

# Luminescent europium tetraazamacrocyclic complexes with wide range pH sensitivity

Thorfinnur Gunnlaugsson and David Parker\*

Department of Chemistry, University of Durham, South Road, Durham, UK DH1 3LE

The complexes  $[\text{EuL}^1]^{3+}$  and  $[\text{EuL}^2]$  function as luminescent pH sensors over an extended pH range; two distinguishable pH switching ranges are observed: the delayed europium emission is switched on in acidic solution, whereas the fluorescence emission spectra show a pronounced pH dependence only in alkaline media.

Luminescent chemosensors offer an attractive method for the detection of various physiological ions and molecules.<sup>1</sup> Fluorescent sensors may be adversely affected by autofluorescence and by light scattering from an active physiological environment.<sup>2</sup> Delayed luminescence affords an attractive means of overcoming some of these obstacles.<sup>3</sup> In solution, the application of lanthanide luminescence, has generated a great deal of interest owing to the long wavelength of the emission (large Stokes' shifts) and the long lifetimes (in the ms range).<sup>4</sup> An example of such a  $\text{Tb}^{\text{III}}$  and  $\text{Eu}^{\text{III}}$  sensory PET (photoinduced electron transfer) system has been reported recently for pH measurement in aqueous solution.<sup>5</sup> Various lanthanide complexes of tetra-substituted derivatives of 1,4,7,10-tetraazacyclododecane (cyclen) have been synthesised either as contrast agents in magnetic resonance imaging<sup>6</sup> or as luminescence probes.<sup>7</sup> In water, these complexes are kinetically stable with respect to dissociation and possess low hydration numbers ( $q \leq 1$ ). In further developing this work, we have recently demonstrated the effect of protons, oxygen and halide anions on the luminescence emission spectra of some  $\text{Eu}^{\text{III}}$  phenanthridinium conjugates.<sup>8</sup> Here we introduce the cationic  $\text{Eu}^{\text{III}}$ -tetraamide  $[\text{EuL}^1]^{3+}$  and the neutral monoamide  $[\text{EuL}^2]$  quinoyl derived conjugates. In addition to acting as an efficient antenna sensitiser<sup>4,6,7</sup> the chromophore can reversibly switch, *via* an energy transfer mechanism,<sup>4</sup> the lanthanide emission on and off as a function of pH. At the same time, the fluorescence emission spectrum is only dependent on the hydroxide ion concentration, so that these conjugates show a dual pH dependence spanning a wide pH range.

The tetraamide ligand  $\text{L}^1$  was synthesised by reaction of the  $\alpha$ -haloamide **1** with 1,4,7,10-tetraazacyclododecane in DMF at 80 °C (4.1 equiv.  $\text{Cs}_2\text{CO}_3$ ). The tribasic ligand  $\text{H}_3\text{L}^2$  was synthesised by reacting the molybdenum tricarbonyl complex of cyclen with the same amide (1 : 1) in DMF- $\text{Cs}_2\text{CO}_3$ , with a subsequent phosphinoxymethylation in THF followed by basic hydrolysis. The  $\text{Eu}^{\text{III}}$  complexes of  $\text{L}^1$  and  $\text{L}^2$  were made by reaction of the ligand with equimolar quantities of europium triflate in acetonitrile.<sup>9</sup>

The absorption spectra in water of  $[\text{EuL}^1]^{3+}$  and  $[\text{EuL}^2]$ , were similar to those observed for the intermediate amide **1**. The spectra showed a pH dependent bathochromic shift ( $\lambda_{\text{max}} = 314$  nm,  $\log \epsilon = 4.18$ ) with an isosbestic point at 296 nm, and revealed the formation of a new band at 261 nm ( $\log \epsilon = 4.0$ ) following protonation with  $\text{CF}_3\text{CO}_2\text{H}$ . The fluorescence emission spectrum of **1** did not show any substantial pH dependence below pH 8 when excited at 330 nm.<sup>†</sup> The same trend was observed for  $[\text{EuL}^1]^{3+}$  and  $[\text{EuL}^2]$ , when excited at 330 nm; the fluorescence emission spectra decreased in intensity in alkaline media, as shown in the pH-luminescence profile of  $[\text{EuL}^1]^{3+}$  (Fig. 1). In contrast, when excited at the isosbestic wavelength, the fluorescence emission spectra increased in intensity in

