 remain sizeable, at 1.5 and 10.3% for the Eu and Tb podates, respectively (Table 4). This points to fairly efficient energy transfer from the ligand to the Tb(5D_4) level. It is noteworthy that the quantum yield of [Tb(H₂L)] increases significantly upon addition of HMPA, which is known to be a good complexation agent for Ln^{III} ions and which removes the water from the inner coordination sphere (2 eqs: +45%, 4, 10, 100 and 500 eqs: +105%). Moreover, a graph of the quantum yield of [Tb(H₂L)] vs. pH (Figure S2, Supporting Information) reflects the distribution curve of this species reasonably well.

Conclusion

The solution studies described in this paper show that podand H₅L gives stable Ln^{III} complexes in water that are resistant toward hydrolysis and show interesting photophysical properties. Thermodynamically stable 1:1 neutral podates [Ln(H₂L)] form in the pH range 3.7–8. No nitrogen atom is involved in the binding, as a result of the protonation of the amine functions, preventing the wrapping of the ligand around the metal ion. The emission lifetimes of the Eu^{III} and Tb^{III} complexes recorded in D₂O and H₂O point to four water molecules completing the coordination sphere of the metal ions. The luminescence study shows that the ligand exhibits a good antenna effect with respect to the Tb^{III} ion, due to efficient intersystem crossing ($^1\pi\pi^*$ - to $^3\pi\pi^*$) and ligand-to-metal energy transfer. Despite the large number of coordinated water molecules, the quantum yields of the metal-centred luminescence in the Tb^{III} (and Eu^{III}) complexes are encouraging and demonstrate that benzoate is a potentially interesting moiety for attachment onto a flexible receptor for Ln^{III} ions.

Experimental Section

Starting Materials and General Procedures: Analytical grade solvents and chemicals (Fluka AG) were used without further purification, except for acetonitrile, which was distilled from CaH₂. Solutions were prepared just before use with freshly boiled, doubly distilled water saturated with N₂. Stock solutions of LnX₃·*n*H₂O (X = ClO₄, CF₃SO₃) were prepared from lanthanide oxides (99.99%, Rhône Poulenc) and the corresponding acid. They were systematically acidified with HCl to a pH of about 4 before titration to avoid hydroxide precipitation. The concentrations were determined by complexometric titrations with a standardized Na₂H₂EDTA solution in urotropine-buffered medium and with xylenol orange as indicator.^[25] Elemental analyses were performed by Dr. Eder, Microchemical Laboratory, University of Geneva.

1-D and 2-D NMR spectroscopic data were collected on Bruker DPX 400 or AM 360 spectrometers. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃, D₂O or CH₃OD and their assignment was based on ¹H coupling and 2-D ¹H-¹³C correlation spectra. The mass spectra were recorded in electrospray ionisation mode on a Finnigan quadrupole mass spectrometer (*T*_{matrix} = 240 °C). The instrument was calibrated with a horse myoglobin standard. The analyses were conducted in positive mode. The ion spray voltage was 4.6 kV. Assignment of the species was based on the isotopic

distribution of the peaks. Electronic UV/Vis spectra were recorded on a Perkin–Elmer Lambda 900 spectrometer. Infra-red spectra were measured on a FT-IR Mattson Alpha Centauri spectrometer (4000–400 cm^{−1}, KBr pellets).

Syntheses (see Scheme 1). Methyl 2-(Bromomethyl)benzoate (1): This compound was synthesized by a known procedure.^[26]

