ORGANIC
LETTERS

2006
Vol. 8, No. 13
2727−2730

Supramolecular Self-Assembly of Mixed f–d Metal Ion Conjugates

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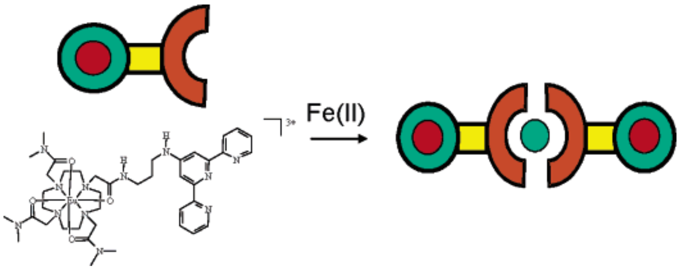
Received March 28, 2006

ABSTRACT



The synthesis of the novel Eu(III) cyclen complex, Eu1, is described. In buffered pH 7.4 water, the Eu(III) emission was "switched on" upon excitation of the *Terpy* antenna. In the presence of various transition-metal ions (e.g., Fe(II) and Ni(II)), both the singlet-excited state and the Eu(III) emission were quenched ("switched off"), whereas in the ground state, an MLCT band was formed, signifying the formation of stable mixed linear trimetallic f–d supramolecular self-assemblies.

There is currently great interest in the development of transition-metal-directed coordination assembly of functional supramolecular systems.[1] Such systems can often be viewed to mimic the nature of biological systems, as well as to replicate the function of switches, motors, and machines.[2,3] The lanthanides have also been used in the construction of such supramolecular assemblies, although relatively few examples exist for comparison.[4,5] Owing to their unique luminescence and paramagnetic properties, in conjunction with their high coordination requirements, the lanthanides have been extensively employed in organic synthesis and catalysis,[6] as luminescent probes and sensors[7] and as MRI contrast agents.[8] We have been interested in the use of lanthanide complexes of cyclen 1,4,7,10-tetraaza-cyclododecane in developing various supramolecular devices.[9−12]

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(1) Some recent examples include: (a) Stadler, A. M.; Puntoriero, F.; Campagna, S.; Kyritsakas, N.; Welter, R.; Lehn, J. M. *Chem.−Eur. J.* **2005**, *11*, 3997. (b) Bonnet, S.; Collin, J. P.; Sauvage, J. P. *Chem. Commun.* **2005**, 3195. (c) Sauvage, J. P. *Chem. Commun.* **2005**, 1507. (d) Leop, S. J. *Chem. Commun.* **2005**, 1511. (e) Constable, E. C.; Housecroft, C. E.; Lambert, J. N.; Malarek, D. A. *Chem. Commun.* **2005**, 3739. (f) Constable, E. C.; Figgemeier, E.; Hougen, I. A.; Housecroft, C. E.; Neuburger, M.; Schaffner, S.; Whall, L. A. *Dalton Trans.* **2005**, 3204. (g) Tominaga, M.; Suzuki, K.; Murase, T.; Fujita, M. *J. Am. Chem. Soc.* **2005**, *127*, 11950. (h) Fujita, M.; Tominaga, M.; Hori, A.; Therrien, B. *Acc. Chem. Res.* **2005**, *38*, 369.

(2) (a) Stoddard, J. F. *Acc. Chem. Res.* **2001**, *34*, 410. (b) Amendola, V.; Fabbrizzi, L.; Mangano, C.; Pallavicini, P. *Acc. Chem. Res.*, **2001**, *34*, 488. (c) de Silva, A. P.; Fox, D. B.; Huxley, A. J. M.; Moody, T. S. *Coord. Chem. Rev.* **2000**, *205*, 41.

(3) (a) *Molecular Motors*; Schilwa, M., Ed.; Wiley-VCH, Weinheim, 2002. (b) Venturi, M.; Credi, A.; Balzani, V. *Molecular Devices and Machines-A Journey into the Nanoworld*; Wiley-VCH: Weinheim, 2003. (c) *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, 2001.