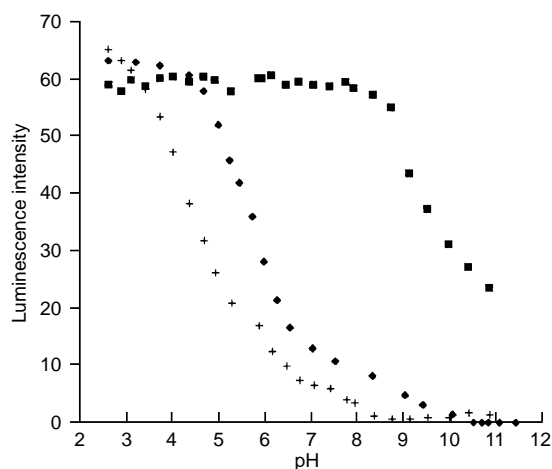
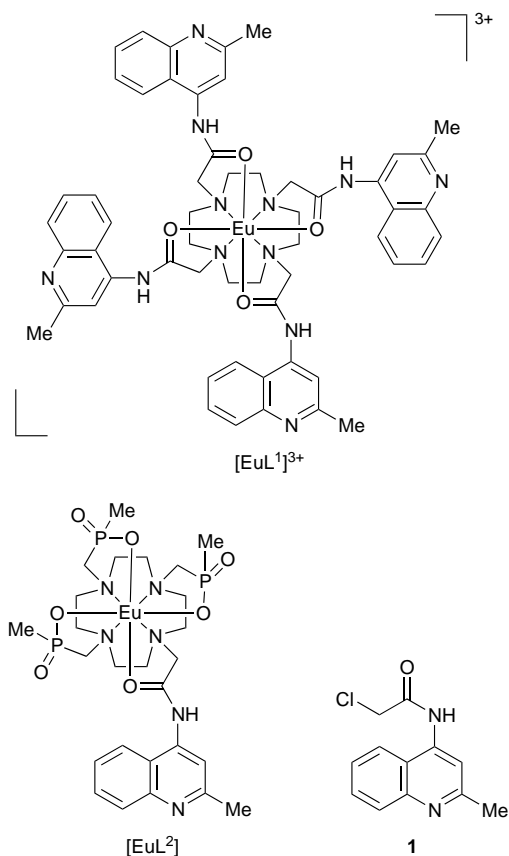
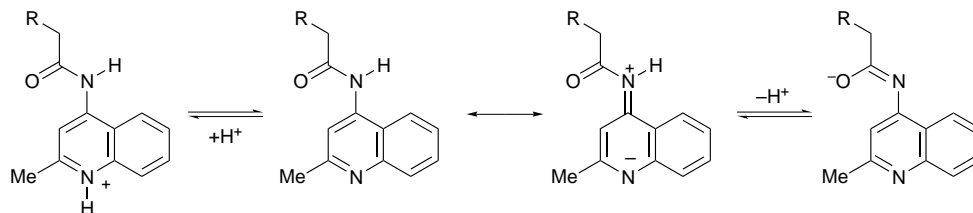


Fig. 1 Enhancement of the luminescence of europium complexes as a function of pH: (■) quinoyl fluorescence in  $[\text{EuL}^1]^{3+}$ ; (+) metal-based emission (594 nm) in  $[\text{EuL}^1]^{3+}$ ; (◆) metal-based emission in  $[\text{EuL}^2]$



Scheme 1

alkaline solution. In both cases,  $\lambda_{\text{max}}$ (fluor.) shifted to longer wavelength in the presence of base, and pH titrations revealed formation of an isoemissive point, for [EuL<sup>1</sup>]<sup>3+</sup> at 377 nm and [for EuL<sup>2</sup>] at 375 nm. The estimated pK<sub>a</sub> values of 9.4(3) and 9.6(3) were determined from these changes for [EuL<sup>1</sup>]<sup>3+</sup> and [EuL<sup>2</sup>], respectively, which relate to the deprotonation of the aryl amide nitrogen.

