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The efficient intramolecular sensitisation of terbium(III) and europium(III) by benzophenone-containing ligands

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The europium and terbium complexes of an octadentate macrocyclic ligand incorporating benzophenone have been prepared; excitation of the ketone, which has a triplet quantum yield of unity, results in very efficient sensitisation of the emissive states of the bound metal ions.

Luminescent lanthanide complexes are of growing interest owing to their application as luminescent labels or probes in biological systems. The long lifetime of the metal centred emission allows the use of time-resolved detection to discriminate between the luminescence of the molecular probe and the ubiquitous, short-lived auto-fluorescence. Complexes need to fulfil a number of criteria, including solubility in water as well as having high kinetic and thermodynamic stability. It is also important that the compounds used are highly emissive and that excitation can be achieved with moderately long wavelength radiation, $\lambda_{ex} > 300$ nm.

Due to the very low extinction coefficients of the lanthanide ions, direct metal excitation is inefficient and it is preferable to sensitise the excited state *via* a suitable chromophore covalently coupled to the ligand. Early studies of the transfer of energy from a chromophore to a chelated lanthanide ion were carried out by Horrocks *et al.* who studied systems in which the metal ions were bound to proteins.[1,2] They assumed that it was the excited singlet state of the chromophore that sensitised the lanthanide ions and carried out calculations based upon the internuclear separations and spectral overlap using the Förster transfer model. However, subsequent experiments have indicated that the triplet state of the chromophore also plays an important role in energy transfer to the metal ion.[3,4] The longer intrinsic lifetime of the triplet state means that it is likely to make the major contribution to metal ion sensitisation.

Ultimately the quantum yield of luminescence, Φ_{lum}, depends upon a number of factors [eqn. (1)], where Φ_T is the triplet yield

$$\Phi_{lum} = \Phi_T \eta_{ET} \eta_{Ln} \qquad (1)$$

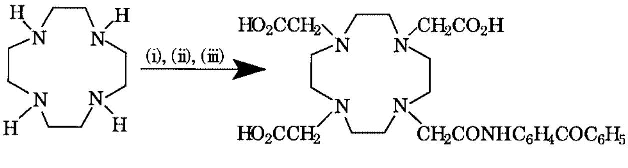
of the chromophore and η_{ET} and η_{Ln} are the efficiencies of energy transfer and metal centred luminescence respectively.

Given this equation it is perhaps surprising that until now the chromophores chosen for incorporation into ligands have triplet quantum yields of less than unity. We report here the use of an aromatic ketone, a substituted benzophenone, which has an n,π* triplet state. Compounds of this type are known to have large triplet quantum yields and have the additional benefit of a small singlet–triplet energy gap. However, there are very few examples of the use of aromatic ketones as sensitisers of lanthanide ions. Substituted 1,3-dicarbonyl compounds have been exhaustively studied as lanthanide ligands since the early work of Weissman.[5] These dicarbonyl ligands form complexes of the type ML_3 but tend to be somewhat unstable in aqueous solution. The three bidentate ligands do not fulfil the higher coordination numbers required by the lanthanide ions, and in some cases another ‘auxiliary ligand’ such as phenanthroline is included.[6]

A more pertinent example is provided by the recent work of Werts *et al.* who reported the formation of a 1 : 1 complex between $Eu(fod)_3$ and Michler’s Ketone, 4,4′-bis(dimethylamino)benzophenone, in benzene solution in which the benzophenone may act as the auxiliary ligand.[7] The complex showed a red-shifted absorption band which extended to almost 450 nm, attributed to the charge transfer nature of the Michler’s Ketone, and was highly luminescent, $\Phi_{lum} = 0.20$, demonstrating that the energy transfer process from the substituted benzophenone to the metal ion was occurring readily. However, the complex is not luminescent in polar solvents, limiting the suitability of this material for more widespread applications. Rodriguez-Ubis *et al.* have reported the synthesis of a polyaminocarboxylate ligand containing an acetophenone and the Eu and Tb complexes were reported to have exceedingly high luminescence quantum yields, $\Phi > 0.9$.[8] Based upon the reported luminescence lifetimes, these values seem surprisingly high and such complexes will not exhibit the same stability as those based upon the azamacrocycles.

