The first lanthanide-containing helicates self-assembled in water

Mourad Elhabiri,[a] Rosario Scopelliti,[a] Jean-Claude G. Bünzli*[a] and Claude Piguet[b]

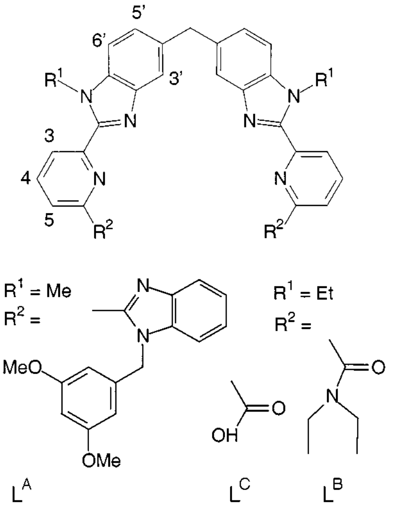
[a] *Institute of Inorganic and Analytical Chemistry, BCH, University of Lausanne, CH-1015-Lausanne, Switzerland. E-mail: jean-claude.bunzli@icma.unil.ch*

[b] *Department of Inorganic, Analytical and Applied Chemistry, Sciences II, University of Geneva, CH-1211 Geneva-4, Switzerland*

Received (in Cambridge, UK) 28th August 1998, Accepted 25th September 1998

Triple-stranded bimetallic helicates $[Ln_2(L^C-2H)_3]$ form in water by a strict self-assembly process and are shown to be thermodynamically very stable ($\log \beta_{23} > 26$) and luminescent (Ln = Eu).

To cope with the demand for efficient light-converting devices arising from the development of time-resolved fluoroimmunoassays, signalling and luminescent labelling technologies,[1–4] including bimetallic probes which provide two probe signals in one stain, co-ordination chemists have developed several strategies. Among these, self-assembly processes[5] based on the induced fit concept[6] have proved efficient in designing lanthanide building blocks with predetermined structural and physicochemical properties.[7] The ditopic ligand L^A was designed to produce the cationic triple-stranded helicate $[Ln_2(L^A)_3]^{6+}$ by strict self-assembly and the resulting complexes exhibit a large stability in MeCN.[8] The $[Eu_2(L^A)_3]^{6+}$ helicate is, however, only weakly luminescent and is water sensitive, two severe handicaps for its use as a probe. A substantial improvement was achieved upon replacing the terminal benzimidazole groups in L^A by carboxamide binding units in L^B, with a large increase in the Eu-centred luminescence and a good resistance of the triple-stranded helicate $[Eu_2(L^B)_3]^{6+}$ toward hydrolysis in MeCN containing up to 2.5 M water.[9] However, biomedical applications require water soluble probes and, to our knowledge, self-assembly of bimetallic lanthanide-containing edifices in water have only been reported for $[Ln_2L_2]$ supramolecular boxes where L is 2,6-bis[*N*,*N*-bis(carboxymethyl)aminomethyl]-4-benzoylphenol and in which the Ln^{III} cations are linked to each other by an aqua bridge inside the cage.[10] In order to test whether the energetic drive leading to the formation of bimetallic helicates in water is able to compensate the large dehydration enthalpy of the lanthanide aquo-ions, we have introduced two carboxylic acid functions in L^C, which led to the quantitative formation of neutral $[Ln_2(L^C-2H)_3]$ triple-stranded helicates. These new compounds are thermodynamically highly stable and luminescent (Ln = Eu) and they are the first examples of such structures self-assembled in water.



Ligand L^C was obtained from the hydrolysis of L^B† and the pK_a of the carboxylic groups were determined by potentiometry to be 4.15 ± 0.05 and 7.05 ± 0.05 (0.1 M Et_4NClO_4). ^1H NMR titration of L^C with $Eu(ClO_4)_3 \cdot xH_2O$, in D_2O at pD = 12.74, points to the exclusive formation of a 2 : 3 species (break at $[Eu]/[L^C] = 0.64$, no hydroxide precipitation before the break point). This speciation is confirmed by spectrophotometric data obtained at pH 7.2 and 298 K in H_2O ($[L^C] = 1.05 \times 10^{-5}$ M, $0 < [Ln] < 1.6 \times 10^{-5}$ M), which can be fitted to eqn. (1) for Ln = La ($\log \beta_{23} = 30 \pm 1$), Eu (26.1 ± 0.4) and Lu (27.3 ± 0.6).‡ Titrations with solutions in MeOH–H_2O 98 : 2 (v/v) yield similar $\log \beta_{23}$ values, 29.6 ± 0.8 (La), 27.8 ± 0.6 (Eu) and 25.9 ± 0.3 (Lu), but data for Eu and Lu have to be fitted to eqns. (1) and (2) with $\log \beta_{22} = 21 \pm 0.6$ (Eu) and 19.1 ± 0.5 (Lu). As a

