COMMUNICATION www.rsc.org/chemcomm | ChemComm

Lanthanide luminescent anion sensing: evidence of multiple anion recognition through hydrogen bonding and metal ion coordination†

Cidália M. G. dos Santos, Pablo Barrio Fernández, Sally E. Plush, Joseph P. Leonard and Thorfinnur Gunnlaugsson*

Received (in Austin, TX, USA) 12th April 2007, Accepted 18th May 2007
First published as an Advance Article on the web 15th June 2007
DOI: 10.1039/b705560a

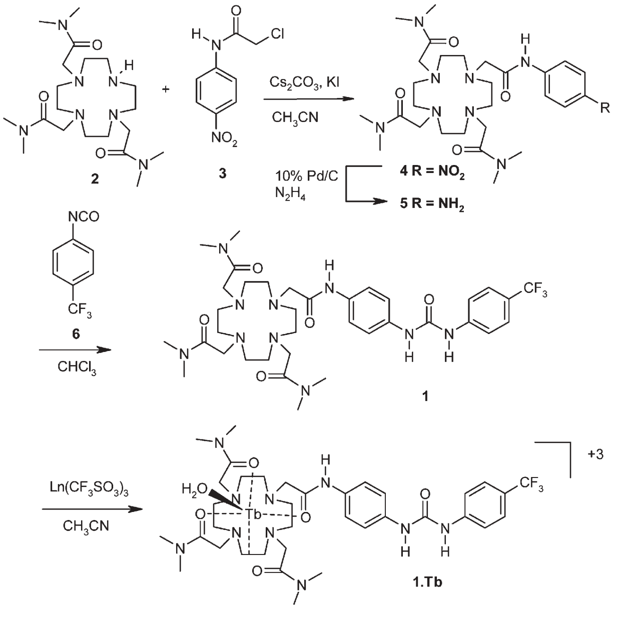
The delayed lanthanide luminescence of the terbium [Tb(III)] diaryl-urea complex 1·Tb is significantly enhanced upon sensing of dihydrogenphosphate ($H_2PO_4^-$) in CH_3CN, which occurs through multiple anion binding through hydrogen bonding interactions and potential metal ion coordination to Tb(III).

The luminescent and colorimetric sensing of anions is both a challenging and highly topical area of research.[1–3] The most common methods for achieving such anion recognition has been *via* the use of: (i) transition metal ion coordination complexes;[4] (ii) ammonium or guanidinium moieties,[5] and (iii) charge neutral hydrogen bonding moieties, such as amides, ureas, thiourea, *etc.*[6] Using heptadentate tri-arm cyclen (1,4,7,10-tetraazacyclododecane) Tb(III) and Eu(III) complexes, we and others have recently demonstrated the sensing of both aliphatic and aromatic carboxylates, *via* the formation of ternary complexes in buffered solution, where the emission was either enhanced or reduced upon coordination of these anions to the f-metal ions.[7,8] Similarly, using chromophores, based on charge neutral receptors, we have developed numerous examples of both fluorescent and colorimetric anion sensors, which can function in both organic and aqueous solutions.[2,9,10] Nevertheless, the combination of these two anion binding interactions in a single molecule, with the aim of achieving maximum luminescent 'output' coupled with high anion affinity, has not been demonstrated to date using members of the f-metal ion family. However, such sensing has recently been shown to work well using d-metal ions.[11] With the objective of demonstrating such dual sensing interactions using f-metal ions, we synthesised the Tb(III) complex **1**·Tb from **1**. Herein, we demonstrate the results from this investigation and prove that this design gives rise to: (a) high anion binding affinity, (b) multiple binding interactions and (c) large Tb-luminescence enhancements.

The Tb(III) $^5D_4$ transition is Laporte-forbidden and direct excitation of Tb(III) is often difficult.[12] Nevertheless, excitation *via* the use of ligand or antennae, gives rise to sensitised emission.[12–14] In **1**, the aryl-urea has a dual role, it can function as both the sensitizing antenna[12] and the hydrogen bonding anion receptor.[2] Therefore, we anticipated that anion binding at the urea moiety would modulate the sensitization process to the lanthanide excited state, and hence, the Tb(III) emission.

