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Sensitization of Europium(III) Luminescence by Benzophenone-Containing Ligands: Regioisomers, Rearrangements and Chelate Ring Size, and Their Influence on Quantum Yields

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A series of europium(III) complexes based on the macrocyclic azacarboxylate structure, DO3A, have been investigated, incorporating benzophenone appended at N10 of the macrocycle via linkers containing amide bonds (H_3DO3A = 1,4,7,10-tetraazacyclododecane-1,4,7-tris-acetic acid). Complexes [EuL$^{1-3}$] incorporate N^{10}–CH_2CONH–*BP* linkers (*BP* = benzophenone), which allow formation of a five-membered chelate ring containing the metal ion upon chelation of the amide oxygen; these three isomeric complexes differ from one another in the substitution position of the *BP* unit, namely para, meta, and ortho for L^1, L^2, and L^3 respectively. The quantum yields of europium luminescence sensitized via the chromophore are found to be highly dependent upon the position of substitution, being 20 times smaller for the ortho compared to the para-substituted complex. A related para-substituted *BP* complex [EuL^4], prepared by an unusual Michael reaction of the azamacrocycle with a *BP*-containing acrylamide, incorporates an additional methylene unit in the linker, namely N^{10}–CH_2CH_2CONH–*BP*. Despite the longer linker, this complex equals the luminescence quantum yield achieved with [EuL^1] (Φ_{lum} = 0.097 and 0.095, respectively, in H_2O at 298 K). Analysis of the pertinent kinetics reveals that the decreased energy transfer efficiency in this complex, arising from the longer donor–acceptor distance, is compensated by an increased radiative rate constant. Under basic conditions, the ortho-substituted complex [EuL^3] undergoes an intramolecular rearrangement to generate an unprecedented complex [EuL^5] incorporating a 4-phenyl-2-hydroxyquinoline unit directly bound to the ring nitrogen. Although this complex is a poor emitter, an analogous complex obtained from 2-amino-acetophenone, which generates 4-methyl-2-hydroxyquinoline during the corresponding rearrangement, is an order of magnitude more emissive while still benefiting from relatively long-wavelength absorption. The emission from this complex is pH sensitive, being dramatically quenched under mildly basic conditions.

Introduction

The sensitization of lanthanide(III) luminescence by organic chromophores was first reported by Weissman 65 years ago.[1] Detailed investigations into the mechanism of energy transfer were made by Crosby and co-workers in pioneering studies during the 1960s.[2,3] They examined the process in the context of the theories of energy transfer that had recently been put forward by Dexter[4] and by Förster,[5] highlighting the importance of the sensitizer triplet state in acting as the donor to energetically appropriate excited states of the lanthanide ions.

Much of the recent interest in this process has been stimulated by the application of lanthanide complexes as luminescent probes and sensors in biological systems.[6–8] Here, the long lifetime of the metal-centered emission, which is normally not quenched by molecular oxygen, allows the

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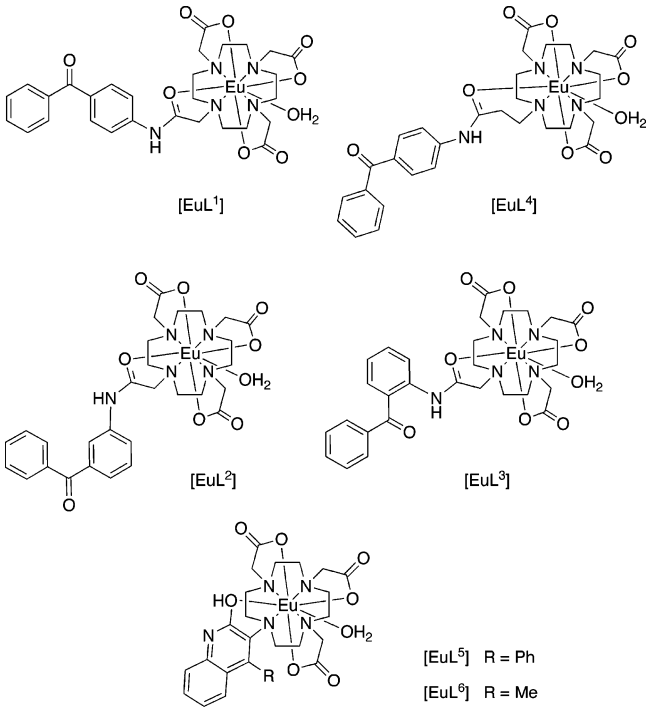
use of time-resolved detection to discriminate between the luminescence of the probe and the ubiquitous, short-lived auto-fluorescence. Only those complexes that are stable and soluble in water, with high thermodynamic and kinetic stability with respect to metal-ion dissociation, are realistic candidates for such applications. These criteria are analogous to those that must be met by gadolinium complexes for use as contrast agents in magnetic resonance imaging (MRI).[9−11] The highly polydentate, seven to nine-coordinating ligands based on aza-carboxylates, -phosphinates, and -phophonates, that have been developed for in vivo use in MRI,[12] are also suitable core ligand structures for biocompatible luminescent complexes because of the high stabilities they offer. On the other hand, to optimize luminescence, it is also necessary to limit the ingress of water molecules into the inner coordination sphere of the metal ion, which otherwise offer the excited states a facile pathway of nonradiative deactivation through energy transfer into O−H vibrations.[13−15] In addition, given the low extinction coefficients of lanthanide f−f transitions (ϵ typically <1 mol^{-1} dm^3 cm^{-1}), the ligand should preferably also incorporate an aromatic-sensitizing group to absorb light more efficiently and populate the lanthanide excited state by energy transfer.[9,16,17,18] A popular strategy for ligand design has been to use the DOTA structure as the core (DOTA = 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetate, the Gd^{3+} complex of which is the MRI contrast agent DOTAREM) and to covalently link the sensitizer unit to one of the four arms through an amide bond (e.g., as in Scheme 1).[11,16,19,20]

The role of the sensitizer triplet state in the energy transfer process has been conclusively confirmed for several chromophores by a combination of triplet−triplet transient

Scheme 1. Structures of the Complexes [EuL^1]−[EuL^6] Investigated in This Study



absorption and time-resolved emission spectroscopy.[21] The overall quantum yield of luminescence, Φ_{lum}, should then be favored by a high value of the quantum yield of triplet formation, Φ_T, of the sensitizer, because

$$\Phi_{lum} = \Phi_T \eta_{et} k_r \tau_{obs} \quad (1)$$

where η_{et} is the efficiency of energy transfer and where the product of k_r (the radiative rate constant of the lanthanide) and τ_{obs} (the observed luminescence lifetime) is the efficiency of emission from the lanthanide, η_{Ln}. Previously, it has been noted that molecules with n,π^* triplet states, such as aromatic ketones, typically have high triplet-quantum yields and small singlet−triplet energy gaps, and hence should be attractive as sensitizers of lanthanide luminescence.[22] We reported high efficiencies of luminescence from Eu^{3+} and Tb^{3+} complexes incorporating benzophenone as a sensitizer in aqueous solution.[22] Acetophenones, also with n,π^* triplet states, similarly proved effective.[23,24] Meanwhile, acridones,[25] azaxanthones, and azathioxanthones[26] have also been explored

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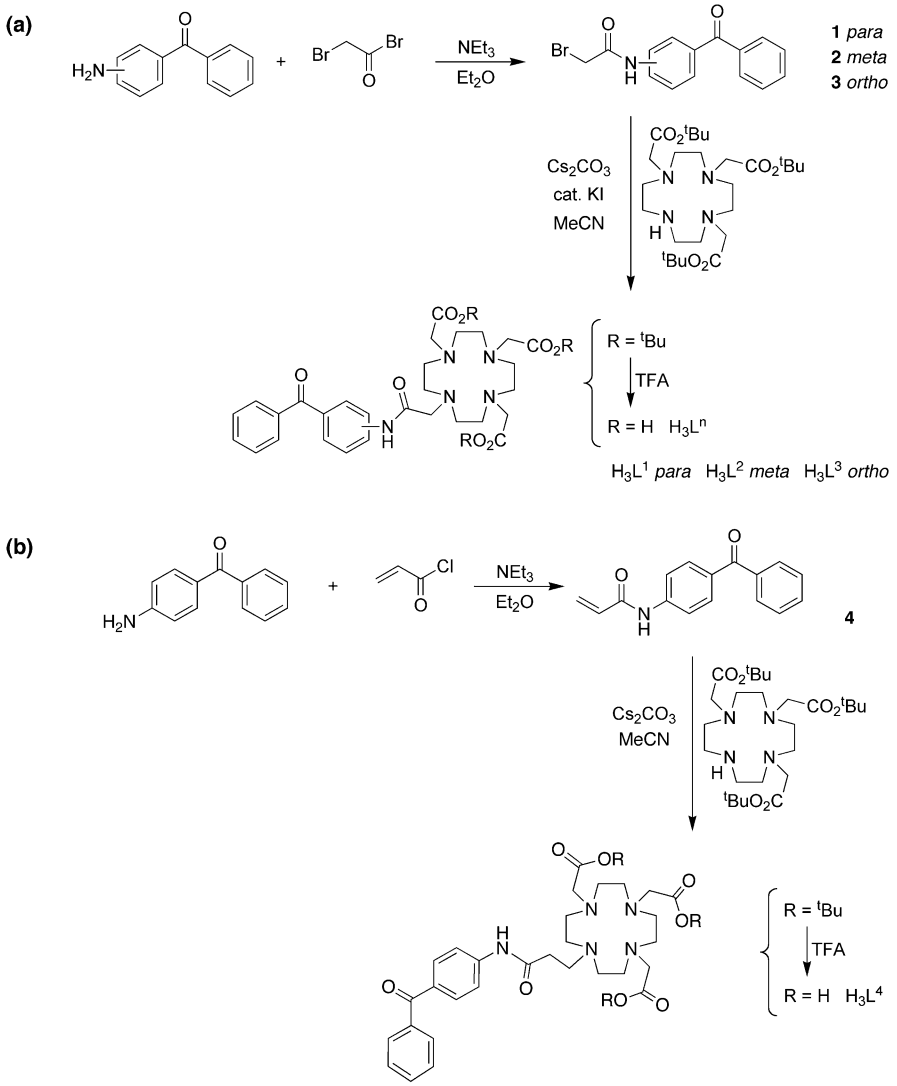
Scheme 2. The Synthetic Strategy Used to Prepare the Para, Meta, and Ortho-Substituted Benzophenone Complexes [EuL^1]−[EuL^3] (*a*), and the Complex [EuL^4] Incorporating the Additional Carbon Atom in the Pendent Amide Arm (*b*)



