

Intramolecular sensitisation of lanthanide(III) luminescence by acetophenone-containing ligands: the critical effect of *para*-substituents and solvent

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Tetraazamacrocyclic ligands have been prepared in which three of the four nitrogen atoms are functionalised with carboxylate donors and the fourth is alkylated with a *para*-substituted acetophenone group $\{-\text{CH}_2\text{C}(\text{O})\text{C}_6\text{H}_4\text{-X}$, where X = H, OMe, NMe₂\}. The europium(III), gadolinium(III) and (for X = H) terbium(III) complexes of these potentially octadentate ligands have been prepared. The unsubstituted and methoxy-substituted ligands sensitise the europium(III) emissive state with high efficiency in aqueous solution. Calculation of the pure radiative lifetime, based on the contribution of the $^5\text{D}_0 \rightarrow ^7\text{F}_1$ transition to the total integrated emission intensity, has allowed an estimate of the efficiency of energy transfer to be made. Sensitisation of europium luminescence also occurs in the complex of the dimethylamino-substituted ligand but the process is highly solvent-dependent: very efficient sensitisation is observed in dichloromethane and DMSO, but the complex is non-emissive in water and only slightly emissive in acetonitrile. UV-Visible absorption spectra indicate that in all the solvents investigated, the carbonyl oxygen of the ligand is directly coordinated to the metal ion. The intensity of the hypersensitive $^5\text{D}_0 \rightarrow ^7\text{F}_2$ transition in the three complexes mirrors the degree of polarisation of the ketone C=O bond.

Introduction

Although first observed 60 years ago,¹ the sensitisation of lanthanide luminescence by organic chromophores is a subject which continues to attract a great deal of attention, owing primarily to its potential use in luminescent probes and sensors and for light amplification and frequency conversion.²⁻⁴ Two characteristic properties of lanthanide luminescence are central to such applications, namely the long lifetimes of emission under ambient conditions and the line-like nature of the emission spectra. Many applications require water-soluble complexes and this poses a challenge in the design and preparation of suitable complexes, since the lanthanide(III) ions have a high affinity for water molecules as ligands and their excited states are efficiently quenched by water. Successful complexes will have high thermodynamic and kinetic stability with respect to metal ion dissociation and ideally saturate the coordination shell of the metal ion, to prevent water molecules from binding. The incorporation of appropriate organic chromophores into the complex to act as efficient sensitisers of the lanthanide excited states is also an important objective in overcoming the problem of the very low extinction coefficients of the Ln³⁺ ions (typically $\epsilon < 1$).

Studies on several chromophores have demonstrated the importance of the triplet state in the energy transfer process.⁵ The overall quantum yield of luminescence, ϕ_{lum} , is determined by the triplet yield of the chromophore (ϕ_{T}), the efficiency of energy transfer (η_{ET}) and the efficiency of metal centred luminescence (η_{Ln}):

$$\phi_{\text{lum}} = \phi_{\text{T}} \cdot \eta_{\text{ET}} \cdot \eta_{\text{Ln}} \quad (1)$$

We have recently demonstrated that aromatic ketones with n, π^* triplet states, which have high triplet quantum yields, are

particularly suitable as sensitisers,⁶ provided that there is a reasonable match between the triplet energy and the emissive level (or a higher excited level) of the lanthanide such that η_{ET} is also optimal (the energy gap should, however, be at least 1500 cm^{-1} if back energy transfer to the chromophore is to be minimised). A striking recent example of ketone-sensitised lanthanide luminescence is to be found in the 1 : 1 complex formed between Eu(fod)₃ (Hfod = 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dione) and Michler's ketone, 4,4'-bis(*N,N'*-dimethylamino)benzophenone, in benzene solution.⁷ Here, the substituted benzophenone acts as an auxiliary ligand and sensitises the metal ion very efficiently. Our recent work investigated stable, water soluble Eu³⁺ and Tb³⁺ complexes of a ligand incorporating a benzophenone group covalently-bound *via* an amide linker, which gave impressive quantum yields in aqueous solution.⁶ We report here on the preparation of related tetraazamacrocyclic ligands incorporating *para*-substituted acetophenone groups directly linked (*via* the CH₂ group) to one of the nitrogen atoms of the macrocycle, such that the ketone oxygen can potentially act as a donor to a bound lanthanide ion. The ketone-sensitised luminescence of the europium complexes of these ligands is described.

