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Lanthanide luminescent switches: modulation of the luminescence of bis-macrocyclic based Tb(III) conjugates in water by H^+, Na^+ and K^+†

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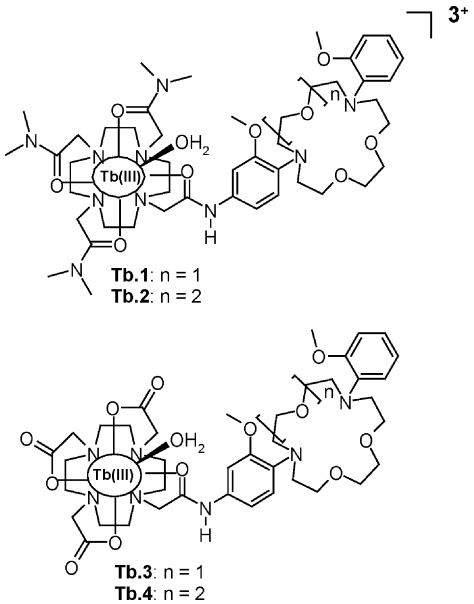
The synthesis of four bis-macrocyclic conjugates made from the coupling of either diaza-15-crown-5 ethers (**1** and **3**) and diaza-18-crown-6 ethers (**2** and **4**) to either amide or carboxylate functionalized cyclen (1,4,7,10-tetraazacyclododecane), and their corresponding cationic Tb(III) complexes, **Tb·1**, **Tb·2**, and neutral complexes **Tb·3** and **Tb·4** are described. The effect on the ground, singlet excited states and the Tb(III) emission, was investigated either as a function of pH or the concentration of several Group I and II cations, upon excitation at 300 nm. The ground state and singlet excited states of the Tb(III) complexes were found to be modulated by ions such as H^+, Na^+ or K^+, signifying the recognition of these ions by the crown ether receptors. In acidic media, below pH 4, the Tb(III) emission was highly pH sensitive, gradually increasing with large orders of magnitude of luminescence enhancements. For **Tb·1** and **Tb·2** complexes, the Tb(III) emission was also '*switched on*' in alkaline media above pH 8. At pH 7.4, the recognition of Na^+ or K^+ also gave rise to a significant change in the Tb(III) emission due to the modulation of the *antenna-receptor* moieties by these ions. For **Tb·1** and **Tb·3** the largest changes were seen for Na^+, whereas for **Tb·2** and **Tb·4** the largest changes were seen for K^+.

Introduction

The development of luminescent signalling systems is an active area of research in supramolecular chemistry.[1–4] These include the development of luminescent switches, logic gate mimics, machines and, in particular, sensors.[1–10] Classically, transition metal ion complexes have often been employed in the design of such luminescent devices.[11] Recently, lanthanide ion complexes have also been developed as alternative metal ion based emission moieties.[1,12,13] Ions like Nd(III), Sm(III), Eu(III), Tb(III), Er(III) and Yb(III), all possess long lived excited states, occurring in the millisecond or microsecond timescale. Moreover, they emit at long wavelengths, with large sharp and narrow emission band structures. However, their excited states are, nevertheless, a Laporte-forbidden f–f transition, which makes direct excitation difficult. Nonetheless, the development of metal sensitization using *antennae*, by covalently incorporating one or more sensitizing chromophore into the coordinating ligand, or by self-assembly, overcomes this drawback.[1,12–14] Furthermore, by modifying the antenna, for instance, by incorporating a receptor moiety as an integrated part of the antenna, it is possible to modulate the sensitization process, which in turn yields responsive luminescent devices.[1,12,13,14]

We are interested in the development of such responsive lanthanide ion complexes and we have developed systems whereupon the emission is either '*switched on*' or '*off*', by cations, anions or neutral molecules.[1,15,16] In this paper we present the synthesis of several Tb(III) complexes **Tb·1**, **Tb·2**, **Tb·3** and **Tb·4**, as Na^+ or K^+ switches, and the photophysical evaluation of these complexes as a function of pH or the concentration of several group I and II ions in pH 7.4 buffered solutions.[17] These bis-macrocyclic complexes comprise of a diaza-15-crown-5 or a diaza-18-crown-6 macrocycle, as combined antenna/receptors, that are tethered to a cyclen (1,4,7,10-tetraazacyclododecane) macrocycle that hosts the Tb(III) ion and function as the luminescence emitting moiety. To the best of our knowledge, these are one of the first examples of such bis-macrocyclic lanthanide based luminescent switches.[18]



Results and discussion

Design and synthesis of ligands 1–4 and their corresponding Tb(III) complexes

Our design is based on the use of the crown ether receptors **7** and **8** as key intermediates (Scheme 1). These are formed by using *o*-anisidine moieties as a part of the crown ether receptor so that the methoxy groups can participate in the coordination of the targeted ions, and as such increase both sensitivity and the selectivity of the Na^+ or K^+ recognition.[19] Indeed, X-ray crystallographic evaluations of these two receptors in the presence of Na^+ and K^+, have indeed shown this to be the case.

† Electronic supplementary information (ESI) available: 22 figures including binding studies of **13** and **14**, various bindings studies of the Tb(III) complexes discussed, the effect of temperature and degassing on the Tb(III) emission and the crystal structure of **14** and the corresponding K^+ complex. See http://dx.doi.org/10.1039/b509230m

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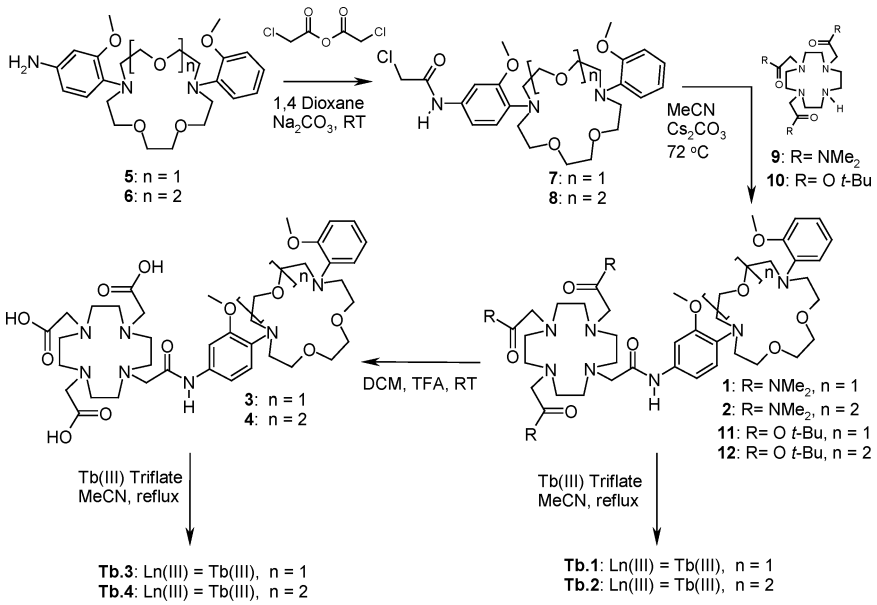


Scheme 1 Synthesis of **1–4** and their corresponding Tb(III) complexes.

The ions were found to be coordinated to the oxygens of the ring, the nitrogens of the aniline units and the two methoxy groups.[20]

The synthesis of ligands **1–4** and their Tb(III) complexes are shown in Scheme 1. The α-chloroamides **7** and **8** were synthesised by stirring the amino compounds **5** and **6**, respectively, in 1,4-dioxane with 1.1 equivalents of α-chloroacetic anhydride and Na_2CO_3 at room temperature. This gave both products in yields of *ca.* 62% following purification by column chromatography. The synthesis of **5** and **6** have previously been reported by us involving the transformation of 2-methoxyaniline in several high yielding steps to give **13** and **14** as intermediates (see later).[20] The nitration of **13** and **14** was achieved using $NaNO_2$ in aerated water and glacial acetic acid. Compounds **5** and **6** were then obtained by catalytic hydrogenolysis. The synthesis of **1**, **2**, **11** and **12** involved stirring equimolar amounts of **7** or **8** with **9**[21a] or **10**[21b] in refluxing MeCN in the presence of Cs_2CO_3. Both **1** or **2**, were obtained in 77% yields in a sufficiently pure state for complexation to Tb(III). It is worth noting that using either flash silica or alumina column chromatography failed to afford the desired products in any purer state. Both **11** and **12** were, successfully purified and obtained as oils in *ca.* 56% yield after treating the crude materials to alumina column chromatography, by initially using DCM–THF (70 : 30) as an eluent, followed by a gradient elution to DCM–THF–MeOH (60 : 30 : 10) as the final solvent system. Both **11** and **12** were finally subjected to acid hydrolysis using TFA in DCM yielding **3** and **4** in 82 and 89% yields, respectively.