(4) (a) Bünzli, J.-C. G. *Acc. Chem. Res.* **2006**, *39*, 53. (b) Bünzli, J.-C. G.; Piguet, C. *Chem. Soc. Rev.* **2005**, *34*, 1048. (c) Bünzli, J.-C. G.; Piguet, C. *Chem. Rev.* **2002**, *102*, 1977. (d) Piguet, C.; Bünzli, J.-C. G. *Chem. Soc. Rev.* **1999**, *28*, 347.

(5) (a) Elhabiri, M.; Hamacek, J.; Bünzli, J.-C. G. *Eur. J. Inorg. Chem.* **2004**, 51. (b) Pope, S. J. A.; Coe, B. J.; Faulkner, S. *Chem. Commun.* **2004**, 1550. (c) Bassett, A. P.; Magennis, S. W.; Glover, P. B.; Lewis, D. J.; Specer, N.; Parson, S.; Williams, R. M.; De Cola, L.; Pikramenou, Z. *J. Am. Chem. Soc.* **2004**, *126*, 9413. (d) Faulkner, S.; Pope, S. J. A. *J. Am. Chem. Soc.* **2003**, *125*, 10526. (e) Cantuel, M.; Bernardinelli, C.; Muller, G.; Riehl, J. P.; Piguet, C. *Inorg. Chem.* **2004**, *43*, 1840. (f) Imbert, D.; Cantuel, M.; Bünzli, J.-C. G.; Bernardinelli, C.; Piguet, C. *J. Am. Chem. Soc.* **2003**, *125*, 15698. (g) Petoud, S.; Cohen, S.; Bünzli, M. J.-C. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2003**, *125*, 13324.

(6) See special issue of : Tetrahedron Symposium in Print on Lanthanide Recent Advances in Rare Earth Chemistry. Kobayashi, S., Ed.; *Tetrahedron* **2003**, *52*, 10339−10597. Special issue of : Chemical Review on Frontiers in Lanthanide Chemistry; Kagan, B., Guest Ed; *Chem. Rev.* **2002**, *102*, 1805−2476.

(7) (a) Parker, D.; Dickins, R. S.; Puschmann, H.; Cossland, C.; Howard, J. A. K. *Chem. Rev.* **2002**, *102*, 1977. (b) Parker, D. *Coord. Chem. Rev.* **2000**, *205*, 109. (c) Reany, O.; Gunnlaugsson, T.; Parker, D. *Chem. Commun.* **2000**, 473. (d) Gunnlaugsson, T. *Tetrahedron Lett.* **2001**, *42*, 8901. (e) Gunnlaugsson, T.; Parker, D. *Chem. Commun.* **1998**, 511.

10.1021/ol060752j CCC: $33.50

Recently, we have become interested in the formation of mixed lanthanide−transition-metal (f−d) based supramolecular self-assemblies. Our strategy is shown schematically in Figure 1 and involves designing ligands such as **A**, which has two metal ion binding sites, one of which is a cyclen-based lanthanide ion center (represented as red circles on green circle backgrounds) and the second of which is a receptor for transition-metal ions. The formation of a supramolecular complex between **A** and transition-metal ions (green circles), used here as the bridging ions, would then be expected to give rise to either linear structures, e.g., **B** (1:2 stoichiometry ratio), or three-directional architectures, e.g., **C** (1:3 stoichiometry ratio), depending on the nature of the second receptor. These kinds of systems can also be viewed as lanthanide luminescent sensors for transition-metal ions, as the lanthanide emission for ions such as Eu(III) and Tb(III) (the excited state being $^5D_0$ and $^5D_4$ for Eu(III) and Tb(III), respectively)[9,13] would be expected to be modulated by the presence of the transition-metal ion employed (see later). Our first attempt consisted of developing **B** using *phen* as the antenna (the ligand in **A**). However, using Cu(II) gave rise to the formation of both **B** and **C** in solution.[12] With the aim of achieving exclusively the formation of **B**, we thus synthesized **1**, a terpyridine (*Terpy*)-based cyclen conjugate. The Eu(III) complex of **1**, **Eu1**, Figure 2, gave rise to the correct supramolecular structure using various transition-metal ions as the bridging ions. Moreover, even though both the absorption and the fluorescence spectra changed upon formation of these assemblies, the most striking changes were observed for the delayed Eu(III) emission, which occurred at long wavelengths. Here, we present the results from these studies, which are to the best of our knowledge the first clear examples of such mixed linear trimetallic f−d supramolecular self-assemblies.

