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FULL PAPER

Acid-amide calixarene ligands for uranyl and lanthanide ions: synthesis, structure, coordination and extraction studies

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The synthesis of a series of calix[4]arene ligands bearing lower rim 1,3-acid-amide functionality for the two-phase solvent extraction of lanthanide and uranyl ions from aqueous wastes is described. X-Ray crystal structure studies demonstrate binding of lanthanide ions at the calixarene lower rim through phenolate, carboxylate and carboxamide oxygen atoms. The crystal structures of a centrosymmetric, dimeric lanthanum(III) and non-centrosymmetric dimeric sodium(I) complexes of a 1,3-acid-dihexylamidecalix[4]arene ligand are detailed. Electrospray mass spectrometry confirms retention of this 2 : 2 dimeric structure for large lanthanide ions and that the smaller lanthanide ions *e.g.* Lu^{3+} form monomeric 1 : 1 calixarene : lanthanide complexes in solution. Extraction studies demonstrate a pH dependent uptake of lanthanide and uranyl cations by 1,3-acid-amide ligands with the nature of the carboxamide substituent largely irrelevant to extraction efficiency. Upper rim modified 1,3-dinitro and de-*tert*-butylcalix[4]arene ligands were prepared and NMR and ES-MS studies confirm uranyl coordination by these novel acid-amide ligands. The 1,3-dinitro and de-*tert*-butyl ligands exhibit superior and more efficient extraction of uranyl cations at lower pH values.

Introduction

A worldwide requirement for the development of efficient extraction agents to remove metal ions from both organic and aqueous effluents for either safe disposal or recycling has motivated research into the coordination properties of calixarene-based ligands.[1] These phenol-based macrocycles have proven to be excellent ligands for the formation of thermodynamically stable metal complexes.[2] In addition, their rigid macrocyclic structure frequently confers remarkable selectivity upon their metal ion coordination behaviour.[3] These characteristics, in particular, have led to their application in the area of nuclear waste remediation where lanthanide and actinide ions are the primary metal cation targets to sequest.[4] With the industrial development of lanthanide complexes in fields as diverse as resonance imaging, screen displays, optics and magnetic materials the requirement for their recovery and recycling is likely to increase markedly.[5]

The ease with which calixarenes can be synthetically modified at both their upper and lower rims has allowed the synthesis of a great diversity of ligands.[6] For coordination studies, functionalisation at the lower rim is generally the more popular allowing exploitation of the calixarene's cone-shape and the chelating ring of oxygen donor atoms that encircle its base.[7] Furthermore, the option to expand the macrocyclic ring by employing calix[*n*]arenes, where $n = 4$, 5, 6 or 8, as the ligand platform provides opportunity to additionally tune the selectivity of these ligands. For example, crystal structures of lanthanide and actinide complexes with a range of calix[4] and higher derivatives have now been reported.[8]

Acid-amide derivatised calixarene ligands (**6**–**8**, **13**, **16**), Fig. 1, have been developed for the extraction of toxic metal ions including lanthanides from aqueous solutions.[9] The 1,3-acid-amide substitution pattern was chosen to provide three proton ionisable groups that would allow formation of charge neutral complexes on coordination with trivalent lanthanide ions; the tripositive oxidation state being the most stable and common for lanthanide ions in aqueous solutions at neutral pH. Furthermore, it was anticipated that extraction would exhibit a marked pH dependence and allow facile decomplexation of extracted ions into small volumes of concentrated acid solutions for recycling or storage purposes, and enable efficient recovery of ligands for reuse. Herein we describe the synthesis of a range of 1,3-acid-amide calix[4]arenes, their coordination chemistry and the results of two-phase solvent extraction

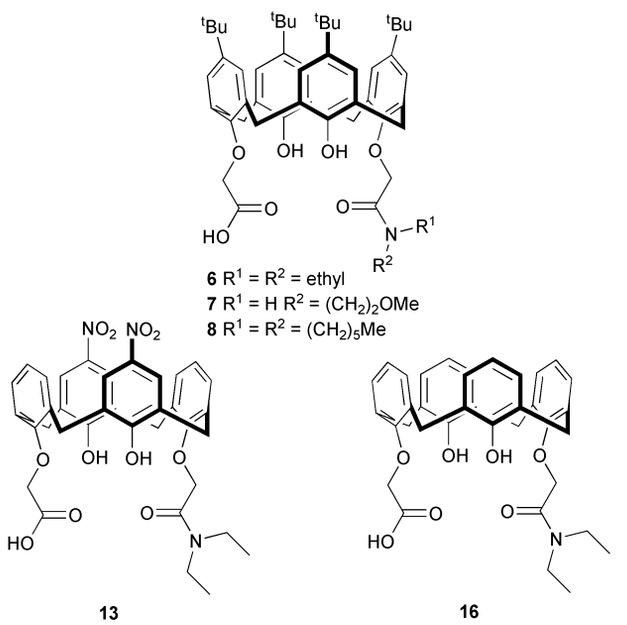

Fig. 1 1,3-Acid-amide calix[4]arene ligands employed.

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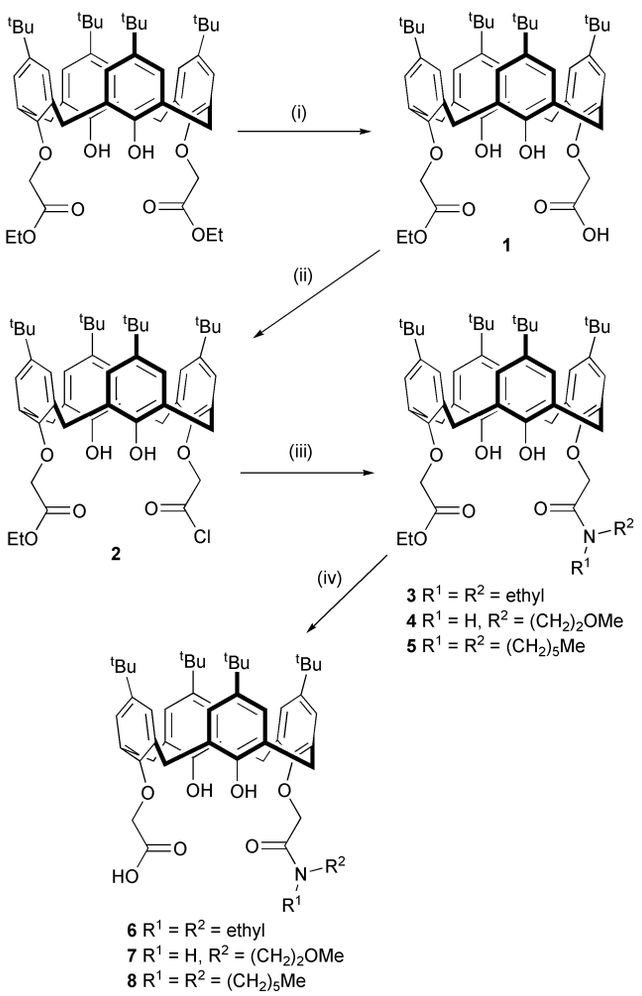
experiments with lanthanide cations. In addition, the characterisation of the likely extractant species is discussed, with the crystal structure of a dinuclear lanthanum complex presented. Finally, we have modified the calix[4]arene acid-amide framework to optimise the extraction of uranyl cations from waste solutions. Nitro- and de-*tert*-butyl-calix[4]arene acid-amide ligands **13** and **16** were prepared and their improved extraction of uranyl from more acidic solutions is described.

Results and discussion

Ligand synthesis

***tert*-Butylcalix[4]arene based ligands.** The ester-amide and acid-amide ligands **3**–**8** were prepared by the procedure outlined in Scheme 1. Hydrolysis of a single ester group of



Scheme 1 Reagents and conditions: (i) 1 equiv. KOH, EtOH; (ii) $(COCl)_2$; (iii) excess amine and Et_3N, CH_2Cl_2; (iv) 1 equiv. KOH, EtOH.

5,11,17,23-tetra-*tert*-butyl-25,27-bis(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene[19] by treatment with one equivalent of potassium hydroxide in refluxing ethanol gave monoacid **1** in good yield (74%). This was converted to the acid-chloride **2** by reaction with thionyl chloride in dichloromethane. This acid-chloride was reacted with a range of amines to yield the ester-amide ligands **3**–**5** (76–88%). Hydrolysis of the remaining ethyl ester to the corresponding acid by potassium hydroxide in refluxing ethanol followed by acidification (HCl) afforded acid-amide ligands **6**–**8** in almost quantitative yield (87–94%). All new ligands **3**–**8** were characterised by ^{1}H NMR, mass spectrometry (FAB and ES) and elemental analysis. ^{1}H NMR spectra were all consistent with the retention of the calixarene cone conformation in solution.