Synthesis of the lanthanide complexes of ligands **1–4** involved stirring the aforementioned ligands and 1.1 equivalents Tb(III) triflate in freshly distilled MeCN for approximately 15 h, under an atmosphere of dry argon, followed by precipitation from dry diethyl ether. The **Tb·1** and **Tb·2** complexes were purified by alumina column chromatography using DCM–THF (30 : 70) as the initial solvent system, followed by a gradient elution using DCM–THF–MeOH (30 : 60 : 10), giving the complexes in yields of *ca.* 35%. However, both **Tb·3** and **Tb·4** were obtained in yields of *ca.* 80% after precipitation from diethyl ether and did not require further purification. The ^{1}H NMR (CD_3CN) spectra of all the complexes showed large chemical shifts for the axial and the equatorial protons of the cyclen ring and the $-CH_2-$ spacers, due to the presence of the paramagnetic lanthanide ion.[22] For **Tb·1**, these resonances appeared at 68.59, 41.76, 23.72, 18.13, 10.36, 8.69, 7.05, 6.77, 6.56, 5.58, 5.25, 4.82, 4.27, 1.42 ppm, respectively, suggesting that the complex adopted a square antiprism geometry around the lanthanide ion in solution.[23] In all cases the ESMS spectrum showed a number of peaks related to the complexes where the isotopic distribution patterns of the Tb(III) complexes were clearly distinguishable.

Ground and singlet excited state investigation of the Tb(III) complexes of 1–4

We carried out investigations of the photophysical properties of this range of complexes as a function of pH, and group I and II metal ions in water, where the changes in the ground state, the singlet excited state and the lanthanide excited state ($^5D_4$) were monitored. The results discussed below, focus on the effect of the ground and the singlet excited state of **Tb·1** and **Tb·2** as representatives of these complexes.

We first evaluated the effect of pH upon the ground state and the singlet excited states of the above complexes. It was foreseen that the ground state properties of these complexes would be greatly effected by pH due to the stepwise protonation of the two aryl amines as well as the potential deprotonation of the secondary amide. In the case of **Tb·1**, at pH ~ 12, (using tetramethyl ammonium hydroxide, TMAOH), two main absorption bands were observed at 211 nm ($\log \varepsilon = 5.43$, determined by linear regression analysis) and 251 nm ($\log \varepsilon = 4.09$) with a shoulder at 279 nm ($\log \varepsilon = 4.03$). Upon acidification (using dilute HCl) to neutral pH, a hypsochromic shift was observed in the 211 nm band with a concomitant hypochromic effect which resulted in the absorption being shifted to 200 nm ($\log \varepsilon = 5.34$). When the pH was decreased further to pH ~ 1, a slight bathochromic shift occurred, resulting in a maximum at 203 nm ($\log \varepsilon = 5.37$) with concomitant hyperchromic effect. Considerable changes were also observed in the longer wavelength band at the 251 nm band and in the shoulder at 279 nm, Fig. 1, which was assigned to the ICT character of the molecule (see later). The 251 nm band experienced a hypochromic effect as the pH was decreased from pH 12 → 6. However, as the pH was decreased even further a second protonation process occurred where a hyperchromic effect was observed for this band. A bathochromic shift was also observed in the 251 nm band as the pH was decreased from pH 12 → 8, which resulted in a shift in the maximum to 279 nm. As the pH was decreased further a hypochromic effect was observed which reached a minimum absorption at *ca.* pH ~ 2, resulting in a decrease in the absorbance intensity of *ca.* 54%. These results clearly demonstrate the complexity of the several protonation steps involved.

We propose that the main changes described above are due to three protonation steps. Two of these we assigned to the

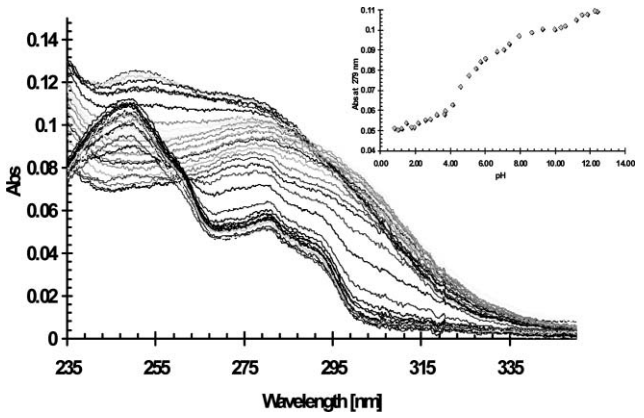


Fig. 1 Absorption spectra of **Tb·1** (10 μM aqueous solution) as a function of pH. See text for description. (Inset: Absorbance of **Tb·1** at 279 nm as a function of pH.).

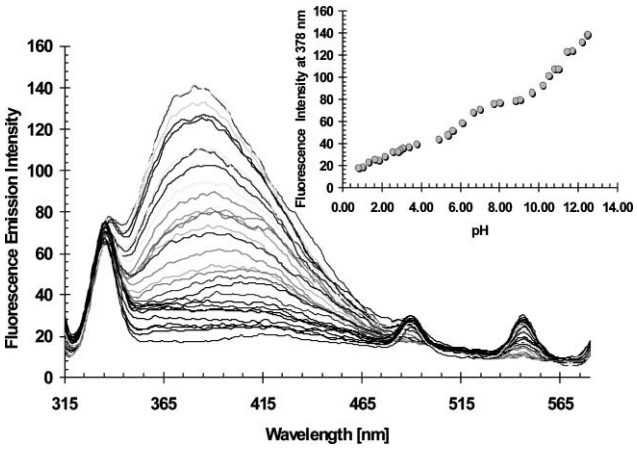


Fig. 2 Fluorescence of **Tb·1** as a function of pH (10 μM solution, slit widths 9 nm, excitation at 300 nm), where the emissions quenched in acidic media. These changes were fully reversible. Note: Emission band at 336 nm is due to Raman scattering of water. (Inset: Fluorescence profile of **Tb·1** as a function of pH at 378 nm (10 μM), excitation at 300 nm.).

protonation both the aniline moieties in **Tb·1**, with pK_{a2} and pK_{a3} of 5.5 (±0.2) and *ca.* 3.0 (±0.2), respectively. Of these two aniline moieties, the one adjacent to the lanthanide ion would be expected to give rise to relatively larger changes in the absorption spectra due to the presence of an internal charge transfer (ICT) process, as a result of the electron donating amine and the electron withdrawing amide. Because of this ICT character, the aniline lone pair is also significantly delocalized and any protonation would be quite difficult, except at low pH. We thus assign the pK_{a3} to this moiety, whereas pK_{a2} is due to the protonation of the remaining aniline moiety. The secondary amide is also adjacent to the lanthanide ion, where it inductively experiences the charge of the lanthanide ion. These combined effects make the secondary amide more acidic and more accessible to deprotonation, and we assign the $pK_{a1} = 11$ (±0.2) to this moiety. A plot of the changes in the absorption spectra at 279 nm as a function of pH is shown in Fig. 1, as an insert, demonstrating these multiple steps. Similar pH studies were performed on all the other complexes, and all showed comparable changes to those reported above.