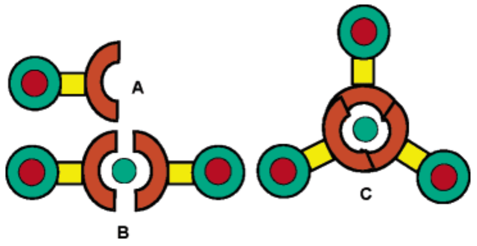


Figure 1. Schematic representation of the two- or three-directional architectures (see text for further explanation). (A) The bifunctional ligand. (B) Linear array of two Ln(III) ion complexes sandwiched between a transition-metal ion. (C) Three-directional array of three Ln(III) complexes with the transition-metal ion centered. Other higher-order arrays can be constructed using these principles.

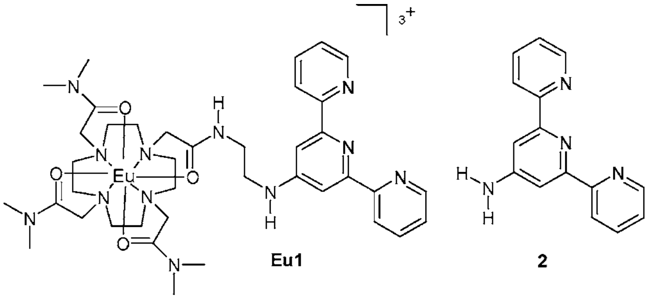
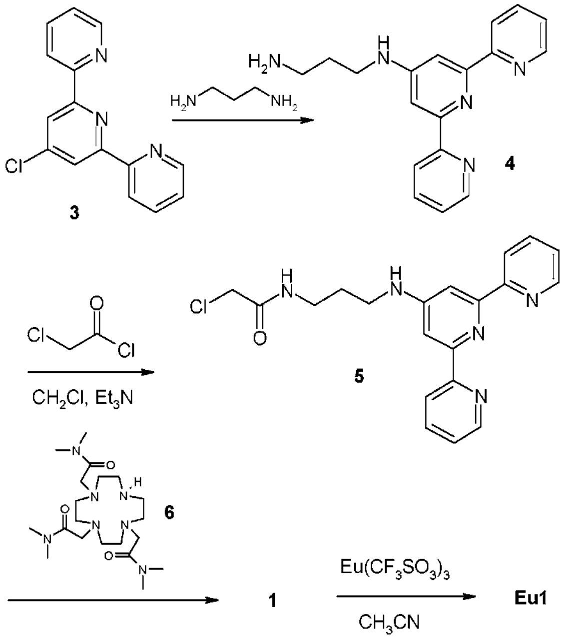


Figure 2. Cyclen-terpyridine target **1**.

Our initial target was to connect the *Terpy* directly into one of the acetamide arms, which involved the synthesis of the amine precursor **2** (Figure 2) from **3** (Scheme 1).[14]

Scheme 1. Synthesis of **1** and the Eu(III) Complex **Eu1**



Unfortunately, although **3** was formed successfully, we were unable to form the amine **2** successfully. We thus turned our emphasis toward an alternative design, **1**, which placed a spacer between the antenna and the coordinated amide (Figure 2). The synthesis of **1** was achieved as shown in

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(8) (a) Merbach, A. E.; Tóth, É. In *The Chemistry Of Contrast Agents In Medical Magnetic Resonance Imaging*; Wiley: West Sussex, England, 2001. (b) Caravan, P.; Ellison, J. J.; McMurray, T. J.; Lauffer, R. B. *Chem. Rev.* **1999**, *99*, 283.