Results and discussion

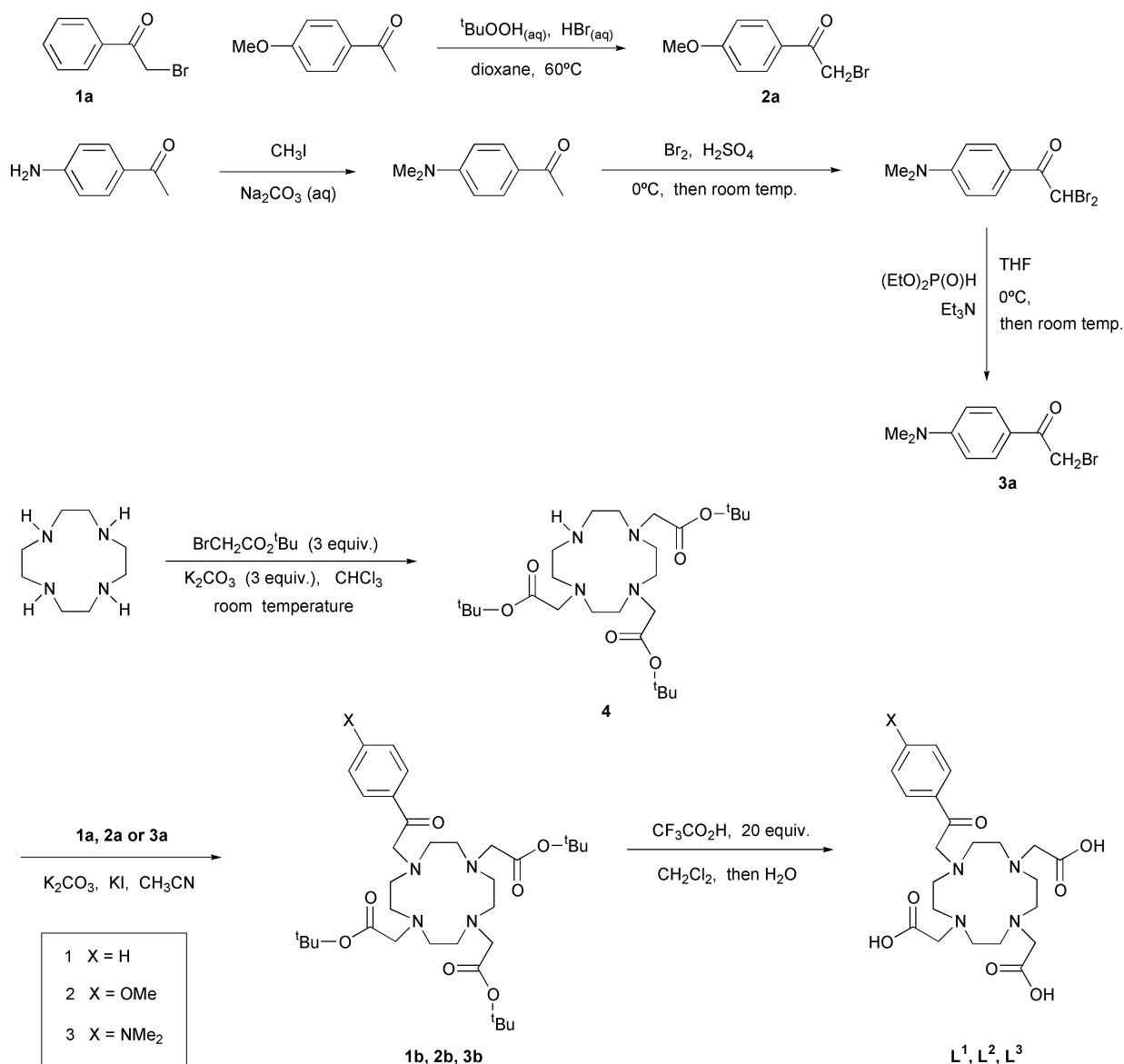
Synthetic routes

Ligands based on the tetraazamacrocyclic 1,4,7,10-tetraazacyclododecane (cyclen) tri- or tetra-*N*-substituted with carboxylate donors are well-known to form lanthanide(III) complexes of exceptional kinetic and thermodynamic stability.^{3,8,9} For example, the Gd³⁺ complex of the tetraacetate is sufficiently stable for use *in vivo* in millimolar quantities as a contrast agent for MRI.⁹ The ketone-substituted ligands L¹-L³ were synthesised in order to explore the efficacy of

acetophenones as sensitizers of the metal excited state in the europium complexes. The synthetic routes to the compounds are summarised in Scheme 1. Reaction of cyclen with three equivalents of *tert*-butylbromoacetate in chloroform at room temperature for 72 hours, in the presence of one equivalent of potassium carbonate, led primarily to the *tert*-butyl ester of DO3A, **4**, which could be separated from small amounts of the tetra- and di-alkylated macrocycle by chromatography on silica. The ester was subsequently alkylated with the appropriate α -bromoacetophenone, **1a–3a**, in acetonitrile in the presence of a catalytic amount of KI and potassium carbonate as the base. Compounds **2a** and **3a** were prepared from the parent *para*-substituted acetophenones. It is well-known that the bromination of arylmethylketones often leads to a complex mixture of products because aromatic ring substitution and bromine addition to the enol form often compete effectively with radical side-chain halogenation. Competitive ring bromination is particularly facile in amino-substituted compounds, due to the activating effect of the electron-donating amino group. We adopted routes to these compounds based on recently described procedures for the efficient, selective preparation of side-chain brominated compounds. The *para*-methoxy-substituted compound was prepared by bromination of 4'-methoxyacetophenone using HBr in the presence of *tert*-butylhydroperoxide, a combination of reagents that has been reported recently

for *in situ* generation of positive halogen species avoiding the hazards associated with the preparation of *tert*-butylhypobromite, and which leads to selective side-chain bromination of acetophenone itself, with no ring bromination.¹⁰ We found this method to be equally selective for side-chain bromination of the *para*-methoxy substituted compound. 2-Bromo-4'-dimethylaminoacetophenone was prepared in three steps from 4'-dimethylaminoacetophenone according to a literature procedure.¹¹

Following alkylation of the secondary amine in **4** with the α -bromoacetones, the *tert*-butyl esters (**1b–3b**) were cleaved using trifluoroacetic acid, to generate the ligands L¹–L³. The europium and gadolinium complexes were prepared by reaction with an equimolar amount of the lanthanide(III) nitrate in aqueous solution and subsequently purified by chromatography on a short column of alumina. The terbium(III) complex of L¹ was prepared similarly. All the complexes were characterised by electrospray mass spectrometry. Although the large paramagnetism and severe line-broadening associated with the gadolinium(III) and terbium(III) ions prohibited NMR analysis, the smaller shifts and narrower line-widths induced by europium(III) allowed the ¹H NMR spectra of the europium complexes to be recorded, revealing in each case the well-established pattern of resonances characteristic of square-antiprismatic complexes found with related ligands.¹²



Scheme 1

Photophysical properties

Absorption spectra. The complexes of L^1 displayed ground-state absorbance maxima at 265 nm in aqueous solution, a value not significantly different from that of the free ligand or acetophenone itself. The corresponding band in the 4'-methoxy-substituted complexes, GdL^2 and EuL^2 , was red-shifted to 305 nm due to conjugation of the electron-donating methoxy group with the carbonyl acceptor; again, the spectrum of the complex was not significantly different from that of the ligand.