The concomitant changes in the fluorescence of **Tb·1** in aqueous solution were also monitored upon excitation at 300 nm, where there was a large change in the absorption spectrum between the alkaline and acidic media, Fig. 1. As with the ground state it was expected that the emission spectra would be pH dependent, and this was indeed found to be the case. At neutral pH a major emission maxima was observed at 378 nm, Fig. 2. Upon titration of a basic solution of **Tb·1** with acid, a decrease was observed in the intensity of this band with a total reduction of 87% at pH ~ 1. A plot of the changes of the intensity as a function of pH is shown in Fig. 2 as an insert. Again, complicated changes were observed, suggesting three protonation/deprotonation steps, which are almost identical to that seen in the ground state. It should also be noted that at pH ~ 4, the Tb(III) emission began to appear, at 490 and 546 nm, respectively (the $J = 6$ and $J = 5$ bands), overlapping with the fluorescence emission. This clearly demonstrated that the lanthanide luminescence was highly pH responsive, but only at low pH. Similar pH experiments were also performed on **Tb·2**, **Tb·3** and **Tb·4**. All showed the same trend as for **Tb·1**.

Ground and singlet excited state investigation Tb(III) complexes of 1–4 as a function of Na^+ and K^+ at pH 7.4

We evaluated the effect of titrating a solution of the respective lanthanide complexes with either Na^+ or K^+ (as Cl^- or AcO^- solutions) In the case of **Tb·2**, a Tb(III) complex designed as a luminescent sensor/switch for K^+, a titration was performed in a 0.1 M TRIS buffered solution at pH 7.4. As demonstrated before, two absorption bands were visible prior to the addition of KOAc. Upon addition of stock solution of KOAc over a range of 1 μM to 0.8 M, a bathochromic shift was observed in the 200 nm band, which was accompanied by a hyperchromic effect that resulted in a formation of a new absorption maximum at *ca.* 223 nm ($\log \varepsilon = 5.03$), and an isosbestic point at *ca.* 248 nm. However, at higher concentrations the isosbestic point was less visible. More importantly, a concomitant hypochromic effect was also observed in the 276 nm band, which resulted in a 33% decrease in the absorption intensity, Fig. 3. The observed changes in the 276 nm band were attributed to the coordination of the aniline nitrogens of the aza crown ring to K^+, which upon binding to the ion are no longer, or only partially, delocalised into the aromatic system, thus reducing the inherent ICT process.

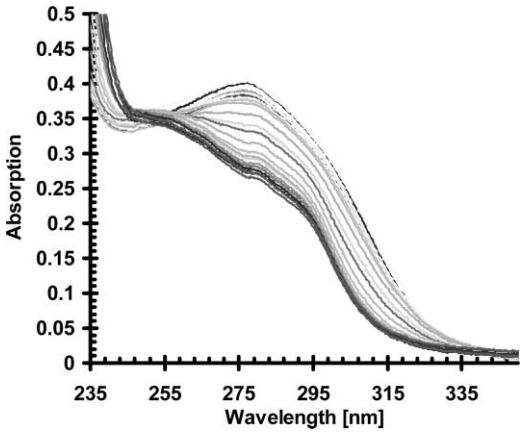
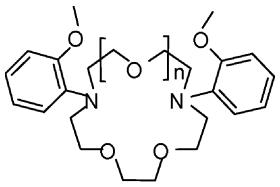


Fig. 3 The changes in the absorption spectra of **Tb·2** (30 μM) as a function of K^+, where the absorption decreases upon increasing K^+ concentration.

Analysis of the changes observed upon titrating **Tb·2** with K^+ indicated 1 : 1 binding. From these changes a binding constant of $\log \beta = 1.3$ (±0.1) was determined for the K^+ binding, which is rather weak. This could be due to the fact that the aniline unit adjacent to the Tb(III) ion makes the nitrogen lone pair more delocalized and less available to participate in the K^+ binding. This became clear by evaluating the changes in the absorption spectra of the model compounds **13** and **14**[20] at 250 nm, when these receptors were subjected to such titrations in MeOH–H_2O (50 : 50) solution. As for the pH titration earlier, the main changes occurred at shorter wavelengths. Nevertheless, there were also changes between 270 and 310 nm. For **14**, a sigmoidal curve indicating a sensitivity to K^+ over two log units from pK_a 2–4, when plotting the changes at 250 nm, from which a binding constant $\log \beta = 3.9$ (±0.1) was determined, which

is significantly stronger binding than seen for the lanthanide complexes. Similar results were observed for **13** with Na^+, which gave $\log\beta = 3.1$ (± 0.1). Studies on all the other lanthanide complexes showed comparable changes in absorption spectra as seen for **Tb·2** in the presence of cations such as Na^+ or K^+ and all showed that the sensitivity for the ions was at a relatively high concentration range.



13: n = 1
14: n = 2

Analysis of the fluorescent emission dependence of all of the lanthanide complexes were also carried out in the presence of either Na^+ or K^+ in a similar manner to that described above for **Tb·2**. The emission spectra of **Tb·1** showed a decrease in the emission of the 378 nm band of almost 50% upon titration with Na^+. The presence of the $J = 6$ and $J = 5$ bands from the Tb(III) emissions were also observed at higher ion concentrations, as seen previously for the pH titration of **Tb·1**; clearly demonstrating that the Tb(III) emission was modulated upon the recognition of the ion by the antenna/receptor. The results for each of the other Tb(III) complexes mirrored those seen here for **Tb·1**.

Lanthanide luminescence investigations of the Tb(III) complexes of 1–4

The lanthanide complexes **Tb·1–4** were all analysed in terms of their lanthanide luminescence with respect to pH, Na^+ and K^+ titration in a similar manner to that discussed above by excitation at 300 nm where there was a significant difference in the absorption spectra between the free and the complexed receptor/antenna. We first evaluated the effect of the pH response of the cationic complex **Tb·1**, in aqueous solution as a function of pH from pH 12 → 1 (using time gating techniques). The Tb(III) emission, corresponding to the $^5D_4 \rightarrow {}^7F_J$ transitions ($J = 6, 5, 4$ and 3, where $^5D_4$ Tb(III), $E = 20\,500\ cm^{-1}$) occurring at 490, 546, 586 and 622 nm, respectively, showed a dramatic sensitivity to its pH environment. The overall changes can be seen in Fig. 4. To investigate this further, the changes in the 546 nm transition were analyzed by plotting them as a function of pH, Fig. 5. From these changes it can be concluded that the Tb(III) emission is *highly* pH dependent, much more so than in the fluorescence spectra. Most importantly, the Tb(III) emission in the pH range of *ca.* 4.1–9.6, is almost fully '*switched off*', whereas in both acidic media (below pH ~ 4) or basic media (above pH ~ 9.6) dramatic changes occurred. From these changes we determined that the Tb(III) emission was '*switched on*' with *ca.* 40 and 14-fold order of magnitude enhancements in acidic media for **Tb·1** and **Tb·2**, respectively, and with *ca.* 22- and 10-fold order of magnitude enhancements in alkaline media for **Tb·1** and **Tb·2**, respectively. Looking at Fig. 5, it is clear that the pH dependence gives rise to an '*inverted-bell-shaped*' pH profile. This pH dependence was found to be fully reversible, and comparable results were also found when this experiment was repeated using other acids such as dilute H_2SO_4, indicating that there was no anion effect.

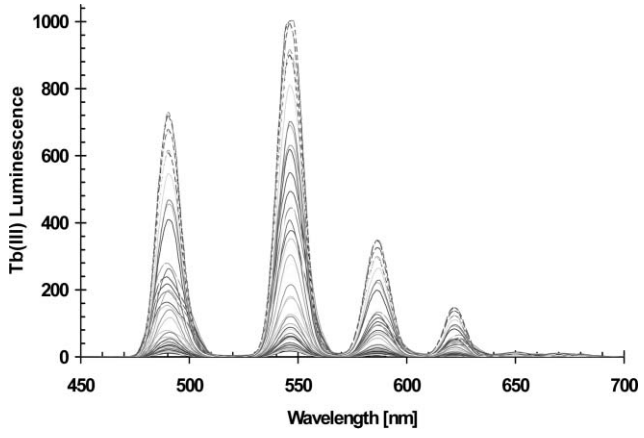


Fig. 4 The overall changes in the Tb(III) emission of **Tb·1** (10 μM; λ_{exc} = 300 nm) as a function of pH from pH 12 → 1.5.

