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Luminescent terbium(III) complexes with pendant crown ethers responding to alkali metal ions and aromatic antennae in aqueous solution†

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The luminescence lifetime of TbL^2 with a pendant 15-crown-5 increased by 65% to 2.95 ms with an [Na^+] concentration of 0.13 M in aqueous solution; the maximum amplification of the luminescence intensity of TbL^1 containing aza-15-crown-5 reached a factor of 47 upon addition of the aromatic antenna *p*-chlorobenzoate 1.

Responsive luminescent lanthanide complexes have recently gained much attention in screening certain analytes, such as H^+,[1,2,3] O_2,[2] X^-,[3] and Zn^{2+},[4] with emission intensity, lifetime and polarization as signal outputs, due to advantages including large Stokes' shifts, long lifetimes, line-like emissions and characteristic wide emission wavelengths.[5] Signal transduction utilising emission lifetime is unaffected by the sample's emission intensity, thereby circumventing many limitations of intensity based limitation.[6] Furthermore, long-lived (in ms scale) lanthanide luminescence has been exploited in various bioassays with time-gating, permitting an easy distinction from the short-lived (in μs scale) background fluorescence present in many biological systems.[5] It has been proved that certain anions can influence the lifetime of the lanthanide luminescence,[7] but the effect of cations has not been well studied. Because Na^+ and K^+ are among the most important ions in physiological surroundings and their concentrations are different in the extracellular and intracellular environments,[8] the signalling of Na^+ and K^+ concentrations *in vivo* and *in vitro* has received particular attention.[9] Since crown ethers are widely used in fluorescent probes for detecting alkali metal ions,[10] in this study we introduce them into the Tb^{3+} luminophors with good water solubility and thermodynamic stability to investigate the influence of alkali metal ions on the lifetime of lanthanide luminescence. Meanwhile, some coordinatively unsaturated Tb^{3+} and Eu^{3+} complexes have been synthesized to trigger luminescence intensity upon the molecular recognition of aromatic antennae at the binding sites,[11] the luminescence-sensing behaviour of these Tb complexes toward the aromatic antennae **1** and **2** in aqueous solution is also explored.

The reaction of cyclam with *N*-chloroacetylaza-15-crown-5 and 2-(2-bromoethoxy)methyl-15-crown-5 achieved a satisfactory yield of 86 and 81%, respectively.[12] After the reduction of 1-(*N*-acetylaza-15-crown-5)-1,4,8,11-tetraazacyclotetradecane with BH_3·THF, treating the two mono *N*-alkylated derivatives of cyclam with *tert*-butyl bromoacetate afforded 1-(functionalised-crown ether)-4,8,11-tris(*tert*-butoxycarbonylmethyl)-1,4,8,11-tetraazacyclotetradecanes. Subsequent deprotection (TFA, CH_2Cl_2) gave the ligands L^1 and L^2, which reacted with $Tb_2(CO_3)_3$ in water to give the desired neutral complexes TbL^1 and TbL^2.‡

Measurements of the luminescence lifetime and the number of bound water molecules of the Tb^{3+} complexes were made in H_2O and D_2O (Table 1), which revealed that TbL^1 possesses two bound water molecules and TbL^2 only one. The luminescence lifetime of TbL^2 in water increased by about 65% from 1.78 ms to 2.95 ms at an [Na^+] concentration of 0.13 M, while the hydration state q^{Tb} decreased from one to nearly zero concomitantly. The luminescence lifetime of TbL^2 also increased with [K^+] and [Li^+] but at different magnitudes (Fig. 1). In a simulated extracellular ionic background (30 mM $NaHCO_3$, 100 mM NaCl, 0.9 mM KH_2PO_4, 2.3 mM/0.13 mM potassium lactate/citrate), the data obtained revealed that the lifetime of TbL^2 can reach 2.97 ms. Interestingly, the luminescence lifetimes of TbL^1 and the known system TbTETA which has one coordinated water like TbL^2, both changed only a little (less than 5%) with [Na^+]. The q^{Tb} of TbL^2 equal to 1 in the absence of Na^+ means the 'bridge' oxygen occupied one coordination site of Tb^{3+} and brought the crown ether **II** close to the cyclen. Upon addition of Na^+, the q^{Tb} value changes from 1