The more strongly donating dimethylamino group has a much larger effect on the $\pi-\pi^*$ singlet excited state in L^3 , shifting the band to 339 nm. Moreover, the band is more red-shifted in the complexes by 30 nm, with a maximum at 372 nm and extending to beyond 400 nm (Fig. 1). This is indicative of a

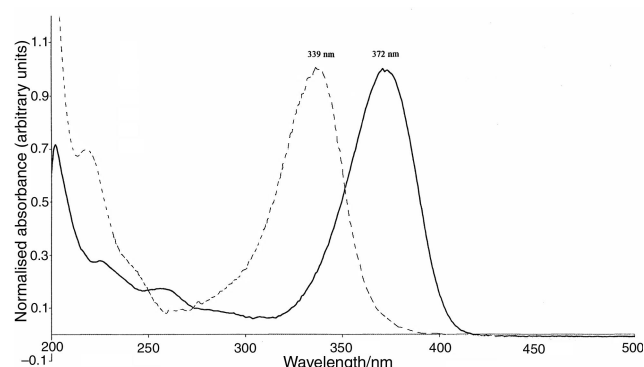


Fig. 1 Absorbance spectra of L^3 (---) and of EuL^3 (—) in ethanol solution at 293 K.

much stronger interaction of the carbonyl group with the metal ion in this case, giving rise to a complex with a higher charge-transfer character. For example, an effect of this type has been reported recently upon coordination of Michler's ketone [4,4'-bis(*N,N*-dimethylamino)benzophenone] to $Eu(fod)_3$ in benzene, where a ground-state complex is formed characterised by an intense absorption band centred at 414 nm.⁷ The authors attribute this to a bathochromic shift of the first singlet-singlet excited state noting that, since excitation of this transition moves the electron density towards the carbonyl group, the presence of the lanthanide ion would be expected to have a large effect on its energy. However, coordination only occurred in non-coordinating solvents. In contrast, in the present instance, the carbonyl group remains bound even in aqueous solution, presumably because the seven other ligating sites of the macrocyclic ligand are able to maintain it in a position suitable for binding.

Such geometric factors should also favour binding of the carbonyl group in the complexes of L^1 and L^2 , despite the fact that no shifts in the absorption bands are observed in these cases. The absence of a red-shift in these complexes does not, however, mean that the carbonyl group remains uncoordinated, as evident from the following control experiment. Upon mixing 4,4'-dimethoxybenzophenone and $Eu(fod)_3$ in toluene, no significant red-shifts nor new bands were observed in the absorption spectra, in contrast to the observations with Michler's ketone. Nevertheless, the europium emission intensity was substantially increased upon excitation at 365 nm, indicative of sensitisation of the metal by the benzophenone and hence complex formation by coordination of the ketone to the lanthanide ion. Moreover, the two complexes were found to contain only one metal-coordinated water molecule (*vide infra*), in contrast to the two water molecules found in complexes of related ligands offering heptadentate coordination (*e.g.* those of 1,4,7,10-tetraazacyclododecane-1,4,7-triacetate, DO3A), lending further support to the proposal that the ketone oxygen is indeed coordinated to the metal.

Phosphorescence of the gadolinium complexes. Aqueous and EPA † solutions of the Gd^{3+} complexes showed no luminescence at room temperature but, upon cooling to 77 K, displayed intense phosphorescence with some vibrational structure, due to emission from the $n-\pi^*$ triplet state of the chromophore. From the positions of the highest energy band in the spectrum, the triplet energy of GdL^1 was determined to be $25600 \pm 200 \text{ cm}^{-1}$ in EPA (25300 cm^{-1} in H_2O). As observed for the singlet excited state, introduction of the methoxy or dimethylamino substituents led to a progressive reduction in the energy of the triplet state: a value of $24500 \pm 200 \text{ cm}^{-1}$ was determined for GdL^2 (EPA and H_2O), and $21000 \pm 200 \text{ cm}^{-1}$ for GdL^3 in EPA (20000 cm^{-1} in H_2O). Phosphorescence lifetimes in EPA at 77 K were determined to be 10.4, 7.9 and 15.9 ms for the three complexes respectively.

EuL^1 and EuL^2 : emission spectra and lifetimes. In each case, the triplet states are much too low in energy to act as sensitizers of the lowest energy excited state of gadolinium(III) [$E(^6P_{7/2}) = 32000 \text{ cm}^{-1}$], but are appropriately placed for potential sensitisation of europium(III) [$E(^5D_0) = 17300$, $E(^5D_1) = 19000 \text{ cm}^{-1}$]. Upon excitation into the $\pi-\pi^*$ bands, both EuL^1 and EuL^2 did indeed display intense metal-centred luminescence, both in alcohol and aqueous solution. The luminescence excitation spectra corresponded well with the ground-state absorption spectra, confirming that the emission was due to sensitisation by the chromophore and (based on previous studies)^{5,6} probably *via* the triplet state of the acetophenone.