In the work presented here we describe the preparation and a photophysical study of ligand **1** in which a benzophenone moiety is coupled to DOTA, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid, *via* an amide linkage. Ligands of this type are known to form lanthanide(III) complexes of exceptional kinetic and thermodynamic stability.[9] Furthermore the macrocyclic ligand effectively excludes water from the metal centre: lanthanide complexes of ligands analogous to **1** typically have only one water molecule bound directly to the metal. Since it is well established that bound water molecules quench the excited states of the metal ions, this protection from water will increase η_{Ln}.

The ligand **1** was prepared according to Scheme 1. Reaction of 1,4,7,10-tetraazacyclododecane with *N*-(4′-benzoylphenyl)-2-chloroethanamide in chloroform at room temperature led to the mono-*N*-alkylated derivative with high selectivity (>85%).[10] Alkylation of the remaining nitrogen atoms with ethyl bromoacetate in the presence of potassium carbonate as a base led to the triethyl ester of **1**, which was purified by column chromatography on alumina, and from which the desired ligand was obtained upon hydrolysis with aqueous base. The complexes were prepared by refluxing an aqueous solution of **1** at pH 6 with $Ln(NO_3)_3 \cdot 5H_2O$.† Initial experiments involved the study of the lanthanum complex. The compounds show a strong absorption band, $\lambda_{max} = 295$ nm, extending to 370 nm. Aqueous and alcoholic‡ solutions of La·**1** showed no luminescence at room temperature. However, upon cooling to 77 K the



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Scheme 1 (i) $ClCH_2CONHC_6H_4COC_6H_5$-*p*, $CHCl_3$, RT; (ii) $BrCH_2CO_2Et$, K_2CO_3; (iii) aq. KOH, ambient temperature.

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Table 1 Luminescence lifetimes and overall quantum yields for emission from the $^5D_0$ state (Eu) and the $^5D_4$ state (Tb) of the complexes of ligand **1**, λ_{ex} 295 nm, 293 K

Compound	$\tau(H_2O)$/ms	$\tau(D_2O)$/ms	$\Phi_{lum}(H_2O)$	$\Phi_{lum}(D_2O)$
Eu·1	0.61 ± 0.02	2.26 ± 0.05	0.095 ± 0.010	0.38 ± 0.04
Tb·1	1.14 ± 0.05	1.74 ± 0.05	0.27 ± 0.03	0.41 ± 0.04

alcoholic solution formed a glass that showed intense phosphorescence, with a strong vibrational progression similar to the spectrum observed from benzophenone itself. The lifetime of the emission was 18.0 ms and from the position of the highest energy band in the spectrum we determined the triplet energy of the ketone to be 282 ± 5 kJ mol^{-1}. The singlet energy of the compound, determined from the absorption spectrum, is 325 ± 5 kJ mol^{-1}. As expected for a compound with an n,π* triplet state, the triplet state properties are not significantly affected by the presence of the heavy atom in the complex and correspond well to the model compound 4-acetamidobenzophenone, $E_T = 282$ kJ mol^{-1}, $\tau_T = 24.0$ ms.

The Eu and Tb complexes showed intense metal centred luminescence in aqueous solution and the intensity of the emission was not affected by degassing the solutions. The luminescence quantum yields and lifetimes in H_2O and D_2O are given in Table 1.§ From the lifetime data we calculate the number of bound water molecules, *q*, to be 1.25 ± 0.05, a figure that is consistent with related complexes.[9] The luminescence excitation spectra corresponded well with the absorption spectra.

Detailed kinetic measurements reveal an interesting insight into the energy transfer mechanisms in the two complexes. The terbium emission, monitored at 545 nm, shows a rise-time that is faster than the response time of the detection system, $\tau_{rise} < 50$ ns. This indicates that the emissive $^5D_4$ state of the terbium ion is formed within this time and hence that the energy transfer step occurs with a rate constant of $>2 \times 10^7$ s^{-1}. By contrast the europium emission shows a more complex kinetic profile. Monitoring the intensity of the $^5D_0 \rightarrow {}^7F_1$ band at 595 nm revealed two components to the rising edge of the signal. The first was very rapid and contributed *ca.* 20% to the signal, whilst the second showed a lifetime of 1.45 ± 0.1 μs. Monitoring the $^5D_1 \rightarrow {}^7F_1$ emission band at 583 nm showed a short-lived emission and indicated that the lifetime of the $^5D_1$ state was 1.45 ± 0.1 μs. Thus we conclude that in the europium complex processes (2)–(4) occur, where BP* indicates the excited triplet state of the benzophenone moiety.