$$2\,Ln^{3+} + 3\,(L^C-2H)^{2-} \rightleftharpoons [Ln_2(L^C-2H)_3] \quad \log \beta_{23} \qquad (1)$$

$$2\,Ln^{3+} + 2\,(L^C-2H)^{2-} \rightleftharpoons [Ln_2(L^C-2H)_2]^{2+} \quad \log \beta_{22} \qquad (2)$$

comparison, helicates formed by L^B in aprotic MeCN display $\log \beta_{23}$ values in the range 24–25 and $\log \beta_{22}$ values in the range 19–20.[9] The large thermodynamic stability of the $[Ln_2(L^C-2H)_3]$ helicates in water is further demonstrated by the partial decomplexation observed in the ^1H NMR spectrum of $[Eu_2(L^C-2H)_3]$ 3.2×10^{-3} M in D_2O upon adding a 20-fold excess of H_2EDTA^{2-}.

Solid complexes have been isolated for Ln = La, Pr, Nd, Eu, Gd, Tb, Tm, Yb, Lu and crystals suitable for crystallographic investigation were obtained for Eu, Tb and Yb.§ The structure of the Eu-helicate is presented in Fig. 1.¶ The asymmetric unit contains two slightly different neutral bimetallic helicates without imposed crystallographic symmetry but with pseudo-D_3 symmetry, as well as 41 water molecules. Molecule A has an Eu···Eu separation of 8.807(3) Å and features two nine-coordinate Eu^{III} ions with marginally different environments [mean Eu–N distances 2.59(3)/2.62(4) Å, mean Eu–O distances 2.40(2)/2.39(2) Å, ionic radius 1.12(3)/1.13(5) Å]. Molecule B displays a larger Eu···Eu separation, 9.044(3) Å, and co-ordination to carboxylic groups is less symmetrical [mean Eu–N distances 2.60(3)/2.59(5) Å, mean Eu–O distances

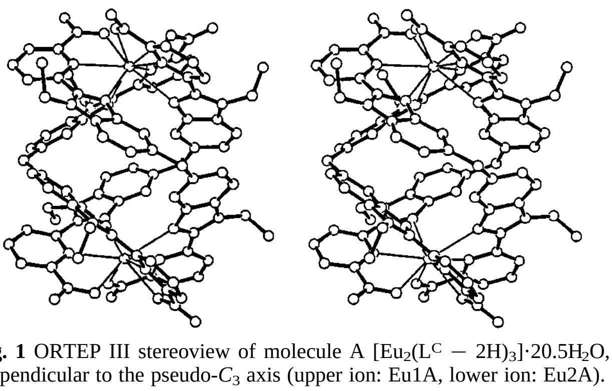


Fig. 1 ORTEP III stereoview of molecule A $[Eu_2(L^C-2H)_3] \cdot 20.5H_2O$, perpendicular to the pseudo-C_3 axis (upper ion: Eu1A, lower ion: Eu2A).

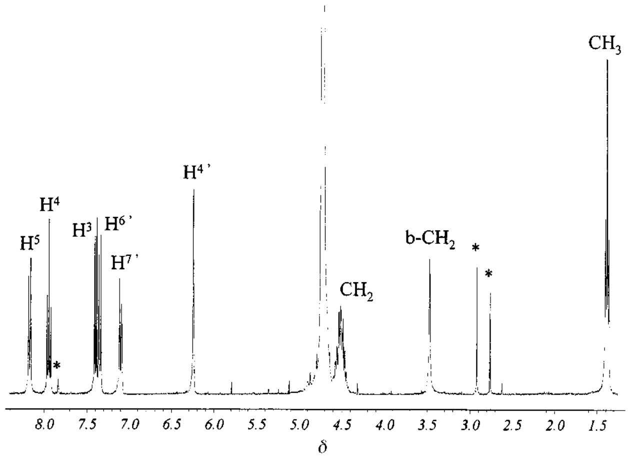


Fig. 2 ^{1}H NMR spectrum of 10^{-4} M $[La_2)L^C - 2H)_3]$ in D_2O at pD = 7 and 303 K, with assignment (b-CH_2: bridging methylene; DMF as internal reference*).