The largest and the most significant pH dependence was observed in the delayed europium emission. The emission was independent of pH in alkaline solution (above pH 10) for [EuL<sup>1</sup>]<sup>3+</sup>, with only very small changes observed for [EuL<sup>2</sup>] (overall, contributing around 8–12% of the total emission). Significant ‘off-on’ luminescence switching was observed when the quinolyl nitrogen was protonated {Fig. 1 for [EuL<sup>1</sup>]<sup>3+</sup>}. The luminescence enhancement was at least 250 for [EuL<sup>2</sup>] ( $\lambda_{\text{exc}} = 330$  nm), while a more modest factor of 30 was obtained with [EuL<sup>1</sup>], in each case observing Eu emission at 594 nm ( $\Delta J = 1$ ).<sup>‡</sup> The europium emission therefore signals the protonation of the remote chromophore, a feature which is not seen in the fluorescence emission spectrum.

Upon protonation of the quinolyl nitrogen atom the  $n-\pi^*$  transition is removed, and the  $\pi-\pi^*$  shifts to lower energy (as revealed by the excitation spectra for [EuL<sup>2</sup>] and [EuL<sup>1</sup>]<sup>3+</sup> as a function of pH). The internal charge transfer (ICT) excited state which is populated in the neutral chromophore is probably modified upon protonation and deprotonation (Scheme 1). The switching between pH 4.5 and 6.5 for [EuL<sup>2</sup>] is in accordance with simple ion-binding equilibria<sup>1,5,8</sup> and a pK<sub>a</sub> value of 5.8(2) was determined. The pH switching of the cationic complex [EuL<sup>1</sup>]<sup>3+</sup> is over a broader range and is shifted by one pH unit lower. In addition a small inflection in the metal-based luminescence is apparent at *ca.* pH 7 for [EuL<sup>1</sup>]<sup>3+</sup> and 8.5 for [EuL<sup>2</sup>]: this feature, apparently not ligand based, could be related to the deprotonation of the proximate water molecule. The extended pH sensitivity range of the tricationic complex, *i.e.* in the region between pH 6.5 and 2.5, may be related to the successive protonation of each of the four nitrogens of the chromophore. The overall pH dependence is then a function of four stepwise equilibria, taking place over almost 4 pH units, rather than the pH range of two associated with a single protonation. In accord with this observation a pH-metric titration of fully protonated [EuL<sup>1</sup>]<sup>3+</sup> revealed that 4 equivalents of base were consumed in the range 2.5–6. Similar behaviour has previously been observed for some fluorescent anthrylazamacrocyclic PET systems,<sup>10</sup> where the switching was considered to be linear over five pH units, although a detailed investigation into this behaviour has not subsequently been reported. In water at pH = 1.80, the luminescence emission lifetimes  $\tau_{\text{H}_2\text{O}}$ , for [EuL<sup>1</sup>]<sup>3+</sup> and [EuL<sup>2</sup>] were measured to be 0.55 and 0.71 ms, respectively, while in D<sub>2</sub>O, the lifetimes were 1.55 and 1.98 ms, respectively, consistent with an overall hydration state of 0.8 (inner + outer sphere) for both [EuL<sup>1</sup>]<sup>3+</sup> and [EuL<sup>2</sup>] (after correcting for the quenching effect of the amide NH oscillators).<sup>9,11</sup>

In summary, the two europium complexes possess distinctly different pH sensitivity. The delayed europium emission is highly dependent on pH changes over the range 3–7 making

these complexes interesting candidates for pH measurement in competitive media.

We gratefully acknowledge the BBSRC for grant support, and Drs Stephen Faulkner and Gareth Williams for helpful discussions.