The synthesis of **1** (Scheme 1), involved the coupling of the tri-arm acetamide cyclen **2**[15] and chloro-*N*-(nitro-phenyl) acetamide, **3**,[16] in dry CH_3CN in the presence of Cs_2CO_3 and KI at 85 °C for 72 h. This gave **4**, which was purified by column chromatography on alumina. This was followed by the reduction of the nitro group, using N_2H_4 in ethanol at 90 °C, in the presence of 10% Pd/C catalyst, to yield **5**, which was reacted with trifluoro-*p*-tolyl isocyanide, **6**, in dry $CHCl_3$ at room temperature, giving **1** in 80% yield. The ^1H-NMR ($CDCl_3$) spectrum of **1**† showed the presence of three characteristic N–H resonances at 9.61, 9.38 and 9.01 ppm. The complex, **1**·Tb, was finally formed in 51% yield by refluxing **1** with one equivalent of $Tb(CF_3SO_3)_3$ in CH_3CN under argon, followed by precipitation from diethyl ether. The ESMS of **1**·Tb showed the expected isotopic distribution pattern and the ^1H NMR (CD_3OD) spectrum showed the shifted resonance for the equatorial and the axial protons of the cyclen and the α-CH_2 due to the presence of the paramagnetic metal ion. Analysis of the excited state lifetimes of the Tb(III) emission in D_2O and H_2O, respectively, gave the hydration state[12,13] ~1, indicating a single metal bound water molecule.

The absorption spectra of **1**·Tb showed a broad band centred around 280 nm in CH_3CN, assigned to the urea antenna moiety. The changes in the spectra were monitored as a function of added anions such as AcO^-, $H_2PO_4^-$, F^- and Cl^- (as their TBA salt solutions). The addition of ions such as AcO^- and $H_2PO_4^-$ caused the absorption maximum to shift towards the red, with concomitant ~20% reduction in the absorption, showing the



Scheme 1 Synthesis of **1** and the Tb(III) sensors **1**·Tb.

School of Chemistry, Centre for Synthesis and Chemical Biology, Trinity College Dublin, Dublin 2, Ireland. E-mail: gunnlaut@tcd.ie; Fax: +353 1 671 2826; Tel: +353 1 896 3459

† Electronic supplementary information (ESI) available: Synthesis and figures 1–14. See DOI: 10.1039/b705560a

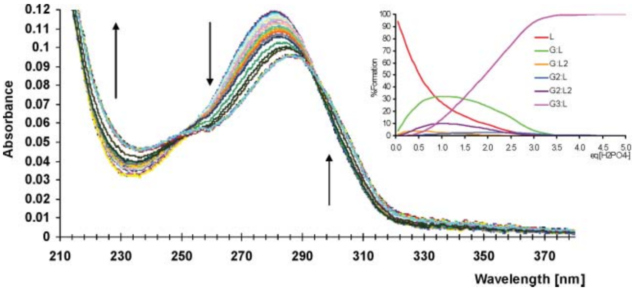


Fig. 1 The changes observed in the absorption spectra of **1**·Tb (4 μM) upon addition of $H_2PO_4^-$ (0–57.3 μM) in MeCN. Arrows indicate the changes upon increasing concentration of $H_2PO_4^-$. Insert: The speciation distribution diagram for the binding of $H_2PO_4^-$.

binding of the anions to the receptor, as demonstrated for $H_2PO_4^-$ in Fig. 1. The titration profile obtained from plotting the absorption changes in Fig. 1, suggested that the anion binding was more complex than a simple 1 : 1 stoichiometry (see ESI†). Fitting these changes, using the nonlinear least squares regression program SPECFIT (see ESI†), gave several binding constants, reflecting that the anions were bound through the proposed 'multiple' binding interactions. These results are summarised in Table 1, for $H_2PO_4^-$, and AcO^-. Here, the stoichiometry (shown as the guest : **1**·Tb ratio $G_n : L_n$) and binding values (log*K*) clearly shows that **1**·Tb initially binds both of these anions with large 1 : 1 binding affinity, where $H_2PO_4^-$ is bound marginally stronger than AcO^-. We assign such a strong anion binding affinity to the neighbouring lanthanide ion, which, being a strong Lewis acid makes the urea protons stronger hydrogen bonding donors.

