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# Ferrocene-appended and bridged calixarene ligands for the electrochemical sensing of trivalent lanthanide ions

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A novel family of ferrocene-derivatised calix[4]arene ligands possessing ester amide and acid amide co-ordination groups has been prepared. UV/VIS, electrospray mass spectrometry and electrochemical co-ordination studies reveal these ligands form thermodynamically 1 : 1 stable complexes with lanthanide ions. Electrochemical studies show these redox-active ligands electrochemically recognise trivalent lanthanide ions *via* significant anodic perturbations of the ferrocene–ferrocenium redox couple. With a ferrocene-bridged calixarene dimer containing ester, amide and phenolic co-ordination functionalities, anodic shifts as large as 200 mV are observed on addition of one equivalent of lanthanide ion.

## Introduction

Molecular sensors are required for the efficient detection of charged and neutral pollutant species within organic and aqueous effluents. In the presence of the substrate molecule or ion the chemical sensor is designed to exhibit a physical response which can easily be detected.[1] In particular redox-active molecular receptors have been designed to sense target guest species *via* means of an electrochemical response. For example, ferrocene-containing ligands have previously been shown electrochemically to sense alkali-, alkaline-earth- and transition-metal ions and more recently anions.[2,3]

Calixarenes when suitably functionalised may serve as excellent hosts or ligands for cations,[4,5] anions[6] and neutral guest species[7] and are excellent platforms upon which to append sensing moieties. These rigid, macrocyclic ligands often exhibit remarkable selectivity in the complexation of metal cations[8] and their potential application in the treatment of metal rich nuclear wastes has been investigated worldwide.[9]

Acid-amide derivatised calixarene ligands (Ac-Am) were developed for the extraction of toxic metal ions including lanthanides from aqueous solutions.[10] These ligands and other simple derivatives have been found selectively to extract a range of lanthanide- and heavy-metal ions from solution. As a further development with these ligands, we chose to introduce an electro-active ferrocene moiety into the calixarene framework to determine whether these compounds could then be exploited electrochemically to sense and detect the presence of lanthanide ions. We report here the preparation of a novel family of ferrocene-appended and bridged calixarenes which complex and electrochemically recognise lanthanide ions.

## Results and discussion

Acid chloride calix[4]arene[10] **1** was condensed with an excess of the appropriate mono-Boc-protected diamine in dichloromethane (DCM) to yield the three Boc-protected amine calixarenes **2**–**4** (see Scheme 1). Treatment of **2**–**4** with chlorocarbonylferrocene gave the ferrocene-appended ester amide calixarenes **5**–**7** which were purified by chromatography on silica and isolated as orange solids in yields of 48–58%. Hydrolysis of **5**–**7** with potassium hydroxide gave acid amide ligands **8**–**10** in good yields, ≈80%. The $^1$H NMR and elemental analysis data were consistent with the proposed compounds **2**–**10**. Electrospray mass spectrometry of **5**–**10** diluted in dichloromethane–methanol solutions gave the protonated, sodium or potassium adducts of the molecular ions.

The condensation of 1,1′-bis(chlorocarbonyl)ferrocene with aminocalixarenes **2**–**4** afforded the ferrocene-bridged calixarenes **11**–**13** in 54–63% yields (Scheme 2). Ligands **11**–**13** were characterised by $^1$H NMR, ES-MS and elemental analysis. The $^1$H NMR spectrum of **12** displays expected peak patterns, which are simplified due to the symmetry of the lower rim 1,3-bis-substituted calix[4]arene derivatives. Amongst the characteristic peaks for **12**, two singlets appear at high field corresponding to 36 protons of the two inequivalent types of *p-tert*-butyl $CH_3$ protons ($\delta$ 0.92 and 1.22) and two singlets at lower field, $\delta$ 6.8 and 7.1, for the aromatic protons of the calix[4]arene phenol units. The resonances arising from the calix[4]arene methylene protons (Ar$CH_2$Ar) appear as two sets of two doublets between $\delta$ 3.3 and 4.3, characteristic of the cone conformation. Notably, the protons of the ferrocene moiety appear as multiplets each corresponding to four protons at $\delta$ 4.28 and 4.68 respectively. Unfortunately, attempts to hydrolyse ester-protected ligands **11**–**13** to their respective free acids using a variety of basic conditions were unsuccessful with decomposition of the calixarene ferrocene framework observed in all cases.

### Co-ordination studies

Previous crystal structure determinations of lanthanide ion binding by acid amide calixarenes show binding at the oxygen rich base of the calixarene cone.[10] The ligand is triply deprotonated with co-ordination to the metal centre by etheric, phenolate, carboxylate and carbonyl amide oxygen atoms. For example with the larger lanthanide ion europium a dimeric structure, [$Eu_2$(Ac-Am)$_2$($EtOH)_2$], is formed through bridging carboxylate moieties from each calixarene ligand. A solvent molecule of crystallisation completes the co-ordination sphere of this eight-co-ordinate lanthanide ion. In contrast the smaller lutetium ion is seven-co-ordinate and monomeric in the solid state.

To determine the interaction of lanthanide ions with the ferrocene-based calixarene ligands **5**–**10**, equivalents of lanthanide nitrate as dmso solvate were added to a solution of