1,4,7-Heptanetriamine-*N,N,N',N',N''*-pentakis(methyl 2-methylbenzoate) (2): Potassium carbonate (10.04 g, 72.7 mmol) was added under nitrogen atmosphere to a solution of diethylenetriamine (500 mg, 4.9 mmol) in freshly distilled acetonitrile (100 mL). The resulting mixture was heated at reflux for 30 min, and a solution of **1** (6.08 g, 26.7 mmol) in dry acetonitrile (50 mL) was added over 2 h. The mixture was stirred and heated at reflux for an additional 12 h and filtered while hot. The solvents were then evaporated to give a black oil, which was dissolved in dichloromethane, washed with brine and dried with Mg₂SO₄, and the solvents were evaporated to dryness. The residue was purified by column chromatography (silica gel; 2% MeOH in CH₂Cl₂). Yield: 1.76 g (43%), orange foam. IR (KBr): $\tilde{\nu}$ = 1711 (C=O), 1452, 1384 cm^{−1}. ¹H NMR (300 MHz, CDCl₃, 25 °C): δ = 2.46 (m, 8 H, CH₂), 3.72 (s, 8 H, CH₂), 3.76 (s, 2 H, CH₂), 3.82 (s, 12 H, CH₃), 3.86 (s, 3 H, CH₃), 7.21 (m, 5 H, ArH), 7.27 (dt, ¹*J* = 7.5, ²*J* = 1.3 Hz, 1 H, ArH), 7.34 (dt, ¹*J* = 7.8, ²*J* = 1.3 Hz, 4 H, ArH), 7.41 (d, *J* = 7.5 Hz, 1 H, ArH), 7.58 (d, *J* = 7.8 Hz, 4 H, ArH), 7.68 (dd, ¹*J* = 7.5, ²*J* = 1.3 Hz, 1 H, ArH), 7.74 (dd, ¹*J* = 7.8, ²*J* = 1.3 Hz, 4 H, ArH) ppm. ¹³C NMR (CDCl₃): δ = 51.7, 51.8 (CH₃), 52.5, 52.6, 57.0, 57.6 (CH₂), 126.3, 129.3, 129.7, 129.9 (CH), 130.1, 130.4 (Cq), 131.3, 131.6 (CH), 141.4 (Cq), 168.2, 168.4 (C=O) ppm. ESI-MS (CH₃CN, H₂O, CH₃CO₂H): *m/z* = 844.3 (calcd. 844.3) [M + H]⁺, 422.8 (calcd. 422.7) [M + 2H]²⁺. C₄₉H₅₃N₃O₁₀ (843.97): calcd. C 69.73, H 6.33, N 4.98; found C 69.72, H 6.31, N 4.96.

1,4,7-Heptanetriamine-*N,N,N',N',N''*-pentakis(2-methylbenzoic acid) (H₅L): Compound **2** (500 mg, 0.59 mmol) was dissolved in a solution of methanol (200 mL) and KOH in water (1 M, 15 mL). The resulting mixture was heated at reflux for 4 h, and the solvents were evaporated. The residue was dissolved in water (400 mL), cooled to 0 °C and acidified to pH 2 with aqueous HCl. The yellow precipitate was collected, washed with water and then diethyl ether, and dried. Yield: 417 mg (91%), yellow solid. IR (KBr): $\tilde{\nu}$ = 3426 br (OH), 2606 br (OH), 1700 (C=O), 1590, 1552, 1451, 1381, 1295, 1145, 1085, 752 cm^{−1}. ¹H NMR (300 MHz, D₂O, 20 °C): δ = 2.8 (m, 4 H, CH₂), 3.3 (m, 4 H, CH₂), 3.63 (s, 2 H, CH₂), 4.44 (s, 8 H, CH₂), 7.2 (m, 1 H, ArH), 7.3–7.4 (m, 14 H, ArH), 7.74 (m, 1 H, ArH), 7.93 (m, 4 H, ArH) ppm. ¹³C NMR (D₂O, 20 °C): δ = 51.1, 55.4, 56.7, 57.9, 58.1 (CH₂), 127.2, 129.6, 130.6, 130.8 (CH), 131.4, 131.6 (quat. C), 133.1, 134.4 (CH), 137.5 (quat. C), 170.7 (C=O) ppm. ESI-MS (CH₃CN, H₂O, CH₃CO₂H): *m/z* = 774.4 (calcd. 774.3) [M + H]⁺, 387.8 (calcd. 387.7) [M + 2H]²⁺. H₅L·H₂O C₄₄H₄₅N₃O₁₁ (791.85): calcd. C 66.74, H 5.73, N 5.31; found C 66.72, H 5.60, N 5.20.