(9) (a) Gunnlaugsson, T.; Leonard, J. P. *Chem. Commun*. **2005**, 3114. (b) Leonard, J. P.; Gunnlaugsson, T. *J. Fluoresc.* **2005**, *15*, 585.

(10) (a) Gunnlaugsson, T.; Leonard, J. P. *Chem. Commun*. **2003**, 2424. (b) Gunnlaugsson, T.; Harte, A. J.; Leonard, J. P.; Nieuwenhuyzen, M. *Chem. Commun.* **2002**, 2134. (c) Gunnlaugsson, T.; Leonard, J. P. *Dalton Trans.* **2005**, 3204.

(11) (a) Gunnlaugsson, T.; Davies, R. J. H.; Kruger, P. E.; Jensen, P.; McCabe, T.; Sinead, M.; Stevenson, C. S.; Fanning, A.-M. *Tetrahedron Lett.* **2005**, *46*, 3761. (b) Gunnlaugsson, T.; Davies, R. J. H.; Nieuwenhuyzen, M.; Stevenson, C. S.; Viguier, R.; Mulready, S. *Chem. Commun.* **2002**, 2136. (c) Gunnlaugsson, T.; O'Brien, J. E.; Mulready, S. *Tetrahedron Lett.* **2002**, *43*, 8493.

(12) Gunnlaugsson, T.; Harte, A. J.; Leonard, J. P.; Senechal, K. *Chem. Commun*. **2004**, 782.

(13) (a) Gunnlaugsson, T.; MacDónaill, D. A.; Parker, D. *J. Am. Chem. Soc*. **2001**, *123*, 12866. (b) Gunnlaugsson, T.; MacDónaill, D. A.; Parker, D. *Chem. Commun*. **2000**, 93.

Scheme 1. Heating **3** at 120 °C in neat 1,3-diamino-propane gave **4** in 89% yield. The reaction of **4**, triethylamine, and chloroacetyl chloride in CH_3CN gave the α-chloroamide **5** in 76% yield after purification (alumina column chromatography; 99:1 CH_2Cl_2/MeOH). The final step involved the coupling of **5** to **6**,[15] by heating under reflux in DMF in the presence of Cs_2CO_3 for 24 h. Ligand **1** was formed in 47% yield after purification using alumina column chromatography (99:1 CH_2Cl_2/MeOH(NH_3)). The reaction of **1** with 1 equiv of europium triflate in CH_3CN under anhydrous conditions gave **Eu1** as an off-white solid in 95% yield after precipitation from diethyl ether, followed by trituration using CH_2Cl_2. Characterization of **Eu1** using ^{1}H NMR (Supporting Information, Figure S1) showed the expected broadly shifted resonances for the axial and equatorial protons of the cyclen ring as well as the α-protons of the pendant arms. The chemical shifts are indicative of square antiprismatic geometry.[7] High-resolution ESMS also confirmed the formation of **Eu1**.[16]

The lanthanide luminescence of **Eu1** was first monitored as a function of pH, in 100% water ($I = 0.1$ M, TMACl). The *Terpy* chromophore functions as an antenna, populating the Eu(III) excited state ($^5D_0$) via sensitization.[9] In water, at pH 7.4, the absorption spectra of **Eu1** showed a band centered at 285 nm ($\epsilon = 23513$ mol^{-1} cm^{-1}), corresponding to the $\pi-\pi^*$ transition of the *Terpy* moiety. Upon excitation of this transition, a broad fluorescence emission was observed centered at 420 nm. The complex also showed the characteristic luminescence bands for Eu(III), appearing at 581, 592, 615, 624, 654, 686, and 702 nm, for the deactivation of $^5D_0 \rightarrow {}^7F_J$ ($J = 0$, 1, 2, 3, and 4). This clearly indicated that the terpyridine moiety was an effective sensitizer for the Eu(III) $^5D_0$ excited state. The emission lifetime (τ_{Eu}) in water (pH = 7.4) was measured to be 0.470 and 0.767 ms in D_2O (pD = 7.0). From these changes, the hydration state (q) of the complex was determined to be 1.2.[9] This indicates that the complex has ca. one metal-bound water molecule, giving an overall nine-coordinated environment.[7a] The pH titration of the complex showed that the Eu(III) emission was also highly pH dependent (Supporting Information, Figure S2), where the Eu(III) emission was switched on above pH ~3 and switched off above pH ~9. These changes can be assigned to protonation of the *Terpy* ligand and deprotonation of the metal-bound water molecule (or an aryl amide), respectively. Moreover, no intensity changes were seen for the Eu(III) emission at pH 7.4 when monitored overnight.