From these changes, the speciation distribution diagram was also determined (shown as insert for $H_2PO_4^-$ in Fig. 1), which demonstrated that initially the 1 : 1 binding event (shown as a green line) dominates, but is then replaced at higher anion concentrations with higher order stoichiometries such as $G_3 : L_1$. Similarly, for AcO^-, both the $G_1 : L_1$ and $G_2 : L_1$ binding stoichiometries were observed. The binding of Cl^- was also observed in the absorption spectra. However, in comparison to the results in Table 1, it was weak and spectral changes only occurred at high anion concentrations. The titration of F^-gave rise to significant changes in the absorption spectra assigned to multiple F^- binding interactions as well as the deprotonation of the urea moiety by F^-, to give HF_2^-.[17] However, the binding constants for F^- were significantly lower than those observed for $H_2PO_4^-$ and AcO^- in Table 1 (see ESI†).

With the aim of further investigating these multiple binding interactions, both the fluorescence and the Tb(III) emission were monitored upon anion titration. For the former, the emission from the antenna (λ_{ex} = 280 nm) gave rise to a broad band centred at 340 nm (see ESI†), that was both weak and significantly polluted by the contribution from the Tb(III) emission, which occurs at longer wavelength. However, upon titration with either $H_2PO_4^-$ or AcO^- the emission was significantly modulated. Even though, the spectra were of poor quality (see ESI†), we were able to obtain binding constants from these changes. These are in reasonable agreement with those obtained for the changes in the ground state, Table 1, further supporting the determined anion binding stoichiometries. However, in contrast to these results, the most significant findings from these investigations were observed in the lanthanide emission, which showed striking changes for the deactivation of the Tb(III) excited state [$^5D_4 \rightarrow {}^7F_J$ (J = 6–3)] upon titration with $H_2PO_4^-$ and excitation at 280 nm.‡

Table 1 Results from the binding constant evaluation of $H_2PO_4^-$ and AcO^-, upon binding to **1**·Tb in CH_3CN[a]

Anion	Technique	Stoichiometry	Log*K*	Std deviation
$H_2PO_4^-$	UV-Vis	G : L	7.07[b]	0.23
		G : L_2	4.87	0.47[c]
		G_2 : L	5.64	0.95[c]
		G_2 : L_2	6.79	0.37
		G_3 : L	7.94[b]	0.21
$H_2PO_4^-$	Fluorescence	G : L	6.86	0.21
		G : L_2	5.15	0.25[c]
		G_2 : L	5.34	0.94[c]
		G_2 : L_2	6.84	0.53[c]
		G_3 : L	7.95[b]	0.20
$H_2PO_4^-$	Tb(III) emission	G : L	7.04[b]	0.14
		G : L_2	4.59	0.24[c]
		G_2 : L	4.90	0.82[c]
		G_2 : L_2	7.20	0.18[c]
		G_3 : L	8.04[b]	0.12
AcO^-	UV-Vis	G : L	6.27	0.116
		G_2 : L	5.84	0.087
AcO^-	Fluorescence	G : L	5.78	0.302
		G_2 : L	5.11	0.511
AcO^-	Tb(III) emission	G : L	6.87	0.475
		G_2 : L	5.12	0.497

[a] Obtained by fitting the spectroscopic data using SPECFIT. [b] Binding constant is large and consequently SPECFIT has difficulties giving accurate determination for log*β*. [c] Species present in less than 10%.