Lifetimes of emission are summarised in Table 1. From the values in H_2O and D_2O , the hydration number q (which provides an indication of the number of metal-bound water molecules) was determined using the Horrocks equation¹³ to be 1.24 and 1.20 for EuL^1 and EuL^2 respectively. After correction for the weaker effect of outer-sphere water molecules,¹⁴ these values are reduced to 1.10 and 1.05 respectively, clearly indicating that there is one metal-bound water molecule in both cases. This is consistent with observations on the complexes of structurally related octadentate amide ligands where a metal-bound water molecule increases the coordination number to nine¹² and, as noted above, supports the proposal that the carbonyl oxygen is coordinated to the metal, preventing the entry of a second water molecule.

The emission spectra of the two complexes EuL^1 and EuL^2 were very similar (Fig. 2). A sharp $^5D_0 \rightarrow ^7F_0$ band of modest intensity at 579.8 nm is observed in each case. The relative contribution of the purely magnetic dipole $^5D_0 \rightarrow ^7F_1$ transition to the total integrated emission intensity is similar for both complexes, but the hypersensitive $^5D_0 \rightarrow ^7F_2$ band is rather more intense in EuL^2 (*vide infra*).

Overall quantum yields of metal-centred luminescence, ϕ_{lum} , upon excitation of the acetophenone group are given in Table 1. In order to assess the efficiency of energy transfer η_{ET} using these quantum yields, an estimate of both ϕ_T and η_{Ln} is required [eqn. (1) above]. Given that the sensitizer has an n,π^* triplet state, and also that the lanthanide ions have high spin-orbit coupling constants, it is appropriate to assume that ϕ_T (the quantum yield of triplet formation) is close to 1.⁶ The efficiency of metal-centred luminescence, η_{Ln} , can be calculated from the observed emission lifetime τ_{obs} , provided that the pure radiative lifetime τ_R is available, since:

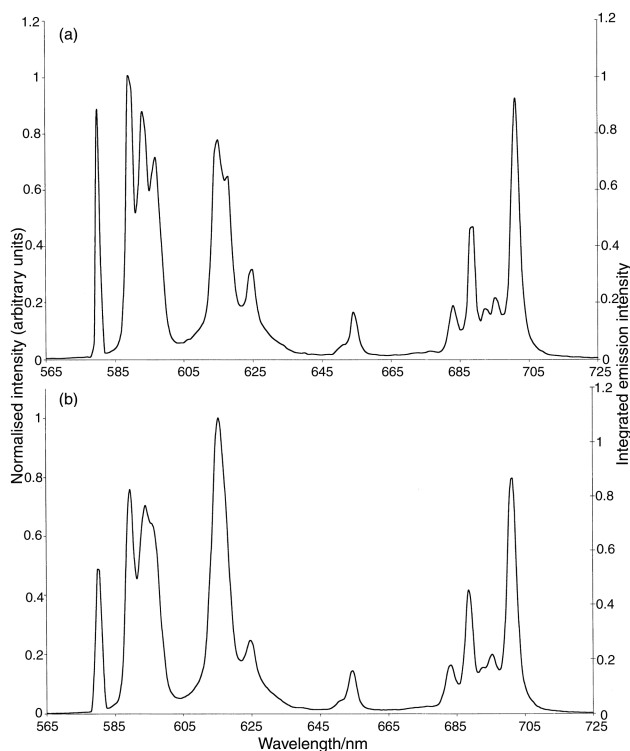
$$\eta_{Ln} = \tau_{obs}/\tau_R \quad (2)$$

† EPA refers to the solvent system: ethanol/isopentane/diethyl ether in the ratio 2/5/5 by volume. This solvent offers excellent properties for measurement of spectra and lifetimes at low temperature, with little tendency for cracking. The solubility of the complexes in EPA, although minimal, is sufficient to obtain solutions with suitable absorbances.

Table 1 Photophysical parameters of the europium and gadolinium (data in *italics*) complexes of L¹–L^{3a}

Complex	E_T/cm^{-1b}	Absorbance $\lambda_{\text{max}}/\text{nm}$	$\tau_{\text{H}_2\text{O}}/\text{ms}^c$	$\tau_{\text{D}_2\text{O}}/\text{ms}^c$	q^d	$\phi_{\text{H}_2\text{O}}^e$	$\phi_{\text{D}_2\text{O}}^e$
LnL ¹	25600 <i>25300</i>	265	0.62	2.26	1.10	0.006	0.021
LnL ²	24500 <i>24500</i>	305	0.63	2.18	1.05	0.098	0.34
LnL ³	21000 <i>20000</i>	375	<i>f</i>	—	—	—	—

^a For the terbium complex of ligand L¹: $\tau_{\text{H}_2\text{O}} = 1.60$ ms, $\tau_{\text{D}_2\text{O}} = 2.6$ ms, $q = 0.98$; $\phi_{\text{H}_2\text{O}} = 0.12$, $\phi_{\text{D}_2\text{O}} = 0.23$. ^b Triplet energy of the acetophenone chromophore ± 200 cm⁻¹, as estimated from the phosphorescence spectra of the gadolinium complexes at 77 K. ^c Lifetimes of the europium-centred emission monitored at 593 nm, 293 K; uncertainty $\pm 5\%$. ^d q is the hydration state (number of coordinated water molecules) as determined from $\tau_{\text{H}_2\text{O}}$ and $\tau_{\text{D}_2\text{O}}$ using the equation of Parker *et al.*¹⁴ ^e Quantum yields of the europium complexes at 293 K, measured using cresyl violet in methanol and rhodamine 101 in acidified ethanol as standards; uncertainty $\pm 10\%$. ^f EuL³ was non-emissive in aqueous solution.

**Fig. 2** Emission spectra of EuL¹ (a) and EuL² (b) in solution in D₂O at 293 K. The excitation wavelength was 265 and 305 nm respectively; excitation and emission bandpasses of 2.5 nm.