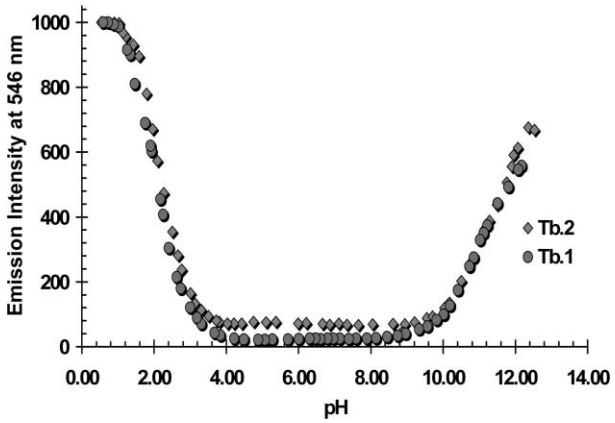


Fig. 5 The changes in the Tb(III) emission at 546 nm for **Tb·1** and **Tb·2** as a function of pH (10 μM, λ_{exc} = 300 nm) using dilute HCl titration of alkaline (TMACl) solution. These changes were fully reversible.

From the changes in the 546 nm transitions shown in Fig. 5, we were able to determine two pK_a values of 2.8 (± 0.2) and 11.2 (± 0.2) for **Tb·1**. As before the latter pK_a was attributed to the deprotonation of the delocalized aniline moiety adjacent to the metal ion. This assignment is also supported by the rational that the aniline furthest from the lanthanide complex is too far to allow an efficient energy transfer (ET) to modulate the Tb(III) emission. This supports the results observed previously for the pH dependence of the singlet excited state, where the Tb(III) emission was only observed in highly acidic media. When this experiment was performed using the structurally similar complex **Tb·2**, Fig. 5, the same pH dependence was observed, and pK_a of 3.0 (± 0.2) and 11.0 (± 0.2) were determined. We also evaluated the changes in the Tb(III) emission in degassed solution, as we have previously demonstrated that Tb(III) having quinoline antennae are prone to quenching due to back energy transfer from the $^5D_4$ to the T_1 of the antenna where it is quenched by O_2. However, for the above Tb(III) complexes, only a minor enhancement was observed, indicating that this quenching pathway was absent.

Similar pH experiments were also performed on the charge neutral triacetate based complexes **Tb·3** and **Tb·4**. At pH = 7, the Tb(III) emissions of both complexes were weak, indicating that the emission was '*switched off*'. When the pH was decreased below pH 4.0, a significant enhancement was observed for the Tb(III) emission where the $J = 5$ transition (at pH 0.3) had been '*switched on*' by a factor of *ca.* 46. Interestingly, both complexes were shown to be pH independent above pH 4.0, Fig. 6. As before, the changes were attributed to the protonation of the aromatic amine of the diaza crown ether adjacent to the Tb(III) centre.

This striking difference between **Tb·1** and **Tb·2**, which display '*on–off–on*' switching as a function of pH, and **Tb·3** and **Tb·4**, showing '*on–off*' switching as a function of pH, is intriguing. The main difference between these four complexes is the coordination environment of the Tb(III) ion, which for **Tb·1** and **Tb·2** consists of four carboxylic amides yielding overall cationic complexes, whereas for **Tb·3** and **Tb·4** the coordination is through a single carboxyl amide (the receptor/antenna) and three acetates, giving an overall charge neutral complex. Hence,

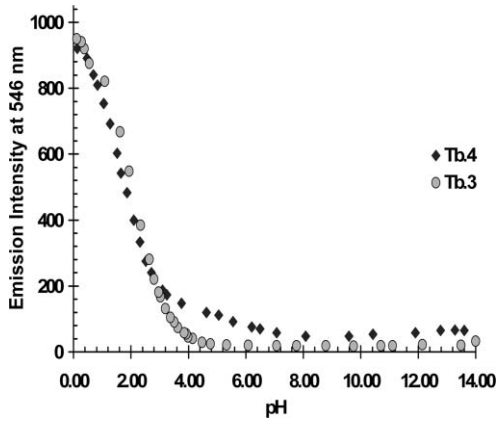


Fig. 6 The changes in the Tb(III) emission of **Tb·3** and **Tb·4** at 546 nm, as a function of pH. These changes were fully reversible.

to investigate the differences in the pH dependence on the basis of a possible coordination effect, we carried out detailed lifetime studies of all of the Tb(III) complexes in H_2O and D_2O, as a function of pH or pD using the Horrrocks equation:[24]

$$q^{Tb(III)} = 5.0[(1/\tau_{H_2O} - 1/\tau_{D_2O}) - 0.06]$$

We conducted a study of our complexes by direct excitation of the lanthanide complexes, at 365 nm as such direct excitation should consequently give information of the coordination environment of the metal ion itself, independent of the efficiency of the sensitization process. The results are presented in Table 1.

The measurements were first recorded at neutral pH and pD, where the emission was, in all cases, '*switched off*'. When recorded in water, lifetimes of 0.16, 0.18, 0.77 and 0.47 ms were determined for **Tb·1–4**, respectively. Noticeably, the overall charge neutral complexes give substantially longer excited state lifetimes than the cationic equivalents. A similar trend was also observed in D_2O. These results clearly support our findings that the coordination environment does additionally affect the lanthanide ion emission. However, the difference between the charge neutral and the cationic complexes were again apparent as the **Tb·1** and **Tb·2** lifetimes were almost identical in both media. At the same time, the neutral complexes were on average 30% longer. As predicted, these results also demonstrate that all the complexes have a single bound water molecule under neutral pH conditions (see q in Table 1).

When the lifetimes were determined in acidic solution at pH ~ 1 considerable changes were observed. Firstly, a significant increase was observed for τ of all the complexes in both H_2O and in D_2O. Lifetimes of 0.91 ms, 1.29 ms, 1.31 ms and 1.23 ms being determined for **Tb·1–4**, respectively when measured in H_2O. This indicated that unlike that at pH 7, all the complexes had similar lifetimes. Furthermore, all the complexes were shown to have $q \sim 1$. Lifetime analysis for **Tb·1** and **Tb·2** at pH ~ 12 produced similar results. However, the most interesting trend was seen for the determination of the q-values between these complexes at pH ~ 12. Here the τ_{H_2O} for **Tb·1** and **Tb·3** on one hand, and **Tb·2** and **Tb·4** on the other hand, were all of similar magnitude. However, only **Tb·1** and **Tb·2** produced meaningful q-values of *ca.* 1, whereas **Tb·3** and **Tb·4** gave inconclusive q-values of −0.35 and −2.5, respectively. Even though, this method does not conclusively explain why the tetra-amide based

Table 1 Determination of excited state lifetimes and q-values

	τ_{H_2O}/ms	k_{H_2O}/ms^{-1}	τ_{D_2O}/ms	k_{D_2O}/ms^{-1}	q (±0.5)
pH 7					
Tb·1	0.16(1)	6.21(1)	0.17(0)	5.88(2)	1.3
Tb·2	0.18(1)	5.52(4)	0.18(9)	5.29(1)	0.9
Tb·3	0.77(8)	1.28(5)	1.04(8)	0.95(4)	1.4
Tb·4	0.47(0)	2.12(7)	0.53(0)	1.88(6)	0.9
pH 1					
Tb·1	0.90(5)	1.10(5)	1.15(9)	0.86(3)	0.9
Tb·2	1.29(3)	0.77(3)	1.99(0)	0.50(2)	1.1
Tb·3	1.31(2)	0.76(2)	2.23(2)	0.44(8)	1.3
Tb·4	1.23(3)	0.81(1)	2.01(7)	0.49(6)	1.3
pH 12					
Tb·1	1.06(4)	0.94(0)	1.55(8)	0.64(1)	1.2
Tb·2	0.42(5)	2.34(8)	0.48(1)	2.07(5)	1.1
Tb·3	1.13(4)	0.88(2)	1.11(9)	0.89(3)	NA
Tb·4	0.41(4)	2.41(5)	0.35(2)	2.84(0)	NA
Saturated with NaCl[a]					
Tb·1	0.43(9)	2.27(8)	0.51(6)	1.93(9)	1.4
Tb·3	0.80(9)	1.23(6)	1.06(5)	0.93(9)	1.2
Saturated with KCl[a]					
Tb·2	0.57(3)	1.74(5)	0.65(2)	1.53(3)	0.8
Tb·4	0.48(9)	2.04(7)	0.56(6)	1.76(8)	1.1

[a] As the q-value does not change in the presence of (saturated concentrations) NaCl or KCl it can be concluded that the complex is kinetically stable in the presence of these ions, and that the chloride anion is not coordinated to the lanthanide ion. Using NaOAc gave similar results, confirming that the counterion was not displacing the metal bound water molecule and hence increasing the Tb(III) emission due to displacement of the quenching water molecule.

ligands show this dual pH behaviour and the carboxylates do not, this experiment suggests a possible change in the Tb(III) coordination environment as a potential cause. One scenario is that the pendent arms can be more affected by the pH than previously anticipated. However, as the pH-titrations were fully reversible it is unlikely that this leads to dissociation of the metal ion from the cyclen moiety. Further studies of model compounds are necessary to fully elucidate this mechanism and we are currently undertaking these investigation.