Preparation of [Ln(H₂L)]·*n*H₂O Complexes (Ln = La, Eu, Tb, Lu): Freshly titrated LnClO₄·*n*H₂O solutions (10^{−3} M, 0.039 mmol) were added over 4 h, at room temperature, to an aqueous solution of H₅L (40 mL, 0.039 mmol, 10^{−3} M, pH = 5.3, adjusted with HCl). The mixture was stirred for an additional 2 h and the resulting white precipitate was filtered, washed successively with water (several times) and diethyl ether, and further dried for 3 days at 65 °C and 0.01 Torr. These complexes being very hygroscopic, variable numbers of water molecules were found when performing microanalyses.

[La(H₂L)]·5H₂O (75%): IR (KBr): $\tilde{\nu}$ = 3422 br (OH), 1554 and 1399 (ν_{as}, ν_s COO), 1606, 1498, 1449, 1294, 1203, 1151, 1120, 1089,

753 cm⁻¹. C₄₄H₅₀LaN₃O₁₅ (999.80): calcd. C 52.86, H 5.04, N 4.20; found C 52.27, H 4.50, N 4.27.

[Eu(H₂L)]·3H₂O (89%): IR (KBr): $\tilde{\nu}$ = 3413 br (OH), 1556 and 1403 (ν_{as}, ν_s COO), 1607, 1490, 1449, 1294, 1202, 1150, 1120, 1094, 752 cm⁻¹. ESI-MS: a stoichiometric mixture of Eu(ClO₄)₃·xH₂O (x = 4.2) and H₃L 10⁻⁴ M in pure methanol gave [EuH₃L]⁺ m/z = 923.4 (calcd. 923.4). C₄₄H₄₆EuN₃O₁₃ (976.81): calcd. C 54.10, H 4.75, N 4.30; found C 53.65, H 4.59, N 4.30.

[Tb(H₂L)]·7H₂O (84%): IR (KBr): $\tilde{\nu}$ = 3416 br (OH), 1556 and 1407 (ν_{as}, ν_s COO), 1608, 1491, 1450, 1295, 1203, 1151, 1120, 1087, 752 cm⁻¹. C₄₄H₅₄N₃O₁₇Tb (1055.83): calcd. C 50.05, H 5.15, N 3.98; found C 49.16, H 4.78, N 3.72. Complexometry: calcd. Tb 15.05; found Tb 15.28 ± 0.28.

[Lu(H₂L)]·4H₂O (92%): IR (KBr): $\tilde{\nu}$ = 3417 br (OH), 1561 and 1410 (ν_{as}, ν_s COO), 1608, 1491, 1450, 1294, 1203, 1152, 1120, 1088, 752 cm⁻¹. C₄₄H₄₈N₃O₁₄Lu (1017.84): calcd. C 51.92, H 4.75, N 4.13; found C 51.98, H 4.41, N 4.14.

Physical Measurements. Potentiometric Titrations: H₇L²⁺ was titrated with a 5.1 mL sample ([H₇L²⁺]_{tot} = 3.7·10⁻³ M, solvent: H₂O/CH₃OH 98:2 v/v) in a thermostatted (20.0 ± 0.1 °C) glass-jacketed vessel under an Ar atmosphere. The ionic strength was fixed with KCl (μ = 0.1 M). The solution was acidified to a pH of about 1.8 (HCl) 30 min before titration. Titrations were carried out with an automatic Metrohm Titrimo 736 GP potentiometer linked to an IBM PS/2 computer (resolution 0.1 mV, accuracy 0.2 mV) and by use of constant volume addition (0.05 mL). An automatic burette (Metrohm 6.3013.210, 10 mL, accuracy 0.03 mL) was used, together with a Metrohm 6.0238.000 glass electrode. The standard base solution (KOH = 0.050 M, μ = 0.1 M, KCl) was added inside the solution through a capillary tip attached to the automatic burette. The data (200 points, drift < 1 mV/min) were mathematically treated by use of the program SUPERQUAD^[27] with a Marquardt algorithm while the distribution of species was calculated with the program Haltafall.^[28] Calibration of the pH meter and the electrode system was performed prior to each measurement with a standardized HCl solution (μ = 0.1 M, KCl) at 20.0 °C: 10 mL of the latter were titrated with a standardized 0.1 M KOH solution at a ionic strength of 0.1, and the electrode potential readings were converted to pH. The ion product of solvent (pK_w = 13.91) and electrode potential were refined by use of the program Scientist[®] by Micromath[®] (Version 2.0).