as sensitizers, the most effective of which also benefit from high triplet-quantum yields.

In this work, we have sought to investigate further the properties and utility of benzophenone as a sensitizer of europium luminescence in single-component, water-soluble complexes. Three distinct areas are explored:

(i) the influence of substitution position (*o*-, *m*-, or *p*-) at the benzophenone unit on the luminescence properties of the complex, revealing that Φ_{lum} is very different for the three regioisomers,

(ii) comparison of the use of a classical three-atom macrocycle-to-sensitizer linker (five-membered chelate ring with the metal ion), with a four-atom linker generated from an acrylamide and giving a six-membered chelate. We demonstrate that the latter can provide an attractive and potentially versatile alternative strategy to the frequently used α-haloamides, without compromising luminescence quantum yields, and

(iii) for the ortho-linked isomer, we report on an unusual rearrangement reaction that leads to unprecedented *N*-arylated complexes and assess the contrasting effectiveness of the resulting 2-hydroxyquinoline pendants as sensitizers of Eu^{3+} luminescence under neutral and basic conditions.

Results and Discussion

Ligand Design and Synthetic Strategy. The synthesis of the three isomeric ligands HL^1−HL^3 was carried out by alkylation of DO3Bu^t (the tris-*tert*-butyl ester of DO3A = 1,4,7,10-tetraazacyclododecane-1,4,7-tris-acetic acid) with the bromoacetamides **1**−**3** obtained upon acetylation of *ortho*, *meta*, and *para*-aminobenzophenone with bromoacetylbromide (part a of Scheme 2). The intermediate DO3Bu^t is attractive in such syntheses of mono-*N*-functionalized DO3A derivatives because it can be obtained upon the alkylation of cyclen with *tert*-butylbromoacetate in the presence of $NaHCO_3$ as the base with reasonable selectivity over the bis and tetrakis compounds.[25] Moreover, after the functionalization of the fourth NH group, the *tert*-butyl groups can be deprotected under mild nonaqueous conditions, using trifluoroacetic acid at room temperature to reveal the desired carboxylate functionality (part a of Scheme 2). In these compounds, there is a three-atom linker (−CH_2−CO−NH−)

between the macrocyclic nitrogen atom and the aromatic ring of the chromophore. As noted above, this arrangement is typical of a large number of structurally related complexes, prepared in a similar manner by alkylation of cyclen with α-haloamides.[11,16,19,20] When the ligands bind to the metal ion, this three-atom linker arrangement favors coordinate-bond formation between the polarizable amide oxygen and the metal and leading to a five-membered chelate ring (Scheme 1, [EuL^{1-3}]).

In a distinctly different strategy for activating the chromophore for *N*-substitution of the macrocycle, acrylamide **4** was prepared by reaction of *para*-aminobenzophenone with acryloyl chloride in the presence of a base. The resulting acrylamide underwent a conjugate Michael addition reaction with DO3Bu^t upon refluxing in acetonitrile solution; after deprotection of the *t*-butyl esters, ligand H_3L^4 was obtained (part b of Scheme 2). In this case, the extended four-atom linker ($-CH_2-CH_2-CO-NH-$) would lead to a six-membered chelate, if the amide carbonyl oxygen does indeed coordinate to the metal ion (Scheme 1, [EuL^4]). The use of such six-membered chelates within DOTA-based lanthanide complexes has scarcely been investigated, despite the plethora of compounds incorporating five-membered chelating amides. Perhaps the most closely related binding motif comes from very recent work by Borbas and Bruce, who elegantly appended rhodamine and nucleobases onto a cyclen ring via peptide coupling reactions with ethylamine units.[27]

The complexation of aminocarboxylate ligands like H_3L^1–H_3L^4 to lanthanide ions is promoted by the presence of a base to take up the three protons released per molecule of ligand. Typically, the protonated ligands are treated with a base to pH ~8, prior to the addition of the lanthanide salt and refluxing of the resulting mixture; strongly basic conditions are normally avoided to prevent the formation of the lanthanide(III) hydroxide.[28] This method led successfully to the europium complexes of ligands H_3L^1, H_3L^2, and H_3L^4, which could be purified by column chromatography on alumina. The novel complex [EuL^4], incorporating the longer four-atom linker, displays a ^{1}H NMR spectrum in D_2O spanning the range +33 to −20 ppm that is very similar to that of [EuL^1]. This indicates that the additional CH_2 unit does not significantly influence the structure of the complex compared to compounds with a conventional amide linker. A total of 26 proton signals (each with integral = 1) are clearly resolved (excluding the aromatic signals and the exchangeable NH): 16 for the cyclen ring, 6 for the acetate arms, and 4 for the amide-containing arm. That the latter four are each resolved is very strong evidence that the amide oxygen is coordinated rigidly to the metal forming the anticipated six-membered chelate; an unbound, freely rotating arm, in contrast, would be expected to lead to only two CH_2 signals of integral = 2. This is consistent with the hydration state of the metal determined by luminscence, which implies an eight-coordinate complex (vide infra). Variable temperature ^{1}H NMR spectra reveal no evidence of loss of rigidity specifically associated with this arm at elevated temperatures (up to 60 °C). The change from the five- to the six-membered chelate has no apparent detrimental effect on the stability of the complex in solution. This is unsurprising, given that the complex is based on the DO3A core, numerous studies having revealed that this core structure can tolerate functionalization of the fourth-ring nitrogen atom by a variety of units, including non-coordinating ones, without loss of stability of the lanthanide complexes.[11,29]

The Ortho-Substituted Isomer: An Unexpected Rearrangement. Attempted complexation of the ortho-linked ligand H_3L^3 under the conditions used to obtain [EuL^{1-2}] and [EuL^4] did not give the expected complex [EuL^3]. The electrospray ionization mass spectrum of the product was indicative of a single europium-containing species, but the observed mass was 18 units lower than for the meta and para isomers, suggesting elimination of a water molecule and possible rearrangement to the complex [EuL^5] (Scheme 1). This was supported by analysis of the ^{1}H NMR spectrum, which showed only six protons assignable to NCH_2CO groups, compared to the total of eight expected and observed for the other isomers. To investigate the resulting compound more fully, identical synthetic conditions were used to prepare the analogous complex of the diamagnetic yttrium-(III) ion. Y^{3+} is comparable in size to Eu^{3+} and binds to DOTA in a similar manner.[30] The simpler ^{1}H NMR spectrum of the resulting diamagnetic complex was consistent with the proposed structure and the presence of the 2-hydroxyquinoline unit.