The pure radiative lifetime of europium(III) in different environments can be estimated from the emission spectrum as follows.¹⁵ The total radiative relaxation rate k_R ($=1/\tau_R$) of the emissive excited state, ⁵D₀, is the sum of the spontaneous emission probabilities, $A(0,J)$, to the lower ⁷F_{*J*} levels.

$$k_R = \sum_J A(0,J) \quad (3)$$

The relative contribution of each ⁵D₀ → ⁷F_{*J*} transition to the spectrum, the branching ratio β , is the ratio of the intensity of the band to the total intensity in the corrected emission spectrum, and is determined by the spontaneous emission probability:

$$\beta(0,J) = A(0,J)/\sum_J A(0,J) = A(0,J)/k_R = A(0,J) \cdot \tau_R \quad (4)$$

The forbidden lanthanide(III) (f–f) emission bands consist of magnetic dipole (MD) and induced electric dipole (ED) transitions. The former are virtually independent of the ion's surroundings, in contrast to the latter where the geometry and ligating atoms have a significant effect on the transition probabilities. The ⁵D₀ → ⁷F₁ (*J1*) band of Eu³⁺ centred at 593 nm is entirely MD and consequently has an oscillator strength that is independent of the ligand field and complex symmetry.¹⁶ Thus,

Table 2 Calculated values of τ_R , η_{Ln} , η_{ET} and $\sum k_{\text{nr}}$ for EuL¹ and EuL² using experimentally determined quantities τ_{obs} , ϕ_{lum} and $[I(0,1)/I_{\text{tot}}]^a$

	EuL ¹		EuL ²	
	H ₂ O	D ₂ O	H ₂ O	D ₂ O
$[I(0,1)/I_{\text{tot}}]$	0.24	0.25	0.22	0.21
τ_R/ms	7.37	7.74	6.65	6.62
k_R/s^{-1}	136	129	150	151
$\tau_{\text{obs}}/\text{ms}$	0.62	2.26	0.63	2.18
η_{Ln}	0.084	0.29	0.094	0.33
ϕ_{lum}	0.058	0.21	0.093	0.34
η_{ET}	0.71	0.72	0.99	1.0
$\sum k_{\text{nr}}/\text{s}^{-1}$	1480	313	1440	308

^a $[I(0,1)/I_{\text{tot}}]$ is the relative contribution of the ⁵D₀ → ⁷F₁ band intensity, $I(0,1)$, to the total integrated emission intensity, I_{tot} ; τ_R is the pure radiative lifetime determined from $[I(0,1)/I_{\text{tot}}]$ using the method described in the text; k_R is the radiative rate constant $=1/\tau_R$; η_{Ln} is the efficiency of metal-centred luminescence obtained using eqn. (2); η_{ET} is the efficiency of energy transfer calculated using eqn. (1) and assuming that $\phi_T = 1$; $\sum k_{\text{nr}}$ (the sum of the non-radiative decay constants) $= [(1/\tau_{\text{obs}}) - k_R]$.

given a value for the spontaneous emission probability $A(0,1)$ of the ⁵D₀ → ⁷F₁ transition and using eqn. (4), it is possible to estimate τ_R from the relative contribution of this band to the experimentally determined emission spectrum:

$$1/\tau_R = A(0,1)/\beta(0,1) = A(0,1)[I_{\text{tot}}/I(0,1)] \quad (5)$$

where $[I_{\text{tot}}/I(0,1)]$ is the ratio of the total integrated intensity of the corrected europium(III) emission spectrum to the intensity of the ⁵D₀ → ⁷F₁ band. The spontaneous emission probability, $A(0,1)$, can be determined directly from the theoretically calculated dipole strength of this transition, leading to a value of 32.4 s⁻¹ in aqueous solution. ‡

For complexes EuL¹ and EuL², the results of these calculations [eqns. (1)–(3)], using the relative contribution of the *J1* band in the corrected emission spectrum together with the experimentally determined values of τ_{obs} and ϕ_{lum} , leads to the values of τ_R , η_{Ln} , η_{ET} and $\sum k_{\text{nr}}$ given in Table 2. It can be seen that the energy transfer efficiencies are high in each case and especially so for the methoxy-substituted system. The introduction of the methoxy substituent lowers the triplet energy by about 1000 cm⁻¹ (Table 1), leading to a better match with the

‡ Application of the Einstein coefficient to express the rate of relaxation from an excited state ψ_j to a final state ψ_j under a magnetic dipole mechanism leads to: $A(\psi_j, \psi_j) = \{64\pi^4\sigma^3/3h(2J+1)\} \cdot n^3 \cdot S_{\text{md}}(\psi_j, \psi_j)$, where σ is the energy gap between the two states (cm⁻¹), n is the refractive index of the medium and $S_{\text{md}}(\psi_j, \psi_j)$ is the magnetic dipole line strength.¹⁷ This last quantity has been calculated theoretically for the ⁵D₀ → ⁷F₁ transition of Eu³⁺ in a number of studies and verified experimentally; we have used the value of Kirby and Richardson¹⁸ (884×10^{-8} Debye²) together with an energy of 17010 cm⁻¹ as the baricentre of the transition and $n = 1.334$ for H₂O, leading to the value of 32.4 s⁻¹.

Table 3 Relative contributions of the $^5D_0 \rightarrow ^7F_J$ bands in the emission spectra of the europium complexes of L^1 , L^2 and L^3 in ethanol solution, 293 K

	EuL ¹	EuL ²	EuL ³
J_0/J_1	1.11	0.40	0.15
J_2/J_1	0.67	1.43	3.22
J_3/J_1	0.20	0.23	0.23
J_4/J_1	0.78	0.97	2.74

acceptor 5D_1 and 5D_0 states of the europium ion. As expected, η_{ET} does not change significantly on going from H_2O to D_2O , and the main factor that limits the observed luminescence quantum yield of these complexes is the rather low efficiency of metal-centred luminescence, even in D_2O .