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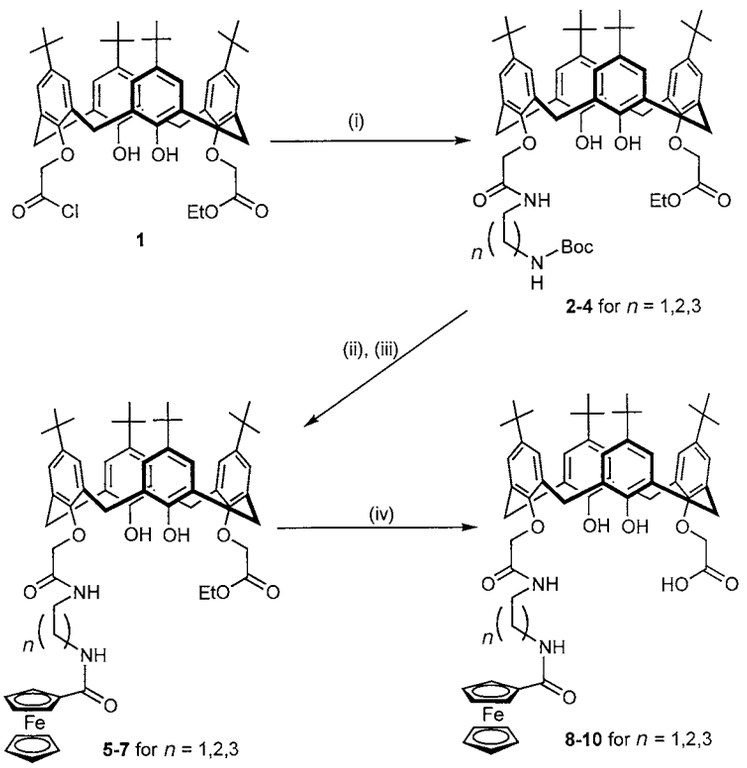
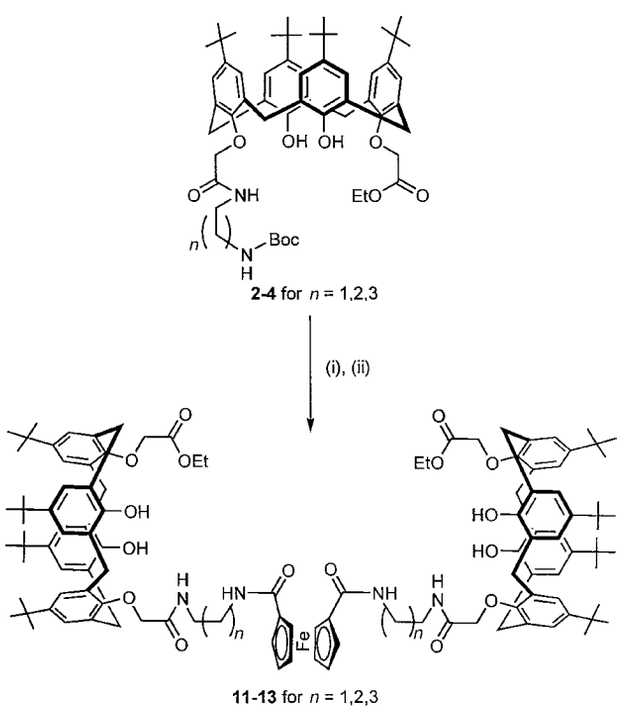



**Scheme 1** Synthesis of ferrocene-appended ligands **5**–**10**. (i) $BocNH(CH_2)_nNH_2$, $Et_3N$; (ii) TFA, DCM; (iii) Chlorocarbonylferrocene, $Et_3N$; (iv) KOH, EtOH, $H^+$.

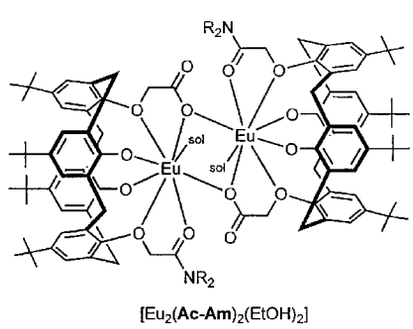



**Scheme 2** Synthesis of ferrocene-bridged ligands **11**–**13**: (i) TFA, DCM; (ii) 1,1′-bis(chlorocarbonyl)ferrocene, $Et_3N$.

**Table 1** Stability constants (log *K*) for the formation of $Ln^{3+}$ (calixarene) complexes in dmso at 298 K [a]

| Ligand | $La^{3+}$ | $Gd^{3+}$ | $Lu^{3+}$ |
|---|---|---|---|
| **5** [a] | 4.58 ± 0.19 | 4.44 ± 0.19 | 4.30 ± 0.18 |
| **6** [a] | 5.31 ± 0.35 | 4.64 ± 0.18 | 4.97 ± 0.18 |
| **7** [a] | 3.17 ± 0.46 | 2.95 ± 0.31 | 4.05 ± 0.22 |
| **8** [b] | 5.48 ± 0.02 | 4.11 ± 0.04 | 4.00 ± 0.04 |
| **9** [b] | 3.67 ± 0.03 | 4.12 ± 0.03 | 3.52 ± 0.07 |
| **10** [b] | 5.18 ± 0.59 | 3.21 ± 0.10 | 3.88 ± 0.05 |

[a] $Ln^{3+} + H_2L \rightleftharpoons [LnL]^+ + 2H^+$. [b] $Ln^{3+} + H_3L \rightleftharpoons [LnL] + 3H^+$.




$[Eu_2(\mathbf{Ac\text{-}Am})_2(EtOH)_2]$

ligand and triethylamine (10 equivalents) in dmso and the UV/VIS spectrum recorded. Successive amounts were added to generate a titration profile, which was analysed using the computer program SPECFIT[11] to obtain information on both the stoichiometry and stability of the metal–ligand complexation (Table 1). In all cases a stoichiometry model of 1 : 1 $Ln^{3+}$:calixarene was determined by analysis of the data. The series of UV/VIS spectra in a typical titration with lanthanum ion is shown in Fig. 1 with two isosbestic points observed at 277 and 295 nm. The observation of isosbestic points in all titrations strongly implicates the presence of only two species in solution, *i.e.* the uncomplexed ligand and the lanthanide–calixarene complex.

The magnitude of the stability constants in dmso (Table 1) demonstrates that all ligands form stable 1 : 1 complexes with lanthanide ions. No trends in stability constants are seen however which can be attributed to the lanthanide contraction. More surprisingly, stability constants for acid amide ligands **8**–**10** are no greater in magnitude than for ester amide ligands **5**–**7**. Previously, extraction studies with acid amide calixarene ligands have shown that trivalent lanthanide ions with the larger ionic radii, *e.g.* lanthanum, are extracted from aqueous solutions into dichloromethane more efficiently than smaller ions such as lutetium.[10] This trend in extraction does not appear

**Table 2** Electrospray mass spectral data (*m/z*) of ligands **7**, **10**, and **13** and their complexes with lanthanide ions

| Species | $La^{3+}$ | $Gd^{3+}$ | $Lu^{3+}$ |
|---|---|---|---|
| $[\mathbf{7}H_{-2}Ln]^+$ | 1211.5 | 1230.5 | 1247.5 |
| $[\mathbf{10}H_{-2}Ln]^+$ | 1183.5 | 1202.5 | 1219.5 |
| $[\mathbf{13}H_{-2}Ln]^+$ | 2103.2 | 2121.1 | 2141.0 |