A likely mechanism for the rearrangement is shown in Scheme 3. This pathway is only open to the *ortho*-aminobenzophenone derivative because only in this case does the attack of the enolate ion result in the formation of a favored six-membered ring. The rearrangement was also found to proceed in the absence of lanthanide(III) ions; refluxing H_3L^3 in aqueous NaOH for 24 h gave a pale-yellow solid whose EI mass spectrum {m/z = 566 ($[M+H]^+$) and 588 ($[M+Na]^+$)} and ^{1}H NMR spectrum were consistent with the rearranged ligand, $[L^5]^{3-}$. Indeed, related rearrangements to form 4-hydroxyquinoline derivatives were observed over a century ago.[31] Interestingly, however, no such reaction was observed for the *t*-butyl-protected ester precursor upon refluxing an ethanolic solution in the presence of an organic base, triethylamine. To establish the generality of the rearrangement, the methyl derivative, [EuL^6], was also prepared via a strictly analogous procedure (Scheme 4), starting from the *N*-alkylation of DO3Bu^t with *N*-(2-acetylphenyl)-2-bromoacetamide (viz. the bromoacetamide formed by acetylation of 2-aminoacetophenone with bromoacetyl bromide). Because the OH group of hydroxyquinolines can be removed, for example, via reduction of the

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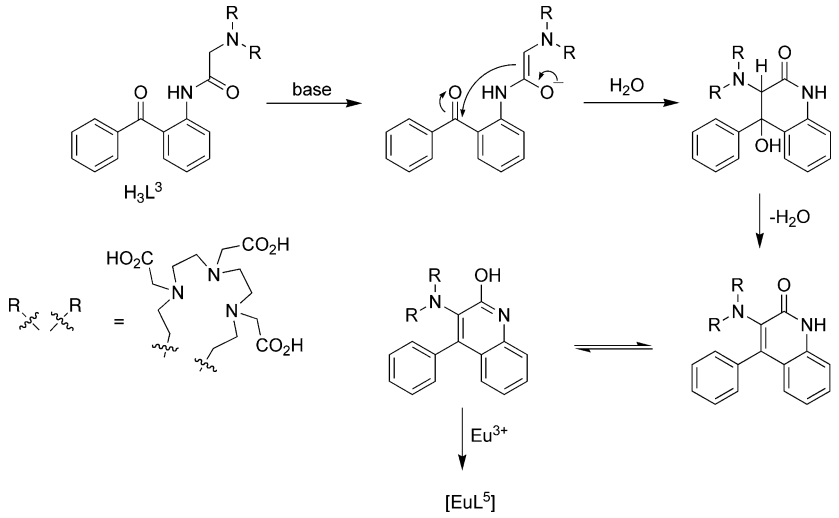
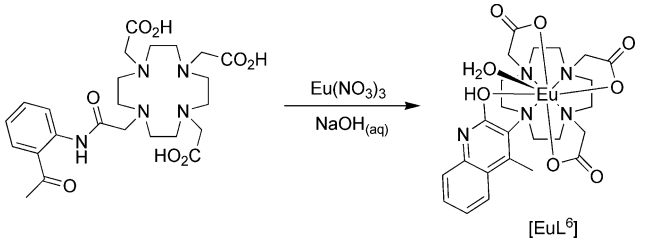
Scheme 3. Suggested Mechanism for the Formation of the Rearranged *ortho*-Aminobenzophenone Derivatized DO3A Complex under Basic Conditions, (i.e., $[EuL^3] \rightarrow [EuL^5]$)



Scheme 4. Rearrangement and Complexation of a 2-Aminoacetophenone Derivatized DO3A Ligand, H_3L^{pre-6}, Generating $[EuL^6]$



tosylate, this rearrangement may be useful as a straightforward route to quinolin-3-yl *N*-arylated macrocycles.

Although crystals of the rearranged complexes $[EuL^5]$ and $[EuL^6]$ suitable for X-ray diffraction analysis could not be obtained, consideration of the likely molecular geometry of the macrocycle is of interest. In complexes of DOTA and *N*-alkylated DO3A derivatives, the *N*-pendent groups are twisted with respect to the N_4 plane, resulting in the typical square-antiprismatic and twisted square-antiprismatic geometries.[32] In $[EuL^5]$ and $[EuL^6]$, however, the direct connection of an aromatic ring to the macrocycle will enforce a planar geometry for the organic part of the five-membered Eu−N−C−C−O ring, restricting the twisting of the N_4 and O_4 planes and potentially inducing a change in the normal puckering of the cyclen ring. Evidence for such a distortion in geometry is provided by the $^1H-^1H$ COSY NMR spectrum, where cross-peaks between protons separated by many bonds may be observed when they are brought into close spatial proximity. A number of additional cross-peaks are observed, of particular note being those between the axial protons at 41.8 and 30.8 ppm, and between the equatorial protons at 1.6 and −9.1 ppm. This is consistent with a change in puckering of the ring from a C_4 symmetric form (Figure 1, geometry **I**) toward a C_2 symmetric form (geometry **II**). In addition, ^1H NMR spectroscopy of Na_3L^5, the crude product from rearrangement of the free ligand, exhibits remarkably well-resolved resonances associated with the CH_2 protons, suggesting that the conformation is restricted even in the absence of a metal ion, in contrast to the normally broad signals associated with the fluxional nature of the noncomplexed ligands. Again, the complex is highly stable in aqueous solution and tolerates, for example, several days at pH 1. As noted above for $[EuL^4]$, this high stability is associated with the DO3A core, which persists essentially irrespective of the nature of the substituent introduced onto the fourth-ring nitrogen atom.

Complexes of aromatic chromophores directly attached to cyclen rings have been little studied, with research almost invariably focusing on compounds with alkyl spacer units. Classical *N*-arylation reactions of cyclen are only achievable with electron-poor arenes such as fluorinated nitrobenzenes, requiring high temperatures and extended reaction times, except for the most-active arylating agents like 2,4,6-trichloro-1,3,5-triazine.[33] Attachment of a wider range of haloarenes by palladium-catalyzed *N*-arylation reactions has been reported recently, but yields are low.[34] To our knowledge, the only reported lanthanide complexes of *N*-arylated cyclens are the Eu(III), Gd(III), and Tb(III) complexes of the *N*-nitrophenyl and anilino derivatives of DO3A,[33b] and there are no previous examples of lanthanide(III) complexes based on cyclen incorporating metal-bound *N*-aryl substituents.

Returning to the synthesis of $[EuL^3]$, it finally proved possible to obtain this complex, without competitive rearrangement, by ensuring that the pH of the solution for complexation was maintained at 6 or below, with the solution being heated to only 40 °C.

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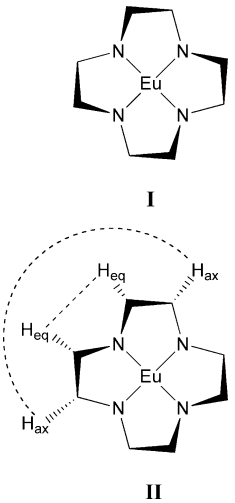

Figure 1. Effect of ring puckering on the geometries of lanthanide(III)-coordinated cyclen derivatives. **I** = C_4-symmetric conformation of the macrocycle normally observed in DOTA complexes. **II** = Dashed lines represent additional $^1H-^1H$ COSY cross-peaks observed in the *N*-aryl-substituted complexes.

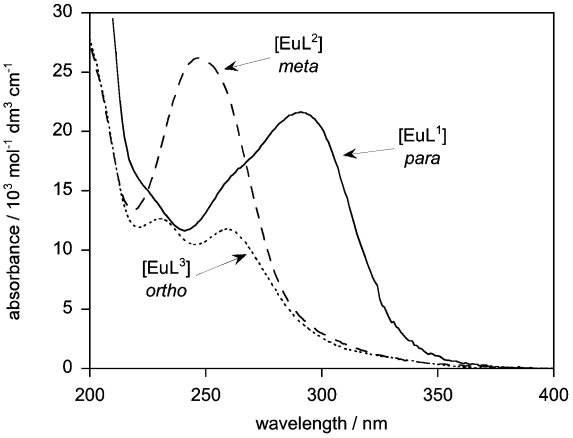

Figure 2. Ground-state absorbance spectra of [EuL^1] (solid line), [EuL^2] (dashed line), and [EuL^3] (dotted line) in aqueous solution at 295 K.

Photophysical Properties of the Europium Complexes. Ground-State Absorption. Absorption spectra of the europium(III) complexes [EuL$^{1-3}$] in the UV−visible region are shown in Figure 2. Two absorption bands are resolved for the ortho isomer [EuL^3] (λ_{max} = 231 and 259 nm), whereas a shoulder at around 262 nm is clearly discernible on the high-energy side of the broad band of [EuL^1] (λ_{max} = 291 nm). The meta isomer [EuL^2], on the other hand, appears to display only a single, rather more-intense band (λ_{max} = 247 nm). However, although only one band may be resolved, ZINDO calculations suggest that two bands should be present for all three isomers, relating to excitation of an electron from a π orbital localized on the unsubstituted phenyl ring and from a π orbital localized on both phenyl rings.[35] Where a single feature is observed, this is probably a combination of two unresolved bands of similar energy. The notable red-shift for the para isomer is attributed to the increased delocalization across the amide group.

(35) ZINDO electronic spectra calculations were performed on 2-amino-*N*-(benzoylphenyl)-acetamide structures at the MM3 optimised geometries using the CaChe 6.1.1 software package, Fujitsu Limited, 2003.