Spectrophotometric Titrations: Electronic spectra were recorded with a Perkin–Elmer Lambda 900 spectrophotometer at 20 °C (210–350 nm, 60 nm min⁻¹ scan speed, spectral width 2 nm) in 1 cm Suprasil[®] quartz cells. Titrations of 10 mL samples were performed in a thermostatted (20.0 ± 0.1 °C), glass-jacketed vessel filled with Ar, at μ = 1 M (KCl); H₇L²⁺ (pH, 2) was titrated with KOH (0.1 M, H₃L (pH, 5.3, HCl) with Ln(ClO₄)₃ (≈ 4.0·10⁻³ M, Ln = La, Eu, Tb, Lu) at pH = 5.3, and [Tb(H₂L)] 2.0·10⁻⁵ M at pH₀ ≈ 2 by KOH (0.050 M). Aliquots of the titrant were added through a Socorex[®] micropipette. The pH values of the titrated solutions were monitored continuously. After a 15 min delay, 3 mL of solution was transferred into the quartz cell with a Teflon[®] syringe. The stability constants were computed by use of the Specfit program.^[29] Differences between the measured and the computed absorbances were less than 7 × 10⁻³ absorbance unit at any wavelength and exhibited statistical behaviour.

NMR Titration: A solution of H₃L (11.6 mg, 7.3·10⁻³ M) was prepared in 2 mL of a D₂O/CD₃OD (95:5, v/v) mixture, by addition of a concentrated KOD/D₂O aliquot (pD₀ ≈ 12). Samples with different pD values were prepared by addition of dilute D₂SO₄/D₂O (Fluka, puriss). Precipitation of ligand occurred at pD values

lower than 3.2. The pH values of the solutions were determined with a Metrohm Titrimo 736 GP potentiometer equipped with a calibrated Metrohm 6.0234.100 glass electrode in H₂O. Ionic strength was not adjusted. The pD values were obtained from the equation pD = pH_{measd.} + 0.4.^[30]

Luminescence Titrations: The solutions {[H₃L]₀ = 2.0·10⁻⁵ M, [Tb(ClO₄)₃]₀ = 2.0·10⁻⁵ M, 10 mL, pH₀ ≈ 2; [KOH]_{tit} = 0.050 M; μ = 0.1 M (KCl)} were identical to those used for the spectrophotometric pH-dependent titration described previously. After a 15 min delay, 3 mL of solution were transferred into a quartz cell and degassed with Ar for 5 min. Absorbance at the excitation wavelength was measured (A < 0.05) and emission (λ_{exc} = 285 nm) and excitation spectra were collected.

