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Highly Luminescent Eu^{3+} and Tb^{3+} Macrocyclic Complexes Bearing an Appended Phenanthroline Chromophore

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A two-component ligand system (**1**) containing 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (**DO3A**) as the hosting unit for the lanthanide cations and an appended asymmetrically functionalized 1,10-phenanthroline (phen) as the chromophore was synthesized. The 1:1 complexes with Eu^{3+}, Gd^{3+}, Tb^{3+}, and Yb^{3+} have been prepared and studied in aqueous solution. For **Gd·1**, a relaxivity value of 2.4 $mM^{-1}\ s^{-1}$ has been measured at 20 MHz and 25 °C, which indicates that there are no water molecules in the first coordination sphere of the metal ion. The analysis of high resolution ^1H NMR spectra of **Yb·1** supports this view and suggests the direct involvement of the phen moiety in the coordination of the metal ion. For **Eu·1** and **Tb·1**, the absorption and luminescence spectra, the overall luminescence efficiencies, and the metal-centered (MC) lifetimes were obtained; coordination features were also determined by comparing luminescence properties in water and deuterated water. For **Eu·1** and **Tb·1**, the overall emission sensitization (se) process in air-equilibrated water was found to be notably effective with $\phi_{se} =$ 0.21 and 0.11, respectively. A detailed study of the steps originating from light absorption at the phen unit and leading to MC sensitized emission was performed.

Introduction

Luminescent and stable complexes of Eu^{3+} and Tb^{3+} are of interest as luminescent probes for diagnostic purposes.[1,2] A great variety of systems have been designed and studied as chelating agents, including, among others, polyaminopolycarboxylates,[3,4] cryptands,[5] calixarenes,[6–8] podands,[9] and helicates.[10,11] The stability constant of the complexes is related to the structural features of the ligand system which must additionally provide an efficient shielding of the Eu^{3+} and Tb^{3+} luminescent centers to prevent undesired interactions with solvent molecules.[12] Accordingly, useful approaches that make use of multichromophoric ligand systems

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have been developed. For instance, encapsulation[3,4,13] and helical wrapping[10] are expected to lead to highly luminescent complexes of Eu^{3+} and Tb^{3+} not only because of structural properties but also because of the many chromophoric units involved in the light absorption. Within this perspective, macrocycles containing bpy or phen (bpy = 2,2′-bipyridine, phen = 1,10-phenathroline) components have been largely employed.[5,6,14] In these cases, the chromophores (L) are arranged to fulfill the coordination requirements of the lanthanide (Ln) cations. Therefore, the antenna-to-cation sensitization step (i.e, the L-to-Ln energy transfer) occurs between partners in a somehow rigid coordination environment. However, most of these systems, with few exceptions,[14] are characterized by a strong quenching of their luminescence in aqueous environments. This is a severe drawback for their application as biological probes.

Recent studies have also pointed out that there may be advantages in the use of somewhat flexible systems, where an “induced fit”[15] takes place between the metal center and some hosting site of the ligand system. Recently, it was shown that a combination of a single chromophore and a polycarboxylate hosting site, provided that they are spatially separated and connected by short chains, can lead to (i) remarkable results in terms of overall sensitized luminescence efficiencies;[16,17] (ii) possible uses for H^+ and O_2 sensing;[18,19] and (iii) implementation of schemes for molecular device operation.[20] Along these lines, we thought that the flexibility issue could be addressed by using a macrocyclic polyaminopolycarboxylic ligand (i.e., 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid, **DO3A**) bearing a flexible sidearm for the connection with a suitable chromophore.[21] Here, we report on the (i) synthesis of such a new ligand incorporating a phen subunit as the chromophore; (ii) luminescence properties of the corresponding Eu^{3+} and Tb^{3+} complexes; and (iii) NMR evidence that the phen moiety is involved in the coordination of the lanthanide ion.

Experimental Section

Materials and Methods. Solvents were purified by using standard methods and dried when necessary. All commercially available reagents were used as received. TLC was carried out on silica gel Si 60-F254. Column chromatography was carried out on silica gel Si 60, mesh size 0.040−0.063 mm (Merck, Darmstadt, Germany). ^1H NMR (300 MHz) spectra were recorded with a Bruker AC 300 spectrometer. Melting points (uncorrected) were determined with a Buchi SMP-20 capillary melting point apparatus.

10-[(9-Methyl-1,10-phenanthrol-2-yl)methyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic Acid Tris(1,1-dimethylethyl) Ester Sodium Perchlorate Complex (4). A suspension of **2** (0.290 g, 1.1 mmol), **3** (0.514 g, 1 mmol), and sodium carbonate (0.210 g. 2 mmol) in 40 mL of acetonitrile was refluxed 24 h under magnetic stirring. The mixture was cooled to room temperature and filtered on a fritted glass, and the filtrate was evaporated to afford a residue. This product was dissolved in 50 mL of CH_2Cl_2 and washed with water (2 × 30 mL) and then with 30% aq $NaClO_4$ (3 × 50 mL). The solvent was removed under reduced pressure and the product purified by column chromatrography (silica gel, CH_2Cl_2/MeOH 96/4) to afford 0.618 g (74%) of **4** as white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 8.22 (1H, d, $J = 8.1$ Hz), 8.15 (1H, d, $J = 8.1$ Hz), 7.75 (2H, s), 7.65 (1H, d, $J = 8.1$ Hz), 7.51 (1H, d, $J = 8.1$ Hz), 4.0 (2H, s), 3.4−2.3 (25H, br m), 1.33 (9H, s), 1.16 (18H, s).^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 172.7, 172.5, 159.1, 145.6, 137.2, 136.9, 128.2, 127.5, 126.8, 125.9, 124.1, 123.8, 82.6, 82.4, 60.9, 56.8, 56.6, 51.8, 50.9 broad, 28.2, 28.1. MS-FAB+: m/z 743 [$M + Na^+$], 721 [$M + H^+$]. Calcd for $C_{40}H_{66}N_6O_6$: 720.

