pH driven self-assembly of a ternary lanthanide luminescence complex: the sensing of anions using a β-diketonate-Eu(III) displacement assay†

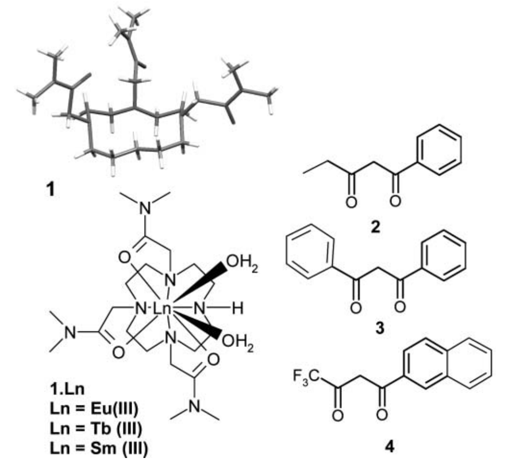
Joseph P. Leonard,* Cidalia M. G. dos Santos, Sally E. Plush, Thomas McCabe and Thorfinnur Gunnlaugsson*

Received (in Cambridge, UK) 9th August 2006, Accepted 27th September 2006
First published as an Advance Article on the web 23rd October 2006
DOI: 10.1039/b611487c

The synthesis and the photophysical evaluation of a novel pH dependent lanthanide luminescent self-assembly in water between a cyclen based europium complex and a β-diketonate is described and its use as a luminescent sensor in displacement assays for anions such as acetate, bicarbonate and lactate, where the Eu(III) emission was quenched upon anion recognition.

The design and synthesis of self-assembly architectures from structurally defined building blocks is at the centre of supramolecular chemistry.[1] Often such structures can be self-assembled, de-assembled, structurally altered or their function modulated by external controls, or inputs, such as light, electrochemistry or by using chemical inputs.[2,3] We are interested in the formation of such functional self-assemblies from lanthanide ions and we have developed both mixed f–d metal ion self-assemblies as well as luminescent lanthanide ternary complexes using coordinating anions and Tb(III) based cyclen complexes.[4–7] In this communication we demonstrate the formation of a new functional luminescent self-assembly ternary complex[8] between the heptadentate europium complex **1**·Eu and the aromatic based β-diketonate **4**. Moreover, we demonstrate that the self-assembly formation is highly pH dependent and that we can employ this assembly at physiological pH as a luminescent sensor for anions.

The β-diketonates are well known to form stable complexes with lanthanide ions usually in 3 : 1 stoichiometry.[9] Moreover, such complexes made from aromatic based β-diketonates can be highly luminescent as demonstrated by Tsukube *et al.*, where the β-diketonates acts as a sensitising antenna for the lanthanide ion.[7,9] However, often such lanthanide complexes have coordinating solvent molecules, such as water, which can quench the lanthanide excited state through O–H vibrational deactivation.[10] Our objective was to take advantage of this quenching process and use coordinatively unsaturated lanthanide complexes, *e.g.* **1**·Ln, which have two metal bound water molecules, and complex these with aromatic β-diketonates such as **2–4**, Scheme 1. This would lead to the formation of ternary self-assembly complexes, provided that the β-diketonates could displace the aforementioned metal bound water molecules, and as such, remove this quenching pathway. We also foresaw that the formation of these self-assemblies could be pH dependent, as both **1**·Ln and the structure of the antennae could be pH dependent.[10] Herein, we present our results, which are, to the best of our knowledge, the first examples of such pH driven self-assembly and the use of this ternary complex as a luminescent sensor for anions, where the Eu(III) emission was quenched or '*switched off*' upon displacing the β-diketonate antenna by the anions.[11]



Scheme 1 The X-ray crystal structure of the protonated (as the HCl salt) form of **1** (Cl$^-$ has been removed for clarity); **1**·Ln and the β-diketonates.