The overall Tb(III) luminescence changes for titrations of $H_2PO_4^-$ are shown in Fig. 2. These results were fully reproducible and clearly demonstrate that the Tb-emission is significantly more sensitive to the anion recognition than seen in either the ground or the singlet excited states. Furthermore, the Tb(III) emission, and hence, the Tb(III) excited state lifetimes (ESI†), are modulated in a two 'step' process, where the initial addition of $H_2PO_4^-$ leads to *ca.* 70% quenching in the Tb(III) emission (*insert* Fig. 2). This is subsequently followed by over *ca.* 90% luminescent enhancement between *ca.* 1 → 3 eq. of $H_2PO_4^-$. This is, to the best of our knowledge, the first time that a lanthanide luminescence is modulated in this manner by an anion.

Moreover, by further analysing the changes in the 546 nm transition *vs.* the number of eq. of $H_2PO_4^-$, it was found that the

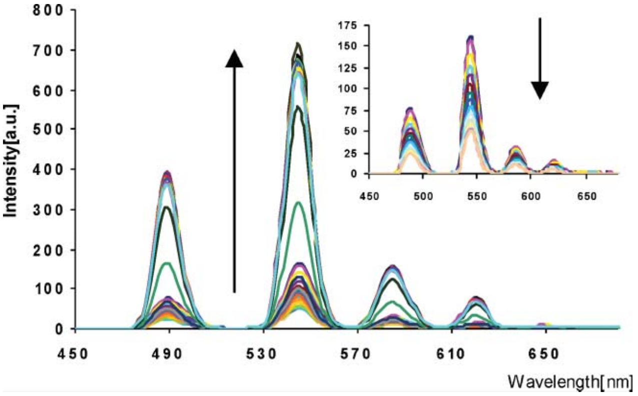


Fig. 2 The Tb(III) emission spectra showing the changes in the intensity of **1**· (4 μM) upon titration with $H_2PO_4^-$ (0 → 57.3 μM) in MeCN. *Inset*: The changes observed upon addition of 0 → 1 eq. of $H_2PO_4^-$, which caused quenching in the Tb(III) emission.

Tb(III) emission enhancements also occurred in a two step process; where the major contribution to these changes took place within the 2 → 3 eq. range of $H_2PO_4^-$. The changes in the 546 nm transition were fitted using the SPECFIT programme. This gave an excellent fit as shown in the ESI,† from which several binding constants were determined. Again, the results from the fitting of the binding isotherm clearly indicated that **1**·Tb senses these anions through multi-step binding interactions and that the binding constants correlate well with that observed from the changes in both the absorption and the fluorescence spectra, Table 1. The speciation distribution diagram obtained from the changes in the Tb(III) emission upon titration with $H_2PO_4^-$ is shown in the ESI† and clearly demonstrates that initially the 1 : 1 stoichiometry is formed with a high binding constant of log$K$ = 7.0. However, after the addition of *ca.* one eq. of anion the $G_3 : L_1$ binding begins to dominate. Interestingly, the 2 : 1 complex only formed in small quantities. In contrast to these results, the titration of **1**·Tb with AcO^- only gave rise to luminescent quenching. Furthermore, only two stoichiometries were determined; namely the G_1:L_1 and G_2:L_1, Table 1 (see ESI†). These results also showed that **1**·Tb selectively sensed $H_2PO_4^-$ over AcO^-. This we confirmed by titrating $H_2PO_4^-$ to a quenched solution of **1**·Tb bound AcO^-. On both occasions, the Tb-emission was '*switched on*' in the same manner as seen above for the titration of $H_2PO_4^-$ in Fig. 2 (See ESI†).