Having established that the emission was switched on at neutral pH, we carried out spectrophotometric titrations of **Eu1** using a series of transition-metal ions at pH 7.4 (HEPES, 0.01 M, $I = 0.1$ M TMACl) where the changes in the ground state, the singlet-excited state, and the delayed Eu(III) emission were all monitored. The changes in the ground state of **Eu1** clearly showed the formation of a ternary complex between **Eu1** and transition-metal ions, Fe(II) (as either the ClO_4^- or Cl^- salt), Co(II), Cu(II), Ni(II), Zn(II), and Cd(II) (as ClO_4^- salts). The changes observed for Fe(II) and Ni(II) (ClO_4^- salts) will be focused on here. For Fe(II), a new band was formed centered at ca. 570 nm, which was assigned to the formation of a new MLCT band upon coordination of these ions to the *Terpy* ligand (Figure 3). This indicated the formation of the desired 2:1 complex **B**, as such MLCT bands are characteristic of such (octahedral) complexes. A small shoulder was also formed at ca. 370 nm due to the changes in the $\pi \rightarrow \pi^*$ transition. Fitting of the spectral changes for the MLCT band, using the nonlinear least-squares regression program SPECFIT, indicated the formation of a 2:1 complex with an overall log $\beta_{2:1}$ of 11.51 (±0.12) (see Supporting Information Figure S3a,b for fitting).[17] For Ni(II), similar spectral changes were seen, with a log $\beta_{2:1}$ of 12.46 (±0.33) determined.[18]

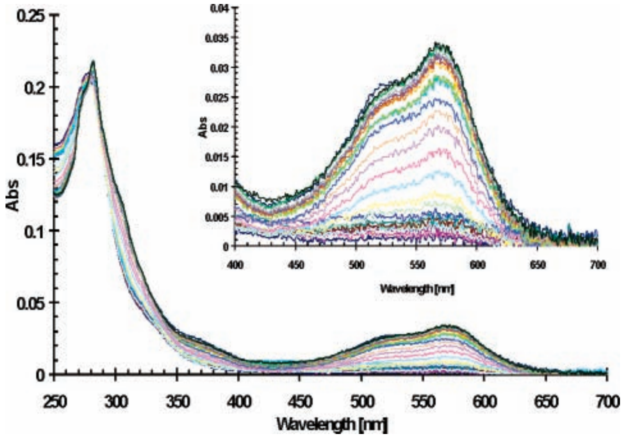

Figure 3. Changes in the absorption spectra of **Eu1** (5.8×10^{-6} M) upon titration with $FeClO_4$ ([Fe(II)] = 0 → 5.8×10^{-5} M) at pH 7.4, $I = 0.1$ M TMACl, showing the formation of the MLCT band. Inset: MLCT band, which was removed upon adding ETDA.

The fluorescence emission spectrum of **Eu1**, when excited at 277 nm, gave rise to a major emission band centered at 422 nm and a smaller band at 348 nm. Upon titration with $FeClO_4$, the long-wavelength emission was quenched as is evident from Figure 4. These changes were assigned to the coordination of Fe(II) to the *Terpy* unit. The fitting of these

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[14] (a) Mutai, T.; Cheon, J.-D.; Arita, S.; Araki, K. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1045. (b) Constable, E. C.; Ward, M. D. *J. Chem. Soc., Dalton Trans.* **1990**, 1405.