$$BP^* + Eu(^7F_0) \xrightarrow{i} BP + Eu(^5D_0) \qquad (2)$$

$$BP^* + Eu(^7F_0) \xrightarrow{ii} BP + Eu(^5D_1) \qquad (3)$$

$$Eu(^5D_1) \xrightarrow{iii} Eu(^5D_0) \qquad (4)$$

Because the triplet state of the benzophenone lies above both the $^5D_1$ and $^5D_0$ levels of the europium ion, 227 and 207 kJ mol^{-1} respectively as illustrated in Fig. 1, energy transfer can and does occur *via* both steps (i) and (ii). These energy steps occur very rapidly, k_i and $k_{ii} > 10^7$ s^{-1}, but the relaxation step (iii) occurs more slowly, $k_{iii} = 6.9 \times 10^5$ s^{-1}. The relatively slow relaxation of the $^5D_1$ state of europium has been observed previously in both the aqua ion and in acetylacetonate complexes,[11] although it should be noted that the contribution of the $^5D_1$ emission to the total emission intensity is negligible, <1%. The decay and grow-in of the emission from the $^5D_1$ and $^5D_0$ states are illustrated in Fig. 2.

In low temperature alcohol glasses both the Eu and Tb complexes showed two sets of emission bands: one showing the characteristic bands associated with the metal centred emission, and one characteristic of the benzophenone. The latter was very

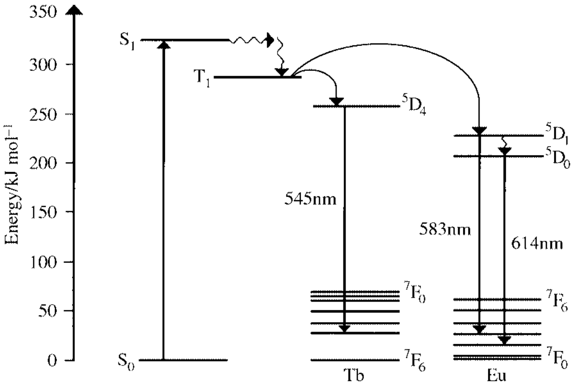

Fig. 1 Energy level diagram showing the energy levels of the chromophore and the two metal ions.