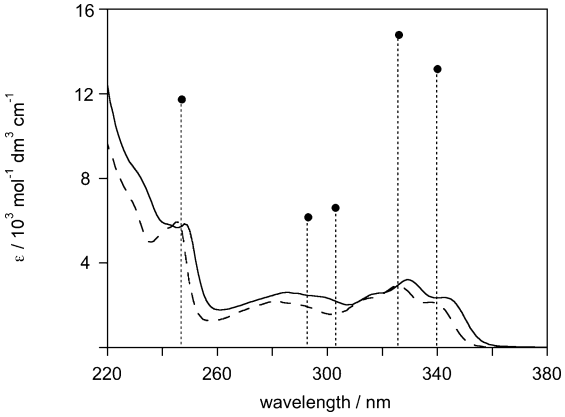

Figure 3. Ground-state absorbance spectra of [EuL^5] (solid line) and [EuL^6] (dashed line) in aqueous solution at 295 K. The literature numerical absorbance data (λ_{max} values) for 3-aminoquinolin-2-ol are included for comparison (filled circles).[36]

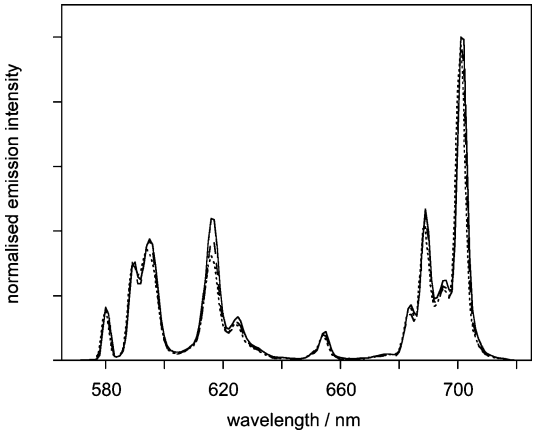

Figure 4. Emission spectra of [EuL^1] (solid line, λ_{ex} = 280 nm), [EuL^2] (dashed line, λ_{ex} = 250 nm), and [EuL^3] (dotted line, λ_{ex} = 280 nm), in aqueous solution at 295 K. Excitation and emission band-passes = 2.5 nm.

In contrast, the rearranged complexes [EuL^5] and [EuL^6] absorb out to a much-longer wavelength (Figure 3), consistent with the proposed quinoline rearrangement product and matching well with literature λ_{max} absorbance values for the model chromophore, 3-aminoquinolin-2-ol.[36] The phenyl-substituted derivative [EuL^5] is a little red-shifted with respect to the methyl-derivative [EuL^6], no doubt due to the increased extent of conjugation in the former.

Luminescence of the Benzophenone-Substituted Complexes [EuL$^{1-4}$]. Upon excitation into the $\pi-\pi^*$ bands of [EuL$^{1-3}$], an emission characteristic of transitions from the $^5D_0$ excited-state of europium(III) is observed (Figure 4). The profiles of the spectra (i.e., the relative intensity of bands and the fine structure of each) are almost identical to one another, suggesting that the environment at the metal is little affected by the substitution position of the chromophore. Luminescence excitation spectra (monitored in the $\Delta J = 2$ band, 615−619 nm) match the absorption spectra, confirming the sensitization of europium(III) emission by the organic chromophore. Notable features include a single, symmetric $\Delta J = 0$ band, consistent with the low symmetry of the complex and with a single emitting species being present.

(36) Baxter, I.; Swan, G. A. *J. Chem. Soc. C* **1967**, 2446.

Table 1. Luminescence Data (Lifetimes, τ_{obs} and Quantum Yields, Φ_{lum}) for the Europium(III) Complexes [EuL$^{1-4}$] in H_2O and D_2O and the Calculated q Values

		[EuL^1] para	[EuL^2] meta	[EuL^3] ortho	[EuL^4] extra C
H_2O	τ/ms[a]	0.61	0.60	0.59	0.61
	Φ_{lum}[b]	0.095	0.015	0.004	0.097
D_2O	τ/ms[a]	2.26	2.22	2.14	2.03
	Φ_{lum}[b]	0.38	0.16	0.027	0.35
q[c]		1.05	1.09	1.08	0.99

[a] Lifetimes of metal-centered emission monitored at 616 nm, 295 K; uncertainty ±5%. [b] Quantum yields of europium emission, $\lambda_{ex} = 280$ nm, 295 K, measured using an aqueous solution of $[Ru(bpy)_3]^{2+}$ as a standard;[46] uncertainty ±20%. [c] q is the hydration state as determined by the equation of Parker et al.[37]

Luminescence lifetimes and quantum yields of [EuL$^{1-3}$] in H_2O and D_2O, together with corresponding values for the six-membered chelate analogue [EuL^4], are summarized in Table 1. The solution hydration numbers, q, (i.e., the number of inner-sphere, metal-bound water molecules) were determined by the empirical relationship devised by Parker et al. (eq 2, where x is the number of N−H oscillators; in this case, $x = 1$).[37] Values of 1.07 and 1.08 were determined for [EuL^2] and [EuL^3] respectively, very close to the value of 1.05 found previously for [EuL^1] and indicative of only a single inner-sphere water molecule in each case.

$$q^{Eu} = 1.2[(\tau_{H_2O}{}^{-1} - \tau_{D_2O}{}^{-1}) - (0.25 + 0.075x)] \quad (2)$$

Significantly, the data for [EuL^4] give a similar value for q of 0.99. These results provide evidence for the binding of the amide carbonyl group to the metal in each case, preventing the entry of a second water molecule. This is fully expected for [EuL$^{1-3}$] incorporating the three-atom linker, where a five-membered chelate will result, on the basis of the large number of structurally related complexes investigated.[11,16,19,20,37] On the other hand, there is little precedence for the use of a four-atom linker to give a six-membered chelate, as in [EuL^4]. It is evident from the q data that the amide oxygen remains bound to the metal ion by forming a six-membered chelate, even in aqueous solution, despite the lower anticipated stability of the six- versus five-chelate ring size. In their system referred to earlier, Borbas and Bruce have also concluded, on the basis of luminescence-based measurement of q, that amide binding in a six-membered chelate persists in aqueous solution.[27] There is a danger of over-interpreting small differences in q values, which are perhaps best considered as guidelines. However, that the value of q for [EuL^4] is slightly less than the very self-consistent values among the series [EuL$^{1-3}$] may perhaps be a genuine reflection of the fact that the potentially quenching N−H oscillator is positioned further from the metal ion in [EuL^4]; the energy transfer being expected to be strongly distance-dependent, the correction factor of 0.075 ms^{-1} in eq 1 is therefore probably a slight overestimate in this case.

Comparison of the relative luminescence quantum yields for the three complexes shows a clear-cut decrease from para-, through meta-, to ortho-substitution. A detailed analysis may be performed by consideration of the parameters in eq 1. Although the natural radiative rate constant, k_r, cannot be directly measured, it has been proposed that an estimate of this parameter may be obtained from the ratio of the integrated emission intensity of the $^5D_0 \rightarrow {}^7F_1$ transition (purely magnetic dipole in character) to the total integrated emission intensity (eq 3, where $A(0,1) \sim 32.4$ s^{-1}).[38]

$$k_r = \frac{A(0,1)}{[I(0,1)/I_{tot}]} \quad (3)$$

Table 2. Calculated Photophysical Parameters for [EuL$^{1-4}$] in H_2O Using the Experimentally Determined Quantities [I(0,1)/I$_{tot}$], k_{obs} (= $1/\tau_{obs}$), and Φ_{lum}

	[EuL^1] para	[EuL^2] meta	[EuL^3] ortho	[EuL^4] extra C
$[I(0,1)/I_{tot}]$[a]	0.21	0.22	0.22	0.16
k_r[b]/s^{-1}	154	147	144	202
k_{obs}/s^{-1}	1640	1670	1690	1640
η_{Ln}	0.094	0.088	0.085	0.12
Φ_{lum}	0.095	0.015	0.004	0.097
η_{et}[c]	1.01	0.17	0.05	0.81
$\sum k_{nr}$[b] / s^{-1}	1490	1520	1550	1440

[a] Estimated uncertainty ±5%. [b] Estimated uncertainty ±10%. [c] Estimated uncertainty ±20%.

The values of the key parameters obtained from this analysis are listed in Table 2. It is clear that, whereas the values of k_r and $\sum k_{nr}$ are of a similar order of magnitude for all three complexes, the emission intensity is limited by the product of $\Phi_T \eta_{et}$. Benzophenone and its simple para-substituted derivatives are known to have triplet-quantum yields of near unity, hence $\Phi_T \sim 1$;[39] meta- derivatives are expected to be similar. Thus, the efficiency of energy transfer from the sensitizing chromophore to the europium(III) ion, η_{et}, is essentially unity for [EuL^1], whereas the decrease in luminescence quantum yield in going to [EuL^2] is seen to arise from a decrease in η_{et}, from 1 to ~0.17. This drop may be due to an increase in the distance between the donor and acceptor, accompanying the rotation of the benzophenone moiety in [EuL^2] about the N−Ar bond into a sterically favored position that is more distant from the metal center. Given the steep distance-dependence of energy transfer mechanisms,[4,5] even a small change in the distance has a significant effect on η_{et}. In the case of [EuL^3], which is by far the most weakly emissive of the three complexes, a further deleterious effect may be the rapid and competitive deactivation of the singlet and triplet states of the sensitizer via vibronic coupling involving an intramolecular hydrogen bond, or an excited-state proton transfer, between the amide NH and the benzophenone C=O.[40,26] In other words, Φ_T is compromised and is probably the limiting factor in determining Φ_{lum} in this instance, rather than η_{et}.

(37) Beeby, A.; Clarkson, I. M.; Dickins, R. S.; Faulkner, S.; Parker, D.; Royle, L.; de Sousa, A. S.; Williams, J. A. G.; Woods, M. *J. Chem. Soc., Perkin Trans. 2* **1999**, 493.

(38) A detailed discussion to this approach is provided in ref 23. See also: Werts, M. H. V.; Jukes, R. T. F.; Verhoeven J. W. *Phys. Chem. Chem. Phys.* **2002**, *4*, 1542.