10-[(9-Methyl-1,10-phenanthrol-2-yl)methyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic Acid Tris(1,1-dimethylethyl) Ester (5). Compound **4** (0.5 g, 0.67 mmol) dissolved in methanol (30 mL) was stirred for 8 h at room temperature in the presence of solid KCl (0.23 g, 3 mmol). The suspension was filtered through Celite, and the solvent was removed under reduced pressure. The residue was transferred into a liquid−liquid extractor by using 2 mL of methanol. Then, 20 mL of water was added, and the mixture was continuously extracted with *n*-pentane (200 mL) for 24 h. The solvent was removed under reduced pressure to yield 0.39 g (90%) of a yellowish thick oil. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 8.25 (1H, d, $J = 8.1$ Hz), 8.18 (1H, d, $J = 8.1$ Hz), 8.11 (1H, d, $J = 8.1$ Hz), 7.7 (2H, s), 7.47 (1H, d, $J = 8.1$ Hz), 4.14 (2H, s), 3.36 (4H, s), 2.92 (3H, s), 2.87 (12 H, m), 2.73 (4H, m), 1.46 (9H, s), 1.38 (18H, s). MS-FAB+: m/z 721 [$M + H^+$]. Calcd for $C_{40}H_{66}N_6O_6$: 720.

10-[(9-Methyl-1,10-phenanthrol-2-yl)methyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic Acid (1). A solution of **5** (0.30 g, 0.42 mmol) in 10 mL of trifluoroacetic acid was stirred at room temperature for 4 h. The solvent was evaporated, and the crude was triturated with diethyl ether to yield a white solid. The solvent was separated, and the residue, dissolved in 2 mL of water, was adsorbed on a short Amberlite XAD 1600T column which was eluted with water until the pH was neutral and then with water/acetonitrile 8/2 (v/v) to recover the product as white solid. ^1H NMR (CD_3OD, 300 MHz) δ (ppm) 8.39 (1H, d, $J = 8.4$ Hz), 8.36 (1H, d, $J = 8.4$ Hz), 8.18 (1H, d, $J = 8.4$ Hz), 7.88 (2H, m), 7.67 (1H, d, $J = 8.4$ Hz), 4.40 (2H, s), 3.62 (2H, s), 3.55 (4H, s), 3.36 (8H, m), 3.10 (8H, m), 2.91 (3H, s). ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 171.4, 170.8, 159.4, 159.2, 145.6, 145.3, 137.5, 137.2, 128.3, 127.4, 126.9, 126.3, 124.3, 61.7, 56.5, 52.1, 51.5, 51.1, 50.6, 25.6. MS-FAB(+): m/z 553 [$M + H^+$]. Calcd for $C_{28}H_{36}N_6O_6$: m/z 552. Anal. Calcd: C, 60.8; H, 6.5; N, 15.2. Found: C, 60.1; H, 6.2; N, 14.7.

2,9-Dimethyl-1,10-phenanthroline-*N*-oxide Dihydrate (7). A solution of neocuproine monohydrate (3.0 g, 13.2 nmmol), in trifluoroacetic acid (15 mL) and H_2O_2 (5 mL), was warmed at 60−65 °C for 4 h. The solvent was removed by evaporation in vacuo, and the residue was neutralized with saturated aqueous Na_2CO_3

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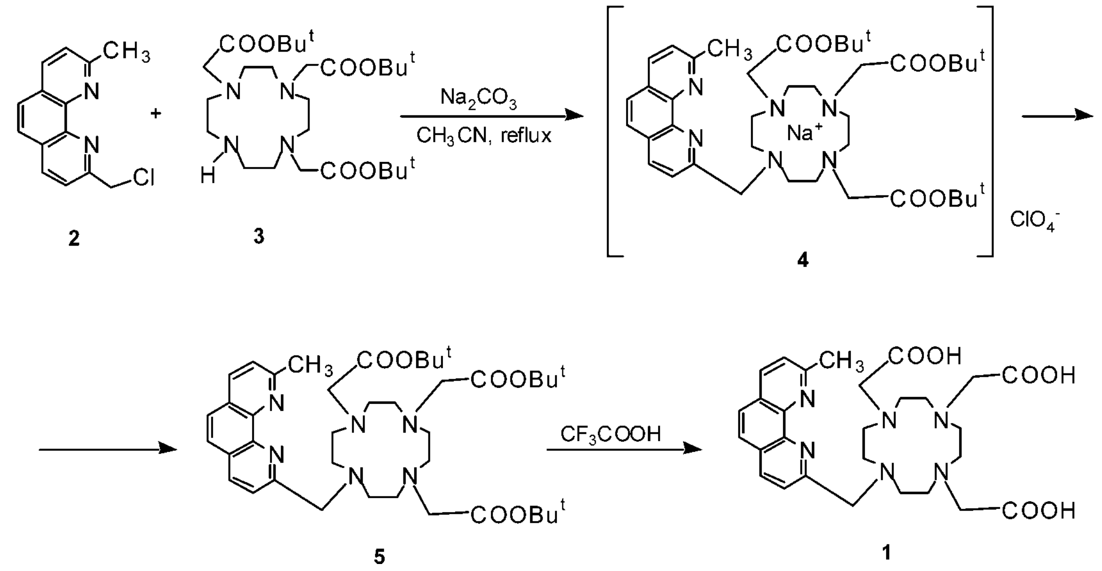
Scheme 1