The synthesis of **1** has previously been described by us, which involved the use of cyclen and the *N*,*N*-dimethyl-α-chloroamide in a single step.[12] The ^{1}H NMR (400 MHz, CDCl$_3$) of **1** showed the expected C_2 symmetry. We were also able to grow crystals of **1**, suitable for X-ray crystal structure analysis, Scheme 1, by slow evaporation from a methanol–CH$_2$Cl$_2$ solution, which confirmed the structure of **1**·HCl.[13] The corresponding Eu(III), Sm(III) and Tb(III) complexes of **1**·Eu, **1**·Sm and **1**·Tb, were all formed from the corresponding lanthanide triflate salts. The X-ray crystal structures of **1**·Eu and **1**·Tb showed that the lanthanide ions were coordinating to the four nitrogens of the ring and the oxygen of the three acetamide arms.[6] In both cases, the remaining two coordination sides were occupied by metal bound water molecules.[6] By measuring the excited state lifetimes of **1**·Eu and **1**·Tb in H$_2$O and D$_2$O, the hydration state (q), the number of metal bound water molecules, was also confirmed to be two in solution.[6,14] We next evaluated the ability of the three antennae, **2–4** to sensitize the lanthanide excited states of **1**·Ln by populating the lanthanide excited states (which under normal conditions is difficult to do directly due to symmetry forbidden f–f transitions)[7] in pH 7.4 buffered solutions and in the presence of 0.1 M TMACl. As the complexes do not have incorporated antenna themselves,[10] we used the λ_{max} for the three β-diketonates as the excitation

---

School of Chemistry, Centre for Synthesis and Chemical Biology, Trinity College Dublin, Dublin 2, Ireland. E-mail: gunnlaut@tcd.ie; Fax: +353 1671 2826; Tel: +353 1 608 3459

† Electronic supplementary information (ESI) available: Potentiometric titrations and general experimental. See DOI: 10.1039/b611487c

wavelengths. Excitation of **1**·Eu, **1**·Sm and **1**·Tb at these wavelengths, in the absence of the antennae did not result in any lanthanide luminescence, as expected. We next carried out spectrophotometric titrations, observing the lanthanide emissions for **1**·Eu, **1**·Sm and **1**·Tb, upon increasing concentrations of **2–4**. For these titrations, *only* the characteristic Eu(III) emission, occurring at 595, 616, 685 and 700 nm for the deactivation of the $^5D_0$ excited state to ^7F_J (J = 1, 2, 3 and 4) was observed.[7] Moreover, the Eu(III) emission was *only* visible upon forming a complex between **1**·Eu and **4** ($\lambda_{\max}$ = 336 nm); **1.Eu-4**. Here the Eu(III) emission was found to be fully '*switched on*' after the addition of *ca.* one equivalent of **4**, Fig. 1, indicating the formation of a 1 : 1 complex in solution.‡ These luminescence changes clearly signified that **4** is able to populate the $^5D_0$ excited state efficiently, which could only occur if the antenna was directly coordinating to the Eu(III) centre, since the efficiency of the energy transfer is distance dependent.[7,9] For these changes a quantum yield of luminescence, Φ_{Eu}, of 0.028 was determined by a method recently developed by Bünzli *et al.*[15] As neither **2** nor **3** were found to modulate the emissions of **1**·Eu, **1**·Sm or **1**·Tb, this strongly suggests that the structural as well as the physical nature (*e.g.* excited state energy, pK_a, *etc*,) of the β-diketonates is crucial to their ability to coordinate to these ions. The formation of the assembly should only be possible by the displacement of the two metal bound water molecules.[6] Indeed $q \sim 0$ (τ_{H_2O} = 0.38 ms and τ_{D_2O} = 0.42 ms upon excitation of **4** at 336 nm) was observed for **1**·Eu, in the presence of two *eq.* of **4**. The structure of the self-assembly **1**·Eu–**4** can also be predicted by analysing the changes for the individual transitions in Fig. 1. Here, the hypersensitive ΔJ = 2, centred at 616 nm, gave rise to the largest changes in the Eu(III) emission. As ΔJ = 2 is sensitive to the change to the local coordination environment we can conclude that **4** is coordinating directly to the ion centre.

We next evaluated formation of the complex as a function of pH, by mixing together in a 1 : 1 stoichiometry **1**·Eu and **4**, and observing the changes in the Eu(III) emission as a function of pH. Here the emission was found to be highly pH sensitive by titrating an acid solution with base, Fig. 2, where maximum intensity was observed around pH 6.5. As before, the largest emission changes were observed for ΔJ = 2 transition. Moreover, the Eu(III) emission changes were also visible under a UV lamp as can be seen in Fig. 3. Here the red Eu(III) emission was only observed upon formation of the self-assembly (recorded at pH 7.5), while in either acid (pH < 4) or alkaline solutions (pH > 9.3), the assembly dissociated and the blue fluorescence emission of **4** was observed.