EuL³: emission spectra and lifetimes. The behaviour of EuL³ is very different from that of the complexes discussed above. The emission spectrum recorded in ethanol solution upon excitation of the dimethylaminobenzene group is shown in Fig. 3.

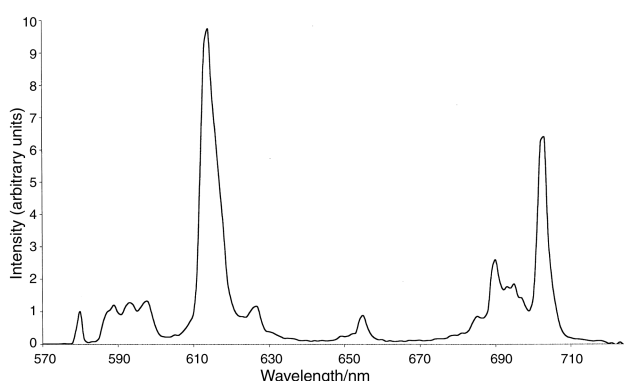


Fig. 3 Emission spectrum of EuL³ in solution in ethanol at 293 K; $\lambda_{ex} = 370$ nm; bandpass = 2.5 nm.

The hypersensitive $\Delta J = 2$ transition now dominates the spectra, being much more intense than the $\Delta J = 1$ band. The ratio of the integrated intensity of each of the $^5D_0 \rightarrow ^7F_J$ bands to the $^5D_0 \rightarrow ^7F_1$ intensity for the three complexes are given in Table 3. A clear trend may be discerned: the relative intensity of the $\Delta J = 2$ transition increases progressively upon going from the unsubstituted to the methoxy- and subsequently the dimethylamino-substituted complexes. The induced electric dipole $\Delta J = 2$ transition in europium is hypersensitive: its intensity is highly dependent on both the coordination geometry and identity of the coordinating atoms. Attempts to explain hypersensitivity have been based on static-coupling models (*eg.* Judd–Ofelt theory) and on dynamic coupling (or ligand polarisation) mechanisms. In the latter, the intensity of hypersensitive transitions is related explicitly to the dipolar polarisabilities of the ligand atoms or groups, (as well as to the geometry of the complex).¹⁹ Thus, the distinctive increase in the intensity of the $\Delta J = 2$ band may be rationalised in terms of the more polarised $Ar=C-O^-$ character of the ketone carbonyl group upon introduction of the increasingly electron-donating methoxy and dimethylamino substituents. The observed trend confirms, then, that the ketone group is coordinated to the metal ion in each of the three complexes.

The total emission intensity of EuL³ was found to be very sensitive to the solvent. In particular, despite the reasonable quantum yields in non-aqueous solvents (Table 4), no emission was detectable in aqueous solution (H_2O or D_2O). For the other solvents examined, luminescence was observed in each case, although the intensity varied erratically (Fig. 4), showing no correlation with the dielectric constant, nor with other solvent parameters such as that of Reichardt. Monoexponential decay

Table 4 Calculated values of τ_R , η_{Ln} , η_{ET} and Σk_{nr} for EuL³ in different solvents^a

	MeOH	EtOH	iPrOH	DMSO
$[I(0,1)/I_{tot}]$	0.14	0.15	0.15	0.12
τ_R/ms	4.31	4.27	4.26	2.79
k_R/s^{-1}	232	234	235	359
τ_{obs}/ms	0.12	0.35	0.69	1.29
η_{Ln}	0.029	0.082	0.16	0.46
ϕ_{lum}	0.014	0.086	0.10	0.35
η_{ET}	0.48	1.05	0.62	0.96
$\Sigma k_{nr}/s^{-1}$	1220	2630	7900	418

^a Parameters are defined in the footnotes to Table 2.

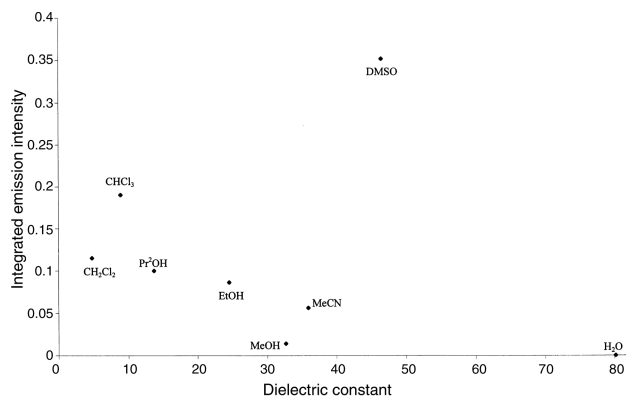


Fig. 4 Integrated emission intensity of EuL³ in several solvents ($\lambda_{ex} = 370$ nm) plotted against dielectric constant.

of the emission was observed in DMSO and alcohol solutions, and the measured lifetime was found to vary substantially with solvent (Table 4). Emission in CH_3CN , CH_2Cl_2 and $CHCl_3$ displayed non-exponential decay kinetics, possibly due to the slow exchange between the two species with and without a metal-bound water molecule.²⁰

The very sensitive dependence of the emission intensity and lifetime on solvent is probably a combination of effects, as revealed by applying the above analysis of spectra and lifetimes to EuL³. The results of this treatment are summarised in Table 4, which show that the solvent has not only an effect on the non-radiative decay pathways, but also a profound influence on both the pure radiative lifetime and the efficiency of energy transfer. The pure radiative lifetime is significantly shorter in DMSO than in alcohols, whilst the non-radiative decay pathways (Σk_{nr}) are less significant, which together account for the substantially higher quantum yield observed in DMSO. The efficiency of energy transfer is close to unity.