So what binding interactions constitute to this complex multiple anion recognition? We propose that the initial anion recognition is due to binding of the anion at the urea moiety of the antenna. This is then followed by a second binding event between these anions and the amide bridge, through anion···H–N hydrogen bonding interactions. We have confirmed this by carrying out UV-vis titrations of an acetamide analogue of the receptor/antenna part of **1**·Tb, which also gave rise to both G_1:L_1 and G_2:L_1 binding for these anions (*cf.* 7 in ESI†). However, the binding constants are lower than observed for **1**·Tb. In the case of binding of $H_2PO_4^-$ to **1**·Tb, the third binding interaction, G_3:L_1 is more difficult to determine without the aid of X-ray crystallography. However, this binding, clearly giving rise to the largest changes in the Tb(III) emission, is most likely taking place through a more direct interaction with the metal ion (and possibly *via* contribution from one of the aryl protons.[18] Contribution from simple electrostatic interactions between the complex and the anion cannot be ruled out either). This may be occurring through the displacement of the aforementioned axial metal bound water molecule. Water is an effective quencher of the $^5D_4$ excited state and displacement of the water generally gives rise to luminescence enhancements.[7,8]§ These changes are also observed in the ground state, which suggests that the Tb(III) ion also affects the electronic properties of the antenna.

In summary, we have developed a novel lanthanide luminescent sensor for anions by incorporating a hydrogen bonding receptor into a sensitizing antenna. Analysis of the ground state, and the emission from the singlet and the Tb(III) excited states, clearly demonstrated the formation of multiple species and hence multiple binding interactions in solution. It also showed that the Tb(III) is extremely sensitive to the changes in the local coordination environment. Furthermore, the selective detection of $H_2PO_4^-$ over AcO^- by **1**·Tb was also observed, with the $H_2PO_4^-$ forming both 1 : 1 and 3 : 1 complexes with **1**·Tb, in CH_3CN. These results represent, to the best of our knowledge, the first examples of the use of a combination of hydrogen bonding anion receptors and f-metal ion coordination for luminescent anion sensing.

We thank Enterprise Ireland, IRCSET and TCD for financial support and Dr John E. O'Brian for running NMR.

Notes and references

‡ The Eu(III) complex of **1**, **1**·Eu, was also formed. However, the emission was very weak in comparison to that of **1**·Tb, as the Eu(III) excited state is quenched by photoinduced electron transfer (*cf.* ESI†).

§ As these measurements are carried out in less competitive CH_3CN solvent the emission enhancement might even be more striking.

1 J. L. Sessler, P. A. Gale and W. S. Cho, *Anion Receptor Chemistry*, Royal Society of Chemistry,Cambridge, UK, 2006.

2 T. Gunnlaugsson, M. Glynn, G. M. Tocci (née Hussey), P. E. Kruger and F. M. Pfeffer, *Coord. Chem. Rev.*, 2006, **250**, 3094.

3 S. E. Garcia-Garrido, C. Caltagirone, M. E. Light and P. A. Gale, *Chem. Commun.*, 2007, 1450; J. W. Steed, *Chem. Commun.*, 2006, 2637; P. A. Gale and R. Quesada, *Coord. Chem. Rev.*, 2006, **250**, 3219; P. A. Gale, *Chem. Commun.*, 2005, 3761; R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419.

4 E. J. O'Neil and B. D. Smith, *Coord. Chem. Rev.*, 2006, **250**, 3068; M. H. Filby and J. W. Steed, *Coord. Chem. Rev.*, 2006, **250**, 3200; S. Goetz and P. E. Kruger, *Dalton Trans.*, 2006, 1277.

5 E. García-España, P. Díaz, J. M. Llinares and Antonio Bianchi, *Coord. Chem. Rev.*, 2006, **250**, 3004; E. A. Katayev, Y. A. Ustynyuk and J. L. Sessler, *Coord. Chem. Rev.*, 2006, **250**, 2952.

6 C. Lin, V. Simov and D. G. Drueckhammer, *J. Org. Chem.*, 2007, **72**, 1742; C. M. G. dos Santos, T. McCabe and T. Gunnlaugsson, *Tetrahedron Lett.*, 2007, **48**, 3135; F. M. Pfeffer, M. Seter, N. Lewcenko and N. W. Barnett, *Tetrahedron Lett.*, 2006, **47**, 5251; D. R. Turner, M. J. Paterson and J. W. Steed, *J. Org. Chem.*, 2006, 1598; E. Quinlan, S. E. Matthews and T. Gunnlaugsson, *Tetrahedron Lett.*, 2006, **47**, 9333; K. Bowman-James, *Acc. Chem. Res.*, 2005, **38**, 671; S. J. Brooks, P. A. Gale and M. E. Light, *Chem. Commun.*, 2005, 4696.