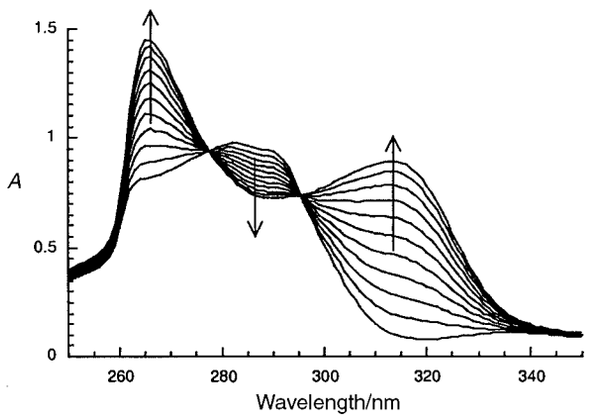



**Fig. 1** UV/VIS spectra of additions of 0.1–1.0 equivalents of $La^{3+}$ to compound **8**.

however to be manifested in higher stability constants for the larger lanthanum ion with the acid amide calixarene ligands (Table 1) as determined by titration in dmso solutions.

The binding of lanthanide ions by compounds **5**–**13** was investigated further by electrospray mass spectrometry (ES-MS) (Table 2). Acetonitrile solutions of ligand ($10^{-5}$ M) and five molar equivalents of lanthanide (as nitrate salt) were employed. For example, with ester **7** the molecular ion $[\mathbf{7}H_{-2}Ln]^+$ was detected exclusively, with no "free" ligand present. Even under conditions of a great excess of lanthanide only the 1:1 species were observed. For acid amide ligand **10**, with the smaller lanthanide ions, gadolinium and lutetium, the 1:1 metal:calixarene species, $[\mathbf{10}H_{-2}Ln]^+$, were observed exclusively. Notably, for the lanthanum complex of **10**, at low cone voltages (≈25 V) the doubly charged species $[\mathbf{10}_2H_{-4}Ln_2]^{2+}$, *m/z* 1183.5, was detected and on moving to higher voltages (≈75 V) the singly charged ion $[\mathbf{10}H_{-2}Ln]^+$, *m/z* 1183.5, was observed. At intermediate cone voltages (≈50 V) a mixture of the overlapping ions was detected. These observations are consistent with our belief that the 2:2 dimeric structure observed in the crystal structures of acid amide–lanthanide complexes with the large lanthanides (*e.g.* La, Eu) can exist in solution.[10]

Ferrocene-bridged bis-calixarenes **11**–**13** were observed by ES-MS to bind lanthanide ions in a 1:1 stoichiometry. Molecular ions corresponding to the species $[\mathbf{13}H_{-2}La]^+$, $[\mathbf{13}H_{-2}Gd]^+$ and $[\mathbf{13}H_{-2}Lu]^+$ were observed; the spectra of the lanthanum and gadolinium complexes are shown in Fig. 2. Even addition of a large excess of lanthanide ion gave only the 1:1 molecular ion.

## Electrochemical studies

The electrochemical properties of ligands **5**–**10** were investigated by cyclic and square-wave (SW) voltammetry in acetonitrile with 0.1 M $NBu_4BF_4$ as supporting electrolyte and referenced to ferrocene–ferrocenium ($Fc–Fc^+$). In all cases, cyclic voltammograms of **5**–**10** gave a single, quasi-reversible one electron oxidation wave for the ferrocene moiety and repeated cycling demonstrated that all ligands were stable under the electrochemical experimental conditions. The $Fc–Fc^+$ couple in ligands **5**–**10** (Table 3) is shifted anodically by approximately 140 mV from that of ferrocene and can be attributed to the electron withdrawing amide substituent.

**Table 3** Electrochemical data and lanthanide electrochemical recognition results

| Compound | $E_{\frac{1}{2}}^a$/mV | $\Delta E_{\frac{1}{2}}^b$/mV | | |
|---|---|---|---|---|
| | | $La^{3+}$ | $Gd^{3+}$ | $Lu^{3+}$ |
| **5** | 144 | 40 (45) | 35 (35) | 35 (40) |
| **6** | 142 | 30 (35) | 25 (30) | 30 (35) |
| **7** | 141 | 60 (65) | 60 (65) | 60 (65) |
| **8** | 145 | 10 (15) | 10 (15) | 25 (25) |
| **9** | 143 | 15 (20) | 35 (40) | 55 (55) |
| **10** | 141 | 15 (15) | 35 (40) | 25 (30) |
| **11** | 153 | 90 (110) | 85 (115) | 80 (100) |
| **12** | 168 | 130 (140) | 195 (220) | 195 (200) |
| **13** | 180 | 120 (140) | 160 (190) | 205 (235) |

[a] Obtained in acetonitrile solution with 0.1 M $Bu_4NBF_4$, references $Fc–Fc^+$. [b] Anodic shifts of respective ferrocene–ferrocenium couple produced by 1 and 2 equivalents of lanthanide cations (at 293 K). Addition of triethylamine caused precipitation and was found to be detrimental to the electrochemical sensing process. The loss of the ligand $Fc–Fc^+$ couple showed that under basic conditions the ligand, or complex of, was the precipitant.

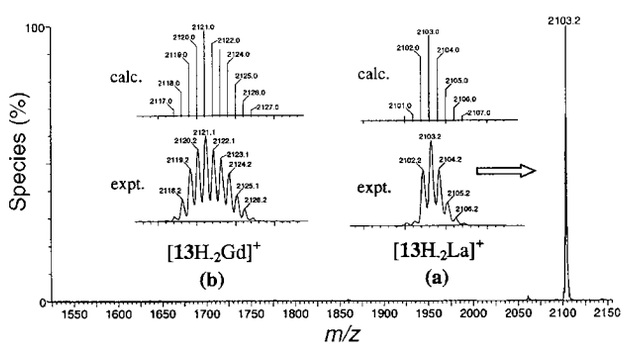



**Fig. 2** ES-MS of $[\mathbf{13}H_{-2}La]^+$ with insets (a) expanded view of $[\mathbf{13}H_{-2}La]^+$ and (b) expanded view of $[\mathbf{13}H_{-2}Gd]^+$.