Switching the Tb(III) emission of Tb·1 and Tb·3 with Na^+ and several other competitive group I and II ions at pH 7.4

As discussed above we had demonstrated that the ground state and the singlet excited states of the antennae were modulated upon recognition of either Na^+ or K^+ (as Cl^- or AcO^- solutions) it was thus anticipated that the same would be the case for the Tb(III) emission. The results of the titration of **Tb·1** in water with NaCl at pH 7.4 are depicted in Fig. 7. It shows that prior to the addition of Na^+ the complex was only weakly emissive, and that upon gradual titration with NaCl solution the emission was gradually '*switched on*', demonstrating that the Tb(III) emission was modulated by Na^+. Of the $^5D_4 \rightarrow {}^7F_J$ transitions, the strongest emission changes were observed for the 546 nm transition with 7-fold enhancement. The changes in the intensity of this band as a function of the concentration of Na^+ and other ions tested are shown in Fig. 8. It is important to note that the luminescent enhancement was not observed until at high concentration and that no further titrations were carried out above 1.23 M. The same concentration dependence

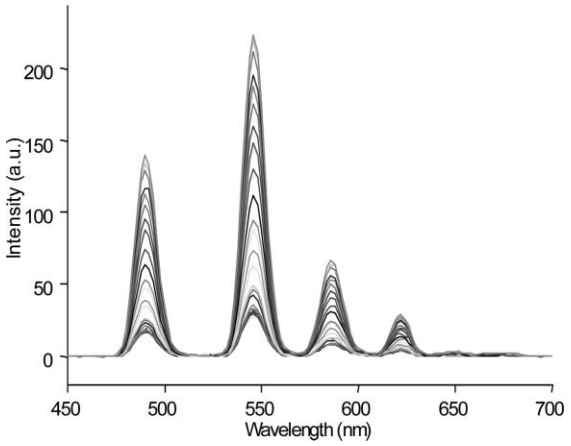


Fig. 7 The changes in the Tb(III) emission of **Tb·1** (4 μM; $\lambda_{exc} = 300$ nm) as a function of Na^+ where the emission is '*switched on*'.

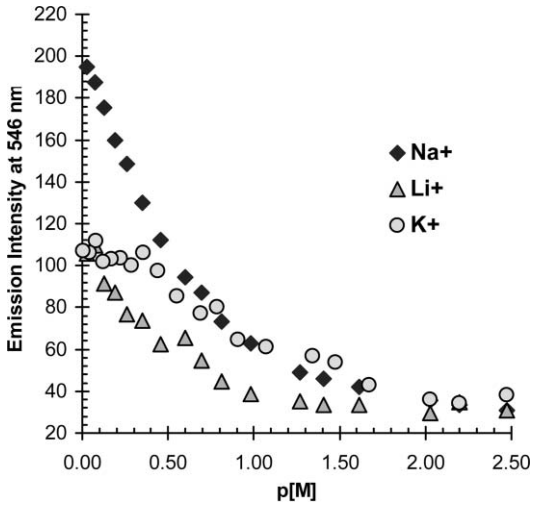


Fig. 8 The changes in the Tb(III) emission of **Tb·1** as a function of pM, where M = Na^+, K^+ and Li^+.

was also observed when these measurements were repeated using NaOAc. However, as the emission was not fully '*switched on*', we were unable to determine accurate binding values from these changes. Similar titration experiments were also performed on **Tb·1** in buffered solutions using KCl or LiCl, Fig. 8. In the case of KCl the emission was enhanced by *ca.* 3-fold after the addition of 1.23 M whereas, a 4-fold enhancement was observed for Li^+ at the same concentration. This demonstrates that the size of the aza crown ether discriminates the selectivity of the recognition process as expected and that Na^+ gives the largest luminescent enhancements and is selectively detected. Similar measurements were carried out on **Tb·3**. Here, the response to Na^+, K^+ and Li^+ mirrored the results observed for **Tb·1**, indicating that, unlike that seen in the pH titrations above, the Tb(III) emission of both systems was modulated to the same extent in the presence of these Group I ions, see ESI.†

The relatively high concentration needed to '*switch the emission on*' for these systems is worth commenting on. We attributed the changes in the sensitivity of the lanthanide ion complexes described herein, in comparison to that observed for **13** and **14** above, to be due to enhanced delocalization of the aniline nitrogen lone pair of the aryl amide moiety adjacent to the luminescent moiety which makes it less available to coordination of either Na^+ or K^+. Although these complexes operate at rather high concentrations this does not however, detract from the fact that the Tb(III) emission can be modulated by an ionic input, *e.g.* a metal based emission can nevertheless be tuned by the recognition of a group I ion species, in kinetically stable lanthanide complexes, with a large order of magnitude difference in their '*off*' to '*on*' stages.

The changes in the lifetime of the Tb(III) excited state in the presence of Na^+ were also measured for these complexes, and the results of these are shown in Table 1. These demonstrated a significant enhancement from 0.16 ms, in the free form, to 0.48 ms upon Na^+ complexation for **Tb·1**. This indicates at least a partial coordination of Na^+ to the aniline nitrogen in a similar way to protonation causing modulation of the Tb(III) emission. From these measurements we determined a value of $q = 1.4$ which indicates that the counter ion Cl^- ion does not displace the metal bound water molecule. The changes in the lifetimes, support the idea that the triplet energy of the antenna/receptor had increased upon binding of Na^+ in a similar way to that discussed previously for the pH titration.

Switching the Tb(III) emission of Tb·2 and Tb·4 with K^+ and several other competitive group I and II ions at pH 7.4

Identical ion titrations to those shown above were performed on **Tb·2** and **Tb·4**, which were designed to be selective towards K^+ ions. As before, the Tb(III) emission was substantially modulated by K^+, as the emission was '*switched on*' in the presence of K^+. These were also significantly larger enhancements than seen for the Na^+ analogues above, with *ca.* 31-fold luminescent enhancement being determined for **Tb·2**. However, again these only occurred at relatively high concentrations. As observed for the Na^+ complexes earlier, the *q*-value was measured to be *ca.* ~ 1, and the lifetimes showed similar trends in comparison to those determined at pH ~ 1 or ~7, Table 1. These titrations were also carried out using a range of other metal chloride salts such as Na^+, Li^+, Mg^{2+} and Ca^{2+} to demonstrate the selectivity of **Tb·2** toward K^+ and the results of these are presented in Fig. 9. Unlike that seen for the smaller diaza-15-crown-5 ethers earlier, no enhancement was observed in the Tb(III) emission when **Tb·2** was titrated with Li^+. This was expected as the receptor of **Tb·2** was designed for K^+ and would be too large to efficiently bind Li^+. For Na^+ the emission was also modulated with *ca.* 6-fold luminescence enhancement. Titrations of **Tb·2** with Ca^{2+} and Mg^{2+} showed 8- and 3-fold enhancements respectively (at higher concentrations).