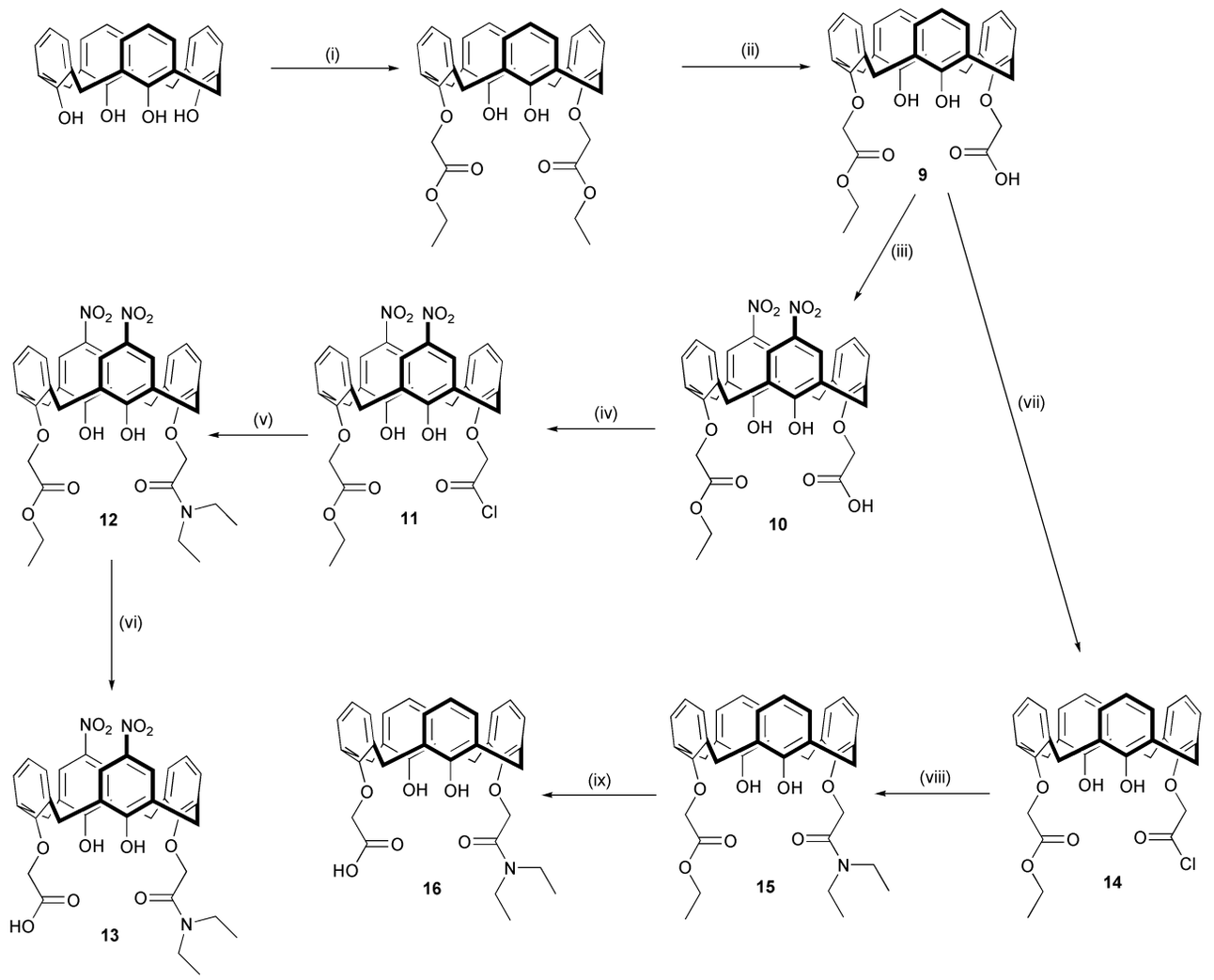
De-*tert*-butyl and nitro ligands. Coordination of uranyl requires deprotonation of a calixarene phenol oxygen atom which would, presumably, be faciliated by the lowering of the pK_a of this donor atom. It was anticipated that upper rim modification of the calixarene by removal of the electron donating *tert*-butyl groups and replacement by less electron donating or more electron withdrawing groups would markedly affect the extraction properties of the acid-amide ligands over a more acidic pH range. Ligands **13** and **16** were prepared by the synthetic routes depicted in Scheme 2. Mono-hydrolysis of 25,27-bis[(ethoxycarbonyl)-methoxy]-26,28-dihydroxycalix[4]-arene[10] employing one equivalent of potassium hydroxide in refluxing ethanol at room temperature furnished **9**, which was nitrated with 10% nitric acid in dichloromethane to afford nitro derivative **10** in 56% yield. This was converted into acid chloride **11** by treatment with oxalyl chloride in dichloromethane. NMR spectroscopy and X-ray crystallography analysis confirmed the cone conformation of acid chloride **11**. Reaction of **11** with excess diethylamine in dichloromethane afforded the amide-ester **12** in 75% yield. The hydrolysis of the ester-amide **12** was performed by the same procedure as the monodeprotection of **9**. The free acid was obtained by suspension of the potassium salt in dichloromethane and treatment with dilute hydrochloric acid, which upon evaporation of the solvent and crystallization from a mixture of dichloromethane and methanol afforded **13** in 80% yield.

For the preparation of ligand **16** the same procedure as above was employed. The ester-amide **15** was prepared from acid-ester **9** *via* acid chloride **14** in 87% yield and the final acid-amide **16** was obtained after crystallization from a mixture of dichloromethane–ethanol in 85% yield.

Lanthanide coordination and extraction investigations

Complexation studies. The complexation behaviours of acid-amide ligands **6**–**8** with lanthanide ions were studied by X-ray crystallography, UV/VIS spectroscopy and electrospray mass spectrometry (ES-MS).

Crystal structures. The crystal structure determinations of the lanthanum and sodium complexes of dihexylcarboxamide ligand **8** have been carried out. Complexation of dihexyl ligand **8** with lanthanum nitrate in a dichloromethane–isopropanol mixture in the presence of triethylamine gave crystals of the dimeric lanthanum complex $[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]$. The resulting X-ray crystal structure complex of $[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]$ is illustrated in Fig. 2. The dimer contains a crystallographic centre of symmetry. In this structure the lanthanum atom is eight-coordinate: it is bound to four oxygen atoms at the bottom rim of one calix[4]arene, the amide oxygen atom O(453), one acid oxygen atom O(253) from this calixarene and the symmetry related acid oxygen atom O(253) from the other calixarene. Finally, a solvent oxygen atom from isopropanol completes the coordination sphere. The make-up of the coordination sphere is thus equivalent to that previously found for the Eu^{3+} and Sm^{3+} complexes of **6**.[9b] These two isomorphous centrosymmetric structures, $[M_2(\mathbf{6} - 3H)(EtOH)_2]$ contain ethanol as the attached solvent molecule. The dimensions of the samarium complex with **6** compared to the lanthanum complex of **8** show little difference between the two structures. The bond lengths for the La^{3+} complex are greater by *ca* 0.10 Å as might be expected but all the angles differ by less than 5° except for O(253)–M–O(453) which differs by 7.5°. The calix[4]arene subunit exhibits a distorted cone conformation with angles between the four phenyl rings and the plane of the four methylene groups 41.5(1), 84.3(1), 43.6(1) and 86.6(1)°, respectively. It is apparent that the hexyl groups have no effect on the coordination sphere because they are directed well away from the metal sites. A search of the Cambridge Crystallographic Database shows that coordination numbers of



Scheme 2 Reagents and conditions: (i) ethylbromoacetate, acetonitrile, K_2CO_3; (ii) 1 equiv. KOH, EtOH; (iii) HNO_3; (iv) $(COCl)_2$; (v) Et_2NH, CH_2Cl_2; (vi) 3.3 equiv. KOH, EtOH; (vii) $(COCl)_2$; (viii) Et_2NH, CH_2Cl_2; (ix) 1 equiv. KOH, EtOH.

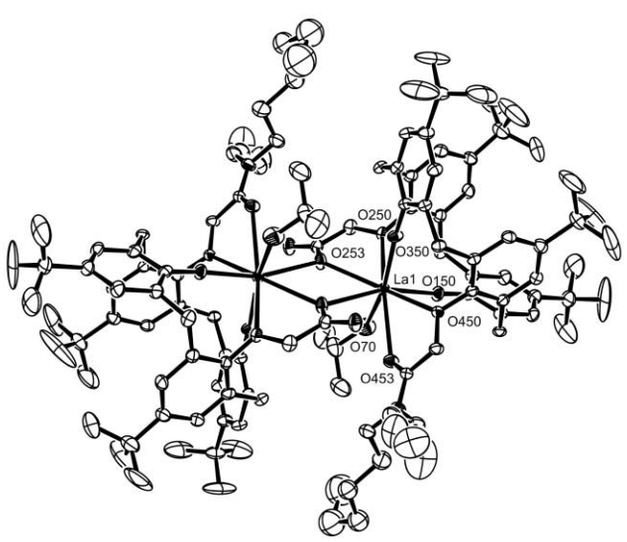


Fig. 2 View of the structure of centrosymmetric dinuclear lanthanum complex $[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]$. Thermal ellipsoids are shown at 15% probability and hydrogen atoms omitted for clarity. Selected bond lengths (Å): La1–O350 2.245(5), La1–O150 2.276(5), La1–O253 2.613(5), La1–O70 2.595(7), La1–O253 ($1 - x$, $2 - y$, $1 - z$) 2.586(6), La1–O453 2.623(5), La–O450 2.667(5), La1–O250 2.683(5).

10–12 are more common than 8 and 9 for La^{3+} and that a coordination number of 8 for the La^{3+}–**8** complex is therefore low. In the present dimer, it is the steric constraints of the calix[4]arene that preclude a higher coordination number. Within the complex, the metal is very strongly bound to the negatively charged oxygen atoms at the bottom rim of the cone as shown by the short La–O distances (La–O(150) 2.276(5), La–O(350) 2.245(5) Å), whereas the other six distances are in a more normal range for La–O distances (2.586(5)–2.683(5) Å). For comparison the Cambridge Database details 37 structures with eight-coordinate lanthanum bonded to at least one oxygen atom. In these structures, the mean La–O bond is 2.506Å and the minimum distance of 2.221 Å is only just longer than the shortest La–O bond in La^{3+}–**8**. Although acid-amide ligands have been shown not to recover sodium in two-phase solvent extraction experiments *vide infra*, the sodium complex of **8** could be prepared by slow crystallisation of a solution of **8** and sodium perchlorate in a mixed dichloromethane–isopropanol–acetonitrile solution.