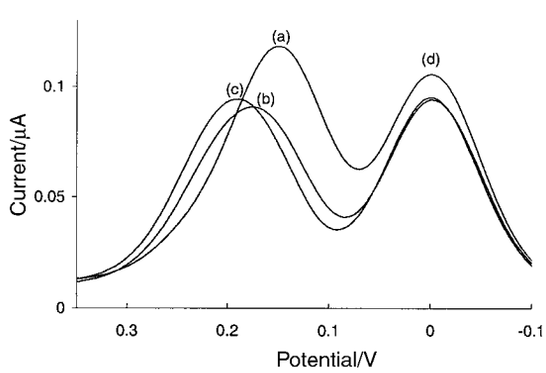



**Fig. 3** Square-wave voltammograms of compound **5** in the presence of (a) 0, (b) 1, (c) 2 equivalents of $Lu^{3+}$ and (d) reference ferrocene (Fc).

Both cyclic and square-wave voltammetry were used to investigate the electrochemical response of the ferrocene unit in compounds **5**–**10** in the presence of varying concentrations of trivalent lanthanide ions. Table 3 shows that in all cases addition of lanthanide ions causes significant anodic shifts in the respective ferrocene–ferrocenium redox couple of **5**–**10** (Fig. 3). The binding of the positively charged lanthanide ion in close proximity to the ferrocene redox centre inhibits the oxidation redox process. Overall the ester amide ligands **5**–**7** showed the greatest potential shifts over the acid amides **8**–**10**, with butyl-spaced **7** exhibiting the largest magnitude of shift, $\Delta E_{\frac{1}{2}} = 60$ mV, on addition of one equivalent of lanthanide ion. Importantly, the addition of a second or further equivalents causes only minimal anodic perturbations (≤5 mV). This is in agreement with the proposed empirical 1:1 binding model determined from UV/VIS titration experiments and, further,

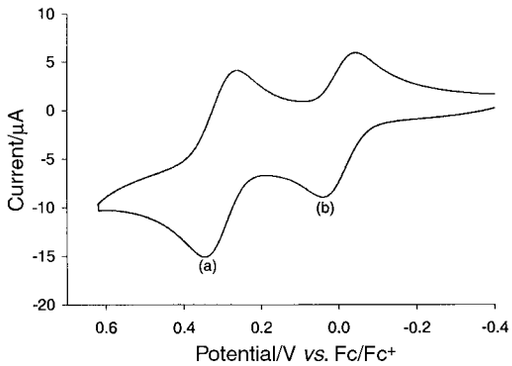



**Fig. 4** Cyclic voltammogram of (a) compound **12** and (b) ferrocene.

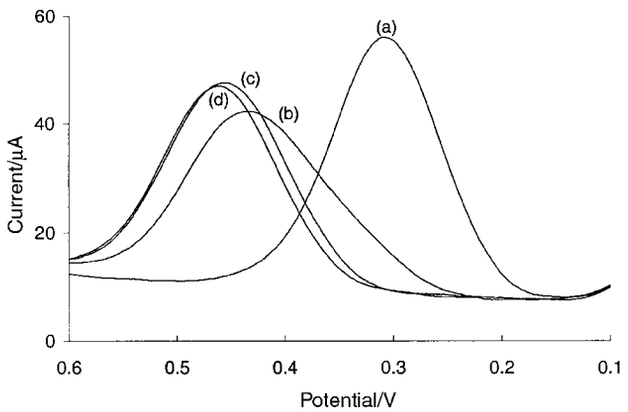



**Fig. 5** Square-wave voltammograms of compound **12** in the presence of (a) 0, (b) 1, (c) 2, (d) 5 equivalents of $La^{3+}$.

suggests strong binding of lanthanide ions under the conditions of the electrochemical experiment. All ester amide ligands **5**–**7** were insensitive to the nature of the lanthanide element, and a very consistent response was observed to whichever lanthanide was added. In contrast acid amide ligands **8**–**10** exhibited generally smaller anodic perturbations. Modest potential shifts with lanthanum ions ($\leqslant$15 mV) were observed for **8**–**10** and the ethyl-spaced ligand **8** exhibited a maximum perturbation with lutetium of 25 mV. The propyl-spaced **9** gave the largest shift increasing from 15 mV for La, through 35 mV for Gd to 55 mV for Lu. The smaller, more charge dense lutetium cation perturbs the ferrocene oxidation more than the large lanthanide ions. A possible rationale as to why ester amide analogues **5**–**7** display greater anodic shifts than their acid amide **8**–**10** counterparts is that only with **8**–**10** can complete charge neutralisation by deprotonation on complexation occur. Charge neutralisation may serve to counter some of the effect of binding an electropositive lanthanide ion in close proximity to the ferrocene redox centre.

Cyclic voltammetry of ferrocene calixarene dimers **11**–**13** gave a single, quasi-reversible oxidation wave, see Table 3 and Fig. 4. Addition of lanthanide ions causes much larger anodic shifts in the oxidation potentials of **11**–**13** (see Table 3) by both CV and SW techniques (see Fig. 3). The propyl- and butyl-spaced dimers **12** and **13** (see Fig. 5) exhibit shifts of 120–205 mV on the addition of one equivalent of lanthanide ions with the smaller lutetium ion causing the largest oxidation potential shift. Again the larger ratio of charge : ionic radius for lutetium causes greater polarisation close to the ferrocene. The addition of a second equivalent of lanthanide results in only a modest shift and from thereon with further additions (up to 5 equivalents) very little perturbation is observed. It is noteworthy that the length of the alkyl spacer has a pronounced effect upon the response of the individual bis-calixarenes to lanthanide ions with the largest shifts observed with the longer chain length. Only **11** gives a similar response across the lanthanide series with **12** and **13** exhibiting larger potential shifts with the smaller and less charge diffuse gadolinium and lutetium ions.

Interestingly the addition of sodium ions (as $NaBF_4$, $NaBPh_4$) and potassium ions (as $KPF_6$, $KNO_3$) to solutions of compounds **5**–**13** caused no significant shifts (<10 mV) in their respective ferrocene oxidation potentials. These experiments provide evidence for the selective binding of lanthanide ions by calixarene ligands **5**–**13**.