Conclusion

In summary, the complexes reported here represent a new class of compound in which an acetophenone group covalently linked to the macrocyclic ligand is able to bind to the coordinated lanthanide ion, promoting efficient energy transfer from chromophore to metal. Introduction of a methoxy substituent into the *para* position of the acetophenone further increases the efficiency, whilst a dimethylamino substituent leads to high emission intensities in non-aqueous solvents only.

Experimental

General

Cyclen was supplied by Strem and used as supplied. The preparation of 4'-dimethylamino-2-bromoacetophenone followed procedures described recently in the literature starting from 4'-aminoacetophenone,¹¹ which was obtained from Aldrich.

2-Bromoacetophenone and 4'-methoxyacetophenone are also available commercially. Chromatography was carried out on silica gel (60, 40–63 μm , Fluorochem) or on alumina (neutral, Brockmann I). Solvents were Analar or HPLC grade, and water was purified by the Milli Q system. Proton and ^{13}C NMR spectra were recorded on a Varian Mercury-200 (200 and 50.3 MHz respectively) or a Unity-300 (300 and 75.5 MHz). Proton spectra were referenced to residual protio solvent resonances and ^{13}C spectra to the solvent carbon resonance. Electrospray mass spectra were measured on a VG Platform II instrument. UV-Visible absorbance spectra were recorded using a Unicam UV-2 spectrometer using quartz cuvettes of 1 cm path-length. Steady-state emission spectra were recorded using an Instruments S.A. Fluoromax and lifetimes were measured using a Perkin-Elmer LS 50B instrument. An Oxford Instruments variable temperature liquid nitrogen cryostat (DN1704) was used for recording the phosphorescence spectra of the chromophores at 77 K. Elemental analyses were carried out using an Exeter Analytical E-440 Analyser.

Syntheses

4'-Methoxy-2-bromoacetophenone, 2a. A solution of *tert*-butylhydroperoxide (70% aq.) (0.42 mL, 3.30 mmol) was added to a cooled mixture of HBr (48% aq.) (0.56 mL, 3.30 mmol) in dioxane (15 mL) and the mixture was stirred for 5 minutes. 4'-Methoxyacetophenone was added to this solution at room temperature and the mixture stirred for 30 minutes, before being heated at 60 °C for 72 h. The solvent was removed under reduced pressure, the residue taken into 10 mL of water and extracted with dichloromethane (3 \times 20 mL). After drying over magnesium sulfate and removal of solvent, the desired product was obtained in 85% yield. δ_{H} (CDCl₃, 300 MHz): 7.95 (2 H, d, J = 8.9, H²), 6.94 (2 H, d, J = 8.9 Hz, H³), 4.39 (2 H, s, CH₂), 3.86 (3 H, s, CH₃). δ_{C} (CDCl₃, 75.5 MHz): 190.0 (C=O), 164.2 (C-COCH₂), 132.3 and 131.4 (aromatic CH), 114.1 (C-OMe), 55.7 (CH₂), 30.9 (CH₃). m/z (ES⁺): 253 (100%, M + Na⁺).

1,4,7-Tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane, 4. *Tert*-butylbromoacetate (3.33 g, 17.08 mmol) in solution in chloroform (100 mL) was added dropwise over 4 hours to a stirred solution of 1,4,7,10-tetraazacyclododecane (1 g, 5.69 mmol) in chloroform (300 mL) in the presence of potassium carbonate (786 mg, 5.69 mmol). After addition was complete, the solution was stirred at room temperature for 72 hours. Inorganic salts were then separated by filtration and the solvent removed from the filtrate under reduced pressure. The residue was purified by chromatography on silica, gradient elution CH₂Cl₂ to 5% MeOH-CH₂Cl₂, R_{f} = 0.5 (7% MeOH-CH₂Cl₂). Yield = 73%. δ_{H} (CDCl₃, 300 MHz): 3.36 (4 H, s, 2 \times CH₂ acetates), 3.27 (2 H, s, CH₂ unique acetate), 3.08–2.86 (16 H, br m, CH₂CH₂ ring), 1.44 [27 H, s, C(CH₃)₃]. Spectrum in agreement with literature data.²¹ m/z (ES⁺): 515 (M + H⁺).

1-(2-Acetophenone)-4,7,10-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane, 1b. A solution of **4** (750 mg, 1.46 mmol), 2-bromoacetophenone (355 mg, 1.75 mmol), potassium carbonate (242 mg, 1.75 mmol) and a catalytic amount of KI in acetonitrile (5 mL) was heated at reflux with stirring for 96 h. The solvent was removed under reduced pressure and the residue taken up into aqueous sodium hydroxide solution (1 M, 10 mL), from which the product was extracted into dichloromethane (3 \times 10 mL). After drying over potassium carbonate and removal of solvent, the crude product was purified by chromatography on alumina, gradient elution from CH₂Cl₂ to 2% MeOH-CH₂Cl₂, R_{f} = 0.5 (2% MeOH-CH₂Cl₂). Yield = 58%. δ_{H} (CDCl₃, 300 MHz): 7.89 (2 H, d, J = 7.5, H²), 7.57 (1 H, t, J = 7.5, H⁴), 7.45 (2 H, t, J = 7.5 Hz, H³), 2.30–3.50 (24 H, br m, CH₂CH₂ ring and CH₂ acetates), 1.45 [27 H, s, C(CH₃)₃]. δ_{C} (CDCl₃, 75.5 MHz): 198.6, 171.8, 134.5, 133.7,

127.7, 126.6, 81.1, 81.0, 59.2, 54.6, 52.5, 52.0 (br), 49 (br), 26.9, 26.8. m/z (ES⁺): 633 (M + H⁺).