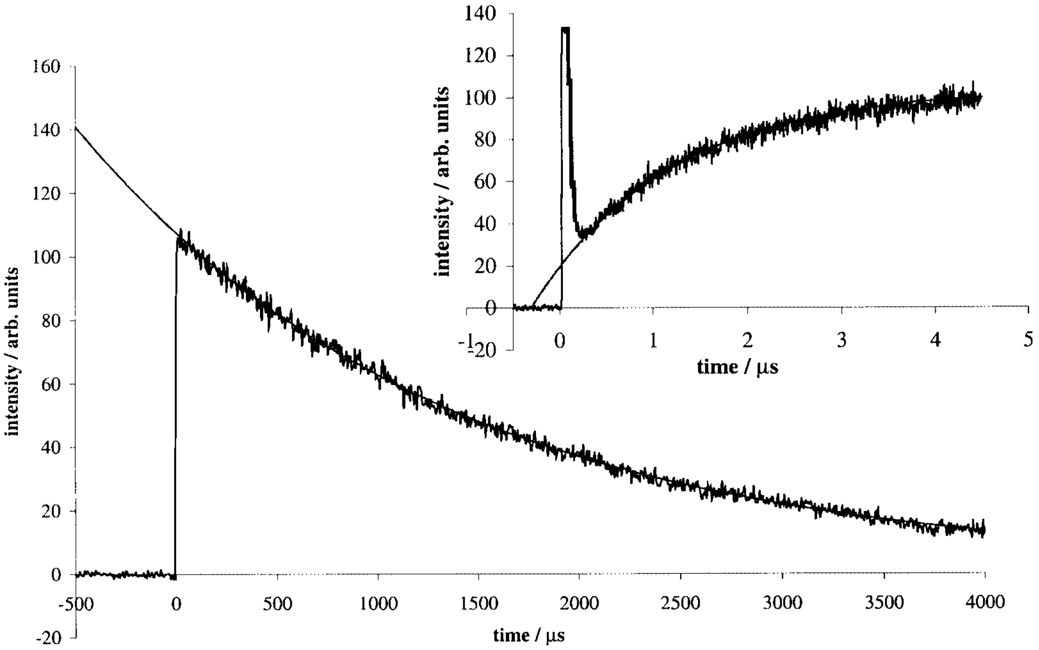

Fig. 2 Time-resolved emission from Eu·1 in D_2O solution, monitoring the $^5D_0 \rightarrow {}^7F_1$ emission at 595 nm. The main curve shows the decay of the $^5D_0$ state, with a lifetime of 2.26 ms. The inset shows the rise-time of the signal, with saturation of the detector between $t = 0$ and $t = 100$ ns due to fluorescence. The characteristic lifetime of this rise is 1.45 ± 0.05 μs.

weak and short lived, with an estimated luminescence quantum yield, $\Phi_P < 0.01$ and lifetime of <200 μs. This indicates that the triplet state of the benzophenone is effectively quenched by the proximate lanthanide acceptor and that the energy transfer step is very efficient. By analogy with the parent chromophore we expect the triplet quantum yield to be unity; hence we deduce that the energy transfer step has a high efficiency, $\eta_{ET} = 0.99$. The observed luminescence quantum yields are in the range 0.095–0.41, suggesting that the efficiency of luminescence is limited by the efficiency of the lanthanide ion luminescence, η_{Ln}, which itself is determined by the relative rates of radiative and non-radiative decay of the ions. The rate of non-radiative decay of the europium $^5D_0$ state is significantly higher than that of the $^5D_4$ state of terbium as illustrated by the empirical proportionality constants known as the '*A* factor', introduced by Horrocks *et al.*, which represent the sensitivity of the excited lanthanide ions to quenching by O–H oscillators.[12] Further refinement of the structures may eliminate the single water molecule bound to the metal ion, which is expected to further reduce the non-radiative deactivation of the metal ions and hence increase η_{Ln}. For example it is known that complexes in which the acetate arms are replaced by phosphinates leave no bound water and hence reduce the non-radiative decay.[13]

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Notes and references

† Selected analytical data for the complexes: [Eu·**1**] *m*/*z* (ES+): 756 [M + Na$^+$]$^+$; ν_{max}/cm^{-1}: 3048, 2929, 2859, 1626, 1596, 1410, 1322, 1284, 1092; ^{1}H NMR: Although a full assignment of the individual resonances in the greatly shifted ^{1}H NMR spectrum by a dipolar shift analysis has not been carried out, the spectrum shows the characteristic pattern of resonances typical of such complexes.[14] δH (200 MHz, D_2O): 33.79 (1H), 30.87 (1H), 29.69 (2H) (H_{ax}); 8.51 (4H), 8.05 (2H), 7.83 (3H) (aromatic H); 1.01 (1H), −0.54 (2H), −3.18 (1H), −3.95 (2H), −5.24 (1H), −7.93 (1H), −8.11 (1H), −8.33 (1H), −10.71 (1H), −12.11 (3H overlapping), −13.35 (1H), −13.78 (1H), −14.79 (2H), −16.21 (1H), −17.47 (1H) (8 H_{eq}, remaining 4 H_{ax}, CH_2CO). [Tb·**1**] *m*/*z* (ES+): 763 [M + Na$^+$]$^+$; IR identical to that of [Eu·**1**]. [La.**1**] m/z (ES+): 743 [M + Na$^+$]$^+$; IR identical to that of [Eu.**1**].

‡ Ethanol:methanol 4 : 1 v/v.

§ Luminescence spectra and quantum yields were recorded using an Instruments SA Fluorolog-3 spectrofluorimeter using steady state excitation. The spectra were fully corrected for the spectral response of the instrument. Quantum yields were recorded relative to quinine sulfate in 1 M H_2SO_4, fluorescein in 0.1 M NaOH, cresyl violet in methanol and Rhodamine 101 in acidified ethanol. Phosphorescence lifetimes were recorded using a ns-pumped spectrometer. Samples were excited at 266 nm using the 4th harmonic of a Q-switched Nd : YAG laser. The luminescence was detected using a photomultiplier (Hamamatsu R928) and recorded using a digital storage oscilloscope (TDS320). Curves were transferred to a PC for analysis using Microsoft Excel. Low temperature spectra were recorded using a cryostat (Oxford Instruments DN1704).

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