Table 1 Selected luminescence lifetimes and derived hydration states of the complexes TbL^1 and TbL^2, in the absence (λ_{em} = 545 nm, λ_{ex} = 246 and 262 nm for TbL^1 and TbL^2, respectively) and presence (λ_{ex} = 246 for TbL^1 and TbL^2) of **1** (295 K, 1×10^{-5} M complex)

Complex	τ_{D_2O}/ms	τ_{H_2O}/ms	q^{Tb}[a] (± 20%)
TbL^1	3.35	1.36	1.9
TbL^2	2.88	1.78	0.8
TbL^1–**1**	3.21	1.71	1.1[b]
TbL^2–**1**	2.75	2.06	0.3[b]
$TbTETA^-$	3.68	2.05	0.8
TbDO3A	3.46	1.35	2.0

[a] Values of q were derived using: $q^{Tb} = 5 \times (1/\tau_{H_2O} - 1/\tau_{D_2O} - 0.06)$ after correcting for the estimated effect of unbound water molecules.[13] [b] After coordination with **1** (10 equiv.), Δq = 0.8 and 0.5 for TbL^1 and TbL^2, respectively.

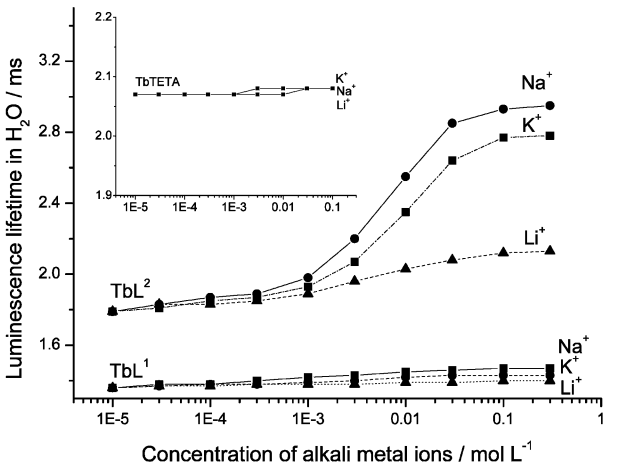

Fig. 1 Plots of the luminescence lifetime of TbL^1, TbL^2 and TbTETA (inset) (λ_{em} = 545 nm) in H_2O as functions of [Na^+], [K^+] and [Li^+] (λ_{ex} = 246, 262 and 228 nm for TbL^1, TbL^2 and TbTETA, respectively) (295 K, 1×10^{-5} M complex, pH = 6.8, I = 2.0 M [Me_4N]Cl, Na^+, K^+ and Li^+ are provided as perchlorate).

† Electronic supplementary information (ESI) available: general experimental procedure, syntheses and characterisation of complexes **1**–**11**. See http://www.rsc.org/suppdata/cc/b2/b206561b/

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to 0, assuming that the interaction arising between the encapsulated Na^+ in the crown ether **II** and the carbonyls in the pendant acetates sterically blocked the only remaining open site so that the inner sphere water was excluded from the first coordination sphere. In the case of TbL^1, which remained a diaqua species in the absence or presence of Na^+, suggests that the crown ether **I** has no significant interaction with the lanthanide centre and the coordination structure of the Tb centre remains unchanged.