and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo to afford a violet solid (3.3 g, 95%). Mp: 118−120 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.73 (3H, s), 2.89 (3H, s), 7.45 (1H, d, $J = 8.2$ Hz), 7.47 (1H, d, $J = 8.2$ Hz), 7.59 (1H, d, $J = 8.2$ Hz), 7.61 (1H, d, $J = 8.7$ Hz), 7.67 (1H, d, $J = 8.7$ Hz), 8.05 (1H, d, $J = 8.2$ Hz).

Spectroscopic and Photophysical Measurements. Absorption spectra were measured in water at room temperature with a Perkin-Elmer Lambda 5 UV−vis spectrophotometer. For the steady-state luminescence experiments, a Spex Fluorolog II spectrofluorimeter equipped with a Hamamatsu R928 phototube was employed. Corrected luminescence spectra were obtained by applying corrections in the range 500−820 nm, owing to the wavelength dependence of the phototube response. Relative luminescence intensities were evaluated from the area (on an energy scale) of the luminescence spectra and with reference to a luminescence standard; both $[Ru(bpy)_3]Cl_2$ ($\phi = 0.028$ in air-equilibrated water[22]) and quinine sulfate ($\phi = 0.546$ in 1 N H_2SO_4[23]) were employed.[24] Luminescence lifetimes on the millisecond time scale were obtained with a Perkin-Elmer LS50B luminescence spectrometer. The experimental uncertainty on the absorption and luminescence maxima is 2 and 1 nm, respectively; that for the ϕ and τ values is 10%.

Titration experiments were performed for 1×10^{-5} M water solutions of ligand **1** by using concentrated solutions of lanthanide salts (as Cl^- or ClO_4^- salts, Fluka). To evaluate the association constant, K_{ML}, the employed spectroscopic data points were fitted to eq 1[25,26]

$$I = I_o + \frac{\Delta I}{2S_o}\left[K_{diss} + X + S_o - \sqrt{(K_{diss} + X + S_o)^2 - 4XS_o}\right] \quad (1)$$

where I is the absorbance (or luminescence intensity) value, I_o and ΔI are the initial value and the overall change in absorbance (or luminescence intensity), respectively, $K_{diss} = 1/K_{ML}$, and X and S_o are the titrant and substrate concentrations, respectively. Results of titration experiments, by using both absorption and luminescence data (see examples in Results and Discussion section), are consistent with a 1:1 association stoichiometry, with $K_{ML} \gg 10^6$ M^{-1}. In any case, complex formation was deemed complete after addition of 2−3 equiv of the lanthanide cation to water solutions of **1**, given that formation of **Gd·DO3A** and **Gd·DOTA** takes place with $K_{ML} > 10^{20}$ M^{-1} (**DOTA** = 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid).[27] Model calculations on the equilibrium between phen-centered and Tb-centered levels were performed by using Matlab 5.0 by MathWorks, Inc., MA.

NMR Measurements. The longitudinal water proton relaxation rate was measured by using a Stelar Spinmaster spectrometer (Stelar, Mede, Pavia, Italy) operating at 20 MHz, by means of the standard inversion−recovery technique (16 experiments, 2 scans).[28] A typical 90° pulse width was 3.5 μs, and the reproducibility of the T_1 data was ±0.5%. The temperature was controlled with a Stelar VTC-91 air-flow heater equipped with a copper−constantan thermocouple (uncertainty of ±0.1 °C). The ^{1}H NMR spectra of **Yb·1** were recorded on a JEOL EX-400 spectrometer (9.4 T), using D_2O (99.8%, Cortec, France) as solvent.

Results and Discussion

Design and Synthesis of the Ligand. Bipartite ligand **1**, see Schemes 1 and 2, features a phen unit as the light absorbing chromophore, which is covalently connected through one methylene spacer to a **DO3A** unit, as the Ln^{3+} coordination site.