The X-ray crystal structure of $[Na_2(\mathbf{8} - H)_2]$ was determined and is illustrated in Fig. 3 The structure of the dimeric $[Na_2(\mathbf{8} - H)_2]$ complex, unlike other calix[4]arene complexes with La^{3+}, Sm^{3+}, and Eu^{3+}, is not centrosymmetric. In the Na^+–**8** complex, the two calix[4]arene axes (defined as the angle between the two planes of four methylene atoms C(17), C(27), C(37), C(47) and C(57), C(67), C(77), C(87)) intersect at 28.2(1)°. The two calixarene subunits have slightly distorted cone conformations where the angles between the phenyl rings and the plane of the four methylene atoms are 63.3, 71.5, 58.8, 63.4° and 54.6, 73.4, 58.5, 65.7° for each subunit respectively. Each sodium atom in the dimeric complex is six-coordinate and bonded to three oxygens at the bottom rim of the cone, the amide oxygen atom

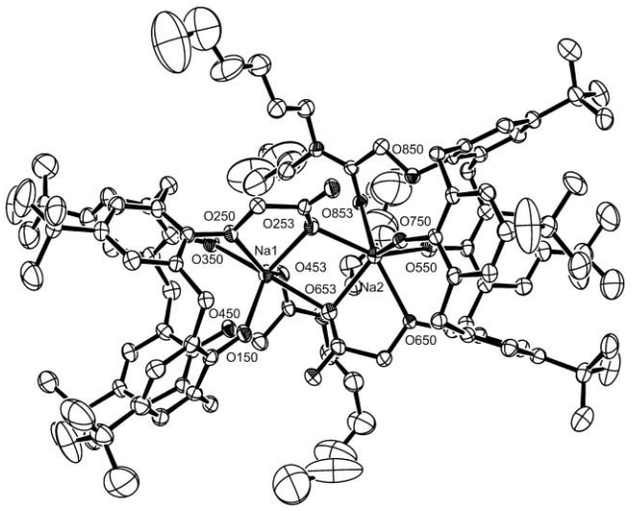


Fig. 3 View of the structure of non-centrosymmetric dinuclear sodium complex $[Na_2(\mathbf{8} - H)_2]$. Thermal ellipsoids are shown at 15% probability and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Na1–O253 2.299(5), Na1–O150 2.370(5), Na1–O653 2.378(5), Na1–O250 2.390(5), Na1–O350 2.443(5), Na1–O453 2.557(5), Na1–O450 2.808(5), Na2–O653 2.341(5), Na2–O253 2.347(5), Na2–O750 2.369(5), Na2–O550 2.398(5), Na2–O650 2.406(5), Na2–O853 2.582(5), Na2–O850 2.810(5).

and two bridging acid oxygen atoms (one from each calixarene). It should be noted that the two sodium atoms remain unbound to the phenolic oxygen atoms (connected to amide groups) at the bottom rim of the calixarene, unlike the lanthanide complexes previously described. Although this is the case, the Na–O distances of Na(1) ··· O(450) and Na(2) ··· O(850) (2.808(5), 2.810(5) Å) suggest that there might be some weak interaction with the remaining phenolic groups. In comparison the other Na–O distances are shorter and in the range 2.299(5)–2.582(5) Å.

In this structure the dimeric complex is formulated as $[Na_2(\mathbf{8} - H)_2]$ with the acid being deprotonated whereas the four phenolic oxygen atoms O(150), O(350) and O(550), O(750), despite being bonded to the metal, retain their hydrogen atoms. This formulation is consistent as the Na–O bonds to these four atoms are not significantly shorter than the other four non-hydrogen Na–O bonds, because in the lanthanum complex, O(150) and O(350) are certainly deprotonated, as the two La–O bonds with the phenolic oxygens are very much shorter than the other La–O bonds. In the sodium dimer, any alternative formulation would require additional cations in the asymmetric unit, though there is much additional electron density in the asymmetric unit, which can be explained in terms of solvent molecules, the presence of small cations though unlikely cannot be entirely ruled out. It is interesting that the sodium structure is different from other structures obtained with lanthanide complexes of calixarene acid-aides and it seems likely that these structural differences are due to the relatively small size of the Na^+ cation which destabilizes the centrosymmetric dimeric structures found for La^{3+}, Sm^{3+}, and Eu^{3+} complexes. As was reported earlier,[9b] this dimeric structure is also unstable for Lu^{3+} which forms a seven-coordinate monomeric structure $[Lu(\mathbf{6} - 3H)(H_2O)]$.

UV/VIS studies. UV/VIS spectroscopy was used to investigate complex formation and stoichiometry with ligands **6**–**8**. Titration experiments for dmso solutions of ligand and the lanthanide ions: La^{3+}, Nd^{3+}, Gd^{3+}, Ho^{3+}, Lu^{3+} in the presence of triethylamine (5 equivalents) were performed and analyzed using the computer program Specfit.[11]

For example, a typical titration profile with ligand **7** and lanthanum nitrate is shown in Fig. 4. The addition of increasing equivalents of cation, up to one equivalent, resulted in the

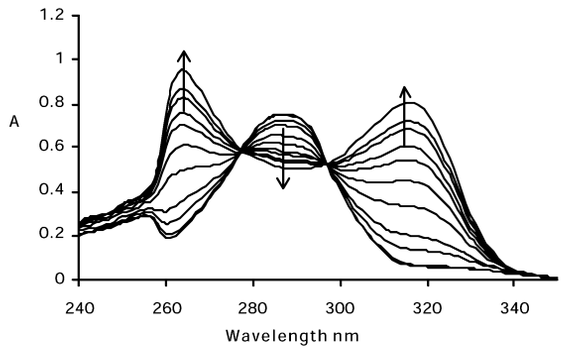


Fig. 4 UV/VIS spectra of additions of 0.1–1.0 equivalents of La^{3+} to **7**.

notable increase of two absorptions at 264 and 315 nm. The observation of two isosbestic points in the titration profile clearly indicates a clean complexation reaction. Addition of further amounts of cation (not shown), up to ten equivalents, caused very little change in the absorption spectrum. These observations show that the formation of the lanthanide complexes is rapid and complete following the addition of one equivalent of the cation. Analysis by Specfit confirmed the empirical 1 : 1 stoichiometry and gave the following stability constants displayed in Table 1. Unfortunately, analysis of the titration data cannot distinguish between the formation of 1 : 1 or 2 : 2 complex stoichiometry in the solution-state. As a consequence of the lanthanide contraction the stability constant of a lanthanide complex may be expected to increase from lanthanum to lutetium, due to the associated increase in Lewis acidity of the lanthanide cation. However, this trend is not observed for the ligands studied here suggesting that the strength of binding cannot be described purely in terms of Lewis acidities and electrostatic interactions. Thus the nature of geometric complementarity and the number of donor atoms required for complexation between the ligand and a lanthanide cation must also be taken into consideration. It is also noted that variation of the carboxamide substituent appears to have little effect upon the stability constants as determined in dmso solution.

Electrospray mass spectrometry (ES-MS). Evidence for the existence of the 2 : 2 lanthanum : calixarene dimer, $[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]$, in solution was provided by electrospray mass spectrometry. Solutions of **8** in dichloromethane and $Ln(NO_3)_3(dmso)_n$ in acetonitrile were mixed prior to injection. With lanthanum, intense molecular ions corresponding to the doubly charged species $[La_2(\mathbf{8} - 2H)_2]^{2+}$ *m*/*z* 1069.0, $[La_2(\mathbf{8} - 2H)_2(dmso)]^{2+}$ *m*/*z* 1108.0 and $[La_2(\mathbf{8} - 2H)_2(dmso)_2]^{2+}$ *m*/*z* 1147.0 were observed. As shown in Fig. 5a, these doubly charged ions were observed at low sample cone voltages, 25 V and upon raising the sample cone voltage to 90 V these 2 : 2 metal : calix dimer peaks were observed to fragment and in the latter case lose dmso solvent, presumably by collision induced dissociation, to give the singly charged species $[La(\mathbf{8} - 2H)]^+$ *m*/*z* 1068.5 exclusively.[12] At intermediate cone voltages the presence of both singly-charged calix : metal monomer and doubly-charged calix : metal dimer ions were observed resulting in a complex isotope distribution pattern at *m*/*z* 1069 (not shown). In contrast, experiments with the smaller gadolinium ion at low sample cone voltage (≈20 V) showed the overlap of both the singly-charged calix : metal monomer and doubly charged calix : metal dimer ions at *m*/*z* 1087. Notably to fragment this dimer to produce exclusively the singly charged species, $[Gd(\mathbf{8} - 2H)]^+$ *m*/*z* 1087.5 a much lower sample cone voltage (≈55 V) (Fig. 5b) was required. For the smallest lanthanide ion, lutetium, only the singly charged 1 : 1 metal : calix species, $[Lu(\mathbf{8} - 2H)]^+$ *m*/*z* 1104.6, was observed irrespective of sample cone voltage (Fig. 5c) or other conditions.[13] These

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

Ligand	La^{3+}	Nd^{3+}	Gd^{3+}	Ho^{3+}	Lu^{3+}
6	6.32 ± 0.14	7.91 ± 0.56	6.02 ± 0.13	5.98 ± 0.66	4.82 ± 0.06
7	5.50 ± 0.09	5.17 ± 0.07	4.60 ± 0.06	4.66 ± 0.05	5.71 ± 0.34
8	7.00 ± 0.26	6.84 ± 0.24	6.86 ± 0.19	5.48 ± 0.07	5.55 ± 0.12

[a] $Ln^{3+} + H_3L = [LnL] + 3H^+$.