2.40(6)/2.41(4) Å, ionic radius 1.12(5)/1.12(4) Å]. As the pH of the mother liquor is *ca.* 7.5–8.2, a partial protonation of the carboxylic groups associated with the presence of hydroxide counter-anions in the asymmetric unit[11] is not likely especially that the mean C–O distances for coordinated (1.27 Å, A and B) and non-coordinated (1.23 Å, A and 1.24 Å, B) O atoms closely match those found in the tris(dipicolinate)anion.[12] Analysis of the coordination polyhedra[13] of the four different metal ions reveals slightly distorted tricapped trigonal prisms. The facial planes of the two distal tripods defined by the three coordinated O atoms from the carboxylates and the three N atoms from the benzimidazole moieties are almost parallel with mean dihedral angles of 3.4° (A) and 6.8° (B) and the interligand ω_i angles[13,14] are in the ranges 11.1–13.6° (A) and 8.1–14.9° (B) (ideal trigonal prism: 0°). The distances between these facial planes, 3.16 Å (A) and 3.23 Å (B), are substantially shorter than that found in the monometallic tris(dipicolinate) Eu-complex (3.44 Å),[12] pointing to a significant compression along the pseudo C_3 axis. The helical twist of the ligand strands (pitch: 23.7 Å, A and 24.4 Å, B) is achieved through rotation about the methylene C–C bond with interplanar angles between the benzimidazole units in the range 66.5–74.6° (A) and 62.4–72.7° (B). The entire structure is held together by an extensive network of water molecules. Preliminary results on the structure of the Tb and Yb helicates reveal an isotypic series of complexes with Ln^{III} environments comparable to those found for Eu^{III}.

The triple helicate structure is maintained in solution, as demonstrated by the observed ^{1}H NMR spectra in D_2O, which imply the formation of a single, inert and compact complex with D_3 symmetry (Fig. 2).[8,9] A preliminary analysis for the complete Ln series, including separation of the contact and dipolar contributions to the chemical shifts points to an isostructural set of helicates. The $[Ln_2(L^C - 2H)_3]$ complexes display interesting photophysical properties. The quantum yield of the ligand-centred luminescence with respect to quinine sulfate (0.044–0.047 at pH 6.8–12.1 in H_2O) increases 10-fold in the La^{III} and Lu^{III} helicates (0.52 at pH 6.8), while it decreases by a factor 2.5 in the Gd^{III} helicate (0.017 at pH 6.7). The $^1\pi\pi^*$ luminescence disappears in the Eu^{III} and Tb^{III} helicates and the characteristic f–f emission bands are observed. The emission spectrum of the $[Eu_2(L^C - 2H)_3](aq)$ is similar to the solid state spectrum, and the Eu($^5D_0$) lifetime of 10^{-8} M solutions amounts to 2.5 ms (H_2O) and 4.6 ms (D_2O). This substantiates the conclusion based on the NMR spectra regarding the solution structure of the helicates and proves that no OH oscillator is interacting directly with the metal ion, the lengthening of the lifetime in D_2O, formally corresponding to an inner-sphere interaction with 0.2 water molecule,[4] can be assigned to second sphere effects.[15] The quantum yield Q^{Eu}_{rel} of the metal-centred luminescence has been measured for solutions in H_2O (pH 7.0) with respect to 10^{-3} M $[Eu(tpy)_3][(ClO_4)_3$ in MeCN[9] and is equal to 1.00 (absolute yield: 1.3%), leading to a detection limit of 10^{-9}–10^{-10} M in H_2O and 10^{-10}–10^{-11} M in D_2O. Although Tb^{III} appears to be effectively sensitized by L^C, Q^{Tb}_{rel} is low (0.038) due to an efficient back transfer process which was evidenced by measuring the Tb($^5D_4$) lifetime of the helicate between 77 K (2.1 ms) and 270 K (0.05 ms), and which arises from a too close proximity of the $L^C(^3\pi\pi^*)$ and Tb($^5D_4$) levels.

In conclusion, strict self-assembly of L^C with Ln^{III} ions in water leads to the formation of a new class of lanthanide carboxylates. The resulting triple-stranded helicates are thermodynamically highly stable and luminescent (Ln = Eu) and the structural control achieved for these architectures is similar to the one provided by pre-organized receptors.

We thank the Swiss National Science Foundation for supporting grants, the Werner Foundation for a grant to C. P. and the Herbette Foundation (Lausanne) for spectroscopic equipment.