The choice for the chromophore is due to careful evaluation of the various steps implied in the antenna-to-cation sensitization process, see Scheme 3. Light absorption and

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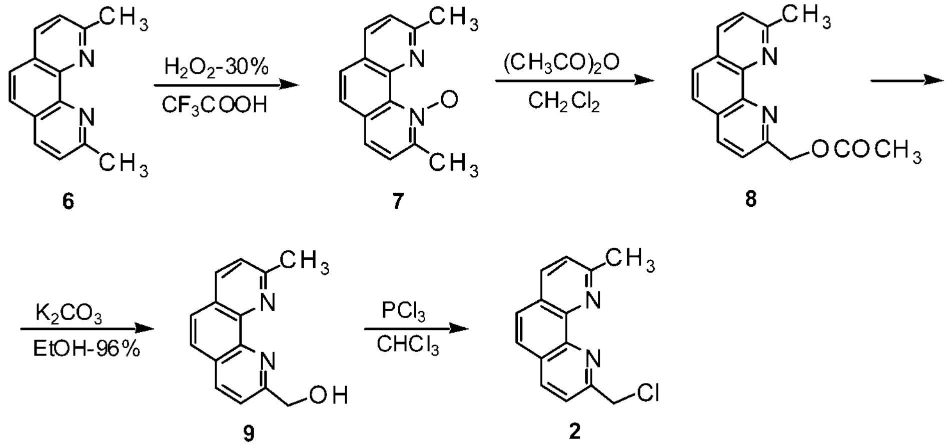
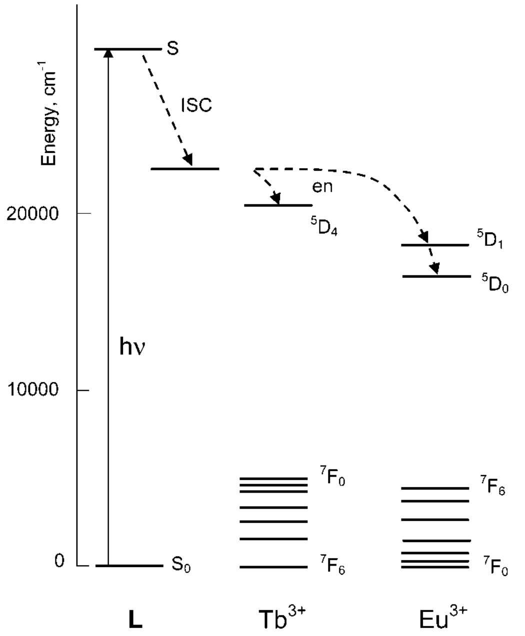
Scheme 2



Scheme 3



singlet state (S) formation at the L chromophore is followed by intersystem crossing (ISC), resulting in population of its lowest-lying triplet (T) level. Subsequent L-to-Ln energy transfer leads to population of a metal-centered (MC) level, which deactivates via radiative and nonradiative paths. Owing to the photophysical properties of phen,[29] a close to unit efficiency for its triplet population is expected (see later). With reference to Scheme 3, the overall efficiency for sensitized emission (se) is

$$\phi_{se} = \phi_{ISC}\,\phi_{en}\,\phi_{lum}{}^{MC} \qquad (2)$$

and optimization of the antenna-to-cation sensitization process requires high efficiencies for all the steps, as we will examine in detail.[30,31]

DO3A was selected as the Ln-chelating subunit because of the high thermodynamic and kinetic stabilities which are well assessed for its lanthanide complexes.[27] Ligand **1** was synthesized according to Schemes 1 and 2. Alkylation of tris(*tert*-butyl) ester, **3**,[32] with 2-chloromethyl-9-methyl-1,-10-phenanthroline, **2**, carried out in CH_3CN at reflux in the presence of Na_2CO_3 as base, and subsequent treatment of the crude, dissolved in CH_2Cl_2, with aqueous $NaClO_4$ afforded sodium complex **4** isolated in 74% yield after column chromatography. The preparation of complex **4** is necessary in order to simplify the chromatographic purification and allows higher yields of isolated product. Decomplexation of **4** was achieved by continuous extraction of the complex, after Cl^- for ClO_4^- counterion exchange, in $H_2O/CH_3OH = 9/1$ (v/v) with *n*-pentane to give very pure **5**, as yellowish thick oil, in 90% yield. Treatment of **5** with CF_3COOH, at room temperature, afforded tricarboxyl derivative **1**, as white solid, in quantitative yield after purification through a nonfunctionalized polystyrene resin.

The preparation of **2** was carried out following the 4-step procedure reported by Newkome and co-workers,[33] starting from commercial neocuproine (Scheme 2). However, differently from Newcome's method, the oxidation of **6** was achieved by using 30% H_2O_2 in CF_3COOH and afforded the corresponding *N*-oxide **7** in 95% yield. All the other steps from **7** to **2** were carried out according to literature[33] and are not detailed in the Experimental Section.

Optical Spectroscopy. Luminescence and photophysical data obtained in water and deuterated water for the **Eu·1** and **Tb·1** complexes are collected in Table 1. In the following, we provide a separate discussion of the absorption and luminescence properties of these and related complexes.

Gd·1. Figure 1 shows the changes of the absorption spectrum of 1×10^{-5} M water solutions of ligand **1**, upon additions of Gd^{3+}. Comparison with literature results for phen ligand[24] indicates that the registered spectral features of **1** (position of band maxima and band intensities) are due to this chromophore. The inset of Figure 1 displays the data

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Table 1. Luminescence and Photophysical Data[a]

	ϕ_{se}[b]	τ_{H_2O}, ms	k_r, s^{-1}	k_{nr}, s^{-1}	τ_{D_2O}, ms	q[c]
Gd·1		$<0.5 \times 10^{-6}$				
Eu·1	0.21	1.24	169	637	1.77	0.0
Tb·1	0.11 (0.55)[d]	0.31 (1.51)[d]	355 (364)[d]	3020 (298)[d]	0.32	0.2

[a] In air-equilibrated water at rt. [b] Luminescence quantum yield upon excitation at 278 nm. [c] Water molecules of the coordination sphere. [d] Degassed sample.