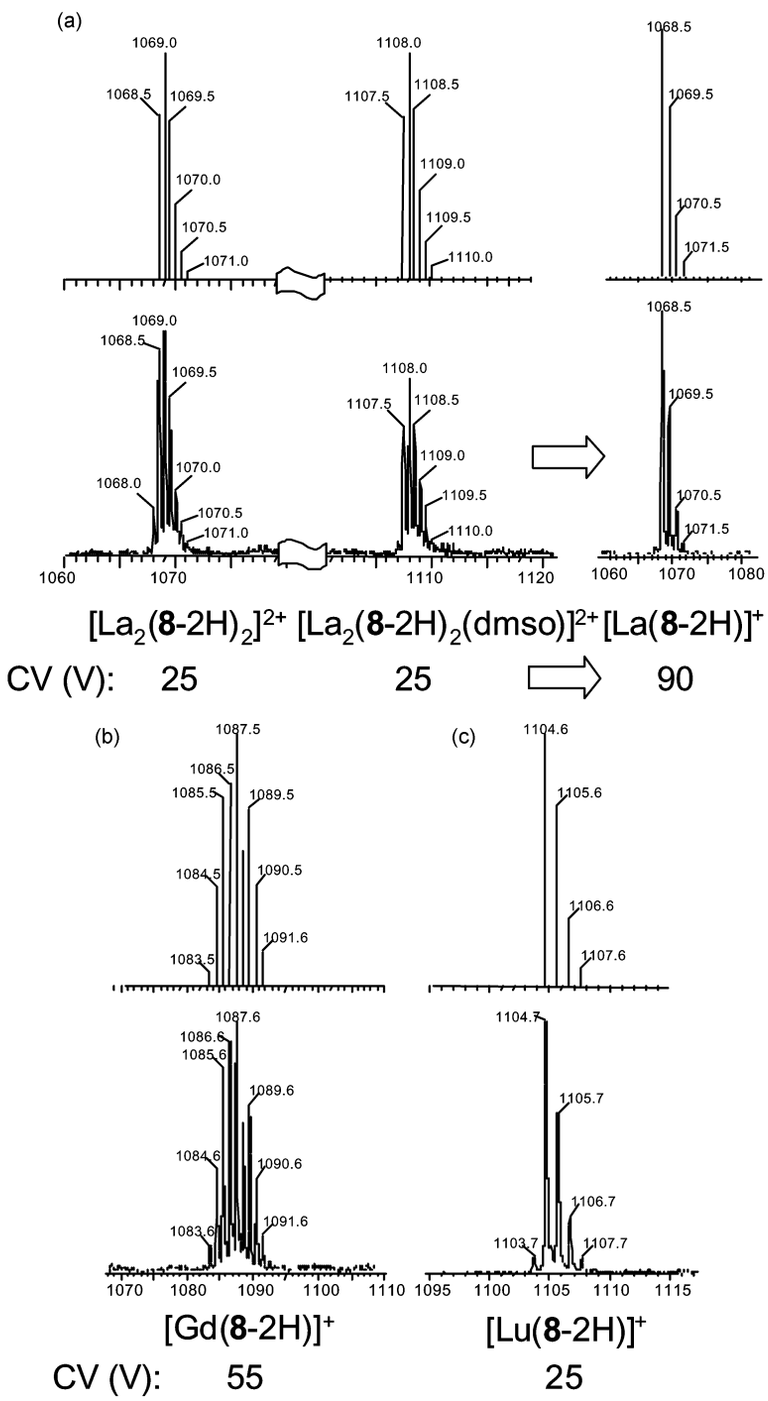


Fig. 5 Electrospray mass spectrometry of (a) lanthanum : calix 2 : 2 dimer and 1 : 1 monomer of **8** at low (25 V) and high (90 V) sample cone voltages; (b) gadolinium and (c) lutetium complexes of **8**. CV = cone voltage.

observations are consistent with previous crystal structure determinations and provide evidence that with the larger lanthanide ions the complexes exist in solution as 2 : 2 calix : metal dimers and that with the smaller lanthanide ions 1 : 1 calix : metal species predominate. Furthermore, they suggest that complexes of the intermediate size lanthanide ions exist in solution as variable and dynamic mixtures of 2 : 2 calix : metal dimer and 1 : 1 calix : metal monomer.

Extraction. Two-phase solvent extraction studies were performed to determine the trivalent lanthanide cation uptake by ligands **6**–**8**. Studies with **6** showed a marked dependence upon pH, with lanthanide extraction being essentially quantitative at pH 6 and above. Initially, extraction experiments were performed in the absence of citrate in the aqueous phase. However, above pH 6 lanthanide hydroxides precipitate which reduces the efficiency of the metal recovery process. For this reason and to buffer the solution, extraction experiments were performed in the presence of a three-fold excess of citrate anion.

The alkyl group on the carboxamide functionality was changed to determine whether this would alter significantly the extraction properties. For example, a more lipophilic dihexylamide substituent was introduced to improve extraction into organic solvents. However, for ligands **7** and **8** and from further studies where the alkyl group was systematically changed, no significant improvement in lanthanide extraction over **6** was observed over the same pH range (see Fig. 6a and 6b).[9,14]

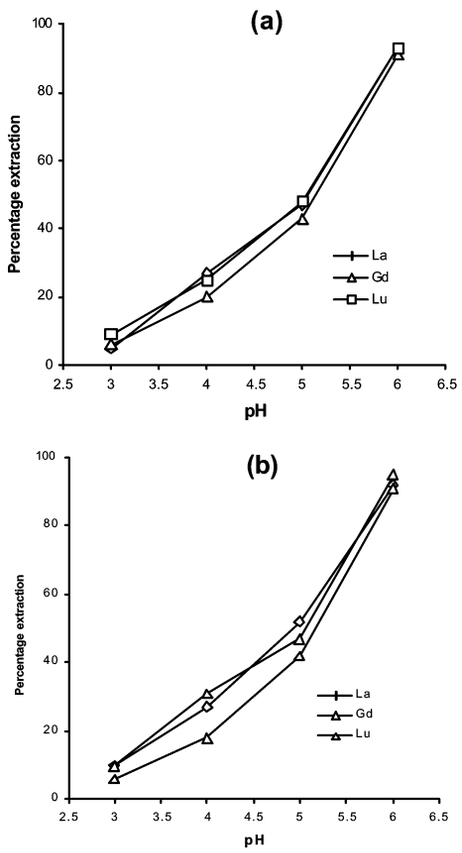


Fig. 6 Extraction of trivalent lanthanide cations by (a) **7** and (b) **8**; conditions: [Ln] = 4.0 mM, [L] = 10 mM, [citrate] = 1.2 mM.

Uranyl extraction and coordination. With their macrocyclic structure and ring of oxygen donor atoms, calixarenes are excellent candidates for the coordination of the uranyl cation (UO_2^{2+}).[15] The known coordination preferences of uranyl are four to six, equatorial, in-plane donor atoms.[16] Acid-amide calixarene ligands coordinate uranyl through deprotonated carboxylate and phenolate moities and a carboxamide donor. This leaves one phenolic oxygen of the calixarene protonated and uncoordinated to the metal cation. A crystal structure determination of **6** with uranyl shows formation of a dimeric 2 : 2 calix[4]arene : uranyl complex, $(UO_2)_2(\mathbf{6} - 2H)_2$, in the solid state with the fourth equatorial site on the uranyl being occupied by a bridging carboxylate of its dimer partner.[9a] Although designed for sequestration of trivalent metal cations 1,3-acid-amide ligands are effective extractants for uranyl ions from aqueous solutions. Uranyl extraction exhibits a marked pH dependency and quantitative extraction at pH 5 or higher.[9a] This pH dependency is attributed primarily to the pK_a values of the phenolic oxygen atoms.

The complexation of uranyl by acid-amide ligands **6**, **13** and **16** was confirmed by ES-MS. Acetonitrile solutions of calix[4]arene ligand and triethylamine turn orange on addition of uranyl acetate and after a day an orange precipitate is deposited. These solids were dissolved in dmf–dichloromethane mixtures and examined by ES-MS. In all three cases intense ions corresponding to the 1 : 1 metal : calix species $[\mathbf{6}(-H)UO_2]^+$ *m*/*z*: 1088.3, $[\mathbf{13}(-H)UO_2]^+$ *m*/*z*: 864.4 and $[\mathbf{16}(-H)UO_2]^+$ *m*/*z*: 954.3 were detected. A previous crystal structure determination showed formation of a 2 : 2 uranyl : calixarene complex in the solid state, however we were only able to observe weak molecular ions corresponding to dimeric species for example, $[\mathbf{16}_2(-H)_3UO_2]^+$ *m*/*z*: 1907.6. This may be a consequence that redissolution of the uranyl complex in the highly coordinating solvent dimethylformamide splits the dimer. Attempts to avoid this by examination of freshly prepared solutions of uranyl cation and ligand allowed to mix for 0.5 h failed to achieve better results. In contrast to the study with lanthanum, no doubly charged ions were observed irrespective of cone voltage.

^{1}H NMR studies confirmed the coordination of uranyl by acid-amide ligands. In the case of free ligand **16** the methylene protons of the ligating carboxy and carbamoyl groups appear as two singlets at δ 4.69 and 4.77 ppm respectively due to free rotation. After complexation[17] these methylene protons become locked in a different chemical environments from one another. Consequently, each proton gives rise to an absorption which appears as a doublet with coupling constants $^2J_{AB}$ = 10–15 Hz. The four AB quartets were identified on the basis of distortion of pairs of lines, interaction constants and COSY spectrum. The 50% decrease of the intensity of the phenolic OH signals indicates removal of a proton from one OH group. This induces different chemical environments for the protons *ortho* to the nitro groups. Appearance of four signals instead of one in the free ligand, for the *ortho* to nitro protons can also indicate the asymmetric dimerisation of uranyl complexes.