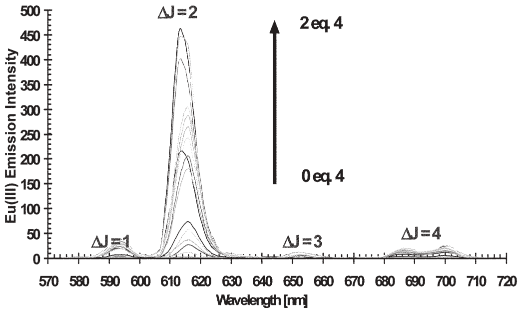


Fig. 1 The changes in the Eu(III) emission of **1**·Eu upon titration with **4** at pH = 7.4 (0.1 M HEPES) and in the presence of 0.1 M TMACl.

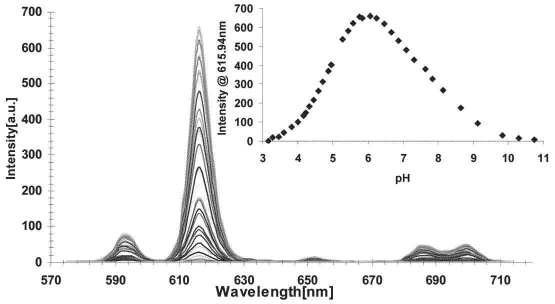


Fig. 2 The changes in the Eu(III) emission of **1**·Eu upon titration with **4** as a function of pH, being switched 'on–off' upon basification. *Insert*: the changes in the 616 nm transition as a function of pH.

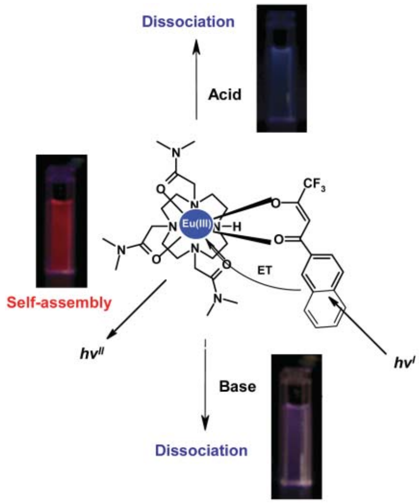


Fig. 3 Schematic representation of the luminescent Eu(III) ternary self-assembly **1**·Eu–**4** at pH 7.5 (red Eu(III) emission) and the dissociation of the assembly in acid at pH 2 and alkaline solution at pH = 12 (blue emission from the β-diketonate).

We also attempted to determine the hydration state of **1**·Eu, in the presence of **4**, at both pH 2 and pH 11. While this gave q = 2.1 in acid (τ_{H_2O} = 0.27 ms and τ_{D_2O} = 0.59 ms upon excitation at 395 nm), we were unable to determine q accurately in alkaline solution, possibly because of the deprotonation of the metal bound water molecules at this pH. Nevertheless, these results demonstrate that the formation of the self-assembly is pH driven.

We also observed the changes in the absorption and the fluorescence emission spectra of **4** as a function of pH. On both occasions significant changes were observed where the ground and the excited states were modulated between pH 4–8.† With the aim of gaining further insight into the nature of the Eu(III) complex pH dependence, we carried out potentiometric pH titrations on **1** and **1**·Eu† using a glass electrode. From these titrations we can conclude that the complex is highly stable with respect to metal dissociation with stability constant log$K$ of 17.17 (±0.02). For **1**, we were only able to determine two pK_a's with the non-linear least squares regression programme HYPERQUAD, these being pK_{a1} = 8.06 (±0.07), pK_{a2} = 2.33 (±0.08).† For **1**·Eu, there are three possible sites for protonation; two assigned to the metal bound water molecules [**1**·EuOH$_2$ and **1**·Eu(OH$_2$)$_2$] and the third one to the pK_a of the secondary amine of the cyclen ring. The latter of these we were unable to determine, as it is expected to be highly