Similar titrations were also performed on **Tb·4**, in buffered pH 7.4 solution. The largest changes were seen for K^+ which

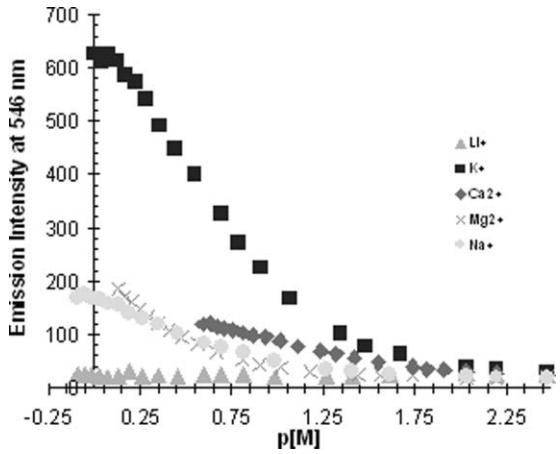


Fig. 9 The changes in the Tb(III) emission of **Tb·2** as a function of pM, where M = Na^+, K^+, Ca^{2+}, Mg^{2+} and Li^+.

resulted in an overall 40-fold luminescent enhancement. The selectivity of this sensor/switch towards K^+ was demonstrated in titration experiments performed using Na^+, Li^+, Ca^{2+} and Mg^{2+} chloride salts. Titrations of **Tb·4** with Ca^{2+} and Mg^{2+} both resulted in a 9-fold enhancement, whereas no change was observed for Li^+. As in the case of **Tb·2**, the luminescence was enhanced for all of the above ions except Li^+. These results clearly indicated that the changes in the receptor part of the conjugate has to take place for modulation of the Tb(III) emission to occur, and that unlike the smaller crown-ether receptors, the Li^+ is not strongly complexed, or recognised, and hence does not lead to modulation of the Tb(III) emission.

When the emission of these complexes was recorded in the presence of high concentrations of either Na^+ or K^+, respectively, but in degassed solutions, no luminescent enhancements were observed indicating the absence of any back energy transfer to the T_1 of the antennae. The stability of all the above complexes was also investigated by recording the delayed lanthanide luminescence over a period of days and weeks. On all occasion the Tb(III) emission was observed under identical experimental conditions, which demonstrated that the complexes were stable to Tb(III) ion dissociation over this period of time.

Conclusion and summary

The synthesis and characterization of several bis-macrocyclic ligands **1–4** and the photophysical evaluation of the Tb(III) lanthanide complexes **Tb·1**, **Tb·2**, **Tb·3** and **Tb·4** were undertaken. Photophysical analysis of these complexes showed that all these complexes were stable in solution, and that both the ground state and the singlet excited states were effected or modulated by the presence of ions such as H^+, Na^+ or K^+. We established that the Tb(III) emission was pH independent over the pH window of 4–8, where it was '*switched off*. In buffered pH 7.4 solution, the Tb(III) luminescence emission was, however, found to be greatly modulated by either Na^+ or K^+, where the sensitivity and the luminescent enhancements was in all cases related to the size of the receptor *e.g.* this was most clearly seen for **Tb·2** and **Tb·4** where Li^+ did not modulate the Tb(III) emission whereas K^+ did.

Experimental

Starting materials were obtained from Sigma Aldrich, Strem Chemicals and Fluka. Columns were run using Silica gel 60 (230–400 mesh ASTM) or Aluminum Oxide (activated, Neutral, Brockmann I STD grade 150 mesh). Solvents used were HPLC grade unless otherwise stated. ^{1}H NMR spectra were recorded at 400 MHz using a Bruker Spectrospin DPX-400 instrument. Tetramethylsilane (TMS) was used as an internal reference standard, with chemical shifts expressed in parts per million (ppm or δ) downfield from the standard. ^{13}C NMR were recorded at 100 MHz using a Bruker Spectrospin DPX-400 instrument. Infrared spectra were recorded on a Mattson Genesis II FTIR spectrophotometer equipped with a Gateway 2000 4DX2–66 workstation. Oils were analyzed using NaCl plates, solid samples were dispersed in KBr and recorded as clear pressed discs. Mass spectroscopy was carried out using HPLC grade solvents. Mass spectra were determined by detection using Electrospray on a Micromass LCT spectrometer, using a Shimadzu HPLC or Water's 9360 to pump solvent. The whole system was controlled by MassLynx 3.5 on a Compaq Deskpro workstation. All spectroscopic studies were carried out on solutions of complexes in water or in buffered solutions at 10, 8 or 4 μM. Buffered solutions consisted of 0.1 M TRIS Buffer and 0.1 M TMACl at pH 7.4. Solutions were 5 mL, 10 mL or 20 mL. Uv-vis spectroscopy analysis was carried out on a Shimadzu UV-2401 PC UV-Vis spectrophotometer. Studies were carried out on fast scan mode with slit widths of 1.0 nm, using matched quartz cells. Excitations were carried out at 300 nm unless otherwise stated. Fluorescence and luminescence measurements were made on a Perkin Elmer LS 50B or Varian Carey Eclipse

General procedure for the formation of α-chloroamides (7 and 8)

Compound **5**, (0.559 g, 1.256 mmol) [or **6**, (0.687 g, 1.40 mmol) in the case of **8**] was placed into a 50 mL single neck RBF along with 1,4-dioxane (99+%, ACS grade) (20 mL). To this was added 1.1 equivalents of Na_2CO_3. This solution was stirred at room temperature. To this a solution of 1,4-dioxane (99+%, ACS grade) (10 mL), containing 1.1 equivalents of α-chloroacetic anhydride was added. The resulting solution was stirred at room temperature overnight. The solution was then reduced and the resulting residue was dissolved in water (50 mL) and the pH was adjusted to pH 1 with conc. HCl. The solution was then washed with DCM (2 × 30 mL). The aqueous phase pH was adjusted to pH 14 with KOH pellets and washed with DCM (2 × 30 mL). The organic phase was dried over $CaCl_2$ and reduced to a crude oil. The oil was run down an alumina column using a gradient elution of DCM to DCM–THF (30 : 70).

2-Chloro-*N*-{3-methoxy-4-[13-(2-methoxyphenyl)-1,4,10-trioxa-7,13-diazacyclopentadec-7-yl]phenyl}acetamide (7). Compound **7** was produced as an oil. (0.409 g, 62.26% yield). Calc. for $C_{26}H_{37}N_3O_6Cl$: [M + H] m/z = 522.2371. Found: 522.2374 (+ 0.6 ppm); δ_H ($CDCl_3$, 400 MHz) 8.30 (s, 1H, N–H), 7.30 (s, 1H, Ar–H), 7.03 (t, 1H, J = 8.0 Hz, Ar–H), 6.98 (d, 1H, J = 5.5 Hz, Ar–H), 6.94–6.83 (m, 4H, Ar–H), 4.18 (s, 2H, Cl–CH_2), 3.83 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.74–3.61 (m, 12H, –OCH_2CH_2O–), 3.49–3.40 (m, 8H, –OCH_2CH_2O–); δ_C ($CDCl_3$, 100 MHz) 163.59, 153.29, 153.0, 140.55, 137.77, 131.72, 122.24, 121.42, 121.10, 120.75, 112.25, 111.95, 105.03, 71.19, 71.05, 70.77, 69.80, 69.80, 69.71, 55.52, 55.39, 53.28, 53.25, 52.65, 52.65, 49.92; MS (MeCN, ES^+) m/z Expected: 521.2. Found: 522.2 (M + H); IR ν_{max}/cm^{-1}: 3033, 3199, 3116, 3055, 2946, 2869, 1684, 1606, 1541, 1509, 1452, 1411, 1350, 1239, 1175, 1110, 1030, 926, 857, 801, 745.