[15] Gunnlaugsson, T.; Leonard, J. P.; Mulready, S.; Nieuwenhuyzen, M. *Tetrahedron* **2003**, *59*, 3231.

[16] **Eu1**: calcd for $C_{40}H_{60}N_{12}O_4Eu$ [M + H peak] m/z = 925.4073, found 925.4031 (+4.5 ppm); ^{1}H NMR (400 MHz, D_2O) 30.4, 8.8, 8.3, 8.1, 7.6, 4.7, 3.2, 2.8, 1.3, 0.4, −1.1, −2.5, −5.5, −7.8, −13.0, −15.7; ^{19}F NMR (376 MHz, D_2O) −79.4; ESMS (MeCN) m/z expected 925.40, found 308.46 (M+)/3, 611.65 (M + 2[Triflate])/2.

[17] The stability of the complex formation is reported as log $\beta_{2:1}$, as the MLCT band reflects the formation of the 2:1 species only, whereas the changes observed in both the fluorescence and the Eu(III) emission reflect the stepwise equilibrium. Fitting (a) over the whole data in Figure 4 gave log $\beta_{2:1}$ = 11.73 (±0.2) and (b) below 400 nm gave log $\beta_{2:1}$ = 11.81 (±0.17). All three fits are within error of each other and are comparable to those determined from the fluorescence and the Eu(III) emission (see later). Fitting these changes to 1:1 complex formation gave unsatisfactory results.

[18] These stability constants are large and, hence, carry a significant error as the individual log K values are approaching the maxima at which they can be determined accurately using this spectroscopic method.

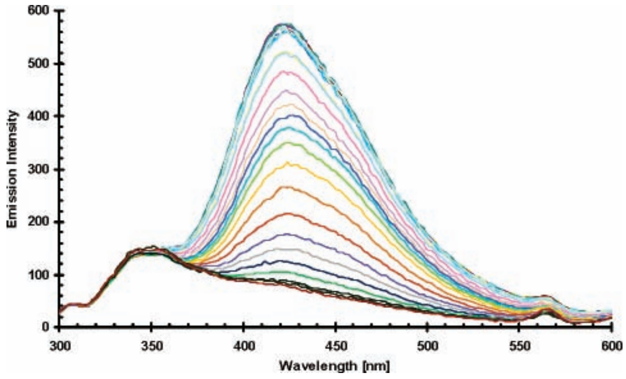

Figure 4. Changes in the fluorescence emission spectra of **Eu1** (5.8×10^{-6} M) upon titration with Fe(II) ([Fe(II)] = 0 → 5.8×10^{-5} M).

changes using SPECFIT indicated the formation of the desired 1:2 complex with an overall log $\beta_{2:1}$ of 11.52 (±0.19) for Fe(II) (Supporting Information, Figure S3c) and a log $\beta_{2:1}$ of 13.35 (±0.45)[18] for Ni(II), both of which are in good agreement with that observed for the absorption changes.

As previously demonstrated, the Eu(III) emission was switched on at pH 7.4. In comparison to the fluorescence changes, the Eu(III) emission is a delayed emission, occurring in the μ−ms time frame and at long wavelengths (in red, with an over 300 nm Stokes shift) with characteristic linelike emission bands. The concomitant changes in the Eu(III) emission upon titration with Fe(II) are shown in Figure 5. These changes clearly show that there was a significant quenching, ca. 95%, for all of the $^5D_0 \rightarrow {}^7F_J$ transitions upon Fe(II) recognition and demonstrate the sensitivity of the Eu(III) emission to changes in the local environment, i.e., the coordination of Fe(II) to the antenna. This quenching is most likely due to energy transfer from $^5D_0$ to ^{3}MLCT upon binding to Fe(II). The reversibility of these changes was also investigated. Adding EDTA to the quenched solution reestablished the emission over time because of dissociation of the assembly.