Coupling of the binding event to a change in the redox potential of a redox-active host can occur *via* a number of communication pathways.[12] If a through space electrostatic interaction is the only interaction in operation, it has been shown that the anodic shift depends on the distance between the binding site and the redox centre, as well as the charge density of the cation.[2,13] Electrochemical experiments performed on a family of ferrocene amide cryptands revealed that there were large anodic shifts of up to 350 mV with trivalent yttrium cation and of approximately 250 mV with lanthanide ions.[2] The magnitude of the anodic shifts observed for the ligands **5**–**10** is modest overall when compared to that of ferrocene cryptands. In this case, the mechanism of electrochemical communication of the lanthanide binding event to the ferrocene redox centre could be a combination of through space and through bond interactions, the latter being possible *via* co-ordination of the amide carbonyl functionality to the lanthanide cation.[12] The large shifts observed for **11**–**13** may be due to partial co-ordination of the lanthanide ion to the chelating amide carbonyls of the bridging ferrocene. Such a mechanism would be consistent with the large anodic shifts observed for ferrocene cryptands with yttrium and lanthanide ions reported by Hall *et al.*[2]

## Conclusion

A novel family of ferrocene-derivatised calix[4]arene ligands possessing ester amide and acid amide co-ordination groups has been synthesized and shown to form thermodynamically stable 1 : 1 complexes with lanthanide ions. Electrochemical methods show that all ligands undergo significant anodic potential shifts of their ferrocene redox centre in the presence of lanthanide ions. Monomeric ferrocene calixarene ligands undergo shifts of up to 60 mV. Notably, ferrocene-bridged calixarene dimers containing ester amide co-ordination functionalities undergo much larger potential shifts, typically 200 mV, on the addition of one equivalent of lanthanide ion.

Previous studies have demonstrated that acid amide type ligands are much more effective lanthanide extractants and chelators than ester amide type ligands.[10] However interestingly, the latter show a superior electrochemical response to the presence of lanthanide ions. In light of these results, the design of future sensing agents will also consider the likely magnitude of the sensor response to the guest and not just the thermodynamic stability of the sensor–guest species. Studies are currently directed towards the functionalisation of ferrocene-appended calixarenes compatible with device manufacture for the detection of lanthanides in aqueous wastes.

## Experimental

### General

Where necessary, solvents were purified prior to use and stored under $N_2$. Unless otherwise stated, commercial grade chemicals were used without any further purification. The acid chloride calix[4]arene **1** was prepared as described previously.[10] Mono-boc-protected diamines were prepared by treating an excess of the corresponding diamine with di-*tert*-butyl dicarbonate.[14] Dichloromethane was pre-dried over calcium chloride and distilled over calcium hydride. NMR spectra were recorded on a Bruker AM 300 instrument or a Varian Unity Plus 500

spectrometer. Correlated NMR experiments using pulsed field gradients were commonly used to assist in characterisation. The Inorganic Chemistry Laboratory Microanalysis Service carried out all elemental analyses. Fast atom bombardment (FAB) mass spectrometry was performed at the University College of Swansea by the EPSRC service. Ultraviolet/visible spectrometry was carried out on a Perkin-Elmer Lambda 6 UV/VIS Spectrophotometer.

Electrospray mass spectrometry was carried out on a Micromass LCT mass spectrometer operating at 3500 kV. For ligand characterisation spectra were collected in methanol–water (90 : 1) solutions. Complexation studies were performed in acetonitrile. Ligands ($1 \times 10^{-3}$ M) were dissolved in dichloromethane, lanthanide nitrate ($5 \times 10^{-3}$ M) in acetonitrile and the two solutions mixed and diluted to $10^{-5}$ M in acetonitrile. The flow rate was 15 μL $min^{-1}$ and the cone voltages were varied to optimise ionisation, but were typically between 25 and 75 V.

Electrochemical measurements were conducted on a Princeton Applied Research Potentiostat/ Galvanostat Model 273. The working electrode was glassy carbon, the counter electrode platinum wire, and the internal reference ferrocene recrystallised from n-hexane. Argon gas saturated with acetonitrile was continually bubbled through the cell to de-oxygenate the solution. The electrochemical solution (5 $cm^3$) consisted of ligand ($5 \times 10^{-3}$ M), $(n\text{-}Bu)_4NBF_4$ (0.1 M) as the supporting electrolyte and ferrocene as an internal reference with acetonitrile as the solvent.

### Boc-protected amino-ester calixarenes 1–3

**Compound 2.** To a solution of the acid chloride **1** (1.17 g, 1.44 mmol) in dichloromethane (20 $cm^3$) a solution of $BocNH(CH_2)_2NH_2$ (0.243 g, 1.51 mmol) and triethylamine (0.161 g, 1.59 mmol) in dichloromethane (50 $cm^3$) was added dropwise over 30 min and stirred for 1 h. The solvent was removed to yield the crude product which was purified by column chromatography ($SiO_2$, dichloromethane–ethyl acetate, 2 : 1, v/v) to yield the product as a white solid (0.95 g, 1.02 mmol, 71%). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 0.92 (s, 9H, $^t$Bu $CH_3$); 0.93 (s, 9H, $^t$Bu $CH_3$); 1.22 (s, 18H, $^t$Bu $CH_3$); 1.27 (t, 3H, $J = 7.0$, $OCH_2CH_3$); 1.29 (s, 9H, O$^t$Bu $CH_3$); 3.32 (d, 4H, $J = 13.5$, $ArCH_2Ar_{eq}$); 3.41 and 3.67 (m, 4H, $NHCH_2CH_2NH$); 4.11 (d, 2H, $J = 13.0$, $ArCH_2Ar_{ax}$); 4.23 (d, 2H, $J = 13.5$, $ArCH_2Ar_{ax}$); 4.26 (q, 2H, $J = 7.0$, $OCH_2CH_3$); 4.49 (s, 2H, $OCH_2CO_2Et$); 4.61 (s, 4H, $OCH_2CONH$); 6.83 and 6.84 (s, 2H, Ar H); 7.04 and 7.05 (s, 2H, Ar H); 7.34 (s, 2H, OH); and 8.72 (t, 2H, $J = 5.8$ Hz, NH): Found: C, 71.0; H, 8.2; N, 2.6. Calc. for $C_{57}H_{78}N_2O_9 \cdot 0.5CH_2Cl_2$: C, 70.6; H, 8.1; N, 2.9%. ES-MS: *m*/*z* 958, $[M + Na]^+$. Boc-protected amines **3** and **4** were prepared in a similar manner.