(39) Sandros, K. *Acta Chem. Scand.* **1969**, *23*, 2815; Chattopadhyay, S. K.; Kumar, C. V.; Das, P. K. *J. Photochem.* **1985**, *30*, 81.

(40) For a structurally related chromophoric unit exhibiting such deactivation, see: Neumann, M. G.; Gehlen, M. H.; Encinas, M. V.; Allen, N. S.; Corrates, T.; Pernado, C.; Catalina, F. *J. Chem. Soc., Faraday Trans.*, **1997**, 1517.

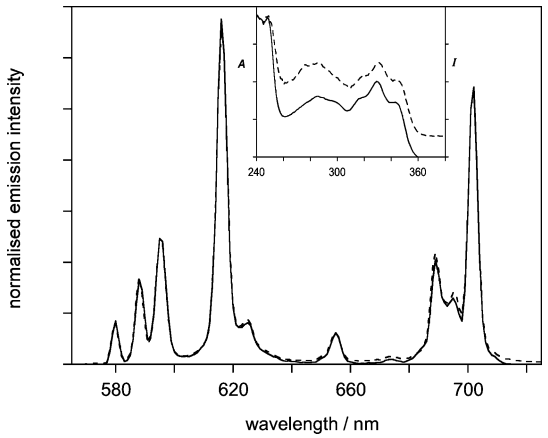

Figure 5. Emission spectra of [EuL^5] and [EuL^6] in aqueous solution at 295 K; $\lambda_{ex} = 340$ nm; band-passes = 2.5 nm. The inset shows the absorption (solid line) and excitation spectra (dashed line, $\lambda_{em} = 619$ nm) of [EuL^5].

The Effect of the Extra Methylene Unit in [EuL^4]. Comparison of the two para-substituted complexes [EuL^1] and [EuL^4] reveals an intriguing result, namely their remarkably similar luminescence quantum yields (Table 1). Consideration of the data derived in Table 2 indicates that, whereas the efficiency of energy transfer η_{et} shows a modest decrease, this is counterbalanced by a significant increase in the radiative rate constant k_r (from around 150 to 200 s^{-1}), promoting luminescence over nonradiative decay from the excited state of the metal. The net result is that Φ_{lum} is almost identical for the two complexes. The decrease in η_{et} is expected because the longer linker in [EuL^4] will lead to a larger separation between the donor sensitizer and the acceptor metal ion. The increase in k_r, on the other hand, was not anticipated, but is presumably due to an increase in asymmetry around the metal ion, perhaps associated with a twisting of the longer arm to allow the amide to coordinate, increasing the oscillator strength of the hypersensitive $\Delta J = 2$ transition and thus the overall radiative rate constant.

The above hypothesis, if correct, might be expected to apply to the corresponding complexes of other lanthanides. The terbium complex [TbL^4] was therefore prepared, and its luminescence compared to that of [TbL^1], which had been studied previously.[22] In this case, the overall luminescence quantum yield actually proved to be higher for the complex with the longer linker: $\Phi_{lum} = 0.27$ and 0.41 for [TbL^1] and [TbL^4] respectively, in H_2O at 298 K; (corresponding values in D_2O are 0.41 and 0.63). For terbium, k_r cannot be estimated simply from the emission spectrum. However, because Φ_{lum} is higher for [TbL^4], despite the longer sensitizer−metal distance that is expected to attenuate η_{et}, this implies that k_r must be substantially increased. The emission and excitation spectra of [TbL^4] are provided in the Supporting Information.

Rearranged Complexes [EuL^5] and [EuL^6]: Sensitization by the 2-Hydroxyquinoline Unit. Upon excitation into the ligand absorption bands of [EuL^5] and [EuL^6], an emission characteristic of transitions from the $^5D_0$ excited state of europium(III) is observed (Figure 5). Luminescence excitation spectra (monitored at 700 nm) match the absorption spectra (shown for [EuL^5] in the inset to Figure 5), confirming the sensitization of europium(III) emission by the organic chromophore. The profiles of the emission spectra for the two complexes are identical, suggesting that the environment at the metal is little affected by substitution at the four position of the quinoline ring. With respect to [EuL$^{1-4}$], there is relatively little variation in the form of the emission spectra (compared, for example, to tris-β-diketonate complexes such as Eu(TTFA)$_3$), evidence that there is a similar set of donor atoms with a similar symmetry. The most notable differences are an increase in intensity of the hypersensitive $\Delta J = 2$ band and a larger separation of the two components of the $\Delta J = 1$ emission band. These changes imply an increase in polarizability of the axial donor,[41] as may perhaps be expected for a change from an amide carbonyl group to a phenol.

Table 3. Luminescence Data (Lifetimes, τ_{obs}, and Quantum Yields, Φ_{lum}) for the Europium(III) Complexes [EuL^5] and [EuL^6] in H_2O and D_2O, and the Calculated q Values

		[EuL^5] R = phenyl	[EuL^6] R = methyl
H_2O	τ/ms[a]	0.62	0.62
	Φ_{lum}[b]	0.003	0.052
D_2O	τ/ms[a]	2.02	2.05
	Φ_{lum}[b]	0.011	0.18
q[c]		1.06	1.04

[a] Lifetimes of metal-centered emission monitored at 616 nm, 295 K; uncertainty ±5%. [b] Quantum yields of europium emission, $\lambda_{ex} = 280$ nm, 295 K, measured using an aqueous solution of $[Ru(bpy)_3]^{2+}$ as a standard;[46] uncertainty ±20%. [c] q is the hydration state as determined by the equation of Parker et al.[37]

Lifetimes for emission in H_2O and D_2O are summarized in Table 3. The solution hydration numbers q were again assessed using eq 2, giving values of 1.06 and 1.04 for [EuL^5] and [EuL^6], respectively. These values indicate that there is only a single inner-sphere water molecule in each case, strongly suggesting the binding of the quinoline hydroxyl substituent in the eighth coordination site.

The luminescence quantum yield of [EuL^6] in H_2O is 0.052 (Table 3). Although at first sight it is inferior to to [EuL^1] and [EuL^4], it should be noted that this performance is achieved at substantially longer excitation wavelengths. In particular, [EuL^6] can be excited at wavelengths of 340−350 nm, where the absorption is still strong ($\epsilon_{440} \sim 2200$ mol^{-1} dm^3 cm^{-1}). Efficient excitation at wavelengths beyond the glass cutoff around 330 nm, and beyond the range of absorption by aromatic amino acids, is important for practical applications in biological media, yet the range of complexes that satisfy this criterion that are stable in water and emit strongly is still relatively limited.[11,16,19,26,42,43,44,45]

Interestingly, the luminescence quantum yield of the phenyl derivative [EuL^5] is an order of magnitude smaller

(41) Dickins, R. S.; Parker, D.; Bruce, J. I.; Tozer, D. J. *Dalton Trans.* **2003**, 1264.
(42) For example, the performance is comparable to a carbostyril-124-substituted cyclen-based complex, but offering a more accessible and lower-cost sensitizer unit: D. Parker and J. A. G. Williams, *J. Chem. Soc., Perkin Trans. 2* **1996**, 1581.
(43) Bekiari, V.; Lianos, P. *Langmuir* **2006**, *22*, 8602.
(44) Vendevyver, C. D. B.; Chauvin, A.-S.; Comby, S.; Bünzli, J.-C. G. *Chem. Commun.* **2007**, 1716.
(45) Yu, J.; Parker, D.; Pal, R.; Poole, R. A.; Cann, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 2294. Pandya, S.; Yu, J.; Parker, D. *Dalton Trans.* **2006**, 2757.

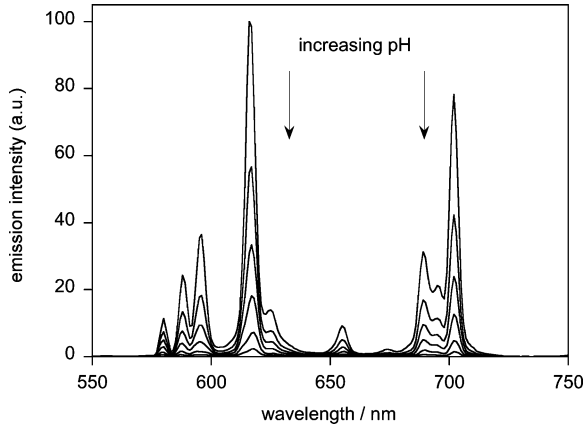

Figure 6. Evolution of the emission spectrum of [EuL^6] in aqueous solution with increasing pH (KOH). The spectra shown are at pH values of 7.4, 8.6, 9.3, 9.8, 10.9, 11.7, acquired under identical condtions: $\lambda_{ex} = 340$ nm, band-passes 3.0 nm, 295 (±1) K.