Luminescence Measurements: Low-resolution luminescence measurements (spectra and lifetimes) were recorded on a Perkin–Elmer LS-50B spectrofluorimeter. Phosphorescence lifetimes (τ) were measured with the instrument in time-resolved mode, on frozen glycerol/water (10:90%) solutions in a quartz capillary or a 1-cm Suprasil[®] cell. They are the average of at least three independent measurements, made by monitoring the decay at the maxima of the emission spectra, enforcing a 0.03–0.04 ms delay. The decays were mono-exponential and were analysed by use of the FLDM program (Perkin–Elmer). Solutions of [Ln(H₃L)]^{(3+/5-)+} were prepared in water at pH = 5.3, with stock solutions of H₃L (2.0·10⁻³ M) and Ln(ClO₄)₃·xH₂O (x ≈ 4.5, Ln = La, Eu, Tb, Lu; ≈ 4·10⁻³ M). Quantum yields of L⁵⁻ (10⁻⁵ M, pH = 12) and [Ln(H₂L)] (Ln = La, Eu, Tb, Lu, 10⁻⁵ M in H₂O) were determined in degassed water relative to quinine sulfate in 0.05 M aqueous H₂SO₄ (absolute quantum yield: 0.546)^[31] and cresol violet (absolute quantum yield: 0.52);^[32] estimated error ± 10%. The number of coordinated water molecules (q) for the Eu and Tb complexes were calculated from q = A(τ_H⁻¹ - τ_D⁻¹ - k_{corr}), where τ_H and τ_D are the lifetimes in H₂O and D₂O respectively, A = 1.2 (Eu) and 5.0 (Tb), and k_{corr} = 0.25 (Eu) and 0.06 (Tb) ms⁻¹.^[24] High-resolution spectra were recorded on a previously described setup.^[33]

Table 4. Absolute quantum yield of the ligand-centred fluorescence in [L]⁵⁻ (pH = 12) and [LnH₂L] (Ln = La, Lu) and of the metal-centred phosphorescence in [LnH₂L] (Ln = Eu, Tb) measured in water at 295 K and pH = 5.3 (values in D₂O are italicised)

Compound	λ _{exc} (nm)	Φ _{abs} (%)
[L] ⁵⁻	268	0.3
[LuH ₂ L]	273	0.4
[LaH ₂ L]	273	0.5
[EuH ₂ L]	270	1.5, 3.3
[TbH ₂ L]	270	10.3, 18.9

Acknowledgments

This work is supported through grants from the Swiss National Science Foundation and the Swiss Federal Office for Science and Education (COST Action D18). We thank Frédéric Gummy for his help in recording the high-resolution luminescence data.

[1] The chemistry of contrast agents in medical magnetic resonance imaging, eds A. E. Merbach and E. Tóth, Wiley, London, 2001.

[2] Z. P. Zheng, *Chem. Commun.* 2001, 2521–2529.

[3] J.-C. G. Bünzli, C. Piguet, *Chem. Rev.* 2002, 102, 1897–1928.