Two-phase solvent extraction experiments showed quantitative recovery of uranyl at pH 5 and above. Again a systematic change of the alkyl group of the carboxamide function failed to improve extraction at lower pH values, with ligands **7** and **8** showing identical performance over the pH range 2–7. Uranyl complexation requires deprotonation of a single phenolic moiety and carboxylic acid to achieve a charge neutral complex. It was anticipated that by lowering the pK_a of the phenolic oxygen atoms of the calixarene ligand uranyl extraction would be improved at lower pH values. For this reason the de-*tert*-butyl and 1,3-dinitro derivatives **13** and **16** were prepared. Extraction experiments with **13** and **16** demonstrated superior uranyl cation recovery for a given concentration of calixarene ligand, see Fig. 7. Previously, extraction experiments as detailed in Fig. 8 with ligands **6**–**8** were performed with a metal : ligand ratio of 1 : 25. However, the extraction efficiency of dinitro-based **13** was so much improved that even with metal : calix ratios of 1 : 1 over 90% of uranyl cation was extracted at pH 7. Consistent with this, the de-*tert*-butyl ligand **7** also exhibited superior extraction performance over ligands **6**–**8**, with 60% uranyl recovery at a 1 : 1 metal : calix ratio. Uranyl extraction with ligands **13** and **16** also showed improved performance at lower pH values (see Fig. 7). This improved performance at lower pH for **13** and **16** compared to **6**, is attributed to more facile proton dissociation in acidic environments from the calixarene ligands' phenol and carboxyl donor atoms due to the presence of their electron withdrawing and less donating substituents respectively.

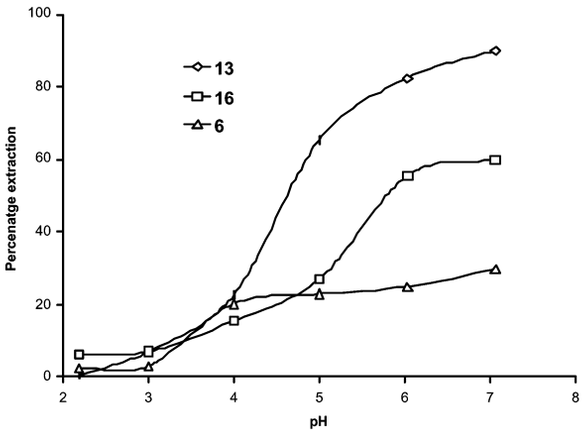


Fig. 7 Extraction of uranyl (UO_2^{2+}) by acid-amide ligands **6**, **13** and **16**; conditions: $[UO_2^{2+}] = 0.2$ mM [L] = 0.2 mM, CH_2Cl_2–H_2O.

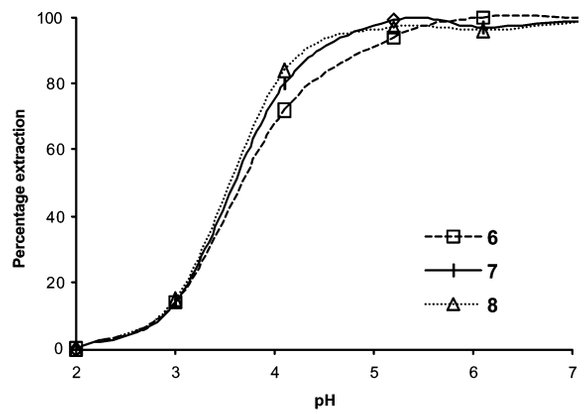


Fig. 8 Extraction of uranyl (UO_2^{2+}) by acid-amide ligands **6**–**8**; conditions: $[UO_2^{2+}] = 0.2$ mM, [L] = 5.0 mM, CH_2Cl_2–H_2O.

Conclusions

The synthesis of a series of *para-tert*-butylcalix[4]arene ligands bearing lower rim 1,3-acid-amide functionality has been achieved. A combination of UV/VIS, X-ray diffraction, NMR and ES-MS studies demonstrate binding of lanthanide and uranyl ions at the base of the calixarene cone through phenolate, carboxylate and carboxamide oxygen atoms. For the larger lanthanide ions and uranyl ion dimeric 2 : 2 calixarene : metal complexes are formed. Two-phase solvent extraction experiments have shown efficient and pH dependent uptake of lanthanide and uranyl cations by 1,3-acid-amide ligands. Introduction of more lipophilic groups at the carboxamide substituent was not found to improve efficiency in two-phase solvent extraction experiments. However, substitution of the upper rim calixarene to introduce 1,3-dinitro groups or removal of the *tert*-butyl groups was found to markedly improve the efficiency of uranyl extraction at both equivalent and lower pH values.

Experimental

General

Where necessary, solvents were purified prior to use and stored under N_2. Unless otherwise stated in the text, commercial grade chemicals were used without any further purification. *para-tert*-Butylcalix[4]arene and calix[4]arene were purchased from Aldrich and O-1,3-alkylated with ethylbromoacetate to afford 5,11,17,23-tetra-*tert*-butyl-25,27-bis(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene and 25,27-bis[(ethoxycarbonyl)-methoxy]-26,28-dihydroxycalix[4]arene respectively.[10,18,19] 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 performed all elemental analyses. Fast atom bombardment (FAB) mass spectrometry was performed at the University College of Swansea by the EPSRC service. UV/VIS spectrometry was performed on a Perkin-Elmer Lambda 6 UV/VIS spectrophotometer.

Electrospray mass spectrometry was performed on a Micromass LCT mass spectrometer operating at 3500 kV. For ligand characterisation, spectra were collected in mixed methanol–water solutions (90 : 1). Complexation studies were performed in acetonitrile. Ligands (1×10^{-3} M) were dissolved in dichloromethane, lanthanide nitrate (5×10^{-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.

For UV/VIS, ES-MS studies and complex preparation lanthanide nitrate salts as their dmso solvates *e.g.* $La(dmso)_4(NO_3)_3$, prepared by the method of Ramalingam and Soundararajan, were employed,.[20] Briefly, this involved crystallization of a solution of $Ln(NO_3)_3$ from a small volume of methanol and dmso.

Dichloromethane and deionised water were used for all extraction experiments. Lanthanide and uranyl standard solutions were purchased from Aldrich and BDH and were diluted for use with ICP calibration as well as the aqueous phase in the extraction studies. For uranyl extractions the concentration of the calix[4]arene ligand was 5 mM in dichloromethane and uranyl concentration was 0.2 mM in water. For lanthanide extractions the concentration of the calix[4]arene ligand was 10 mM in dichloromethane and the concentrations of La^{3+}, Gd^{3+} and Lu^{3+} cations were 0.4 mM in water. Equal volumes of organic and aqueous solutions were used (10 cm^3) in all solvent extraction experiments over the range pH 3–6 for the lanthanide cations and pH 2–7 for the uranyl cation. Prior to extraction, the aqueous layer was pH adjusted with 1 M LiOH or HCl where appropriate. Citric acid was neutralised with 1 M LiOH prior to use. Three molar equivalents of citrate when compared to the amount of cation present were added to the aqueous phase. The organic–aqueous layers were stirred in sealed flasks for 1 h and allowed to stand for 0.5 h. The organic and aqueous layers were separated and the metal cation concentration in the aqueous layer determined by ICP-AES. A Thermo Jarrell Ash atomscan 25 sequentially inductively coupled plasma atomic emission spectrometer (ICP-AES) was used to determine cation concentrations. It consists of a vacuum monochromator, a fully automated ICP source with a variable observation height and an autosampler. The equipment is controlled by the Thermo Jarrell Ash Thermospec™ version 5.2 software package.

Crystal structure determinations

Crystal data for $[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]\cdot 2CH_2Cl_2$ and $[Na_2(\mathbf{8} - H)_2]\cdot 2MeCN\cdot(CH_3)_2CO\cdot EtOH\cdot 2.5H_2O$ are given in Table 2 together with refinement details. Data for both crystals were collected with Mo-Kα radiation using the MARresearch Image Plate System. The crystals were positioned at 70 mm from the image plate. 95 Frames were measured at 2° intervals with a counting time of 5 min. Data analysis was carried out with the XDS program.[21] Default refinement details are described here while differences for specific structures are included below. Structures were solved using direct methods with the SHELXS program.[22] All non-hydrogen atoms, apart from those disordered and in solvent molecules, were refined anisotropically. Hydrogen atoms on the carbon atoms and nitrogen atoms were

Table 2 Crystal data and structure refinement for $[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]$ and $[Na_2(\mathbf{8} - H)_2]$

	$[La_2(\mathbf{8} - 3H)_2(^iPrOH)_2]\cdot 2CH_2Cl_2$	$[Na_2(\mathbf{8} - H)_2]\cdot 2MeCN\cdot(CH_3)_2CO\cdot EtOH\cdot 2.5H_2O$
Empirical formula	$C_{128}H_{170}Cl_4La_2N_2O_{16}$	$C_{129}H_{185}N_4Na_2O_{18.5}$
Formula weight	2426.39	2146.90
Wavelength/Å	0.71073	0.71073
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$C2/c$
a/Å	15.717(17)	38.60(5)
b/Å	16.040(19)	24.30(3)
c/Å	16.265(13)	29.79(4)
α/°	114.26(1)	(90)
β/°	90.25(1)	99.01(1)
γ/°	110.44(1)	(90)
Volume/Å^3	3450	27593
Z, D_c/Mg cm^{-3}	1, 1.168	8, 1.027
μ/mm^{-1}	0.744	0.070
Reflections collected	8954	37125 (R_{int} = 0.0994)
Data/restraints/parameters	8954/37/692	23584/36/1355
Final R indices [$I > 2\sigma(I)$] $R1$	0.0659	0.1091
$wR2$	0.1792	0.2843
R indices (all data) $R1$	0.0875	0.2520
$wR2$	0.1993	0.3533
Largest diff. peak, hole/e Å^{-3}	1.805, −1.156	0.448, −0.244

included in calculated positions and given thermal parameters equivalent to 1.2 times those of the atom to which they were attached. Hydrogen atoms on water molecules and oxygen atoms bonded to the metals, could not be located and were not included. In the lanthanum complex one of the hexyl moieties was disordered over two possible sites, and occupancy factors were refined to 0.59(2) and 0.41(2) respectively. In both complexes the dimensions of the hexyl chains were constrained. Both structures were refined on F^2 till convergence using Shelxl.[23] All calculations were carried out on a Silicon Graphics R5000 Workstation at the University of Reading. In the lanthanum complex, the two dichloromethane molecules in the asymmetric unit were both refined with 50% occupancy. In the sodium complex, two acetonitrile solvent molecule were refined with full occupancy, one acetone solvent molecule was refined with full occupancy and two ethanol molecules with 50% occupancy and 5 water molecules with 50% occupancy.