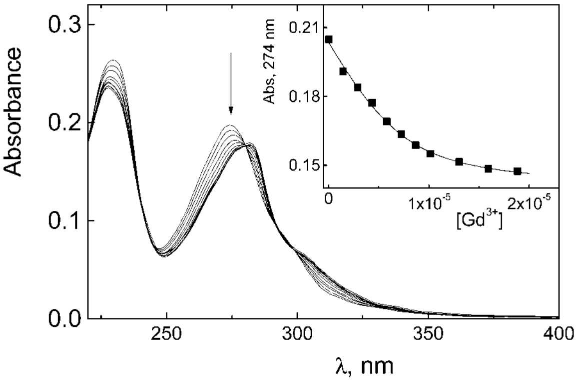

Figure 1. Titration of the absorption spectrum of 1 × 10^{-5} M water solution of **1** by addition of aliquots of Gd^{3+}. The inset shows the absorbance changes at $\lambda = 274$ nm; the full line results from the fitting procedure, see text.

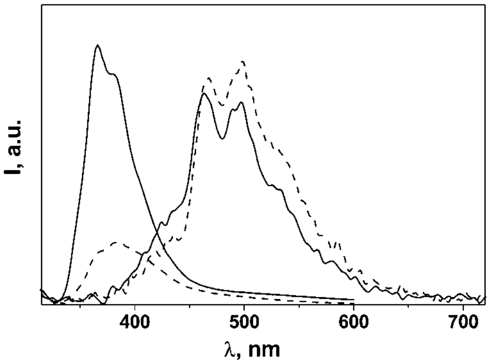

Figure 2. Room-temperature fluorescence (left) and 77 K phosphorescence (right) spectra for **1** (full line) and **Gd·1** (dashed line); $\lambda_{exc} = 278$ nm.

points corresponding to the absorbance values registered at 274 nm. The plateau region is approached for ~1 equiv of Gd^{3+}, consistent with a 1:1 association process, as expected on the basis of electrostatic and structural arguments. This is consistent with previous studies indicating that **DOTA** and **DO3A** in water coordinate lanthanide cations with log $K_{ML} > 20$.[27]

It can be noted that the absorption profile of **Gd·1**, as registered at the end of the titration experiment, mainly exhibits changes in the intensity and position of the band around 272−280 nm. Only modest variations are apparent in the low-energy region of the spectrum, $\lambda > 280$ nm, which is the spectral portion usually growing significantly in intensity upon coordination of phen or bpy ligands to Ln^{3+} cations.[24] As it is well-known, these cations require saturation of 8−9 coordination positions,[34,35] and the fact that for **Gd·1** the absorption profile (of phen origin) is not markedly affected by the presence of the cation center suggests that the N atoms of the phen unit are not equally engaged in the coordination. The same finding was registered for the cases of Eu^{3+} and Tb^{3+}, and in following paragraphs, we provide some evidence regarding possible structural features.

Figure 2 shows the room-temperature fluorescence spectrum of **1** and **Gd·1**, whose observed lifetimes were $\tau_f = 1.1$ and <0.5 ns, respectively; no MC luminescence was observed. The fluorescence spectra, ascribable to the lowest-lying singlet level (S) of phen chromophore (Scheme 3), peak in the same spectral region and exhibit similar profiles. On this basis, the reduction of the fluorescence intensity for **Gd·L** is likely attributable to the heavy-atom effect brought about by the Gd center. As a consequence, improved ISC processes (with a rate constant k_{ISC}) are observed for **Gd·1**, in accord with

$$\phi_{ISC} = k_{ISC}\tau_f \tag{3}$$

where τ_f is given by

$$\tau_f = \frac{1}{k_r + k_{nr} + k_{ISC}} \tag{4}$$

and k_r and k_{nr} are rate constants for radiative and nonradiative processes. It is interesting to compare the fluorescence parameters for phen and phenanthrene, its homonuclear counterpart. In the latter case, fluorescence takes place with $\tau_f = 60$ ns and $\Phi_f = 0.13$, and the singlet deactivates to the triplet with $\phi_{ISC} = 0.85$.[29] For phen, $\tau_f \approx 2$ ns, $\Phi_f \approx 0.004$, and the presence of heteroatoms (with respect to the case of phenanthrene) should enhance the intersystem crossing processes.[36] On this basis, in accord with eqs 3 and 4, for phen, one expects $\phi_{ISC} > 0.85$. In turn, for the phen chromophore within the **Gd·1** complex (and for the **Eu·1** and **Tb·1** cases as well), the further enhancement of ISC processes due to the heavy-atom effect should result in ϕ_{ISC} most likely close to unity.

In Figure 2, the phosphorescence spectrum of the **Gd·1** complex is also shown, as obtained at 77 K; the measured τ_P was 0.53 s. From the structured phosphorescence profile, an energy level $E_T = 21830$ cm^{-1} is derived in correspondence to highest energy band maximum (458 nm). The lack of MC luminescence and the observation of phen-centered phosphorescence are consistent with the fact that the lowest-lying MC excited level ($^6P_{7/2}$) of the Gd center is located at 32150 cm^{-1},[34] that is, well higher in energy than the phosphorescent level of the phen chromophore, E_T. It is worth noting that the triplet level for 1,10-phenanthroline is $E_T^{phen} = 22100$ cm^{-1},[31] so that E_T of **Gd·1** appears only slightly bathochromically shifted upon complexation. The determination of E_T of **Gd·1** is useful while discussing the phen → M energy transfer which occurs within **Eu·1** and **Tb·1**, given that for the latter complexes this same E_T value can be assumed. For an easier discussion of the various steps involved in sensitization of the MC luminescence within **Eu·1** and **Tb·1**, we will refer to Scheme 3.

