Reversible anion binding in aqueous solution at a cationic heptacoordinate lanthanide centre: selective bicarbonate sensing by time-delayed luminescence

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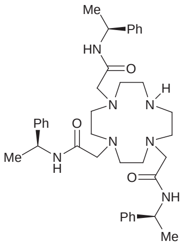
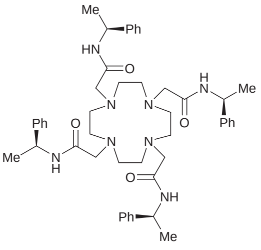
Reversible displacement of up to two metal bound water molecules at a coordinately unsaturated, cationic lanthanide centre is signalled by increases in the luminescence intensity or lifetime of the emissive lanthanide: selective chelation of hydrogencarbonate is consistent with emission spectroscopic, ESMS and CPL measurements.

Intrigued by the prospect of using a charged luminescent lanthanide receptor for the time-gated signalling of anion binding (hinted at by a brief communication[1]), we set out to prepare well-defined coordinately unsaturated Tb and Eu complexes wherein stepwise displacement of quenching metal-bound water molecules by a given anion would be signalled by increases in the lifetime or emission intensity of the lanthanide luminescence. Accordingly the enantiopure complexes $[EuL^1]^{3+}$ and $[TbL^1]^{3+}$ were devised, wherein the remote chiral centre at carbon determines the chirality of the complex in a similar fashion to that established with the Ln complexes of L^2.[2] In aqueous solution, the complexes complete their coordination number by binding two displaceable water molecules.



L^1



L^2

Reaction of 3 equiv. of (*R*)-*N*-(2-chloroethanoyl)-2-phenylethylamine with 1-(4-methoxyphenylsulfonyl)-1,4,7,10-tetraazacyclododecane (Cs_2CO_3, DMF, 70 °C) followed by reductive deprotection (Na, aq. NH_3, EtOH–THF) allowed isolation of the heptadentate, tri-*N*-substituted ligand L^1 (mp 64 °C), following chromatography on neutral alumina (CH_2Cl_2 to 1% MeOH–CH_2Cl_2). Complexation with $Eu(CF_3SO_3)_3$ or $Tb(CF_3SO_3)_3$ in anhydrous MeCN gave tripositive complexes. Analysis of $[EuL^1]^{3+}$ by ^1H NMR spectroscopy in D_2O and CD_3OD revealed only one set of four distinct broadened resonances for the most shifted axial ring proton (293 K, D_2O: +27.0, +16.1, +13.5, +8.8 ppm). A low temperature EXSY spectrum at −20 °C, clearly indicated that there were four stereoisomeric complexes (in a ratio of *ca.* 3.5 : 1 : 0.5 : 0.25) undergoing exchange by arm rotation but not ring inversion at this temperature.

The luminescence lifetimes for each complex were measured in H_2O and D_2O, initially in the absence and presence of a 10-fold excess of a selection of halides and oxyanions (Table 1). Such measurements allow the estimation of the number of coordinated water molecules ($q' = 2$ for each in the absence of added anions). A correction has been made in each case to account for the quenching effect of closely diffusing OH and amide NH oscillators.[3] In the presence of base ($I = 0.14$ NaCl), the lifetime of $[TbL^1]^{3+}\cdot(OH_2)_2$ increased by almost 50% and the q' value fell from 1.9 to 0.4, consistent with deprotonation and concomitant displacement of the second water molecule by Cl^-—leaving one quenching OH oscillator. The labilisation of metal bound water molecules following deprotonation is well-known with di- and poly-aqua metal ion species.[4]

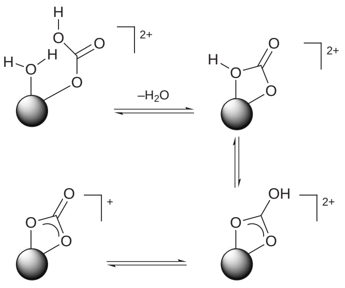
Lifetimes for $[TbL^1]^{3+}$ in the presence of $I^-/Br^-/Cl^-$ and NO_3^- (pH 5.5–6.5) were virtually unchanged, whereas F^-, acetate and sulfate competed with H_2O for binding and led to the displacement of up to one of the quenching water molecules. Most striking was the behaviour of hydrogencarbonate (pH 6.5) and carbonate (pH 11) in which *both* water molecules were displaced leading to a large change in the measured lifetime (Table 1). This pattern of behaviour was echoed in lifetime measurements with $[EuL^1]^{3+}$, suggesting formation of a chelated adduct with HCO_3^-/CO_3^{2-} (Scheme 1).[5]