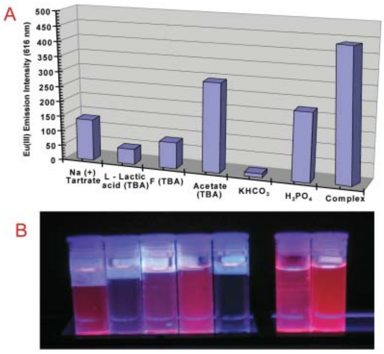


Fig. 4 (A) The changes in the recorded Eu(III) emission at 616 nm at pH 7.4. The tertiary complex is shown for comparison. **B**) The changes observed under a UV-Vis lamp clearly showing naked eye intensity changes for the same anions in **A**. TBA = tetrabuytlammonium salts.

acidic due to the presence of the Eu(III) ion. However, we were able to determine two pK_a values of 7.06 (±0.08) and 6.53 (±0.02), assigned to the deprotonation of the two metal bound water molecules. From the speciation diagram (see ESI†) it can be seen that when the Eu(III) emission is *ca.* 90% enhanced (Fig. 2), the pH is *ca.* 6 and that the most dominant species in solution is in fact the **1**·$Eu(OH_2)_2$. Hence, the binding of **4** to **1**·$Eu(OH_2)_2$ within the pH window of 4–7 is associated with the deprotonation of the α-proton in **4** (*c.f.* ESI for the spectro-photometric pH titration of 4), and not the metal bound waters. In more alkaline solution the formation of **1**·EuOH and **1**·$Eu(OH)_2$ prevents the binding of the antenna due to electrostatic repulsion.

The self-assembly ternary complex **1**·Eu–**4** can also be considered as a potential luminescent sensor, as it should be possible to replace the coordinating antenna with other suitable coordinating ligands such as anions.[6,8,16] This could possibly give rise to the formation of lanthanide based 'displacement assays', complimentary to those developed by Anslyn *et al.*,[11] where, the Eu(III) emission would be expected to be reduced upon displacement of **4**, as energy transfer from the antenna would be prevented. To evaluate this hypothesis, we carried out quantitative analysis by adding various anions ($\sim$1 mM) to a solution of the above ternary complex at pH 7.4 (emission *ca.* 50% '*switched on*') in the presence of 0.1 M TMACl. Upon addition of anions such as Br^-, ClO_4^-, PF_6^- and NO_2^- to **1**·Eu–**4** no significant Eu(III) emission changes were observed, while for I^- and $H_2PO_4^-$ the Eu(III) emission at 616 nm was reduced in intensity by 20–40%.† This indicates that some displacement of the antenna had occurred. In contrast to these results, the use of sodium tartarate, lactic acid, F^-, $CH_3CO_2^-$, $KHCO_3$ gave more pronounced luminescent changes as can be seen in Fig. 4A for the 616 nm transition. Moreover, these changes were also clearly distinguishable by the naked-eye under a UV lamp, Fig. 4B. We also carried out more detailed anion titrations on **1**·Eu–**4** using sodium tartarate, lactic acid and $NaHCO_3$ at pH 7.5, which showed that the Eu(III) emission was gradually reduced.† These results clearly demonstrate that such self-assembly ternary lanthanide complexes can be employed in the sensing of anions in a displacement type assay. To the best of our knowledge, such anion sensing has not been demonstrated before using lanthanide based luminescent ternary complexes.

In summary, we have demonstrated the successful formation of a luminescent Eu(III) ternary complex **1**·Eu–**4** in water, where the self-assembly is highly pH dependent, and that the resulting complex can be employed as a luminescent sensor for anions (at pH 7.4), where the β-diketonate antenna **4** is displaced with concomitant changes in the Eu(III) emission.

We thank Enterprise Ireland, IRCSET and TCD for financial support.

Notes and references

‡ Upon addition of excess of **4** to **1**·Eu, the Eu(III) emission was significantly reduced. However, no such dissociation occurred when these titrations were carried out in MeOH.

1 J. D. Badjic, V. Balzani, A. Credi, S. Silvi and J. F. Stoddart, *Science*, 2004, **303**, 1845; K. S. Chichak, K. S. S. J. Cantirill, A. R. Pease, S. H. Chiu, G. W. V. Cave, J. L. Atwood and J. F. Stoddart, *Science*, 2004, **304**, 1308; P. Thordarson, E. J. A. Bijsterveld, A. E. Rowan and R. J. M. Nolte, *Nature*, 2003, **424**, 915.