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(35) Richardson, F. S. *Chem. Rev.* **1982**, *82*, 541.
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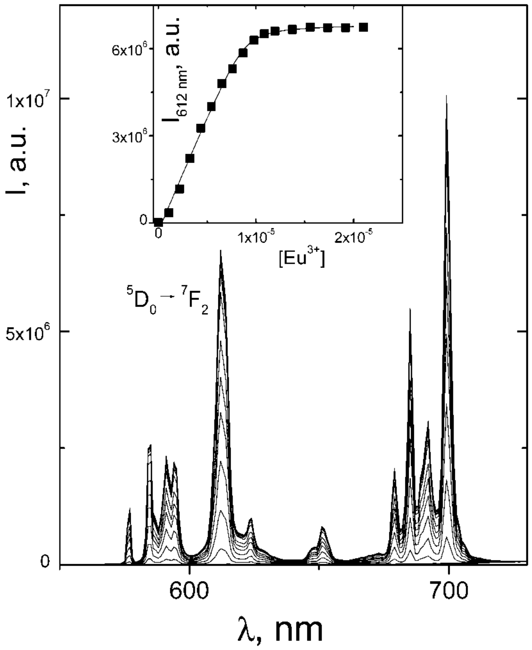
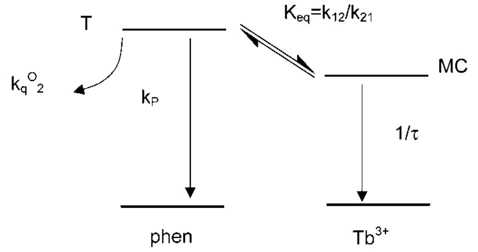


Figure 3. Increase of the luminescence intensity of 1×10^{-5} M water solution of **1** by addition of aliquots of Eu^{3+}; $\lambda_{exc} = 278$ nm. The inset shows the luminescence intensity changes detected at $\lambda = 612$ nm; the full line results from the fitting procedure, see text.

Eu·1. The absorption spectra registered upon titration of 1×10^{-5} M water solutions of **1** with Eu^{3+} are identical to those already seen for titration with Gd^{3+} (Figure 1). The MC $^5D_0$ level of Eu^{3+} is well lower than E_T ($\Delta E \approx 4500$ cm^{-1}), and sensitization of the MC luminescence is observed. This allows observation of the changes of luminescence intensity for **1** upon addition of Eu^{3+}. Figure 3 illustrates results obtained using λ_{exc} 278 (corresponding to an isosbestic point for the absorption spectra of **1** upon Eu^{3+} addition). The inset of Figure 3 shows results from the fitting procedure in accord with eq 1, where I is luminescence intensity observed at 612 nm (corresponding to the $^5D_o \rightarrow {}^7F_2$ transition, which appears as the strongest luminescent band[35] when no phototube correction for the fluorimeter is taken into account) and ΔI is the final increase of luminescence intensity at this wavelength.

Tb·1. For the case of Tb^{3+}, and with regard to the 1:1 stoichiometry, the small changes of the ground-state absorption profile upon cation coordination, and the value for the association constant for formation of the complex in water, titration experiments by using absorption spectra gave results quite similar to those seen above for **Gd·1** and **Eu·1**. The MC $^5D_4$ level of Tb^{3+} is lower than E_T ($\Delta E \approx 1400$ cm^{-1}, Scheme 3), and sensitization of the MC luminescence is observed. However, ΔE is not so large to prevent back energy transfer, as demonstrated by O_2-degassing experiments. Argon bubbled solutions of the **Tb·1** complex show a 5-fold increase of the luminescence intensity registered for the case of the air-equilibrated sample; thus, the determined sensitized luminescence quantum yield is $\phi_{se} = 0.11$ for the air-equilibrated case and 0.55 for the O_2-free case (see Table 1). At the same time, the lifetime for the MC luminescence is found to be 0.31 and 1.51 ms, respectively.

Scheme 4



This outcome prompted us to model the room-temperature equilibrium between the ligand-centered triplet level, T, and the MC luminescent level of Tb^{3+}, with an energy gap between the two levels $\Delta E = 1400$ cm^{-1}, see Scheme 4. The rate for the T phosphorescence decay was $k_P = 1/(35\ \mu s)$,[29] and the rate constant for competitive diffusional quenching by oxygen was $k_q^{O2} = 2.0 \times 10^6\ s^{-1}$, as evaluated from $k_{diff} \times [O_2]$, with $k_{diff} = 7 \times 10^9\ M^{-1}\ s^{-1}$, and $[O_2] = 0.29 \times 10^{-3}$ M.[29]

The experimental findings could be reproduced for k_{12} (the forward energy transfer rate constant) $\approx 5 \times k_q^{O2}$ [with the backward energy transfer $k_{21} = k_{12} \exp(-\Delta E/RT)$]. Accordingly, the phen → Tb^{3+} energy transfer step was evaluated to be $k_{en} \approx 1 \times 10^7\ s^{-1}$.