Further support for the distinctive nature of the anion adduct was provided by examination of the Eu emission spectra wherein the hypersensitive $\Delta J = 2$ transition at 618 nm is particularly sensitive to coordination environment.[2] The intensity ratio of the $\Delta J = 2 : \Delta J = 1$ emission bands was 4 : 1 (10-fold excess of anion in D_2O) for HCO_3^-, and the other values measured were all lower (*e.g.* F^-, 4 : 3; $H_2PO_4^-$, 2 : 1). A titration of the change in the intensity of one component of the 620 nm band as a function of added bicarbonate ($[Eu{\cdot}L^1]^{3+} = 2 \times 10^{-3}$ M, 0–40 mM $NaHCO_3$, 293 K, 0.1 M MES buffer,

Table 1 Effect of added anions (10 mM complex) on the rate constants (±10%) for depopulation of the excited states of $[Eu{\cdot}L^1]^{3+}$ and $[Tb{\cdot}L^1]^{3+}$, and corrected inner-sphere hydration numbers, q'

Complex/anion	k_{H_2O}/ms^{-1}	k_{D_2O}/ms^{-1}	$\Delta k_{corr.}/ms^{-1}$	q'_{is} (±0.15)
$[Tb{\cdot}L^1]^a$ ($CF_3SO_3^-$)	0.84	0.39	0.39	1.91
OH^- (pH 11)	0.59	0.45	0.08	0.39
F^-	0.61	0.36	0.19	0.93
I^-, Br^- or Cl^-	0.87	0.39	0.42	2.06
NO_3^-	0.84	0.42	0.36	1.76
$CH_3CO_2^-$	0.74	0.42	0.26	1.27
SO_4^{2-}	0.66	0.37	0.23	1.13
$H_2PO_4^-$	0.57	0.37	0.14	0.69
Citrate	0.55	0.41	0.08	0.39
HCO_3^-	0.54	0.45	0.03	0.15
CO_3^{2-c}	0.53	0.46	0.01	0.05
$[Eu{\cdot}L^1]^d$ ($CF_3SO_3^-$)	3.85	1.54	1.81	2.14
CO_3^{2-}	2.33	1.64	0.19	0.24
HCO_3^{-b}	2.44	1.67	0.27	0.34
$H_2PO_4^-$	2.63	1.54	0.59	0.74
SO_4^{2-}	2.94	1.67	0.77	0.96
$CH_3CO_2^-$	3.45	1.69	1.26	1.58
F^-	2.70	1.39	0.81	1.01

[a] Corrections for Tb complexes were to allow for the effect of closely diffusing OH oscillators ($-0.06\ ^{-1}$ in Δk) and used $q'_{is} = A'\Delta k_{corr.}$ where $A' = 4.9$. [b] Unchanged in 0.14 M NaCl; reduces to $q' = 0.25$ in 50 mM HCO_3^-. [c] At pH 11. [d] For Eu complexes, the correction for closely diffusing OH oscillators was −0.25 and −0.08 ms^{-1} for each amide NH, with $A' = 1.25$.



Scheme 1

Figs. 1 and 2), revealed an increase in the intensity of the band, with a switching factor of six, consistent with reversible formation of a 1 : 1 adduct. A similar titration with added dihydrogenphosphate showed much less change, with an enhancement factor of two in the range 0–5 mM. It is well known that hydrogenphosphate prefers to bind in a monodentate manner,[6] while carboxylates and carbonates often chelate, particularly to metal centres in higher coordination numbers.[7] Support for the existence of such a species came from ESMS, where in addition to the observation of an $[TbL^1OH]^+$ species at 831, peaks at 875.2 and 876.2 were apparent, together with 437.6/438.2 (m/z), whose relative abundance was in agreement with the isotope pattern calculated for $[TbL^1 + HCO_3]^+$ [calc.: 875.34 (100%) and 876.34 (51%)]. The structure of the excited state of lanthanide complexes is probed sensitively by circularly polarised luminescence (CPL).[8] CPL spectra for $[EuL^1]^{3+}$ in the presence of $CF_3SO_3^-$, $H_2PO_4^-$ and HCO_3^- (at pH 6.5 in an 0.1 M MES buffer) (Fig. 3) were measured. Distinctively different CPL spectra were found in the presence of both HCO_3^- and HPO_4^{2-} consistent with a pronounced change in the helicity of the 'anion-bound' europium excited-state structure.