2-Chloro-*N*-{3-methoxy-4-[16-(2-methoxyphenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl]phenyl}acetamide (8). Compound **8** was produced as an oil. (0.490 g, 61.67% yield). Calc. for $C_{28}H_{41}N_3O_7Cl$: [M + H] m/z = 566.2633. Found: 566.2642 (+ 1.6 ppm); δ_H ($CDCl_3$, 400 MHz) 8.39 (s, 1H, N–H), 7.34 (s, 1H, Ar–H), 7.17–7.11 (m, 2H, Ar–H), 6.98–6.95 (m, 2H, Ar–H), 6.91 (t, 1H, J = 8.0 Hz, Ar–H), 6.85 (d, 1H, J = 8.0 Hz, Ar–H), 4.21 (s, 2H, Cl–CH_2), 3.85 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.60–3.51 (m, 24H, –OCH_2CH_2O–); δ_C ($CDCl_3$, 100 MHz) 163.64, 153.38, 153.15, 139.40, 136.55, 132.00, 122.50, 121.80, 121.53, 120.77, 112.29, 111.89, 104.94, 70.58, 69.98, 69.88, 55.57, 55.42, 52.79, 52.73, 42.98; MS (MeCN, ES^+) m/z Expected: 565.2. Found: 566.2 (M + H); IR ν_{max}/cm^{-1} 3272, 3186, 3106, 3042, 2936, 2872, 1688, 1607, 1543, 1502,

1453, 1411, 1352, 1288, 1240, 1174, 1109, 1031, 991, 914, 858, 815, 730.

General synthesis of 1, 2, 11 and 12

Compound **7**, (0.2815 g, 0.658 mmol) [or **8**, (0.468 g, 0.828 mmol) in the case of **2**] and 1 equivalent of **9** [or **10** in the case of **11** and **12**] was placed into a 50 mL single-neck RBF. To this was added 1 equivalent of Cs_2CO_3 and 40 mL of dry MeCN. The solution was kept under dry conditions in an argon atmosphere and stirred at 72 °C for 72 h. The resulting mixture was cooled to room temperature and filtered through Celite. In the case of **1** and **2**, MeCN was removed under vacuum and the crude material dissolved in $CHCl_3$ (40 mL). This was washed with water (5 × 20 mL). The organic phase was separated dried over $MgSO_4$ and reduced to give the desired product in a relatively pure state. (Yields *ca.* 70%). In the case of **11** and **12**, MeCN was removed under vacuum to produce a crude oil. The crude oil was dissolved in a small quantity of DCM and placed onto a dry alumina column that was washed with DCM–THF (70 : 30) which was slowly changed by gradient dilution to DCM–THF–MeOH (60 : 30 : 10).

***N*-{3-Methoxy-4-[13-(2-methoxyphenyl)-1,4,10-trioxa-7,13-diazacyclopentadec-7-yl]phenyl}-2-(4,7,10-tris(dimethylcarbamoyl)-methyl-1,4,7,10-tetraazacyclododec-1-yl)acetamide (1).** Compound **1** was formed in *ca.* 77% yield. Calc. for $C_{46}H_{77}N_{10}O_9$: [M + H] m/z = 913.5875. Found: 913.5858 (−1.9 ppm); δ_C ($CDCl_3$, 100 MHz) 170.30, 170.21, 170.07, 153.0, 152.6, 151.3, 140.16, 135.60, 125.29, 122.06, 121.30, 120.66, 120.50, 111.55, 104.25, 71.01, 70.89, 70.82, 70.51, 69.47, 55.17, 54.74, 54.36, 53.13, 52.92, 52.33, 52.21, 51.84, 36.82, 36.26, 35.23, 34.92; MS (MeCN, ES^+) m/z Expected: 912.5. Found: 913.5 (M + H), 456.9 (M + 2H)/2; IR ν_{max}/cm^{-1} 3420, 2937, 2855, 1647, 1510, 1451, 1403, 1260, 1238, 1217, 1108, 1030, 859, 810, 747, 629, 489.

***N*-{3-Methoxy-4-[16-(2-methoxyphenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl]phenyl}-2-(4,7,10-tris(dimethyl)-carbamoylmethyl-1,4,7,10-tetraazacyclododec-1-yl)acetamide (2).** Compound **2** was formed in *ca.* 77% yield. Calc. for $C_{48}H_{81}N_{10}O_{10}$: [M + H] m/z = 957.6137. Found: 957.6188 (+5.3 ppm); δ_C ($CDCl_3$, 100 MHz) 170.28, 170.22, 170.07, 153.08, 152.80, 143.61, 138.80, 135.58, 125.27, 122.37, 121.63, 121.22, 120.47, 111.43, 104.16, 70.26, 69.54, 55.15, 54.78, 54.30, 52.93, 52.52, 52.42, 51.83, 36.82, 36.25, 35.22, 34.93; MS (MeCN, ES^+) m/z Expected: 956.6. Found: 957.6 (M + H), 979.0 (M + Na) 478.9 (M + 2H)/2; IR ν_{max}/cm^{-1} 3417, 2955, 2923, 2854, 1644, 1538, 1504, 1454, 1402, 1260, 1240, 1104, 1030, 812, 750.

[4,7-Bis-*tert*-butoxycarbonylmethyl-10-({3-methoxy-4-[13-(2-methoxyphenyl)-1,4,10-trioxa-7,13-diazacyclopentadec-7-yl]phenylcarbamoyl}methyl)-1,4,7,10-tetraazacyclododec-1-yl]-acetic acid *tert*-butyl ester (11). Compound **11** was formed in *ca.* 57% yield. Calc. for $C_{52}H_{86}N_7O_{12}$: [M + H peak] m/z = 1000.6334. Found: 1000.6307 (−2.8 ppm); δ_C ($CDCl_3$, 100 MHz) 172.58, 172.09, 170.18, 152.52, 151.20, 140.13, 135.48, 134.93, 122.05, 121.16, 120.64, 120.55, 112.27, 111.63, 105.35, 81.57, 81.52, 70.69, 70.41, 69.45, 67.63, 56.47, 55.50, 55.31, 55.08, 53.04, 52.72, 52.41, 52.22, 27.69, 27.62; MS (MeCN, ES^+) m/z Expected: 999.6. Found: 1000.6 (M + H), 1022.6 (M + Na), 500.7 (M + 2H)/2; IR ν_{max}/cm^{-1} 3428, 2975, 2854, 1728, 1681, 1607, 1504, 1454, 1368, 1312, 1228, 1166, 1106, 1008, 852, 756, 597.

[4,7-Bis-*tert*-butoxycarbonylmethyl-10-({3-methoxy-4-[16-(2-methoxyphenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl]phenylcarbamoyl}methyl)-1,4,7,10-tetraazacyclododec-1-yl]acetic acid *tert*-butyl ester (12). Compound **12** was formed in *ca.* 36% yield. Calc. for $C_{54}H_{90}N_7O_{13}$: [M + H peak] m/z = 1044.6597. Found: 1044.6619 (+ 2.1 ppm); δ_H ($CDCl_3$, 400 MHz) [Partial NMR only] 10.82 (1H, N–H), 7.36 (d, 1H J = 8.52 Hz, Ar–H), 7.29 (s, 1H, Ar–H), 6.99 (d, 1H, J = 7.5 Hz, Ar–H), 6.82–6.78 (m, 2H, Ar–H), 6.75 (t, 1H, J = 7.5 Hz, Ar–H), 6.68 (d, 1H, J = 8.0 Hz, Ar–H), 1.32 (s, 9 H, *tert*-butyl CH_3), 1.30 (s, 18 H, *tert*-butyl CH_3); δ_C ($CDCl_3$, 100 MHz) 172.37, 171.94, 170.03, 152.60, 151.00, 135.31, 134.75, 127.67, 122.07, 120.90, 120.18, 112.02, 111.18, 104.95, 81.54, 81.31, 69.69, 69.28, 67.42, 55.30, 55.11, 54.89, 52.39, 52.14, 27.51, 27.44; MS (MeCN, ES^+) m/z Expected: 1043.6. Found: 1044.6 (M + H), 1066.7 (M + Na), 522.8 (M + 2H)/2; IR ν_{max}/cm^{-1} 3420, 2974, 2857, 1728, 1680, 1607, 1512, 1454, 1368, 1311, 1165, 1105, 1008, 852, 755, 598.

General synthesis of 3 and 4

The triester, **11** (or **12**) (0.162 mmol) was placed into a 25 mL single neck RBF. To this was added DCM (12 mL) and TFA (5 mL). The solution was stirred for 24 h at room temperature. The solvent was removed under reduced pressure and the acid chased off by the addition and evaporation of successive portions of DCM (2 × 10 mL), MeOH (2 × 10 mL) and diethyl ether (2 × 10 mL). The resulting residue was dissolved into MeOH (0.25 mL) to which ether (10 mL) was added dropwise yielding the desired product as a solid. This was filtered off, washed with cold ether and dried under vacuum. Both gave yields of >80%.