Structural and Relaxivity Properties of the Complexes. The relaxivity represents the increment of the water proton nuclear magnetic relaxation rate induced by a millimolar concentration of a paramagnetic complex and is routinely used as a measure of the efficacy of Mn^{2+}- and Gd^{3+}-based MRI contrast agents.[37] This relaxation enhancement is the result of the electron−nucleus dipolar interaction modulated by rotation of the complex, electron spin relaxation of the metal ion, and chemical exchange of the coordinated water molecules. The analysis of the pH, temperature, and magnetic field dependence of the relaxivity enables much detailed structural and dynamic information on paramagnetic metal complexes to be obtained.[38] In the absence of water molecules in the inner coordination sphere of the metal ion, the relaxivity of a complex is reduced to the contribution of the outer sphere solvent molecules closely diffusing near the paramagnetic center, but yet, it is detectable. The outer sphere component of the relaxivity is typically of the order of 2−3 $mM^{-1}\ s^{-1}$ at 20 MHz and 25 °C for Gd^{3+} chelates with polyaminopolycarboxylic ligands.[37,39] The relaxivity of **Gd·1** as measured at 20 MHz and 25 °C in aqueous solution is 2.4 $mM^{-1}\ s^{-1}$, a value which is strongly indicative of the absence of any coordinated water molecule in the inner coordination sphere of Gd^{3+}. The relaxivity is constant from pH 4 to 12 to indicate that the integrity and the hydration of the complex are unchanged in this range. This result indicates that the phen moiety is involved in the coordination of the

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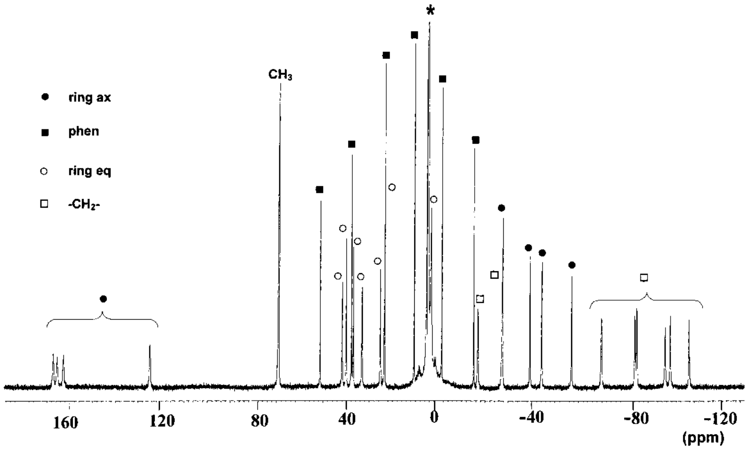

Figure 4. 400 MHz ^{1}H NMR spectrum of **Yb·1** in D_2O at pH = 7.2 and 25°C. The peak labeled with an asterisk represents the residual HDO resonance.

Gd^{3+} ion and prevents the access of the solvent molecules to the metal center.

More insights into the solution structure of the **Ln·1** complexes were obtained from analysis of the ^{1}H NMR spectra of the Yb^{3+} derivative. This ion is well suited to this type of analysis because it couples in the high resolution spectra of its complexes a large chemical shift range and a relatively limited paramagnetically induced line broadening. Furthermore, the isotropic shift is largely dipolar in origin and thus more directly amenable to the obtainment of structural information.[40] The 400 MHz ^{1}H NMR spectrum of **Yb·1** in D_2O at pH = 7.2 and 25 °C is reported in Figure 4. The spectrum consists of 30 resonances which correspond to the 31 nonequivalent protons of the complex (1 peak is masked by the broad signal of HDO) and cover a chemical shift range of more than 260 ppm. All the resonances have the same relative intensity, with the exception of the resonance at 66.7 ppm (relative intensity 3) easily attributable to the methyl group. By comparison with published data on structurally related complexes, it is possible to partially assign the resonances.[41] The low field chemical shift values of the 4 axial protons of the macrocyclic ring are particularly diagnostic and suggest for the complex a square-antiprismatic (SAP) structure, in analogy with the major isomer present in the corresponding **Yb·DOTA** complex.[42] This structural arrangement implies coordination of the N atom (adjacent to the methylenic group) of the phen unit to originate a five-membered ring, of particular stability in this class of complexes.[43] Interestingly, unlike most of the lanthanide complexes with DOTA-like ligands, only one isomer is observed over the temperature range 0−80 °C. This might be rationalized in terms of (i) increased stabilization of the SAP isomeric form at the end of the lanthanide series with respect to the DOTA complexes;[44] and (ii) high activation energy for the isomerization process due to the steric crowding of the phen moiety.

The signals of the protons of the phen moiety cover a chemical shift range of about 80 ppm (−14/+67 ppm) and show a marked paramagnetic shift. In particular, the chemical shift (+67 ppm) of the methyl group suggests a position very close to the paramagnetic center. Furthermore, these spectral features remain unchanged in the temperature range 1−80 °C, to indicate a marked structural rigidity of the metal complex.