CCDC reference numbers 181508 and 181509.

See http://www.rsc.org/suppdata/dt/b2/b202442j/ for crystallographic data in CIF or other electronic format.

Syntheses

5,11,17,23-Tetra-*tert*-butyl-25-carboxymethoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene (1). Potassium hydroxide (0.68 g, 12.2 mmol) was added to 5,11,17,23-tetra-*tert*-butyl-25,27-bis(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene[19] (10.0 g, 12.2 mmol) slurried in ethanol and the mixture stirred. The resulting mixture was then heated at reflux for 2 h, cooled and filtered to yield the crude product as its potassium salt. This was taken up in the minimum amount of ethanol, concentrated hydrochloric acid (5 cm^3) in water (16 cm^3) was added and the mixture stirred for 30 min. The resulting solution was filtered, and the solvent removed to yield the product as a white solid (6.86 g, 74%), mp 178–181 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 0.93 (s, 9H, ^{t}Bu CH_3); 1.03 (s, 9H, ^{t}Bu CH_3); 1.28 (s, 18H, ^{t}Bu CH_3); 1.34 (t, 3H, J = 7.3, OCH_2CH_3); 3.35 (d, 2H, J = 13.2, ArCH_2Ar$_{eq}$); 3.39 (d, 2H, J = 13.3, ArCH_2Ar$_{eq}$); 3.73 (q, 2H, J = 7.4, OCH_2CH_3); 4.30 (d, 2H, J = 13.4, ArCH_2Ar$_{ax}$); 4.32 (d, 2H, J = 13.2, ArCH_2Ar$_{ax}$); 4.61 (s, 4H, OCH_2CO); 6.62 (s, 2H, OH); 6.89 (s, 2H, ArH); 7.05 (s, 4H, ArH); 7.06 (s, 2H, ArH). Found: C, 73.6; H, 8.2%. Calc. for $C_{50}H_{64}O_8\cdot 0.5K$: C, 73.9; H, 7.9%. ES-MS: m/z 816, $[M + Na]^+$.

5,11,17,23-Tetra-*tert*-butyl-25-(chlorocarbonyl)methoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene (2). Thionyl chloride (0.18 g, 1.51mmol) was slowly added to **1** (1.00 g, 1.25 mmol) in dichloromethane (50 cm^3), and the resulting mixture heated at reflux overnight. On cooling the solvent was removed and the resulting solid triturated with dichloromethane, to yield the product as a white solid (0.70 g, 67%), which was used without further purification.

5,11,17,23-Tetra-*tert*-butyl-25-(diethylcarbamoyl)methoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene (3). To a solution of **2** (2.0 g, 2.52 mmol) in dichloromethane was added dropwise a solution of diethylamine (0.74 g, 10 mmol) in dichloromethane. The resulting solution was stirred for 2 h and the solvent removed under reduced pressure. To the resulting sticky, pale oil, water (25 cm^3) and ethanol (25 cm^3) were added and the mixture stirred to produce a white precipitate that was removed by filtration and recrystallized from petroleum ether (bp 40–60 °C) to afford the title compound as a white solid (1.65 g, 77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 0.98 (s, 9H, ^{t}Bu CH_3); 1.00 (s, 9H, ^{t}Bu CH_3); 1.23 (s, 18H, ^{t}Bu CH_3); 1.3 (m, 9H, NCH_2CH_3, OCH_2CH_3); 3.30 (m, 4H, ArCH_2Ar$_{eq}$); 3.50 (m, 4H, NCH_2CH_3); 4.28 (q, 2H, $CO_2CH_2CH_2$); 4.43 (m, 4H, ArCH_2Ar$_{ax}$); 4.74 (s, 4H, OCH_2); 6.81 (s, 2H, ArH); 6.83 (s, 2H, ArH); 6.97 (s, 4H, ArH); 7.29 (s, 2H, OH). Found: C, 76.8; H, 9.0; N, 1.5%. Calc. for $C_{54}H_{73}O_7N$: C, 76.5; H, 8.7; N, 1.65%. ES-MS: m/z 871, $[M + Na]^+$.

5,11,17,23-Tetra-*tert*-butyl-25-(methoxyethoxycarbamoyl)-methoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]-arene (4). Prepared by the same method as **3** to afford a white solid (0.92 g, 88%), mp 109–113 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.92 (s, 9H, ^{t}Bu CH_3); 0.93 (s, 9H, ^{t}Bu CH_3); 1.23 (s, 18H, ^{t}Bu CH_3); 1.28 (t, 3H, J = 7.0, OCH_2CH_3); 3.25 (s, 3H, OCH_3); 3.32 (d, 2H, J = 14.0, ArCH_2Ar$_{eq}$); 3.33 (d, 2H, J = 13.5, ArCH_2Ar$_{eq}$); 3.58 (t, 2H, J = 6.3, $CH_2CH_2OCH_3$); 3.69 (m, 2H, $CONHCH_2CH_2$); 4.14 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.27 (d, 2H, J = 12.5, ArCH_2Ar$_{ax}$); 4.25–4.29 (m, 2H, OCH_2CH_3); 4.48 (s, 2H, OCH_2CO_2OEt); 4.62 (s, 2H, OCH_2CON); 6.82 (s, 2H, ArH); 6.83 (s, 2H, ArH); 7.04 (s, 4H, ArH); 7.30 (s, 2H, OH); 8.74 (t, 1H, J = 5.8, NH). Found: C, 73.8; H, 8.5; N, 1.5%. Calc. for $C_{53}H_{71}O_8N\cdot 0.5Na$: C, 73.9; H, 8.3; N, 1.6%. FAB-MS: m/z 850, $[M]^+$.

5,11,17,23-Tetra-*tert*-butyl-25-(dihexylcarbamoyl)methoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene (5). Prepared by the same method as **3** to afford a white solid (0.95 g, 76%), mp 175–78 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.80–0.84 (m, 6H, $CH_2CH_2CH_3$); 0.91 (s, 18H, ^{t}Bu CH_3); 0.95 (s,

18H, ^{t}Bu CH_3); 1.20–1.22 (m, 3H, OCH$_2$CH_3); 1.23–1.30 (m, 16H, CH$_3$CH_2CH_2CH_2CH_2CH$_2$N); 3.25 (d, 4H, J = 13.0, ArCH_2Ar$_{eq}$); 3.31–3.35 (m, 4H, CH_2N); 4.23 (q, 2H, J = 7.2, OCH_2CH$_3$); 4.37 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.46 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.71 (s, 4H, OCH_2CO); 6.77 (s, 2H, ArH); 6.82 (s, 2H, ArH); 6.94 (d, 2H, J = 2.5, ArH); 6.95 (d, 2H, J = 2.5, ArH); 7.28 (s, 2H, OH). Found C, 76.2; H, 9.4; N, 1.2%. Calc. for $C_{62}H_{89}O_7N\cdot H_2O$: C, 76.1; H, 9.4; N, 1.4%. FAB-MS: m/z 983, [M + Na]$^+$.

5,11,17,23-Tetra-*tert*-butyl-25-(diethylcarbamoyl)methoxy-27-carboxymethoxy-26,28-dihydroxycalix[4]arene (6). A solution of potassium hydroxide (67 mg, 1.2 mmol) in ethanol (40 cm^3) was added to **3** (1.00 g, 1.18 mmol) in ethanol (10 cm^3). The resulting mixture was heated under reflux with stirring for 2 h, cooled to room temperature and reduced to a small volume (5 cm^3). Concentrated hydrochloric acid (10 cm^3) was added and the white precipitate that formed was removed by filtration and washed with water (25 cm^3). The crude product was recrystallized from dichloromethane–hexane to afford a white solid (0.91 g, 94%). ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 0.98 (s, 9H, ^{t}Bu CH_3); 1.03 (s, 9H, ^{t}Bu CH_3); 1.20 (s, 18H, ^{t}Bu CH_3); 3.28 (t, 6H, J = 7.0, NCH$_2$CH_3); 3.33 (d, 2H, J = 13.0, ArCH_2Ar$_{eq}$); 3.36 (d, 2H, J = 13.0, ArCH_2Ar$_{eq}$); 3.49 (q, 4H, J = 7.2, NCH_2CH$_3$); 4.18 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.25 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.59 (s, 2H, OCH_2CO$_2$H); 4.72 (s, 2H, OCH_2-CON); 6.88 (s, 2H, ArH); 6.95 (s, 2H, ArH); 7.00 (d, 2H, J = 2.5, ArH); 7.04 (d, 2H, J = 2.5, ArH); 7.76 (br s, 2H, OH). ν_{max}/cm^{-1} 3432, 2961, 1746, 1649, 1484, 1361, 1301, 1202, 1124, 1058. Found: C, 74.7; H, 8.2; N, 1.7%. Calc. for $C_{52}H_{69}O_7N\cdot H_2O$: C, 74.5; H, 8.5; N 1.7%. ES-MS: m/z 854, [M + Na]$^+$.