**Compound 3.** White solid (0.45 g, 35%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.04 (s, 9H, $^t$Bu $CH_3$); 1.27 (s, 9H, $^t$Bu $CH_3$); 1.44 (s, 18H, $^t$Bu $CH_3$); 1.46 (t, 3H, $J = 7.0$, $OCH_2CH_3$); 1.50 (m, 2H, $CH_2CH_2CH_2$); 3.45 (m, 2H, $NHCH_2$); 3.51 (d, 4H, $J = 13.0$, $ArCH_2Ar_{eq}$); 4.22 (m, 2H, $OCH_2CH_3$); 4.33 (d, 2H, $J = 13.0$, $ArCH_2Ar_{ax}$); 4.49 (d, 2H, $J = 13.0$ Hz, $ArCH_2Ar_{ax}$); 4.65 (s, 2H, $OCH_2CO$); 6.39 (s, 2H, OH); 7.03, 7.24 (s, 4H, Ar H); and 8.76 (m, 2H, NH). Found: C, 73.8; H, 8.6; N, 2.6. Calc. for $C_{57}H_{78}N_2O_9$: C, 73.4; H, 8.5; N, 2.95%. ES-MS: *m*/*z* 972, $[M + Na]^+$.

**Compound 4.** White solid (0.83 g, 58%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.08 (s, 9H, $^t$Bu $CH_3$); 1.10 (s, 9H, $^t$Bu $CH_3$); 1.42 (s, 18H, $^t$Bu $CH_3$); 1.46 (t, 3H, $J = 7.0$, $OCH_2CH_3$); 1.55 (s, 9H, O$^t$Bu $CH_3$); 1.70–1.80 and 1.80–1.90 (m, 2H, $NHCH_2CH_2$); 3.20–3.30 (m, 2H, $NHCH_2$); 3.50 (d, 2H, $J = 13.0$, $ArCH_2Ar_{eq}$); 3.50 (d, 2H, $J = 13.5$, $ArCH_2Ar_{eq}$); 3.60–3.70 (m, 2H, $NHCH_2$); 4.29 (d, 2H, $J = 13.0$ Hz, $ArCH_2Ar_{ax}$); 4.44–4.46 (m, 4H, $OCH_2CH_3$ and $ArCH_2Ar_{ax}$); 4.65 (s, 2H, $OCH_2CO_2Et$); 4.78 (s, 2H, $OCH_2CONH$); 6.99 (s, 2H, Ar H); 7.00 (s, 2H, Ar H); 7.20 (s, 4H, Ar H); 7.38 (s, 2H, OH); and 8.85 (m, 2H, NH). Found: C, 70.8; H, 8.6; N, 2.5. Calc. for $C_{59}H_{82}N_2O_9 \cdot 0.5CH_2Cl_2$: C, 71.1; H, 8.3; N, 2.8%. ES-MS: *m*/*z* 986, $[M + Na]^+$.

### Ferrocene-appended ester amide calixarenes 5–7

**Boc removal.** To a solution of crude Boc-diamine calix[4]arene (3.50 g, 3.69 mmol) in dichloromethane (150 $cm^3$), trifluoroacetic acid (2.0 $cm^3$) was added and stirred for 1 h. The solvent was removed under reduced pressure, the resulting solid redissolved in dichloromethane, triethylamine (3 $cm^3$) added and then stirred for 30 min. Removal of the solid afforded a yellow oil which was used directly without further purification.

**Compound 5.** To a stirred solution of the aminocalix[4]arene (1.00 g, 1.20 mmol) in dichloromethane (100 $cm^3$) a solution of the ferrocenecarbonyl chloride (0.35 g, 1.41 mmol) in dichloromethane (50 $cm^3$) was added dropwise over 30 min. The resulting solution was stirred for 2 h, the solvent removed and the crude product subject to column chromatography ($SiO_2$, dichloromethane–ethyl acetate, 2 : 1 v/v) to yield the product as an orange-red solid (0.73 g, 0.696 mmol, 58%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.90 (s, 9H, $^t$Bu $CH_3$); 0.91 (s, 9H, $^t$Bu $CH_3$); 1.22 (s, 18H, $^t$Bu $CH_3$); 1.25 (t, 3H, $J = 7.1$, $OCH_2CH_3$); 3.31 (d, 2H, $J = 14.0$, $ArCH_2Ar_{eq}$); 3.34 (d, 2H, $J = 13.0$, $ArCH_2Ar_{eq}$); 3.62–3.65 (m, 2H, $CH_2CH_2NHCOFc$); 3.76–3.79 (m, 2H, $NHCH_2CH_2$); 4.10 (d, 2H, $J = 13.5$, $ArCH_2Ar_{ax}$); 4.11 (s, 5H, Fc H); 4.17 (d, 2H, $J = 13.5$, $ArCH_2Ar_{ax}$); 4.18–4.19 (m, 2H, Fc H); 4.26 (q, 2H, $J = 7.0$, $OCH_2CH_3$); 4.53 (s, 2H, $OCH_2CO$), 4.55 (s, 2H, $OCH_2CO$); 4.60–4.61 (m, 2H, Fc H); 6.82 (s, 4H, Ar H); 7.04 (s, 4H, Ar H); 7.16 (t, 1H, $J = 4.5$, NH); 7.32 (s, 2H, OH); and 9.00–9.02 (t, 1H, $J = 4.5$ Hz, NH). Found: C, 69.30; H, 7.70; N, 2.31. Calc. for $C_{63}H_{78}FeN_2O_8 \cdot 0.5CH_2Cl_2$: C, 70.0; H, 7.3; N, 2.6%. ES-MS: *m*/*z* 1069.9, $[M + Na]^+$. Ferrocene ester amides **6** and **7** were prepared in a similar manner.

**Compound 6.** Yield 0.60 g (48%). $^1$H NMR: (500 MHz, $d_6$-DMSO): $\delta$ 1.17 (s, 18H, $^t$Bu $CH_3$); 1.24 (s, 18H, $^t$Bu $CH_3$); 1.89 (m, 2H, $NHCH_2CH_2CH_2NH$); 1.33 (m, 3H, $OCH_2CH_3$); 3.38 (d, 2H, $J = 14.0$, $ArCH_2Ar_{eq}$); 3.52 (d, 2H, $J = 13.5$, $ArCH_2Ar_{eq}$); 3.54 (m, 4H, $NHCH_2CH_2CH_2NH$); 4.10 (m, 2H, $OCH_2CH_3$); 4.21 (s, 5H, Fc H); 4.28 (d, 2H, $J = 13.5$, $ArCH_2Ar_{ax}$); 4.33 (d, 2H, $J = 13.0$, $ArCH_2Ar_{ax}$); 4.40 and 4.53 (s, 5H, Fc H); 4.85 and 4.87 (s, 2H, $OCH_2CO$); 7.23 and 7.24 (s, 4H, Ar H); 7.88 (m, 1H, NH); 8.21 (s, 2H, OH); and 8.82–8.84 (t, 1H, $J = 4.5$ Hz, NH). Found: C, 70.4; H, 7.6; N, 2.5. Calc. for $C_{64}H_{82}FeN_2O_8 \cdot 0.5CH_2Cl_2$: C, 70.2; H, 7.4; N, 2.5%. ES-MS: *m*/*z* 1083.5, $[M + Na]^+$; 1099.5 $[M + K]^+$.