Table 4. Calculated Photophysical Parameters for [EuL^5] and [EuL^6] in H_2O Using the Experimentally Determined Quantities τ_{obs}, Φ_{lum}, and [I(0,1)/I$_{tot}$]

	[EuL^5]	[EuL^6]
$[I(0,1)/I_{tot}]^a$	0.16	0.17
τ_{obs}/ms	0.62	0.62
$k_r{}^b$/s^{-1}	197	196
$\sum k_{nr}{}^b$ / s^{-1}	1420	1420
Φ_{lum}	0.003	0.052
$\Phi_T\eta_{et}{}^c$	0.03	0.43

[a] Estimated uncertainty ±5%. [b] Estimated uncertainty ±10%. [c] Estimated uncertainty ±20%.

than that for the methyl derivative [EuL^6], despite similar luminescence lifetimes. Analysis using eqs 1 and 3 reveals that this difference stems exclusively from a difference in the product of $\Phi_T\eta_{et}$ between the two complexes (Table 4). Possible origins of this difference include: (i) phenyl substitution on the hydroxyquinoline chromophore having a detrimental effect upon the triplet-quantum yield, Φ_T; (ii) the value of η_{et} being lowered by increased separation between the sensitizer and the metal center, perhaps due to the additional steric demand associated with the phenyl group; (iii) the energy of the sensitizer triplet state being lowered by phenyl substitution, perhaps to such an extent that back-energy transfer is introduced, serving to attenuate the overall efficiency of luminescence. We note, however, that degassing the sample led to no increase in Φ_{lum}, contrary to what has frequently been observed in those instances where back-energy transfer plays a role.[21]

The intense emission of an aqueous solution of [EuL^6] is almost completely eliminated upon increasing the pH. The effect is fully reversible; the emission is restored upon the addition of dilute acid. Representative emission spectra at a selection of pH values between 7.4 and 11.7 are shown in Figure 6. Evidently, the complex undergoes a reversible deprotonation over this range, which is most likely associated with the −OH group of the hydroxyquinoline (or its zwitterionic form). The dramatic quenching of the emission is probably due to the increase in electron density of the chromophore that accompanies deprotonation, facilitating the transient oxidation, and hence deactivation, of its excited state by a photoinduced electron transfer or ligand-to-metal charge-transfer process. Such quenching, in which the Eu^{3+} center is transiently reduced, is not uncommon for europium(III),[9] being the most readily reduced of the lanthanide(III) ions. The quenching is also accompanied by a change in the spectral profile: the hypersensitive $\Delta J = 2$ band is enhanced relative to the $\Delta J = 1$ bands. Such a change is suggestive of an increase in the polarizability of the axial donor, which would be consistent with deprotonation of the bound −OH group.[41]

Summary and Concluding Remarks. The use of amide linkers for the incorporation of organic sensitizers into the macrocyclic azacarboxylate skeleton, DO3A, has emerged over the past decade as an important method for accessing robust, water-soluble luminescent lanthanide complexes. The demonstration in this work that, for a given sensitizer, a longer four-atom linking unit (H_3L^4 versus H_3L^{1-3}) can provide a facile route to equally efficient emitters, could open up an alternative methodology for introducing a wide range of functionalities. Indeed, the superior results for [TbL^4] compared to [TbL^1], in terms of the overall luminescence quantum yield, suggest that a detailed assessment of complexes incorporating the sensitizer within a six- as opposed to five-membered chelate may be particularly rewarding.

Within the series of isomeric complexes [EuL$^{1-3}$], the position of substitution of the benzophenone-sensitizing moiety is found to be crucial in determining Φ_{lum}, probably reflecting small changes in the sensitizer−acceptor distance (e.g., the decreased efficiency in going from para- to meta-substituted systems) or the introduction of deactivating pathways for the sensitizer excited state, as in [EuL^3]. An unusual rearrangement reaction open to the latter complex leads to a rare example of an *N*-arylated azamacrocyclic complex. The corresponding rearranged complex [EuL^6], obtained starting from 2-aminoacetophenone, emits with reasonable efficiency in water and can be excited at practicable wavelengths around 350 nm, making it a potentially interesting system for applications in aqueous media. Its pH-sensitive emission over mildly basic conditions could also render it useful as a luminescent pH sensor amenable to time-resolved detection methods.

Experimental Section

Cyclen was purchased from Strem and used as supplied. The three isomeric *ω*-amino-benzophenones are commercially available and were obtained from Aldrich. The synthesis and characterization of [EuL^1] have been described previously.[22] Chromatography was carried out on a silica gel (60, 40−63 *μ*m, Fluorochem) or on alumina (neutral, Brockman I). Solvents were Analar or HPLC grade, and water was purified by the Milli Q system. Proton and $^{13}C\{^1H\}$ NMR spectra were recorded on Varian instruments operating at the frequencies indicated; proton spectra were referenced to residual protio solvent resonances and ^{13}C to the solvent carbon resonance. Electrospray mass spectra were measured on a VG Platform II, or a Micromass LCT spectrometer, with methanol as the carrier solvent; high-resolution spectra were recorded at the EPSRC National Mass Spectrometry Service Centre, Swansea.

Synthesis and Characterization. The procedures used for the synthesis of *N*-(3-Benzoyl-phenyl)-2-bromo-acetamide, **2**, *N*-(2-Benzoyl-phenyl)-2-bromo-acetamide, **3**, *N*-(2-Acetyl-phenyl)-2-

bromo-acetamide, and *N*-(4-Benzoyl-phenyl)acrylamide, **4**, and the details of their characterization are described in the Supporting Information.

10-((3-Benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester), (*t*-Bu)$_3$L^2. 1,4,7,10-Tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester) (3.76 g, 7.31 mmol), *N*-(3-benzoyl-phenyl)-2-bromo-acetamide, **2**, (2.32 g, 7.29 mmol), cesium carbonate (7.36 g, 22.6 mmol), and a few grains of potassium iodide were stirred in acetonitrile (150 mL) at room temperature under a nitrogen atmosphere for 2 days. The progress of the reaction was followed by TLC (silica, CH_2Cl_2/MeOH, 95/5). The solvent was removed under reduced pressure, and the residue was added to water (100 mL) and then extracted into dichloromethane (3 × 100 mL). Drying over $MgSO_4$ and the removal of the solvent under reduced pressure gave the desired product (*t*-Bu)$_3$L^2 as a brown solid (4.77 g, 87%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 11.16 (1H, br s, NH), 8.65 (1H, d, J = 7.9, H^6), 8.49 (1H, s, H^2), 8.33 (2H, d, J = 7.6, H$^{2'}$), 7.90−8.12 (5H, m, H^4, H^5, H$^{3'}$ & H$^{4'}$), 3.71 (2H, s, CH_2), 3.68 (2H, s, CH_2), 3.65 (4H, s, CH_2), 3.26−3.40 (12H, m, NCH_2CH_2N), 3.14 (4H, br s, NCH_2-CH_2N), 1.93 (9H, s, ^{t}Bu), 1.89 (18H, s, ^{t}Bu). MS(ES+) m/z = 774 ([M+Na]$^+$).

[EuL^2]. A solution of 10-((3-benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester) (3.55 g, 4.72 mmol) in 80% TFA in dichloromethane (50 mL) was stirred at room temperature for 3 days. The reaction could be followed by ^{1}H NMR (D_2O). Removal of the solvent under reduced pressure followed by washing with dichloromethane (2 × 100 mL) and then diethyl ether (2 × 100 mL) gave 10-((3-benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris-(acetic acid), H_3L^2, as a pale-brown solid, which was used without further purification. ^{1}H NMR (D_2O, 400 MHz) δ = 7.84 (1H, s, arom), 7.76 (3H, d, J = 7.5, arom), 7.71 (1H, t, J = 7.3, arom), 7.49−7.58 (4H, m, arom), 3.86 (8H, br s, CH_2), 3.29 (16H, br s, NCH_2CH_2N). MS(ES+) m/z = 584 ([M+H]$^+$), 606 ([M+Na]$^+$). This was redissolved along with europium(III) nitrate pentahydrate (3.00 g, 7.01 mmol) in water (100 mL). The solution was adjusted to pH 6 with NaOH solution (2 mol dm^{-3}) and heated under reflux at 100 °C for 24 h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was redissolved in ethanol, and all of the undissolved material was removed by filtration. Removal of the solvent under reduced pressure and purification of the residue by column chromatography (alumina, CH_2Cl_2/MeOH, gradient elution from 100/0 to 95/5) gave the desired product as a colorless solid (1.67 g, 48%), mp >250 °C. ^{1}H NMR (D_2O, 500 MHz) δ = 34.2 (1H, s, H_{ax}), 31.4 (1H, s, H_{ax}), 30.2 (1H, s, H_{ax}), 30.0 (1H, s, H_{ax}), 8.7−7.8 (9H, m, arom), 1.1 (1H, s, H_{eq}), −0.5 (2H, s, H_{eq} & $H_{ax'}$), −3.0 (1H, s, H_{eq}), −3.9 (2H, s, H_{eq} & $H_{ax'}$), −5.1 (1H, s, $H_{eq'}$), −7.9 (2H, s, $H_{eq'}$ & $H_{eq'}$), −8.1 (1H, s, $H_{eq'}$), −10.7 (1H, s, CH_2CO), −11.9 (1H, s, $H_{ax'}$), −12.2 (1H, s, CH_2CO), −12.5 (1H, s, $H_{ax'}$), −13.8 (1H, s, CH_2-CO), −13.9 (1H, s, CH_2CO), −14.9 (1H, s, CH_2CO), −15.1 (1H, s, CH_2CO), −16.2 (1H, s, CH_2CO), −17.5 (1H, s, CH_2CO). MS-(ES+) m/z = 756 ([M+Na]$^+$). HRMS(ES+) m/z = 734.1702 ([M+H]$^+$); calc. for $EuC_{29}H_{35}N_5O_8$, 734.1692. Anal. Calcd for $C_{29}H_{34}N_5O_8Eu(H_2O)_{2.5}$: C, 44.8; H, 5.1; N, 9.0. Found C, 43.9; H, 5.4; N, 8.8.