The luminescence intensities of TbL^1 and TbL^2 in H_2O both increased strongly upon addition of *p*-chlorobenzoate **1**, whose triplet state energy was assumed to be high enough to sensitise the Eu^{3+} and Tb^{3+} luminescence[14] (Fig. 2). Upon excitation at 246 nm, maximum amplification factors of 47 and 5 were achieved for TbL^1 and TbL^2, respectively. Excitation spectra of TbL^1 and TbL^2 (λ_{em} = 545 nm) in the presence of **1** showed similar spectra features (shape and position of the bands) as the absorption spectra of **1**, which indicates that **1** acts as a sensitiser for Tb^{3+} luminescence. Quantum yields of 0.51% (before adding **1**) and 4.6% (10 equiv. of **1** added) were recorded for TbL^1 (298 K, H_2O) upon excitation at 246 nm. Table 1 shows that after the complexation with **1** (10 equiv.), one water molecule on average was effectively displaced from the inner sphere of Tb^{3+} centre, suggesting the possibility that the carboxylate binds the Tb centre directly.[15] The inset of Fig. 2 shows that when the Na^+ in **1** was replaced by tetrabutylammonium cation, the maximum amplification factor decreased from 49 to less than 7. TbDO3A, which contains two coordination water molecules, similarly to TbL^1, shows much less effective sensitisation of the luminescence toward aromatic antenna **1**. The luminescence intensity of TbDO3A was increased less than a factor of 3 upon addition of 20 equiv. of **1** in the aqueous solution. The luminescence studies above suggest that a ditopic receptor composed of the unsaturated Tb^{3+} centre and crown ether **I** jointly facilitates the detection of benzoate.[16] In such a system, the crown ether is used for effective complexation with Na^+ cation, so that the carboxylate anion can be brought in a close proximity to the Tb^{3+} ion, then the efficient energy transfer from the aromatic antennae to the lanthanide centre is possible. Furthermore, the two labile water coordination positions in the inner coordination sphere, together with the fact that there is no remarkable interaction between the Tb^{3+} centre and crown ether **I**, may also attribute to the intensity amplification.

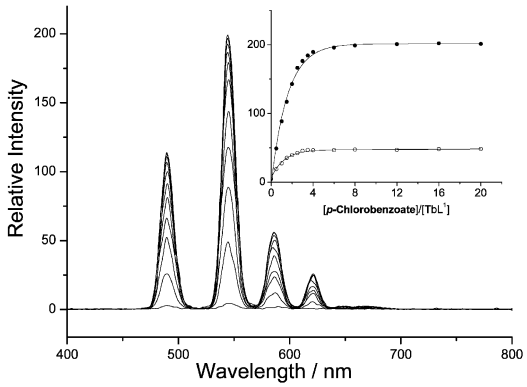

Fig. 2 Emission traces of TbL^1 in H_2O upon addition of *p*-chlorobenzoate **1** (λ_{ex} = 246 nm). The intensities are given relative to the intensity of TbL^1 in the absence of sensitizer at 545 nm. Inset: luminescence intensities, monitored at 545 nm, plotted as a function of [**1**]/[TbL^1] (●) and [**2**]/[TbL^1] (○) ratio, respectively; the lines represent the fit to a 1 : 1 binding model (295 K, pH = 7.4, 0.1 M triethanolamine/HCl).

The lifetime change of the TbL^2 as a function of [Na^+], [K^+] in aqueous solution, suggests that lifetime measurements may be applied in biological systems depending on the physiologically important [Na^+] and [K^+] ranges. The enhancement of the luminescence intensity over the sensitiser provides the opportunity for TbL^1 to act as a luminescence sensor for the detection of aromatic guests, moreover, its Gd complex with two hydration states may have potential applications in MRI (Magnetic Resonance Imaging).

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Notes and references

‡ All new compounds were characterised by ^1H NMR, FAB-MS, ESI-MS and elemental analysis. *Selected analytical and spectroscopic data*: TbL^1: MS (ESI) *m*/*z* 776.6 $[M + H]^+$; calc. for $C_{28}H_{51}N_5O_{10}Tb{\cdot}5H_2O$: C 38.80, H 7.09, N 8.08, found: C 38.48, H 6.77, N 8.01%. TbL^2: MS (ESI) *m*/*z* 807.4 $[M + H]^+$; calc. for $C_{29}H_{51}O_{12}N_4Tb{\cdot}3H_2O$: C 40.47, H 6.67, N 6.51, found: C 40.25, H 6.33, N 6.38%.

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