5,11,17,23-Tetra-*tert*-butyl-25-(ethoxymethoxycarbamoyl)-methoxy-27-carboxymethoxy-26,28-dihydroxycalix[4]arene (7). Prepared by the same method as **6** to afford a white solid (0.79 g, 91%), mp 239–242 °C. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H 1.04 (s, 9H, ^{t}Bu CH_3); 1.09 (s, 9H, ^{t}Bu CH_3); 1.27 (s, 18H, ^{t}Bu CH_3); 3.39 (d, 2H, J = 13.2, ArCH_2Ar$_{eq}$); 3.47 (d, 2H, J = 13.3, ArCH_2Ar$_{eq}$); 3.53 (s, 3H, OCH_3); 3.70 (m, 2H, NHCH_2-CH$_2$OCH$_3$); 3.71 (t, 2H, J = 7.5, CH$_2$CH_2OCH$_3$); 4.12 (d, 2H, J = 12.5, ArCH_2Ar$_{ax}$); 4.17 (d, 2H, J = 12.5, ArCH_2Ar$_{ax}$); 4.54 (s, 2H, OCH_2CO$_2$H); 4.63 (s, 2H, OCH_2CON); 6.92 (s, 2H, ArH); 6.99 (s, 2H, ArH); 7.06 (s, 2H, ArH); 7.08 (s, 2H, ArH); 7.71 (s, 2H, OH); 8.89 (t, 1H, J = 5.8, NH); ν_{max}/cm^{-1} 3368, 2955, 1746, 1681, 1555, 1484, 1362, 1300, 1196, 1126, 1053. Found: C, 73.5; H, 8.5; N, 1.6%. Calc. for $C_{51}H_{67}O_7N\cdot NaH_2O$: C, 73.3; H, 8.3; N, 1.7%. FAB-MS: m/z 844, [M + Na]$^+$.

5,11,17,23-Tetra-*tert*-butyl-25-(dihexylcarbamoyl)methoxy-27-carboxymethoxy-26,28-dihydroxycalix[4]arene (8). Prepared by the same method as **6** to afford a white solid (0.95 g, 87%), mp 129–133 °C. ^{1}H NMR (500 MHz, CDCl$_3$): δ_H 0.81–0.85 (m, 6H, CH$_2$CH$_2$CH_3); 0.97 (s, 9H, ^{t}Bu CH_3); 1.02 (s, 9H, ^{t}Bu CH_3); 1.19 (s, 18H, ^{t}Bu CH_3); 1.24–1.27 (m, 16H, NCH$_2$CH_2CH_2-CH_2CH_2CH$_3$); 3.16–3.20 (m, 2H, NCH_2CH$_2$); 3.32 (d, 2H, J = 13.5, ArCH_2Ar$_{eq}$); 3.36 (d, 2H, J = 13.5, ArCH_2Ar$_{eq}$); 3.38–3.42 (m, 2H, NCH_2CH$_2$); 4.18 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.24 (d, 2H, J = 13.5, ArCH_2Ar$_{ax}$); 4.59 (s, 2H, OCH_2CO$_2$OH); 4.71 (s, 2H, OCH_2CON); 6.87 (s, 2H, ArH); 6.94 (s, 2H, ArH); 6.99 (d, 2H, J = 2.5, ArH); 7.09 (d, 2H, J = 2.5, ArH); 7.76 (br s, 2H, OH). ν_{max}/cm^{-1} 3432, 2959, 1747, 1649, 1483, 1362, 1300, 1194, 1125, 1058. Found: C, 75.7; H, 9.0; N, 1.1%. Calc. for $C_{60}H_{85}O_7N\cdot 0.5NaH_2O$: C, 75.6; H, 9.1; N, 1.5%. FAB-MS: m/z 955, [M + Na]$^+$.

25-Carboxymethoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxycalix[4]arene (9). Potassium hydroxide (0.72 g, 12 mmol) in water : ethanol (0.8 : 5 cm^3) was added over 2 h to a stirred suspension of 25,27-bis[(ethoxycarbonyl)-methoxy]-26,28-dihydroxycalix[4]arene (7.20 g, 12 mmol) in ethanol (70 cm^3) under reflux. The resulting mixture was maintained under reflux for a further 2 h and following cooling to 3–4 °C a white suspension that formed was removed by filtration to afford the potassium salt of ester-acid **9** in 85% yield (6.24 g). This was suspended in a vigorously stirred mixture of dichloromethane (300 cm^3) and hydrochloric acid (100 cm^3, 5%) and heated under reflux (0.5 h). Following cooling to room temperature the organic layer was separated, dried over magnesium sulfate, concentrated to 20 cm^3 volume and hexane (80 cm^3) was gradually added. The white microcrystalline product was separated, washed with hexane and dried at 60–70 °C to afford the acid-ester **9** (5.72 g, 84%). ^{1}H NMR (500 MHz, dmso-d$_6$): δ_H 1.26 (t, 3H, J = 7.0, CH_3); 3.40 (d, 4H, J = 13.0, ArCH_2Ar$_{eq}$); 4.26 (q, 2H, J = 7.0, OCH_2CH$_3$); 4.33 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 4.36 (d, 2H, J = 13.0, ArCH_2Ar$_{ax}$); 7.13, 7.20 (2 × d, 8H, J = 7.5, OCH_2C(O)O); 7.90 (s, 2H, OH). Found: C, 71.51; H, 5.67%. Calc. for $C_{34}H_{32}O_8$: C, 71.82; H, 5.67%. ES-MS: m/z 569.2, [M + H]$^+$; 591.2, [M + Na]$^+$.

25-Carboxymethoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxy-5,17-dinitrocalix[4]arene (10). To a vigorously stirred solution of the potassium salt of **9** (5.5 g, 9 mmol) in dichloromethane (200 cm^3) a mixture of concentrated hydrochloric acid (50 cm^3) and nitric acid (68%, 50 cm^3) in water (250 cm^3) and two drops of acetic anhydride were added. After 0.5 h stirring at room temperature the organic layer was separated, washed with water (100 cm^3), dried over magnesium sulfate and evaporated. The orange residue was purified by column chromatography on silica gel (Merck Kieselgel 60, 230–400 mesh) using a mixture of dichloromethane–ethyl acetate–acetic acid (95 : 5 : 0.3) as eluant. A broad yellow band was collected, evaporated and the solid residue crystallized from ethanol (40 cm^3) to give the pure dinitro derivative **10** as pale yellow powder (3.7 g, 56%). ^{1}H NMR (500 MHz, CDCl$_3$): δ_H 1.25 (t, 3H, J = 7.5, CH_3); 3.37–3.41 (overl. d, 4H, ArCH_2Ar$_{eq}$); 4.24 (q, 2H, J = 7.5, OCH_2CH$_3$); 4.40 (d, 2H, J = 13.5, ArCH_2Ar$_{ax}$); 4.35 (d, 2H, J = 13.5, ArCH_2Ar$_{ax}$); 4.59, 4.62 (2 × s, 4H, OCH_2C(O)O); 6.73–6.76 (overl. t, 2H, ArH); 6.87 (d, 2H, ArH); 6.90 (d, 2H, ArH); 8.03 (s, 2H, ArH); 8.80 (br s, 2H, OH). FAB-MS: m/z 659, [M + H]$^+$; 681, [M + Na]$^+$.

25-(Chlorocarbonyl)methoxy-27-(ethoxycarbonyl)methoxy-26,28-dihydroxy-5,17-dinitrocalix[4]arene (11). To a stirred solution of dinitro derivative **10** (3.64 g, 5.5 mmol) in dichloromethane (40 cm^3) oxalyl chloride (1.4 cm^3, 11 mmol) and two drops of DMF were added. The mixture was stirred at room temperature for 1 h, refluxed for 2 h and then crystallized by addition of hexane (50 cm^3) at 3–4 °C. The crystalline product was separated, washed with hexane (2 × 10 cm^3) and dried over phosphorous pentoxide *in vacuo* to give the title compound in a quantitative yield (3.8 g). ^{1}H NMR (500 MHz, CDCl$_3$): δ_H 1.39 (t, 3H, J = 7.0, CH_3); 3.54 (d, 2H, J = 13.5, ArCH_2Ar$_{eq}$); 3.57 (d, 2H, J = 13.5, ArCH_2Ar$_{eq}$); 4.38–4.42 (m, 6H, OCH_2CH$_3$, ArCH_2Ar$_{ax}$); 4.73 (s, 2H, OCH_2C(O)O); 5.13 (s, 2H, OCH_2-C(O)Cl); 6.88–6.91 (overl. t, 2H, ArH); 7.00 7.04 (d, 4H, ArH); 8.04 (s, 4H, ArH); 8.52 (s, 2H, OH).

25-(*N*,*N*-Diethylcarbamoyl)methoxy-27-(ethoxycarbonyl)-methoxy-26,28-dihydroxy-5,17-dinitrocalix[4]arene (12). To a stirred solution of acid chloride **11** (3.8 g, 5.5 mmol) in dichloromethane (50 cm^3) diethylamine (1.33 g, 18.3 mmol) in dichloromethane (10 cm^3) was added over 10 min at 16–20 °C. The yellow reaction mixture was stirred at room temperature for 1 h, whereupon water (25 cm^3) and concentrated aqueous hydrochloric acid (3 cm^3) were added. After stirring for 20 min the organic layer was separated, washed with water (40 cm^3), dried over magnesium sulfate and reduced in volume. The pale yellow product was recrystallized from dichloromethane–methanol, separated, washed with methanol and dried at 60–70 °C to give the title compound (2.94 g, 75%). ^{1}H NMR (500 MHz,

dmso-d_6): δ_H 1.11 (t, 6H, J = 7.0, NCH_2CH_3); 1.15 (t, 6H, J = 7.0, NCH_2CH_3); 1.26 (t, 3H, J = 7.0, OCH_2CH_3); 3.30 (q, 4H, J = 7.0, NCH_2CH_3); 3.40 (q, 4H, J = 7.0, NCH_2CH_3); 3.60 (d, 4H, J = 13.0, $ArCH_2Ar_{eq}$); 3.67 (d, 4H, J = 13.0, $ArCH_2Ar_{eq}$); 4.23 (q, 2H, J = 7.0, OCH_2CH_3); 4.34 (d, 4H, $ArCH_2Ar_{ax}$); 4.35 (d, 4H, $ArCH_2Ar_{ax}$); 4.79, 4.91 (2 × s, 4H, $OCH_2C(O)N$ and $OCH_2C(O)O$); 6.79 (t, 2H, J = 7.5, Ar*H*); 6.84 (t, 2H, J = 7.5, Ar*H*); 7.08 (d, 4H, J = 7.5, Ar*H*); 7.15 (d, 4H, J = 7.5, Ar*H*); 8.19 (s, 4H, Ar*H*); 9.56 (s, 2H, O*H*). Found: C, 63.63; H, 5.31; N, 5.55%. Calc. for $C_{38}H_{39}N_3O_{11}$: C, 63.95; H, 5.51; N, 5.89%. FAB-MS: *m*/*z* 714.3, $[M + H]^+$; 736.3 $[M + Na]^+$.