## Notes and References

\* david.parker@durham.ac.uk

† The fluorescence emission spectrum of **1** gave spectra consistent with a weak internal charge transfer excited state. In solvents of increasing polarity (CH<sub>2</sub>Cl<sub>2</sub>, Et<sub>2</sub>O, MeCN, MeOH, H<sub>2</sub>O) a bathochromic shift was observed in  $\lambda_{\text{max}}$  and at pH 3 the ICT band was less apparent.

‡ These large enhancement factors are not explained simply by the suppression of photoinduced electron transfer following N-protonation (although this effect contributes a factor of *ca.* 3 per N, as seen by excitation at the isosbestic wavelength). Only when protonated, do the Eu complexes significantly absorb photons at 330 nm.

- 1 *Fluorescent Chemosensors for Ions and Molecular Recognition*, ed. A. W. Czarnik, ACS Symp. Ser., Washington DC, 1993; R. A. Bissell, A. P. de Silva, H. Q. N. Gunaratne, P. L. M. Lynch, G. E. M. Maguire and K. R. A. S. Sandanayake, *Chem. Soc. Rev.*, 1992, **21**, 187; R. A. Bissell, A. P. de Silva, H. Q. N. Gunaratne, P. L. M. Lynch, G. E. M. Maguire, C. P. McCoy and K. R. A. S. Sandanayake, *Top. Curr. Chem.*, 1993, **168**, 223; A. W. Czarnik, *Acc. Chem. Res.*, 1994, **27**, 302.
- 2 A. Mayer and S. Neuenhofer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1044; E. F. G. Dickson, A. Pollak and E. P. Diamandis, *J. Photochem. Photobiol. B*, 1995, **27**, 3.
- 3 R. A. Bissell, A. P. de Silva, *J. Chem. Soc., Chem. Commun.*, 1991, 1148; R. Grigg, J. M. Holmes, S. K. Jones and W. D. J. A. Norbert, *J. Chem. Soc., Chem. Commun.*, 1994, 185.
- 4 J.-C. G. Bunzli, in *Lanthanide Probes in Life, Chemical and Earth Sciences, Theory and Practice*, ed. J.-C. G. Bunzli and G. R. Choppin, Elsevier, New York, 1989, p. 219; D. Parker and J. A. G. Williams, *J. Chem. Soc., Dalton Trans.*, 1996, 3613; *J. Chem. Soc., Perkin Trans. 2*, 1995, 1305; A. Beeby and S. Faulkner, *Chem. Phys. Lett.*, 1997, **266**, 116; A. Beeby, R. S. Dickins, S. Faulkner, D. Parker and J. A. G. Williams, *Chem. Commun.*, 1997, 1401.
- 5 A. P. de Silva, H. Q. N. Gunaratne and T. E. Rice, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2116.
- 6 D. Parker, in *Comprehensive Supramolecular Chemistry*, ed. J.-M. Lehn, D. D. Macnicol, J. L. Atwood, J. E. Davis, D. N. Reinhoudt and F. Vogtle, Pergamon, Oxford, 1996, vol. 10, ch. 17, pp. 487–536; D. Parker, *Chem. Br.*, 1994, 818.
- 7 A. Beeby, D. Parker and J. A. G. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1565; A. Beeby, M. Murru, D. Parker and J. A. G. Williams, *J. Chem. Soc., Chem. Commun.*, 1993, 1116; S. Aime, M. Botta, D. Parker and J. A. G. Williams, *J. Chem. Soc., Dalton Trans.*, 1996, 17.
- 8 D. Parker, K. Senanayake and J. A. G. Williams, *Chem. Commun.*, 1997, 1777; D. Parker and J. A. G. Williams, *Chem. Commun.*, 1998, 245.
- 9 D. Parker and J. A. G. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1581.
- 10 E. U. Akkaya, M. E. Huston and A. W. Czarnik, *J. Am. Chem. Soc.*, 1990, **112**, 3590.
- 11 R. S. Dickins, D. Parker, A. S. de Sousa and J. A. G. Williams, *Chem. Commun.*, 1996, 697.

Received in Cambridge, UK, 19th November 1997; 7/08342D