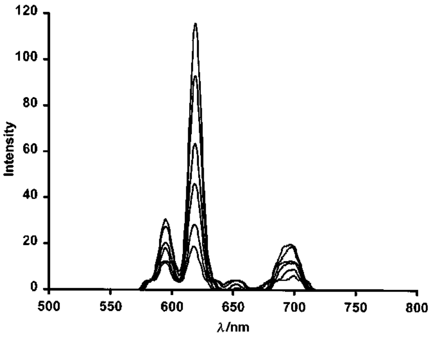


Fig. 1 Variation of luminescence intensity at 620 nm for $[EuL^1](CF_3SO_3)_3$ (pH 6.4 to 7.3 in 0.1 M MES buffer, 293 K, 1 mM) as a function of added $NaHCO_3$ in the range 1–30 mM. Emission intensities and lifetimes were unchanged (±7%) in the presence of 140 mM NaCl and in control experiments varying pH only (Perkin Elmer LS50B fluorimeter).

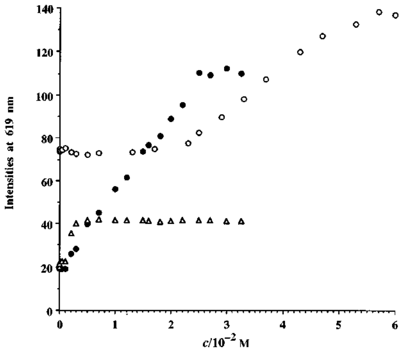


Fig. 2 Increase in the Eu emission intensity as a function of added $NaHCO_3$ (●; 293 K, pH 6.5–7.3 in an 0.1 M MES buffer, $\lambda_{exc.}$ 257 nm), NaH_2PO_4 (△) and $NaHCO_3$ (○) in a simulated clinical background of anions ($H_2PO_4^-$ 0.9 mM, 2.3 mM lactate, 145 mM Cl$^-$, 0.13 mM citrate)

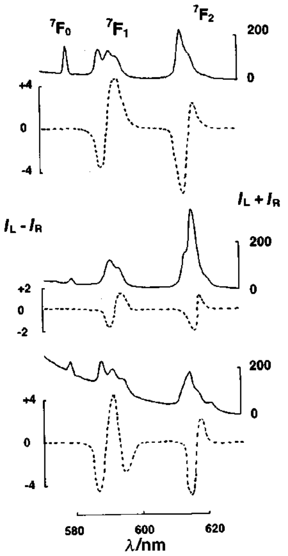


Fig. 3 Circularly polarised luminescence spectra for $[EuL^1](CF_3SO_3)_3$ (pD 6.9, 293 K, 1.0 mmol dm^{-3} in 0.1 M MES) (upper), and in the presence of 10 mM $H_2PO_4^-$ (bottom) and 40 mM HCO_3^- (centre). With $H_2PO_4^-$, the three $\Delta J = 1$ components have alternating signs while with HCO_3^- the highest energy component is absent and the signs are reversed.

In summary, measurements of the luminescence lifetime or intensity of emissive, coordinatively unsaturated enantiopure lanthanide complexes in aqueous media afford a new way of signalling the presence of selected oxyanions. Such systems may also act as simple models for studying anion binding in water that is relevant to the mode of action of alkaline phosphatase and carbonic anhydrase.

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Notes and References

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1 N. Sabbatini, M. Guardigli, J.-M. Lehn and G. Mathis, *J. Alloys Compds.*, 1992, **180**, 363.

2 R. S. Dickins, J. A. K. Howard, C. W. Lehmann, J. M. Moloney, D. Parker and R. D. Peacock, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 521; R. S. Dickins, J. A. K. Howard, J. M. Moloney, D. Parker, R. D. Peacock and G. Siligardi, *Chem. Commun.*, 1997, 1747.

3 D. Parker and J. A. G. Williams, *J. Chem. Soc., Dalton Trans.*, 1996, 3613; M. P. O. Wolbers, F. C. J. M. van Veggel, J. W. Hofstraat, F. A. J. Geurts and D. N. Reinhoudt, *J. Chem. Soc., Perkin. Trans. 2*, 1997, 2275.

4 D. T. Richens, *The Chemistry of Aqua Ions*, Wiley, Chichester, 1997.

5 In Scheme 1, chelation in principle may involve attack by bound bicarbonate at the metal centre or nucleophilic attack by the bound OH group at the trigonal carbonyl centre: such mechanisms may be distinguishable by appropriately controlled isotope incorporation experiments in $^{18}OH_2$.

6 B. Schneider and M. Kabelac, *J. Am. Chem. Soc.*, 1998, **120**, 161.

7 C. J. Carrell, H. L. Carrell, J. Erlebacher and J. P. Glusker, *J. Am. Chem. Soc.*, 1988, **110**, 8651.

8 J. P. Riehl and F. S. Richardson, *Chem. Rev.*, 1986, **86**, 1; E. Huskowska, C. L. Maupin, D. Parker, J. A. G. Williams and J. P. Riehl, *Enantiomer*, 1997, **2**, 381.

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