1-(4'-Methoxy-2-acetophenone)-4,7,10-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane, 2b. Compound **2b** was prepared in a similar manner, starting from **4** (800 mg, 1.55 mmol), potassium carbonate (258 mg, 1.86 mmol) and 4'-methoxy-2-bromoacetophenone (426 mg, 1.86 mmol). The solvent was again acetonitrile and the reaction time 96 h at reflux. Work-up and purification was carried out in the same way, and the desired compound eluted from the column under very similar conditions to **1b**; yield 55%. δ_{H} (CDCl₃, 300 MHz): 7.77 (2 H, d, J = 8.7, H²), 6.82 (2 H, d, J = 8.7 Hz, H³), 3.76 (3 H, s, OCH₃), 3.40–2.10 (24 H, m, CH₂CH₂ ring and CH₂ acetates), 1.34 [27 H, s, C(CH₃)₃]. δ_{C} (CDCl₃, 50.3 MHz): 197.6, 172.5, 163.7, 130.4, 129.7, 128.5, 113.7, 113.5, 81.9, 81.8, 59.6, 55.5, 55.4, 53 (br), 49 (br), 27.7, 27.6. m/z (ES⁺): 685 (M + H⁺).

1-(4'-Dimethylamino-2-acetophenone)-4,7,10-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane, 3b. This compound was prepared similarly, from **4** (750 mg, 1.46 mmol), caesium carbonate (570 mg, 1.75 mmol) and 4'-dimethylamino-2-bromoacetophenone (354 mg, 1.46 mmol). Solvent, reaction time, work-up and purification was as above, with the desired compound requiring slightly more polar conditions for elution from the column (R_{f} = 0.5 in 4% MeOH-CH₂Cl₂); yield 53%. δ_{H} (CDCl₃, 200 MHz): 7.76 (2 H, d, J = 9.0), 6.61 (2 H, d, J = 9.0 Hz), 3.60–2.10 (24 H, m, CH₂CH₂ ring, CH₂ acetate), 3.05 [6H, s, N(CH₃)₂], 1.45 [27 H, s, C(CH₃)₃]. δ_{C} (CDCl₃, 75.5 MHz): 196.5, 173.0, 172.8, 153.8, 129.8, 123.7, 110.7, 82.0, 81.9, 59.4, 55.9, 55.7, 53 (br), 49 (br), 40.1, 28.0. m/z (ES⁺): 698 (M + Na⁺).

L¹-L³. The tris-acetate ligands L¹-L³ were prepared by hydrolysis of the tris-*tert*-butylesters using the following procedure. Trifluoroacetic acid (20 equiv.) was added to a solution of the tris-ester (200 mg) in dichloromethane (5 mL), and the solution stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the residue washed with more dichloromethane (3 \times 5 mL). Water was then added, and the pH adjusted to 6–7 using HCl (aqueous, 1 M).

Lanthanide(III) complexes. The lanthanide(III) complexes were prepared by addition of an equimolar amount of the lanthanide(III) nitrate to an aqueous solution of the ligand (concentration *ca.* 40 mM). After refluxing for 24 h, alumina (2 g) was added and the solvent removed under reduced pressure until the solid was dry and free-flowing. The alumina with adsorbed complex was added to the top of a short column of alumina, and eluted with CH₂Cl₂/20% MeOH-CH₂Cl₂. The electrospray ionisation mass spectrum of each complex gave, as the major peak, [M + H⁺] or [M + Na⁺]. Owing to the large paramagnetism associated with the gadolinium(III) and terbium(III) ions, analysis by NMR is not feasible for these complexes, but is possible for europium(III) where the shifts are not as large and the line-widths narrower. A full assignment of the individual resonances, however, requires a dipolar shift analysis which is beyond the objectives of the current work; nevertheless, the spectra show very clearly the characteristic pattern of resonances shown previously to be typical of such complexes, in which the rigidity imposed by the metal ion leads to the inequivalence of the four protons of each ethylene unit in the macrocycle.¹²

For example, for [EuL³], δ_{H} (D₂O, 200 MHz): 36.3 (1 H), 32.0 (1 H), 31.4 (1 H), 30.6 (1 H) (H_{ax}); 6.1 (4 H, aromatic H); 3.3 (6 H, N(CH₃)₂); 1.8 (1 H), -1.2 (1 H), -1.7 (1 H), -2.6 (1 H), -3.0 (1 H), -4.6 (1 H), -6.2 (1 H), -7.1 (1 H), -8.8 (3 H overlapping), -10.4 (1 H), -11.5 (1 H), -12.9 (1 H), -14.8 (4 H overlapping), -15.7 (1 H), -16.7 (1 H) (8 H_{eq}, remaining

4 H_{ax}, CH₂CO). *m/z* (ES⁺): 680.1612 (M + Na⁺, calculated value for C₂₄H₃₄N₅O₇EuNa = 680.1568).

Similarly, *m/z* (ES⁺): EuL¹: 635 (M + Na⁺); GdL¹: 618 (M + H⁺); TbL¹: 619 (M + H⁺); EuL²: 667.1266 (M + Na⁺, calculated value for C₂₃H₃₁O₈N₄EuNa = 667.1252); found C 36.82, H 4.89, N 7.32% (C₂₃H₃₁O₈N₄Eu·5H₂O requires C 37.60, H 5.59, N 7.63%); GdL²: 671 (M + Na⁺); found C 36.84, H 4.82, N 7.45% (C₂₃H₃₁O₈N₄Gd·5H₂O requires C 37.35, H 5.55, N 7.58%); GdL³: 685 (M + Na⁺).

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