25-(*N*,*N*-Diethylcarbamoyl)methoxy-27-carboxymethoxy-26,28-dihydroxy-5,17-dinitrocalix[4]arene (13). To a stirred solution of ester-amide **12** (2.60 g, 3.6 mmol) in acetone (30 cm^3) a solution of potassium hydroxide (0.67 g, 12 mmol) in water (0.7 cm^3) and ethanol (7 cm^3) was added and stirred at room temperature (21–23 °C) for 3.5 h. The precipitated orange potassium salt of **13** was separated, washed with acetone (2 × 5 cm^3) and dried (yield 2.10 g). This was suspended in a vigorously stirred mixture of dichloromethane (70 cm^3) and dilute hydrochloric acid (30 cm^3, 5%) and after 0.5 h the organic layer was separated, dried over magnesium sulfate and reduced in volume. The product was recrystallized from dichloromethane–ethanol to afford acid-amide **13** (1.98 g, 80%). ^{1}H NMR (500 MHz, dmso-d_6): δ_H 1.11 (t, 6H, J = 7.0, NCH_2CH_3); 1.15 (t, 6H, J = 7.0, NCH_2CH_3); 3.32 (q, 4H, J = 7.0, NCH_2CH_3); 3.40 (q, 4H, J = 7.0, NCH_2CH_3); 3.64 (d, 2H, J = 13.5, $ArCH_2Ar_{eq}$); 3.65 (d, 2H, J = 13.5, $ArCH_2Ar_{eq}$); 4.34 (d, 2H, J = 13.5, $ArCH_2Ar_{ax}$); 4.41 (d, 2H, J = 13.5, $ArCH_2Ar_{ax}$); 4.89, 4.72 (2 × s, 4H, $OCH_2C(O)N$ and $OCH_2C(O)O$); 6.82 (overl.t, 2H, J = 7.5, Ar*H*); 7.09 (d, 2H, J = 7.5, Ar*H*); 7.15 (d, 2H, J = 7.5, Ar*H*); 8.16 (s, 4H, Ar*H*); 9.68 (br s, 2H, O*H*). Found: C, 62.92; H, 5.14; N, 5.41%. Calc. for $C_{36}H_{35}N_3O_{11}$: C, 63.06; H, 5.14; N, 6.13%. FAB-MS: *m*/*z* 686.4, $[M + H]^+$; 708.4, $[M + Na]^+$.

25-(*N*,*N*-Diethylcarbamoyl)methoxy-27-(ethoxycarbonyl)-methoxy-26,28-dihydroxycalix[4]arene (15). The reactive intermediate **14** was prepared as follows. To a stirred solution of **9** (2.00 g, 3.5 mmol) in dichloromethane (30 cm^3) oxalyl chloride (2 cm^3) and two drops of DMF were added. The mixture was refluxed for 2 h and reduced to a solid residue *in vacuo* at 40–50 °C to afford crude acid chloride **11** (2.10 g). To a stirred solution of acid chloride **14** (2.10 g, 3.4 mmol) in THF (50 cm^3) diethylamine (0.98 g, 13.5 mmol) in THF (5 cm^3) was added over 10 min and the mixture was stirred at 50–55 °C for 0.5 h. The solid (Et_3NHCl) was removed by filtration and the filtrate evaporated to dryness. The solid residue was dissolved in dichloromethane (50 cm^3); washed with water (20 cm^3); the organic layer was separated, dried over magnesium sulfate, evaporated and the crude product was triturated with hot ethanol (10 cm^3) to give the pure ester-amide **15** (2.0 g, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.21 (t, 6H, J = 7.0, NCH_2CH_3); 1.25 (t, 6H, J = 7.0, NCH_2CH_3); 1.34 (t, 3H, J = 7.0, OCH_2CH_3); 3.39 (d, 2H, J = 13.0, $ArCH_2Ar_{eq}$); 3.40 (d, 2H, J = 13.0, $ArCH_2Ar_{eq}$); 3.50 (overl. q, 4H, J = 7.0, NCH_2CH_3); 4.31 (q, 2H, J = 7.0, OCH_2CH_3); 4.48 (d, 2H, J = 13.0, $ArCH_2Ar_{ax}$); 4.52 (d, 2H, J = 13.0, $ArCH_2Ar_{ax}$); 4.76 (s, 4H, $OCH_2C(O)N$ and $OCH_2C(O)O$); 6.64 (t, 2H, J = 7.5, Ar*H*); 6.74 (overl. t, 2H, J = 7.5, Ar*H*); 6.91 (overl. d, 4H, J = 7.5, Ar*H*); 7.04 (d, 4H, J = 7.5, Ar*H*); 7.89 (s, 2H, O*H*). Found: C, 72.87; H, 5.74; N, 2.27%. Calc. for $C_{38}H_{41}NO_7$: C, 73.14; H, 6.63; N, 2.25%. ES-MS: *m*/*z* 624.3, $[M + H]^+$; 646.3, $[M + Na]^+$.

25-(*N*,*N*-Diethylcarbamoyl)methoxy-27-carboxymethoxy-26,28-dihydroxycalix[4]arene (16). To a stirred solution of esteramide **15** (1.5 g, 2.4 mmol) in acetone (25 cm^3) a solution of potassium hydroxide (0.15 g, 2.4 mmol) in water (0.3 cm^3) and ethanol (3 cm^3) was added over 3 h and stirring continued at room temperature overnight. The precipitated potassium salt of **16** was separated, washed with acetone (2 × 5 cm^3) and dried (yield 1.32 g). This was suspended in a vigorously stirred mixture of dichloromethane (40 cm^3) and dilute hydrochloric acid (15 cm^3, 5%). After 0.5 h the organic layer was separated, dried over magnesium sulfate and evaporated to dryness. Recrystallisation from dichloromethane–ethanol afforded a white crystalline product (1.2 g, 85%). ^{1}H NMR (500 MHz, dmso-d_6): δ_H 1.12 (t, 6H, J = 7.0, NCH_2CH_3); 1.17 (t, 6H, J = 7.0, NCH_2CH_3); 3.45–3.67 (m, 8H, NCH_2CH_3 and $ArCH_2Ar_{eq}$); 4.33 (d, 4H, J = 13.0, $ArCH_2Ar_{ax}$); 4.39 (d, 4H, J = 13.0, $ArCH_2Ar_{ax}$); 4.77, 4.69 (2 × s, 4H, $OCH_2C(O)N$ and $OCH_2C(O)O$); 6.54 (t, 2H, J = 7.5, Ar*H*); 6.75 (overl. t, 2H, J = 7.5, Ar*H*); 7.01 (d, 2H, J = 7.5, Ar*H*); 6.98 (d, 2H, J = 7.5, Ar*H*); 7.08 (d, 4H, J = 7.5, Ar*H*); 8.18 (br s, 2H, O*H*). Found: C, 72.43; H, 5.97; N, 2.38%. Calc. for $C_{36}H_{37}NO_7$: C, 72.59; H, 6.26; N, 2.35%. ES-MS: *m*/*z* 596.3, $[M + H]^+$; 618.3, $[M + Na]^+$.

$[La_2(8 - 3H)_2(^iPrOH)_2]$. To a solution of **8** (100 mg, 0.11 mmol) in dichloromethane (20 cm^3) was added $La(dmso)_4(NO_3)_3$ (70 mg, 0.11 mmol) in acetonitrile (5 cm^3) and triethylamine (50 μL). The solution was allowed to stir for 2 h, filtered and the filtrate layered with isopropanol (30 cm^3). After 2 weeks colourless crystals of the title complex suitable for an X-ray diffraction study had formed. The sample was dried under vacuum. Found: C, 66.5; H, 7.7; N, 1.4%. Calc. for $C_{126}H_{166}La_2N_2O_{16}$: C, 67.1; H, 7.5; N, 1.2%. ES-MS: *m*/*z* 1069.0, $[La_2(8 - H)_2]^{2+}$.

$[Na_2(8 - H)_2]\cdot 2MeCN\cdot(CH_3)_2CO\cdot EtOH\cdot 2.5H_2O$. To a solution of **8** (50 mg, 0.055 mmol) in dichloromethane (20 cm^3) was added sodium perchlorate (100 mg, 0.8 mmol) in acetonitrile (10 cm^3). The solution was stirred for 2 h, filtered and layered with isopropanol (30 cm^3). After 3 weeks colourless crystals of the title complex suitable for an X-ray diffraction study had formed. Found: C, 73.0; H, 9.2; N, 2.1%. Calc. for $C_{129}H_{185}N_4Na_2O_{18.5}$: C, 72.6; H, 8.7; N, 2.6%. ES-MS: *m*/*z* 955, $[8 + Na]^+$.

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