**Compound 7.** Yield 0.70 g (56%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.07 and 1.15 (s, 18H, $^t$Bu $CH_3$); 1.23 (t, 3H, $J = 7.5$, $OCH_2CH_3$); 1.54 (m, 2H, $CH_2CH_2CH_2CH_2$); 1.64 (m, 2H, $CH_2CH_2CH_2CH_2$); 3.18 (d, 2H, $J = 12.5$, $ArCH_2Ar_{eq}$); 3.29 (d, 2H, $J = 13.5$, $ArCH_2Ar_{eq}$); 3.47 (m, 4H, $NHCH_2CH_2$); 4.00 (m, 2H, $OCH_2CH_3$); 4.10 (m, 2H, Fc H); 4.16 (d, 2H, $J = 13.0$, $ArCH_2Ar_{ax}$); 4.27 (d, 2H, $J = 13.0$ Hz, $ArCH_2Ar_{ax}$); 4.23 (m, 5H, Fc H); 4.40 (s, 2H, $OCH_2CO_2Et$); 4.74 (s, 2H, Fc H); 4.76 (s, 2H, $OCH_2CO$); 7.13 and 7.14 (s, 2H, Ar H); 7.15 (s, 4H, Ar H); 7.75 (m, 1H, NH); 8.10 (s, 2H, OH); and 8.67 (m, 1H, N*H*). Found: C, 70.8; H, 8.0; N, 2.4. Calc. for $C_{65}H_{82}FeN_2O_8 \cdot 0.5CH_2Cl_2$: C, 70.4; H, 7.5; N, 2.5%. ES-MS: *m*/*z* 1097.7, $[M + Na]^+$; 1113.7 $[M + K]^+$.

### Ferrocene-appended acid amide calixarenes 7–9

**Compound 8.** A solution of compound **5** (0.68 g, 0.645 mmol) and sodium hydroxide (0.312 g, 7.80 mmol) in ethanol (35 $cm^3$)–water (1 $cm^3$) was heated under reflux (0.75 h). The solvent was removed under reduced pressure and to the residual sodium salt were added dichloromethane (20 $cm^3$) and dilute

hydrochloric acid (20 $cm^3$; 5 $cm^3$ conc. HCl in 50 $cm^3$ water). After stirring (5 min) the organic layer was separated, washed with water (10 $cm^3$), dried over $MgSO_4$ and the solvent removed to afford the product as an orange solid (0.56 g, 81%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.95 and 0.99 (s, 9H, $^t$Bu $CH_3$); 1.23 (s, 18H, $^t$Bu $CH_3$); 3.32 (d, 2H, $J$ = 13.0, ArC$H_2$Ar$_{eq}$); 3.37 (d, 2H, $J$ = 13.5, ArC$H_2$Ar$_{eq}$); 3.63 (q, 4H, $J$ = 6.0, NC$H_2$C$H_2$N); 4.13 (d, 2H, $J$ = 13.0, ArC$H_2$Ar$_{ax}$); 4.19 (s, 5H, Fc H); 4.24 (d, 2H, $J$ = 13.0, ArC$H_2$Ar$_{ax}$); 4.34 (s, 2H, Fc H); 4.51 (s, 2H, OC$H_2$-$CO_2$H); 4.65 (s, 2H, OC$H_2$CON); 4.71 (s, 2H, Fc H); 6.72 (m, 1H, N$H$COFc); 6.87 and 6.91 (s, 2H, Ar H); 7.06 (s, 4H, Ar H; 7.54 (s, 2H, OH); and 8.96 (t, 1H, $J$ = 4.5 Hz, N$H$COCH$_2$). Found: C, 69.8; H, 7.5; N, 2.5. Calc. for $C_{61}H_{74}FeN_2O_8$·2$H_2O$: C, 69.4, H, 7.5, N, 2.6%. ES-MS: $m/z$ 1042.5, $[(M + Na)]^+$.

**Compound 9.** Yield 0.20 g (77%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.93 and 0.97 (s, 9H, $^t$Bu $CH_3$); 1.21 (s, 18H, $^t$Bu $CH_3$); 1.95 (m, 2H, $CH_2CH_2CH_2$); 3.30 (d, 2H, $J$ = 13.0, ArC$H_2$Ar$_{eq}$); 3.35 (d, 2H, $J$ = 13.0, ArC$H_2$Ar$_{eq}$); 3.42 (q, 2H, $J$ = 7.0, $CH_2CH_2$NHCOFc); 3.51 (q, 2H, $J$ = 7.5, NHC$H_2$CH$_2$); 4.12 (d, 2H, $J$ = 13.0, ArC$H_2$Ar$_{ax}$); 4.11 (m, 5H, Fc H); 4.22 (d, 2H, $J$ = 13.5, ArC$H_2$Ar$_{ax}$); 4.32 (s, 2H, Fc H); 4.49 (s, 2H, OC$H_2$CO$_2$H); 4.63 (s, 1H, $CO_2$H); 4.65 (s, 2H, OCH$_2$CON); 4.75 (s, 2H, Fc H); 6.84 and 6.88 (s, 2H, Ar H); 6.98 (br s, 1H, $CH_2$N$H$COFc); 7.04 and 7.05 (s, 2H, ArH); 7.53 (br s, 2H, OH); and 8.85 (t, 1H, $J$ = 6.0 Hz, $CH_2$N$H$CO). Found: C, 69.2; H, 7.7; N, 2.4. Calc. for $C_{62}H_{76}FeN_2O_8$·2$H_2O$: C, 69.65; H, 7.5; N, 2.6%. ES-MS: $m/z$ 1055.6, $[M + Na]^+$.