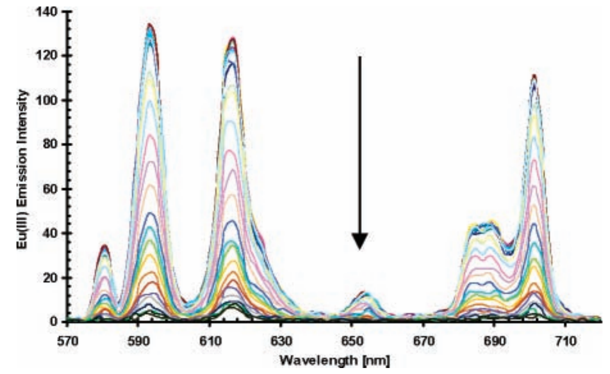

Figure 5. Changes in the Eu(III) emission upon titration of **Eu1** (5.8×10^{-6} M) upon titration with Fe(II) ([Fe(II)] = 0 → 5.8×10^{-5} M).

Analysis of the changes for Fe(II) (as ClO_4^-) gave an overall log $\beta_{2:1}$ of 11.58 (±0.13) [log K_1 = 6.12 (±0.13), log K_2 = 5.46 (±0.19)] (Supporting Information, Figure S3d). The titration of **Eu1** using Fe(II) (chloride) gave similar results [log K_1 = 6.35 (±0.15), log K_2 = 4.81 (±0.13)]. Ni(II) complexation to **Eu1** gave similar spectral changes, with a log $\beta_{2:1}$ of 13.41 (±0.42) [log K_1 = 7.14 (±0.28), log K_2 = 6.27 (±0.42)] determined.[18] Similarly, for Co(II), log K_1 = 6.34 (±0.11) and log K_2 = 5.88 (±0.13) were determined, whereas for Cu(II), log $K_1 < 1$ and log K_2 = 13.75 (±0.22) were measured. These results clearly showed the same binding stoichiometry (2:1) signifying the formation of the desired linear trinuclear f−d self-assembly architecture **B**.

In the case of the d^{10} transition-metal ions, no MLCT bands were seen for Zn(II) and Cd(II), as expected. Moreover, the fluorescence and the Eu(III) emission were enhanced, in contrast to the quenching observed above, possibly due to reduction in LMCT upon coordination to these ions. Hence, the nature of the bridging ion can also be determined from these changes, e.g., switching off vs switching on for the d^{10} ions. For these later ions, log $\beta_{2:1}$ = 11.97 (±0.22) with log $K_1 < 1$ and log $\beta_{2:1}$ = 11.13 (±0.25) [log K_1 = 5.63 (±0.12), log K_2 = 5.50 (±0.25)] were determined for Zn(II) and Cd(II), respectively.

The real attractiveness of monitoring the changes in the Eu(III) emission, over that of the ground and the singlet-excited state, lies in the fact that these changes occur at long wavelength and with delayed emission, giving rise to significantly improved signal-to-noise ratios (cf. Supporting Information Figure S3a−d). More importantly, the Eu(III) ion is an *impartial luminescent reporter*, as it does not participate directly in the binding of the transition-metal ions. Hence, the changes observed in Figure 5 can be used as a direct measure of the coordination changes occurring at the antenna and therefore of the formation of the self-assembly complex **B**.

In summary, we have developed new cyclen-based mixed trinuclear f−d self-assemblies in aqueous solution. Here, the changes in the ground and the singlet-excited states and, in particular, the long-wavelength lanthanide emission were used independently to determine the structural nature of the resulting assembly in solution. To the best of our knowledge, these are the first examples of such linear f−d assemblies that can be reversibly formed. Moreover, by simple replacement of the lanthanide metal ion, for instance, with Nd(III) or Yb(III), the formation of such self-assemblies can also be monitored in the NIR, as can Er(III), which has potential application for telecommunication. We are currently developing these types of self-assemblies.

Acknowledgment. We would like to thank EI, TCD, and CSCB for financial support, Dr. John O'Brien for NMR, and Drs. Paul E. Kruger and Susan Quinn for useful discussions and help during the writing of this manuscript.

Supporting Information Available: Synthesis and characterization of **Eu1** and Figures S1−S3. This material is available free of charge via the Internet at http://pubs.acs.org.

OL060752J