10-((2-Benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester), (*t*-Bu)$_3$L^3. 1,4,7,10-Tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester) (1.88 g, 3.65 mmol), *N*-(2-benzoyl-phenyl)-2-bromo-acetamide (1.16 g, 3.65 mmol), cesium carbonate (3.68 g, 11.3 mmol), and a few grains of potassium iodide in acetonitrile (75 mL) were stirred at room temperature under a nitrogen atmosphere for 2 days. The progress of the reaction was followed by TLC (silica, CH_2Cl_2/MeOH, 95/5). The solvent was removed under reduced pressure, and the residue was added to water (50 mL) and then extracted into dichloromethane (3 × 50 mL). Drying over $MgSO_4$ and removal of the solvent under reduced pressure gave the desired product, (*t*-Bu)$_3$L^3, as a brown solid (2.40 g, 87%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 11.27 (1H, br s, NH), 8.23 (1H, d, J = 8.1, H^6), 7.79 (2H, d, J = 8.0, H$^{2'}$), 7.56 (1H, tt, J = 7.4, 1.2, H$^{4'}$), 7.51 (1H, td, J = 8.1, 1.5, H^5), 7.42−7.47 (3H, m, H^3 & H$^{3'}$), 7.12 (1H, td, J = 7.5, 1.0, H^4), 3.35 (2H, s, CH_2), 3.25 (4H, s, CH_2), 3.11 (2H, s, CH_2), 2.72−2.91 (16H, m, NCH_2CH_2N), 1.46 (9H, s, ^{t}Bu), 1.39 (18H, s, ^{t}Bu). MS(ES+) m/z = 752 ([M+H]$^+$), 774 ([M+Na]$^+$).

[EuL^3]. A solution of 10-((2-benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris-(acetic acid *tert*-butyl ester) (154 mg, 0.20 mmol) in 80% TFA in dichloromethane (2 mL) was stirred at room temperature for 3 days. The reaction could be followed by ^{1}H NMR (D_2O). Removal of the solvent under reduced pressure followed by washing with dichloromethane (3 × 20 mL) and then diethyl ether (3 × 20 mL) gave 10-((2-benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid) as a pale-brown solid, which was used without further purification. ^{1}H NMR (D_2O, 400 MHz) δ = 7.72 (2H, d, J = 7.8, arom), 7.66 (1H, t, J = 7.5, arom), 7.64 (1H, t, J = 8.1, arom), 7.48−7.53 (3H, m, arom), 7.46 (1H, d, J = 8.1, arom), 7.40 (1H, t, J = 7.9, arom), 2.70−3.97 (24H, br m, CH_2). MS(ES+) m/z = 584 ([M+H]$^+$), 606 ([M+Na]$^+$). This was redissolved along with europium(III) nitrate pentahydrate (95 mg, 0.22 mmol) in water (3 mL), the solution was carefully adjusted to pH 6 with NaOH solution (2 mol dm^{-3}) (NOTE: The reaction must not be carried out under more basic conditions, otherwise [EuL^5] is obtained), and heated to 40 °C for 24 h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was redissolved in ethanol and all of the undissolved material was removed by filtration. Removal of the solvent under reduced pressure and purification of the residue by column chromatography (alumina, CH_2Cl_2/MeOH, gradient elution from 100/0 to 85/15) gave the desired product as a colorless solid (82 mg, 55%), mp >250 °C. ^{1}H NMR (D_2O, 500 MHz) δ = 33.95 (1H, s, H_{ax}), 31.01 (1H, s, H_{ax}), 29.37 (1H, s, H_{ax}), 28.71 (1H, s, H_{ax}), 7.00−10.00 (9H, m, arom), 1.60 (1H, s), 1.39 (1H, s), −1.01 (1H, s), −3.15 (1H, s), −3.81 (1H, s), −4.78 (1H, s), −4.91 (1H, s), −8.04 (1H, s), −8.48 (2H, s), −9.89 (1H, s), −11.58 (1H, s), −12.44 (1H, s), −13.31 (1H, s), −13.55 (1H, s), −13.68 (1H, s), −14.37 (1H, s), −15.48 (1H, s), −16.50 (1H, s), −18.29 (1H, s). MS(ES+) m/z = 756 ([M+Na]$^+$). Anal. Calcd for $C_{29}H_{34}N_5O_8Eu(H_2O)_4$: C, 43.3; H, 5.3; N, 8.7. Found C, 43.1; H, 5.4; N, 8.5.

Europium(III) 10-(2-Hydroxy-4-phenylquinolin-3-yl)-1,4,7,-10-tetraazacyclododecane-1,4,7-trisacetate [EuL^5]. A solution of 10-((2-benzoyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester), (*t*-Bu)$_3$L^3, (1.78 g, 2.37 mmol) in 80% TFA in dichloromethane (25 mL) was stirred at room temperature for 3 days. The reaction could be followed by ^{1}H NMR (D_2O). Removal of the solvent under reduced pressure followed by washing with dichloromethane (3 × 50 mL) and then diethyl ether (3 × 50 mL) gave 10-((2-benzoyl-phenylcarbamoyl)-methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid) as a pale-brown solid, which was used without further purification. This was redissolved along with europium(III) nitrate pentahydrate (1.03 g, 2.41 mmol) in water (30 mL). The solution made basic (to pH 8) with NaOH solution (2 mol dm^{-3}) and heated under reflux at 100 °C for 24 h. After cooling to room temperature, the solvent

was removed under reduced pressure. The residue was redissolved in ethanol and all of the undissolved material was removed by filtration. Removal of solvent under reduced pressure and purification of the residue by column chromatography (alumina, CH_2Cl_2/MeOH, gradient elution from 100/0 to 50/50) gave [EuL^4] as a colorless solid (1.14 g, 68%), mp >250 °C. ^{1}H NMR (D_2O, 500 MHz) δ = 41.8 (1H, s, H_{ax}), 41.2 (1H, s, H_{ax}), 35.3 (1H, s, H_{ax}), 30.8 (1H, s, H_{ax}), 8.9 (1H, s, arom), 8.3 (2H, s, arom), 7.2 (1H, s, arom), 6.5 (1H, s, H_{eq}), 5.7 (1H, s, arom), 5.5−4.0 (4H, obscured by H_2O, arom), 3.6 (1H, s, H_{eq}), 1.6 (1H, s, $H_{eq'}$), −1.9 (1H, s, H_{eq}), −2.6 (1H, s, $H_{ax'}$), −5.6 (1H, s, $H_{eq'}$), −5.9 (1H, s, H_{eq}), −6.7 (1H, s, $H_{ax'}$), −9.1 (1H, s, $H_{eq'}$), −10.7 (1H, s, $H_{eq'}$), −13.1 (1H, s, $H_{ax'}$), −14.0 (1H, s, $H_{ax'}$), −14.9 (1H, s, CH_2CO), −16.0 (1H, s, CH_2CO), −18.0 (1H, s, CH_2CO), −18.9 (1H, s, CH_2CO), −19.2 (2H, s, CH_2CO). MS(ES+) m/z = 716 ([M+H]$^+$), 738 ([M+Na]$^+$). MS(ES-) m/z = 714 ([M−H]$^-$). HRMS(ES+) m/z = 733.1862 ([M+NH$_4$]$^+$); Calcd for $EuC_{29}H_{36}N_6O_7$, 733.1852. Anal. Calcd for $C_{29}H_{32}N_5O_7Eu(H_2O)$: C, 47.5; H, 4.7; N, 9.6. Found C, 47.0; H, 4.9; N, 9.0.

A sample of the yttrium complex of this ligand, [YL^5], was also prepared in an analogous manner to that for (t-Bu)$_3$L^3, (156 mg, 0.21 mmol) and yttrium(III) nitrate (85 mg, 0.31 mmol), giving the desired product as a colorless solid (87 mg, 62%), mp >250 °C. ^{1}H NMR (D_2O, 400 MHz) δ = 7.67 (1H, t, J = 7.5, arom), 7.58−7.63 (4H, m, arom), 7.39−7.42 (2H, m, arom), 7.23 (1H, t, J = 7.6, arom), 7.02 (1H, d, J = 8.1, arom), 1.16−4.20 (22H, m, CH_2). MS(ES+) m/z = 674 ([M+Na]$^+$).