- [4] L. H. Slooff, A. van Blaaderen, A. Polman, G. A. Hebbink, S. I. Klink, F. C. J. M. Van Veggel, D. N. Reinhoudt, J. W. Hofstra, *J. Appl. Phys.* **2002**, *91*, 3955–3980.
- [5] J.-C. G. Bünzli, C. Piguet, in *Encyclopedia of Materials: Science and Technology* (Eds.: K. H. J. Buschow, R. W. Cahn, M. C. Flemings, B. Ilshner, E. J. Kramer, S. Mahajan), Elsevier Science Ltd, Oxford, **2001**, *10*, Ch. 1. 10. 4, 4465–76.
- [6] V. W. W. Yam, K. K. W. Lo, *Coord. Chem. Rev.* **1999**, *184*, 157–240.
- [7] G. Mathis, in *Rare Earths* (Eds.: R. Saez Puche, P. Caro), Editorial Complutense, Madrid, **1998**, 285–97.
- [8] D. Parker, *Coord. Chem. Rev.* **2000**, *205*, 109–130.
- [9] D. J. Bornhop, D. S. Hubbard, M. P. Houlne, C. Adair, G. E. Kiefer, B. C. Pence, D. L. Morgan, *Anal. Chem.* **1999**, *71*, 2607–2615.
- [10] G. Zucchi, A.-C. Ferrand, R. Scopelliti, J.-C. G. Bünzli, *Inorg. Chem.* **2002**, *41*, 2459–2465.
- [11] F. M. Ramirez, L. J. Charbonnière, G. Muller, R. Scopelliti, J.-C. G. Bünzli, *J. Chem. Soc., Dalton Trans.* **2001**, 3205–3213.
- [12] C. Piguet, J.-C. G. Bünzli, *Chem. Soc. Rev.* **1999**, *28*, 347–358.
- [13] M. Elhabiri, R. Scopelliti, J.-C. G. Bünzli, C. Piguet, *J. Am. Chem. Soc.* **1999**, *121*, 10747–10762.
- [14] N. Fatin-Rouge, E. Tóth, D. Perret, R. H. Backer, A. E. Merbach, J.-C. G. Bünzli, *J. Am. Chem. Soc.* **2000**, *122*, 10810–10820.
- [15] J.-C. G. Bünzli, in *Rare Earths* (Eds.: R. Saez Puche, P. Caro), Editorial Complutense, Madrid, **1998**, 223–259.
- [16] W. Shrodt, H. Büchner, U. E. Steiner, *J. Inf. Recording* **1996**, *23*, 79–84.
- [17] M. Bredol, U. Kynast, C. Ronda, *Adv. Mat.* **1991**, *3*, 361–367.
- [18] J. L. Sudmeier, C. N. Reilly, *Anal. Chem.* **1964**, *36*, 1698–1706.
- [19] K. N. Raymond, G. Muller, F. Matzanke, *Top. Curr. Chem.* **1984**, *123*, 49–102.
- [20] J. R. Duffield, F. Marsicano, D. R. Williams, *Polyhedron* **1991**, *10*, 1105–1111.
- [21] H. J. Maria, S. P. McGlynn, *J. Chem. Phys.* **1970**, *52*, 3399–3402.
- [22] M. Latva, H. Takalo, V. M. Mikkala, C. Matachescu, J.-C. Rodriguez-Ubis, J. Kankare, *J. Lumin.* **1997**, *75*, 149–169.
- [23] J.-C. G. Bünzli, in *Lanthanide Probes in Life, Chemical and Earth Sciences. Theory and Practice* (Eds.: J.-C. G. Bünzli, G. R. Choppin), Elsevier Science Publ. B. V., Amsterdam, **1989**, chapter 7, 219–93.
- [24] A. Beeby, I. M. Clarkson, R. S. Dickins, S. Faulkner, D. Parker, L. Royle, A. S. de Sousa, J. A. G. Williams, M. Woods, *J. Chem. Soc., Perkin Trans. 2* **1999**, 493–504.
- [25] G. Schwarzenbach, *Complexometric Titrations*, Chapman & Hall, London, **1957**.
- [26] D. A. Quagliato, P. M. Andrae, E. M. Matelan, *J. Org. Chem.* **2000**, *65*, 5037–5042.
- [27] P. Gans, A. Sabatini, A. Vacca, *J. Chem. Soc., Dalton Trans.* **1985**, 1195–1200.
- [28] N. Ingri, W. Kakolowicz, L. G. Sillen, B. Warnqvist, *Talanta* **1967**, *14*, 1261–1286.
- [29] H. Gampp, M. Maeder, C. J. Meyer, A. D. Zuberbühler, *Talanta* **1986**, *33*, 943–951.
- [30] K. Mikkelsen, S. O. Nielsen, *J. Phys. Chem.* **1960**, *64*, 632–637.
- [31] S. R. Meech, D. C. Phillips, *J. Photochem.* **1983**, *23*, 193–217.
- [32] D. Magde, J. H. Brannon, T. L. Cremers, J. Olmsted, III, *J. Phys. Chem.* **1979**, *83*, 696–699.
- [33] R. Rodriguez-Cortinas, F. Avecilla, C. Platas-Iglesias, D. Imbert, J.-C. G. Bünzli, A. de Blas, T. Rodriguez-Blas, *Inorg. Chem.* **2002**, *41*, 5336–5349.
- [34] P. Letkeman, A. E. Martell, *Inorg. Chem.* **1979**, *18*, 1284–1289.

Received October 4, 2002

[I02550]