7 S. Pandya, J. Yu and D. Parker, *Dalton Trans.*, 2006, 2757; S. J. A. Pope, B. P. Burton-Pye, R. Berridge, T. Khan, P. J. Skabara and S. Faulkner, *Dalton Trans.*, 2006, 2907; J. H. Yu and D. Parker, *Eur. J. Org. Chem.*, 2005, 4249; T. Gunnlaugsson, A. Harte, J. P. Leonard and M. Nieuwenhuyzen, *Chem. Commun.*, 2002, 2134.

8 S. E. Plush and T. Gunnlaugsson, *Org. Lett.*, 2007, **9**, 1919; J. P. Leonard, C. M. G. dos Santos, S. E. Plush, T. McCabe and T. Gunnlaugsson, *Chem. Commun.*, 2007, 129; A. J. Harte, P. Jensen, S. E. Plush, P. E. Kruger and T. Gunnlaugsson, *Inorg. Chem.*, 2006, **45**, 9465.

9 T. Gunnlaugsson, H. D. P. Ali, M. Glynn, P. E. Kruger, G. M. Hussey, F. M. Pfeffer, C. M. G. dos Santos and J. Tierney, *J. Fluoresc.*, 2005, **15**, 287.

10 T. Gunnlaugsson, P. E. Kruger, P. Jensen, J. Tierney, H. D. P. Ali and G. M. Hussey, *J. Org. Chem.*, 2005, **70**, 10875; T. Gunnlaugsson, A. P. Davis, G. J. E. O'Brein and M. Glynn, *Org. Biomol. Chem.*, 2005, **3**, 48; T. Gunnlaugsson, A. P. Davis, G. M. Hussey, J. Tierney and M. Glynn, *Org. Biomol. Chem.*, 2004, **2**, 1856; T. Gunnlaugsson, A. P. Davis, J. E. O'Brien and M. Glynn, *Organic Lett.*, 2002, **4**, 2449.

11 P. Plitt, D. E. Gross, V. M. Lynch and J. L. Sessler, *Chem.–Eur. J.*, 2007, **13**, 1374; T. Mizuno, W. H. Wei, L. R. Eller and J. L. Sessler, *J. Am. Chem. Soc.*, 2002, **124**, 1134.

12 T. Gunnlaugsson and J. P. Leonard, *Chem. Commun.*, 2005, 3114; J. P. Leonard and T. Gunnlaugsson, *J. Fluoresc.*, 2005, **15**, 585.

13 D. Parker, R. S. Dickins, H. Puschmann, C. Cossland and J. A. K. Howard, *Chem. Rev.*, 2002, **102**, 1977; D. Parker and J. A. G. Williams, *J. Chem. Soc., Dalton Trans.*, 1996, 316.

14 T. Gunnlaugsson and J. P. Leonard, *Dalton Trans.*, 2005, 3204; T. Gunnlaugsson, A. J. Harte, J. P. Leonard and K. Senechal, *Chem. Commun.*, 2004, 782; T. Gunnlaugsson and J. P. Leonard, *Chem. Commun.*, 2003, 2424; T. Gunnlaugsson, A. J. Harte, J. P. Leonard and K. Senechal, *J. Am. Chem. Soc.*, 2003, **125**, 12062.

15 T. Gunnlaugsson, J. P. Leonard, S. Mulready and M. Nieuwenhuyzen, *Tetrahedron*, 2004, **60**, 105.

16 A. J. Harte and T. Gunnlaugsson, *Tetrahedron Lett.*, 2006, **47**, 6575.

17 T. Gunnlaugsson, P. E. Kruger, T. Clive Lee, R. Parkesh, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett.*, 2003, **44**, 6575.

18 V. S. Bryantsev and B. P. Hay, *J. Am. Chem. Soc.*, 2005, **127**, 8282.