2 E. R. Schofield, J. P. Collin, N. Gruber and J. P. Sauvage, *Chem. Commun.*, 2003, 188; S. Bonnet, J. P. Collin, J. P. Sauvage and E. R. Schofield, *Inorg. Chem.*, 2004, **43**, 8346.

3 J. V. Hernandez, E. R. Kay and D. A. Leigh, *Science*, 2004, **306**, 1532; V. Bermudez, N. Capron, T. Gase, f. G. Gatti, F. Kajzar, D. A. Leigh, F. Zerbetto and S. W. Zhang, *Nature*, 2000, **406**, 608.

4 K. Sénéshal-David, J. P. Leonard, S. E. Plush and T. Gunnlaugsson, *Org. Lett.*, 2006, **8**, 2727.

5 T. Gunnlaugsson, J. P. Leonard, K. Sénéchal and A. J. Harte, *Chem. Commun.*, 2004, 782; T. Gunnlaugsson, J. P. Leonard, K. Sénéchal and A. J. Harte, *J. Am. Chem. Soc.*, 2003, **125**, 12062.

6 T. Gunnlaugsson, A. Harte, J. P. Leonard and M. Nieuwenhuyzen, *Supramol. Chem.*, 2003, **15**, 505; T. Gunnlaugsson, A. Harte, J. P. Leonard and M. Nieuwenhuyzen, *Chem. Commun.*, 2002, 2134.

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

8 S. J. A. Pope, B. P. Burton-Pye, R. Berridge, T. Khan, P. J. Skabara and S. Faulkner, *Dalton Trans.*, 2006, 2907; R. S. Dickins, T. Gunnlaugsson, D. Parker and R. D. Peacock, *Chem. Commun.*, 1998, 1643; C. Li and W.-T. Wong, *Chem. Commun.*, 2002, 2034.

9 R. K. Mahajan, I. Kaur, R. Kaur, S. Uchida, A. Onimaru, S. Shinoda and H. Tsukube, *Chem. Commun.*, 2003, 2238; H. Tsukube and S. Shinoda, *Chem. Rev.*, 2002, **102**, 2389; H. Tsukube, S. Shinoda and H. Tamiaki, *Coord. Chem. Rev.*, 2002, **226**, 227; P. G. Sammes and G. Yahioglu, *Nat. Prod. Rep.*, 1996, 1.

10 S. Faulkner and B. P. Burton-Pye, *Chem. Commun.*, 2005, 259; M. P. Lowe and D. Parker, *Chem. Commun.*, 2000, 707.

11 A. T. Wright and E. V. Anslyn, *Chem. Soc. Rev.*, 2006, **35**, 14; S. L. Wiskur, H. Ait-Haddou, J. J. Lavigne and E. V. Anslyn, *Acc. Chem. Res.*, 2001, **34**, 963.

12 T. Gunnlaugsson, J. P. Leonard, S. Mulready and M. Nieuwenhuyzen, *Tetrahedron*, 2003, **59**, 3231.

13 SAINT-NT and SHELXTL, Brüker AXS Madison, Wisconsin, 1998, G. M. Sheldrick, University of Göttingen, Göttingen, Germany, 1998;*Crystal data*: $C_{20}H_{42}N_7O_3$,Cl, M = 464.06, monoclinic, a = 15.1926(14), b = 11.0971(10), c = 15.5763(14) Å, β = 111.215(2)°, U = 2448.1(4) $Å^3$, T = 123 K, space group $P2_1/n$, Z = 4, μ(Mo-Kα) = 0.191 mm^{-1}, 25078 reflections collected, 6074 unique, (R_{int} = 0.0256), R = 0.0549, w$R2$ [$I > 2\sigma(I)$] = 0.1247. CCDC 616591. Crystallographic data in CIF or other electronic format can be found at 10.1039/b611487c.

14 A. Beeby, I. M. Clarkson, R. S. Dickins, S. Faulkner, D. Parker, L. Royle, A. S. de Sousa, J. A. G. Williams and M. Woods, *J. Chem. Soc., Perkin Trans. 2.*, 1999, 493.

15 A. S. Chauvin, F. Gumy, D. Imbert and J. C. G. Bünzli, *Spectrosc. Lett.*, 2004, **37**, 517.

16 P. A. Gale, *Acc. Chem. Res.*, 2006, **39**, 465; P. A. Gale, *Chem. Commun.*, 2005, 3761; 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, 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.