10-((2-Acetyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(Acetic Acid *tert*-Butyl Ester), H$_3$L^{pre-6}. 1,4,7,10-Tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester) (1.88 g, 3.65 mmol), *N*-(2-acetyl-phenyl)-2-bromo-acetamide (934 mg, 3.65 mmol), cesium carbonate (3.69 g, 11.3 mmol), and a few grains of potassium iodide in acetonitrile (75 mL) were stirred at room temperature under a nitrogen atmosphere for 2 days. The progress of the reaction was followed by TLC (silica, CH_2Cl_2). The solvent was removed under reduced pressure, and the residue was added to water (50 mL) and then extracted into dichloromethane (3 × 50 mL). Drying over $MgSO_4$ and removal of the solvent under reduced pressure gave the desired product as a brown solid (1.93 g, 76%). Attempted purification by column chromatography (silica, CH_2Cl_2/MeOH) at this stage resulted in decomposition, and therefore the product was used directly in the next step, with purification being carried out after the complexation step. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 12.27 (1H, br s, NH), 8.67 (1H, d, J = 8.5, arom), 7.83 (1H, d, J = 7.9, arom), 7.51 (1H, t, J = 7.7, arom), 7.11 (1H, 7.6, arom), 3.39 (2H, s, CH_2), 3.28 (4H, s, CH_2), 3.20 (2H, s, CH_2), 2.75−3.00 (16H, m, NCH_2CH$_2$N), 1.45 (9H, s, ^{t}Bu), 1.41 (18H, s, ^{t}Bu). MS(ES+) m/z = 690 ([M+H]$^+$), 712 ([M+Na]$^+$).

[EuL^6]. A solution of 10-((2-acetyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid *tert*-butyl ester), H$_3$L^{pre-6}, (440 mg, 0.64 mmol) in 80% TFA in dichloromethane (5 mL) was stirred at room temperature for 3 days. Removal of the solvent under reduced pressure followed by washing with dichloromethane (3 × 25 mL) and then diethyl ether (3 × 25 mL) gave 10-((2-acetyl-phenylcarbamoyl)methyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(acetic acid) as a pale-brown solid, which was used without further purification. ^{1}H NMR (D_2O, 400 MHz) δ = 8.06 (1H, d, J = 8.8, arom), 8.03 (1H, d, J = 8.0, arom), 7.64 (1H, t, J = 7.8, arom), 7.34 (1H, t, arom), 3.90 (8H, br s, CH_2), 3.34 (16H, br s, NCH_2CH$_2$N), 2.67 (3H, s, Me). This was redissolved along with europium(III) nitrate pentahydrate (412 mg, 0.96 mmol) in water (15 mL). The solution was made basic with NaOH solution (2 mol dm^{-3}) and heated under reflux at 100 °C for 24 h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in ethanol and all of the undissolved material was removed by filtration. Removal of the solvent under reduced pressure and purification of the residue by column chromatography (alumina, CH_2Cl_2/MeOH, gradient elution from 100/0 to 50/50) gave the desired product as a colorless solid (150 mg, 36%), mp >250 °C. ^{1}H NMR (D_2O, 500 MHz) δ = 43.1 (1H, s, H_{ax}), 42.4 (1H, s, H_{ax}), 35.4 (1H, s, H_{ax}), 30.3 (1H, s, H_{ax}), 6.8 (1H, s, H_{eq}), 5.8 (1H, s, arom), 5.6 (1H, s, arom), 5.6 (1H, s, arom), 5.2 (1H, s, H_{eq}), 3.9 (1H, s, arom), 3.3 (3H, s, Me), 1.1 (2H, s, $H_{eq'}$), −1.3 (1H, s, $H_{ax'}$), −2.0 (1H, s, H_{eq}), −5.0 (1H, s, $H_{eq'}$), −6.4 (1H, s, $H_{ax'}$), −6.8 (1H, s, H_{eq}), −9.6 (1H, s, $H_{eq'}$), −11.5 (1H, s, $H_{eq'}$), −13.7 (1H, s, $H_{ax'}$), −14.3 (1H, s, CH_2CO), −15.1 (1H, s, $H_{ax'}$), −15.5 (1H, s, CH_2CO), −17.7 (1H, s, CH_2-CO), −18.9 (1H, s, CH_2CO), −20.2 (1H, s, CH_2CO), −20.3 (1H, s, CH_2CO). MS(ES+) m/z = 676 ([M+H]$^+$). HRMS(ES+) m/z = 676.1291 ([M+Na]$^+$); Calcd for $EuC_{24}H_{30}N_5O_7Na$, 676.1255. Anal. Calcd for $C_{24}H_{30}N_5O_7Eu(H_2O)_4$: C, 39.8; H, 5.3; N, 9.7. Found C, 39.3; H, 5.3; N, 9.5.

10-((4-Benzoyl-phenylcarbamoyl)ethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-tris(Acetic Acid *tert*-Butyl Ester), (t-Bu)$_3$L^4. The tris-(*tert*-butyl)ester of DO3A (500 mg, 0.97 mmol), potassium carbonate (137 mg, 1.07 mmol), and *N*-(4-benzoylphenyl)acrylamide, **4** (243 mg, 0.97 mmol), were stirred in acetonitrile (20 mL) at reflux for 48 h. The solvent was removed under a vacuum, and the residue was taken up into aqueous NaOH (1M, 20 mL), from which the product was extracted into dichloromethane (3 × 20 mL). The residue was purified by column chromatography over alumina. The column was first washed with dichloromethane before the title compound was eluted using 97% CH_2Cl_2/3% MeOH (R_f = 0.5 by TLC on alumina in 98% CH_2Cl_2/2% MeOH); (497 mg, 67%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 8.1−7.2 (9H, m, arom), 3.4−2.2 (26H, br m, ring, acetate CH_2, NCH_2), 1.45 (27H, s, ^{t}Bu). MS-(ES+): m/z = 788 (M+Na$^+$).

[EuL^4] and [TbL^4] were prepared by the hydrolysis of (t-Bu)$_3$L^4 using TFA in dichloromethane followed by treatment of a neutralized aqueous solution with the respective lanthanide nitrate salt, as described for complexes [EuL^2] and [EuL^3] above. R_f = 0.5 by TLC on alumina in 90% CH_2Cl_2/10% MeOH in both cases. **[EuL^4].** ^{1}H NMR (D_2O, 500 MHz, all 35 nonexchangeable protons are resolved, although definitive assignment of each one is not possible) δ = 32.5 (1H, s, H_{ax}), 32.1 (1H, s, H_{ax}), 31.0 (1H, s, H_{ax}), 29.7 (1H, s, H_{ax}), 10.4 (2H, s, arom), 8.35 (2H s, arom), 7.70 (2H, s, arom), 7.50 (1H, s, arom), 7.38 (2H, s, arom), 0.9 (1H, s), 0.7 (1H, s), 0.5 (1H, s), −1.0 (1H, s), −2.1 (1H, s), −2.6 (1H, s), −2.9 (1H, s), −4.5 (1H, s), −5.3 (1H, s), −6.1 (1H, s), −7.5 (1H, s), −8.1 (1H, s), −8.6 (1H, s), −10.2 (1H, s), −11.9 (1H, s), −12.0 (1H, s), −13.5 (1H, s), −15.7 (1H, s), −16.5 (1H, s), −17.1 (1H, s), −18.7 (1H, s), −19.4 (1H, s). MS(ES+) m/z = 745 (M+H)$^+$. HRMS(ES+) m/z = 768.1648 (M+Na)$^+$; Calcd for $C_{30}H_{36}N_5O_8$-Na^{151}Eu, 768.1652. Anal. Calcd for $C_{30}H_{36}N_5O_8Eu(H_2O)_4$: C, 44.0; H, 5.4; N, 8.6. Found C, 43.4; H, 5.7; N, 8.2. **[TbL^4].** MS(ES+) m/z = 745 (M+H)$^+$. HRMS(ES+) m/z = 776.1715 (M+Na)$^+$; Calcd for $C_{30}H_{36}N_5O_8NaTb$, 776.1712. Anal. Calcd for $C_{30}H_{36}N_5O_8$-$Tb(H_2O)_{3.5}$: C, 44.1; H, 5.3; N, 8.6. Found C, 43.7; H, 5.4; N, 8.0.

Photophysical Measurements. Absorption spectra were measured on a Biotek Instruments XS spectrometer, using quartz cuvettes of 1 cm path length. Steady-state luminescence spectra were measured using a Jobin Yvon FluoroMax-2 spectrofluorimeter, fitted with a red-sensitive Hamamatsu R928 photomultiplier tube; the spectra shown are corrected for the wavelength dependence of the detector, and the quoted emission maxima refer to the values

after correction. Luminescence quantum yields were determined by the method of continuous dilution, using $[Ru(bpy)_3]Cl_2$ in air-equilibrated aqueous solution ($\phi = 0.028$)[46] as the standard; estimated uncertainty in ϕ is ±20% or better. The quantum yields of the europium(III) complexes obtained in this way displayed excellent consistency with the relative values obtained by using [EuL^1] as a secondary standard.

Samples for time-resolved measurements were excited at 355 nm using the third harmonic of a Q-switched Nd:YAG laser. The luminescence was detected with a Hamamatsu R928 photomultiplier tube and recorded using a digital storage oscilloscope, before transfer to a PC for analysis. The estimated uncertainty in the quoted lifetimes is ±5%.

(46) Nakamaru, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2697.

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Supporting Information Available: Excitation spectra of Eu(III) complexes, emission and excitation spectra of [TbL^4], details of synthesis and characterization of the aromatic precursors, and ^{1}H NMR spectra of the Eu(III) and Y(III) complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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