Notes and references

† L^C: ^{1}H NMR [$(CD_3)_2SO$]; δ 1.38 (t, *J* 6.59 Hz, ethyl CH_3), 4.20 (s, bridging CH_2), 4.87 (q, *J* 6.55 Hz, ethyl CH_2), 8.10 (d, *J* 6.12 Hz, H^3 or H^5), 8.46 (dd, *J* 7.45/1.76 Hz, H^3 or H^5), 8.14 (t, *J* 7.45 Hz, H^4), 7.64 (s, H$^{4'}$), 7.26 (d, *J* 8.35 Hz, H$^{6'}$), 7.58 (d, *J* 8.35 Hz, H$^{7'}$). ^{13}C NMR [$(CD_3)_2SO$, HSQC]; δ 61.86 (bridging CH_2), 60.54 (CH_2, ethyl), 34.76 (CH_3, ethyl), 158.95 (C^3 or C^5), 144.36 (C^3 or C^5), 145.98 (C^4), 138.24 (C$^{4'}$), 131.10 (C$^{6'}$), 145.12 (C$^{7'}$). ES-MS: *m/z* 547.5 (M + H$^+$), 588.8 (M + H$^+$ + MeCN), 607.4 (M + H$^+$ + MeCN + H_2O). IR (KBr): 1718 (s, C=O), 2931, 2966 (m, aliphatic C–H), 3030, 3066 (w, aromatic C–H), 3421 cm^{-1} (OH). Elemental analysis for $C_{31}H_{26}N_6O_4 \cdot 1.5H_2O$. Calc: C, 64.91; H, 5.10; N, 14.65. Found: C, 65.09; H, 5.15; N 14.70%.

‡ These data correspond to pLn values ($[Ln^{III}]_t = 10^{-6}$ M, $[L^C]_t = 10^{-5}$ M. F. Vögtle, *Supramolecular Chemistry*, Wiley, Chichester, 1991, pp. 92–95) of 11.55 (La), 9.60 (Eu) and 10.19 (Lu).

§ $[Eu(L^C - 2H)_3] \cdot 9H_2O$. Calc. C, 53.36; H, 4.32; N, 11.30. Found: C, 53.20; H, 4.32; N, 12.01%.

¶ $C_{93}H_{72}N_{18}O_{12}Eu_2 \cdot 20.5H_2O$, $M = 2306.93$, monoclinic, space group $P2_1/c$, $a = 24.808(10)$, $b = 36.285(10)$, $c = 23.701(10)$ Å, $\beta = 110.30(3)°$, $U = 20\,009(13)$ Å^3, $Z = 8$, $\mu = 1.333$ mm^{-1}, $T = 185$ K, 93 431 reflections measured, 28 393 independent reflections, 2630 parameters, $R_F = 0.0609$, wR_2 [$I > 2\sigma(I)$] = 0.1402. CCDC 182/1036.

1 A. P. De Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515.
2 I. Hemmilä, T. Stahlberg and P. Mottram, *Bioanalytical Applications of Labelling Technologies*, Wallac Oy; Turku, 1995.
3 C. H. Evans, *Biochemistry of the Lanthanides*, Plenum, New York, 1990.
4 *Lanthanide Probes in Life, Chemical and Earth Sciences: Theory and Practice*, eds. J.-C. G. Bünzli and G. R. Choppin, Elsevier Science Publ. B. V., Amsterdam, 1989.
5 S. J. Langford and J. F. Stoddart, *Pure Appl. Chem.*, 1996, **68**, 1255.
6 D. E. Koshland Jr., *Angew. Chem. Int. Ed. Engl.*, 1994, **33**, 2375.
7 J.-C. G. Bünzli, S. Petoud, C. Piguet and F. Renaud, *J. Alloys Compds.*, 1997, **249**, 14.
8 C. Piguet, J.-C. G. Bünzli, G. Bernardinelli, G. Hopfgartner and A. F. Williams, *J. Am. Chem. Soc.*, 1993, **115**, 8197.
9 N. Martin, J.-C. G. Bünzli, V. McKee, C. Piguet and G. Hopfgartner, *Inorg. Chem.*, 1998, **37**, 577.
10 M. Latva, P. Makinen, S. Kulmala and K. Haapakka, *J. Chem. Soc., Faraday Trans.*, 1996, **92**, 3321.
11 R. Baggio, M. T. Garland and M. Perec, *Inorg. Chem.*, 1997, **36**, 950.
12 P. A. Brayshaw, J.-C. G. Bünzli, P. Froidevaux, J. M. Harrowfield, Y. Kim and A. N. Sobolev, *Inorg. Chem.*, 1995, **34**, 2068.
13 C. Piguet, J.-C. G. Bünzli, G. Bernardinelli, C. G. Bochet and P. Froidevaux, *J. Chem. Soc., Dalton Trans.*, 1995, 83.
14 F. Renaud, C. Piguet, G. Bernardinelli, J.-C. G. Bünzli and G. Hopfgartner, *Chem. Eur. J.*, 1997, **3**, 1646.
15 R. S. Dickins, D. Parker, A. S. de Sousa and J. A. G. Williams, *Chem. Commun.*, 1996, 697.

Communication 8/06730I