[4,7-Bis(carboxymethyl)-10-({3-methoxy-4-[13-(2-methoxyphenyl)-1,4,10-trioxa-7,13-diazacyclopentadec-7-yl]phenylcarbamoyl}methyl)-1,4,7,10-tetraazacyclododec-1-yl]acetic acid (3). Compound **3** was formed in *ca.* 82% yield. Calc. for $C_{40}H_{62}N_7O_{12}$: [M + H peak] m/z = 832.4456. Found: 832.4462 (+0.6 ppm); δ_H (CD_3CN, 400 MHz) 10.88 (br s, 1H), 8.41 (br s, 1H), 7.57 (br s, 2H, Ar–H), 7.51 (s, 1H, Ar–H), 7.38–7.36 (m, 2H, Ar–H), 7.12–7.10 (m, 1H, Ar–H), 7.04 (s, 1H, Ar–H), 3.84 (br s, 6H), 3.61 (br s, 10H), 3.43–3.38 (m, 16H), 3.18 (br s, 20H); MS (MeCN, ES^+) m/z Expected: 831.44. Found: 832.3 (M + H), 854.3 (M + Na), 416.6 (M + 2H)/2, 278.1 (M + 3H)/3; IR ν_{max}/cm^{-1} 3429, 3104, 2958, 2924, 2854, 1683, 1504, 1461, 1375, 1355, 1203, 1181, 1127, 1104, 828, 801, 721, 689, 620, 598, 516.

[4,7-Bis(carboxymethyl)-10-({3-methoxy-4-[16-(2-methoxyphenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl]phenylcarbamoyl}methyl)-1,4,7,10-tetraazacyclododec-1-yl]acetic acid (4). Compound **4** was formed in *ca.* 89% yield. Calc. for $C_{42}H_{66}N_7O_{13}$: [M + H peak] m/z = 876.4719. Found: 876.4722 (+ 0.4 ppm); δ_H (CD_3CN, 400 MHz) 10.88 (br s, 1H), 8.64 (br s, 1H), 7.59 (br s, 1H), 7.45 (br s, 1H), 7.27 (br s, 3H), 7.18 (s, 1H,), 7.07–7.01 (br m., 3H, Ar–H), 4.25–4.08 (br m., 4H, Ar–H), 3.80 (br s, 9H), 3.48 (s, 27H), 3.15 (br s, 12H), 2.65 (br s, 2H); δ_C (CD_3CN, 100 MHz) 173.18, 169.82, 169.43, 165.46, 154.50, 138.10, 126.41, 123.68, 121.12, 118.12, 115.26, 111.59, 102.99, 68.52, 66.62, 57.68, 56.36, 55.12, 54.45, 53.96, 53.36, 53.17, 52.84, 50.99, 49.33, 48.37, 46.80, 44.01; MS (MeCN, ES^+) m/z Expected: 875.4. Found: 876.5 (M + H), 898.5 (M + Na), 439.1 (M + 2H)/2, 292.8 (M + 3H)/3; IR ν_{max}/cm^{-1} 3429, 3104, 2957, 2921, 2880, 1688, 1512, 1462, 1353, 1202, 1178, 1123, 1093, 827, 764, 719, 690, 618, 569, 513.

General synthesis of Tb(III) complexes

Compounds **1** or **2** (~100 mg, ~0.1 mmol) and Ln(III) triflouromethane sulfonate (0.1 mmol) were added to a 5 mL single neck RBF that contained 3 mL of freshly dried MeCN. The solution was freeze–pump–thawed three times, placed under an argon atmosphere and left stirring at reflux for 24 h. The resulting solution was cooled to room temperature and then dropped slowly onto dry diethyl ether (50–70 mL). In the case of **Tb·1** and **Tb·2** the diethyl ether was decanted to leave these complexes in a crude state. These were dissolved in a small quantity of DCM and placed onto dry alumina plugs that were washed with DCM–THF (70 : 30) which was slowly changed by gradient dilution to DCM–THF–MeOH (60 : 30 : 10) to

afford the desired products. In the case of **Tb·3** and **Tb·4**, a white precipitate was collected. The solvent was decanted off and the white solid was washed with cold ether (2 × 5 mL). The resulting solid was dried under vacuum.

Tb·1. was formed in 36% yield. Calc. for $C_{46}H_{77}N_{10}O_9Tb$: [M + H peak] $m/z = 1072.5128$. Found: 1072.5160 (+ 3.0 ppm); δ_H (CD_3CN, 400 MHz) 68.59, 41.76, 23.72, 18.13, 10.36, 8.69, 7.05, 6.77, 6.56, 5.58, 5.25, 4.82, 4.27, −1.42; δ_F (CD_3CN, 376 MHz) −77.68; MS (MeCN, ES^+) m/z Expected: 1072.51. Found: 356.92 (M/3), 609.82 (M + [Triflate])/2, 684.76 (M + 2[Triflate])/2; IR ν_{max}/cm^{-1} 3425, 2955, 2924, 2873, 1624, 1560, 1511, 1461, 1356, 1258, 1158, 1119, 1082, 1030, 957, 823, 756, 638, 573, 517.

Tb·2. was formed in 32% yield. Calc. for $C_{51}H_{82}N_{10}O_{20}S_3F_9Tb{\cdot}2THF$: C, 41.07; H, 5.72; N, 8.12. Found: C, 40.93; H, 5.44; N, 7.63;. Calc. for $C_{48}H_{81}N_{10}O_{10}Tb$: [M + H peak] $m/z = 1116.5391$. Found: 116.5390 (−0.1 ppm); δ_H (CD_3CN, 400 MHz) 77.2 (br s), 55.7 (br s), 46.9 (br s), 22.51 (br s), 17.52 (br s), 15.65 (br s), 9.31–8.62 (m), 5.39 (br s), 4.77 (br s), 3.85 (br s), 3.55 (br s), 2.92 (br s), 2.51 (br s), 1.74 (br s), −73.14 (s), −89.81 (s), −97.28 (s); δ_F (CD_3CN, 376 MHz) −78.52; MS (MeCN, ES^+) m/z Expected: 1116.53. Found: 371.60 (M/3), 631.84 (M + [Triflate])/2, 706.74 (M + 2[Triflate])/2; IR ν_{max}/cm^{-1} 3427, 2924, 2877, 1624, 1561, 1511, 1461, 1411, 1354, 1258, 1159, 1119, 1088, 1030, 957, 823, 756, 638, 573, 516.

Tb·3. was formed in 93% yield. Calc. for $C_{40}H_{59}N_7O_{12}Tb$: [M + H peak] $m/z = 988.3475$. Found: 988.3458 (−1.7 ppm); δ_H (CD_3CN, 400 MHz) 7.13, 3.38, 1.94, 1.09, −3.56; MS (MeCN, ES^+) m/z Expected 987.34. Found: 988.26 (M + H), 494.67 (M + 2H)/2, 1010.34 (M + Na), 505.65 (M + Na)/2; IR ν_{max}/cm^{-1} 3481, 3111, 2987, 2927, 1612, 1504, 1460, 1408, 1276, 1257, 1165, 1086, 1030, 802, 760, 721, 639, 574, 517.

Tb·4. was formed in 98% yield. Calc. for $C_{42}H_{63}N_7O_{13}Tb$: [M + H peak] $m/z = 1032.3737$. Found: 1032.3741 (+ 0.4 ppm); δ_H (CD_3CN, 400 MHz) 7.65, 7.28, 6.98, 6.18, 5.48, 4.04, 3.59, 3.43, 1.34, 1.28, 1.14, 0.75, −1.47; MS (MeCN, ES^+) m/z Expected: 1031.37. Found: 1032.23 (M + H), 516.56 (M + 2H)/2, 344.73 (M + 3H)/3; IR ν_{max} (cm^{-1}) 3444, 2924, 2885, 1611, 1545, 1459, 1408, 1260, 1169, 1080, 1031, 841, 802, 761, 721, 640, 575, 518.

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