**Compound 10.** Yield 0.40 g (78%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.91 and 0.93 (s, 9H, $^t$Bu $CH_3$); 1.24 (s, 18H, $^t$Bu $CH_3$); 1.64 and 1.74 (m, 2H, $CH_2CH_2CH_2CH_2$); 3.30 (d, 2H, $J$ = 13.5, ArC$H_2$Ar$_{eq}$); 3.33 (d, 2H, $J$ = 13.5, ArC$H_2$Ar$_{eq}$); 3.39 and 3.45 (m, 2H, NHC$H_2$CH$_2$CH$_2$C$H_2$NH); 4.09 (m, 5H, Fc H; 2H, Fc H); 4.30 (d, 4H, $J$ = 13.5, ArC$H_2$Ar$_{ax}$); 4.46 (s, 2H, OC$H_2$CO$_2$H); 4.61 (s, 1H, $CO_2$H); 4.67 (m, 2H, OCH$_2$CO; 2H, Fc H); 6.44 (br m, 1H, $CH_2$N$H$COFc); 6.82 (s, 2H, Ar H); 7.07 (s, 4H, Ar H); 7.39 (s, 2H, OH); and 8.72 (t, 1H, $J$ = 4.5 Hz, $CH_2$N$H$CO). Found: C, 69.9; H, 7.7; N, 2.4. Calc. for $C_{63}H_{78}FeN_2O_8$·2$H_2O$: C, 69.9; H, 7.6; N, 2.6%. ES-MS: $m/z$ 1070.6, $[(M + Na)]^+$.

**Compound 11.** To a solution of compound **2** (0.925 g, 1.11 mmol) in dichloromethane (50 $cm^3$) a solution of ferrocene bis(carbonyl chloride) (0.200 g, 0.610 mmol) in dichloromethane (25 $cm^3$) was added dropwise over 15 min and stirred (2 h). The solvent was removed and the crude product subjected to column chromatography ($SiO_2$, dichloromethane–ethyl acetate 2 : 1, increased to pure methanol) to yield the product as a dark orange solid (0.668 g, 63%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.93 (s, 36H, $^t$Bu $CH_3$); 1.22 (s, 36H, $^t$Bu $CH_3$); 1.28 (t, 6H, $J$ = 8.0, OCH$_2$C$H_3$); 3.33 (d, 8H, $J$ = 13.0, ArC$H_2$Ar$_{eq}$); 3.61 (q, 4H, $J$ = 5.0, $CH_2CH_2$NHCOFc); 3.76 (q, 4H, $J$ = 5.3, NHC$H_2$CH$_2$); 4.05 (d, 4H, $J$ = 13.0, ArC$H_2$Ar$_{ax}$); 4.06 (m, 8H, Fc H); 4.12 (d, 4H, $J$ = 13.0, ArC$H_2$Ar$_{ax}$); 4.25 (q, 4H, $J$ = 7.2, OC$H_2$CH$_3$); 4.53 (s, 4H, OCH$_2$CO); 6.84 (s, 8H, Ar H); 7.04 (s, 4H, Ar H); 8.17 (m, 2H, NH); and 9.19 (t, 2H, $J$ = 5.2 Hz, NH). Found: C, 67.8; H, 6.6; N, 2.4. Calc. for $C_{116}H_{148}FeN_4O_{16}$·2$CH_2Cl_2$: C, 68.1; H, 7.4; N, 2.7%. ES-MS: $m/z$ 1933.5, $[M + Na]^+$.

**Compound 12.** Yield 2.07 g (54%). $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 0.92 (s, 36H, $^t$Bu $CH_3$); 1.22 (s, 36H, $^t$Bu $CH_3$); 1.24 (t, 3H, $J$ = 7.5, OCH$_2$C$H_3$); 1.88 (m, 4H, $CH_2CH_2CH_2$); 3.31 (d, 4H, $J$ = 13.5, ArC$H_2$Ar$_{eq}$); 3.32 (d, 4H, $J$ = 13.0, ArC$H_2$Ar$_{eq}$); 3.41 and 3.66 (m, 4H, NHC$H_2$CH$_2$); 4.11 (d, 4H, $J$ = 13.0, ArC$H_2$Ar$_{ax}$); 4.21 (d, 4H, $J$ = 13.5, ArC$H_2$Ar$_{ax}$); 4.23 (q, 4H, $J$ = 7.2 Hz, OC$H_2$CH$_3$); 4.28 (m, 4H, Fc H); 4.51 and 4.60 (s, 4H, OCH$_2$CO); 4.68 (m, 4H, FcCO); 6.83 and 7.05 (s, 8H, Ar H); 7.31 (s, 4H, OH); 7.54 and 8.81 (m, 2H, NH). Found: C, 71.2; H, 7.8; N, 2.7. Calc. for $C_{118}H_{152}FeN_4O_{16}$·$CH_2Cl_2$: C, 70.6; H, 7.7; N, 2.8%. ES-MS: $m/z$ 1961.5, $[M + Na]^+$.

**Compound 13.** Yield 0.793 g, 0.403 mmol (58%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.04 and 1.05 (s, 18H, $^t$Bu $CH_3$); 1.12 (s, 36H, $^t$Bu $CH_3$); 1.19 (t, 6H, $J$ = 7.0, OCH$_2$C$H_3$); 1.52 (m, 2H, $CH_2CH_2CH_2$NHCOFc); 1.57 (m, 2H, $CH_2CH_2CH_2$-$CH_2$NHCOFc); 3.15 (m, 4H, OC$H_2$CH$_3$); 3.37 (d, 4H, $J$ = 13.0, ArC$H_2$Ar$_{eq}$); 3.39 (d, 4H, $J$ = 12.5, ArC$H_2$Ar$_{eq}$); 4.12 (d, 4H, $J$ = 13.5, ArC$H_2$Ar$_{ax}$); 4.19 (d, 4H, ArC$H_2$Ar$_{ax}$; 5H, Fc H); 4.37 and 4.38 (s, 2H, Fc H); 4.64 (s, 4H, OC$H_2$CO$_2$Et); 4.73 (s, 2H, OCH$_2$CON); 7.10 and 7.11 (s, 4H, ArH); 7.13 (s, 8H, Ar H); 7.90 (t, 2H, $J$ = 5.8, $CH_2$N$H$COFc); 8.08 (s, 4H, OH); and 8.64 (t, 2H, $J$ = 5.5 Hz, $CH_2$N$H$CO). Found: C, 70.7; H, 8.1; N, 2.7. Calc. for $C_{120}H_{156}FeN_4O_{16}$·$CH_2Cl_2$: C, 70.9; H, 7.8; N, 2.7%. ES-MS: $m/z$ 1989.1, $[M + Na]^+$.

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