The lack of coordinated water molecules, the high degree of stereochemical rigidity of the complex, and the marked paramagnetic isotropic dipolar shift of the phen protons represent a strong indication that the second N atom (adjacent to the methyl group) of the phen unit is located in a nearly apical position, above the NO_3 upper square plane of the antiprism. However, these NMR data alone do not allow us to discriminate between the occurrence in solution of 9-coordinate Ln complexes, where both N atoms of the phenantroline belong to the inner coordination sphere of the metal ion, or 8-coordinate Ln complexes, where the access of the water molecules is only sterically hindered.

Structural and Photophysical Properties of the Complexes. Table 1 lists luminescence efficiencies (ϕ_{se}) and lifetimes (τ) observed for the Eu^{3+} and Tb^{3+} complexes dissolved in water and deuterated water. The number of coordinated molecules (q, uncertainty ±0.5) at the metal centers, also reported in Table 1, was estimated on the basis of the following equations[12]

$$q^{Eu} = 1.2(1/\tau_{H_2O} - 1/\tau_{D_2O} - 0.25) \tag{5}$$

$$q^{Tb} = 5(1/\tau_{H_2O} - 1/\tau_{D_2O} - 0.06) \tag{6}$$

The results of Table 1 regarding the hydration number are in full agreement with the relaxometric properties of **Gd·1**. On the other hand, the small changes of the absorption

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spectra of **1** as registered upon Ln^{3+} titration (see Figure 1) indicate that the cation does not cause a strong perturbation of the electronic properties of the phen chromophore. This supports the view that the N atoms of the phen unit of **1** are not equally involved in the coordination of the metal center, at odds with what usually happens for most of the bpy and phen ligand systems.[5,24]

In conclusion, with reference to the various steps depicted in Schemes 3 and 4, the efficiency for the overall sensitization process (see eq 2), of water solutions of both **Eu·1** and **Tb·1** (O_2-free case), is characterized by unitary ϕ_{ISC} and ϕ_{en} values. This is due to the fact that (i) light absorption at the phen chromophore results in efficient population of its triplet level, and that (ii) the phen → M energy transfer process is much faster then the competing phosphorescence path, $k_{en} \gg k_P$; of course, in the case of Tb^{3+}, competition against diffusional quenching by dissolved O_2 must be taken into account. This allows some conclusion to be reached about reference limits attainable for the overall sensitization efficiency, ϕ_{se} (Scheme 3, eq 2), that includes the intrinsic luminescence efficiency at the metal center.

$$\phi_{lum}^{MC} = \frac{k_r^{MC}}{k_r^{MC} + k_{nr}^{MC}} \qquad (7)$$

In fact, absolute quantum yield and lifetime values obtained after direct excitation of Eu^{3+} and Tb^{3+} dissolved in water yielded the radiative rate constants, $k_r^{Eu} = 170$ and $k_r^{Tb} = 210\ s^{-1}$, contributing to deactivation of their luminescent levels.[34] On the other hand, as shown in a pivotal work by Horrocks and Sudnick,[45] for *no* OH oscillators (from measurements in D_2O) coordinated at the ions, $k_{nr}^{Eu} = 380$ and $k_{nr}^{Tb} = 120\ s^{-1}$. Use of these values leads to $\phi_{lum}^{Eu} = 0.31$ and $\phi_{lum}^{Tb} = 0.64$ (eq 7) that could be regarded as the largest attainable values for ϕ_{lum} due to the intrinsic properties of the cations.[46] On this basis, for the investigated systems **Eu·1** and **Tb·1** (O_2-free case), the found overall ϕ_{se} is 73% and 86%, respectively, of the reference upper limit. Such high luminescence quantum yields have only seldom been reported; for instance, $\phi_{lum}^{Tb} = 0.44$ (in water, air-equilibrated conditions) was registered for a complex based on a tetraazacyclododecane-benzylphosphinate ligand for which no water molecules were found in the coordination sphere.[47]

Conclusions

In complexes of ligand **1** with lanthanide ions, the phenanthroline subunit directly participates to the coordination of the metal ion. Furthermore, the rigidity and spatial arrangement of this chromophore prevent the access of any water molecule into the first coordination sphere of the metal ion. This feature has been exploited to achieve Eu^{3+} and Tb^{3+} complexes which are characterized by high luminescence efficiencies in water. This result has been achieved by using a ligand system whose absorption properties were significant for $\lambda < 300$ nm. Of course, for a system to be employed for biological purposes, (i) a longer wavelength for the absorption maximum should be available, as indicated by recent studies in the area,[7,16b,17a,30] and (ii) the product of the extinction coefficient at the employed excitation wavelength and the observed luminescence quantum yield should favorably compare with other antenna systems.[5]

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(46) Xiao and Selvin, ref 16a, for Eu^{3+} and Tb^{3+} hosted within **DOTA** in D_2O, found the following metal-centered rate constants: $k_r^{Eu} = 220$, $k_r^{Tb} = 287$, $k_{nr}^{Eu} = 221$, and $k_{nr}^{Tb} = 96\ s^{-1}$; this results in $\phi_{lum}^{Eu} = 0.50$ and $\phi_{lum}^{Tb} = 0.75$. In the conditions employed by these authors, the shielding against high-frequency oscillators within the first coordination sphere is expected to be very efficient (which allows a satisfactory determination of the somewhat elusive *intrinsic* metal-centered nonradiative contribution, see refs 17b, 34, 35, 45). In this regard, the overall ϕ_{se} found by us for **Eu·1** and **Tb·1** (water solvent) amounts to be 42% and 73% (O_2-free case), respectively, of the reference upper limit.

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