

## Tri-ionizable calix[4]arene ligands: synthesis and lanthanide ion complexation

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### Abstract

New proton-ionizable *p*-*tert*-butylcalix-4-arene ligands with three *N*-(X)sulfonyl oxyacetamide groups and one methoxy group on the lower rim capable of forming electroneutral complexes with trivalent lanthanide ions are synthesized. Variation of the electron-withdrawing ability of X (Me, Ph, C<sub>6</sub>H<sub>4</sub>-4-NO<sub>2</sub>, CF<sub>3</sub>) is used to tune the ligand acidity. Conformations of the ligands in CDCl<sub>3</sub> are investigated by variable temperature NMR spectroscopy. By potentiometric titration, complexation of La<sup>3+</sup>, Eu<sup>3+</sup>, and Yb<sup>3+</sup> by the tri-ionizable complexing agents in MeOH is probed.

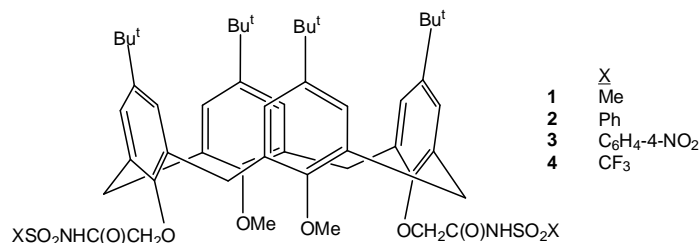
**Keywords:** Proton-ionizable calixarene, lanthanide ion complexation, potentiometric titration

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### Introduction

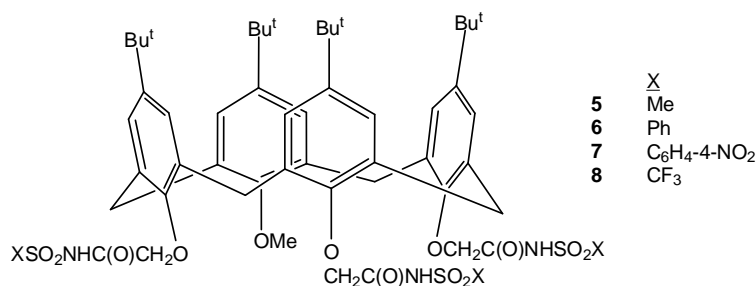
Calixarene scaffolds are frequently employed in the development of new ligands for selective metal ion recognition and separation.<sup>1-9</sup> By attachment of functional groups to the lower rim of calix[4]arene, new metal ion complexing agents with high selectivity have been discovered. Of special interest in our laboratories are calix[4]arenes with pendent proton-ionizable groups<sup>10,11</sup> since these ligands generally provide stronger binding of cationic species than their neutral analogues. Also when the number of acidic sites in the side arms of the ligand matches the charge on the metal ion an electroneutral complex is formed. For a solvent extraction process, this eliminates the need to transport one or more anions from an aqueous phase into the organic diluent, thereby markedly enhancing metal ion extraction efficiency. This is especially important when highly hydrophilic aqueous phase anions of chloride, nitrate, and sulfate are involved. For example, we have found that lower-rim 1,3-disubstituted *N*-(X)sulfonyl *tert*-butylcalix-[4]

arene-carboxamides **1-4** (Figure 1) exhibit efficient and highly selective extraction of heavy metal species  $\text{Pb}^{2+}$  and  $\text{Hg}^{2+}$ .<sup>10-11</sup> The acidity of the ligand was ‘tuned’ by variation of the electron-withdrawing ability of X.<sup>12</sup>



**Figure 1.** Structures of previously studied di-ionizable *p*-*tert*-butylcalix[4]arene ligands.

We now turn our attention to complexing agents for trivalent lanthanide ions. Herein we report the synthesis of tri-ionizable *p*-*tert*-butylcalix[4]arene analogues **5-8** (Figure 2) and the initial evaluation of their complexation of selected trivalent lanthanide ions in MeOH by potentiometric titration. In this series of ligands, variation of the electron-withdrawing properties of X should change the acidity. Some conformational flexibility is anticipated due to the small methyl group that is used to cap the fourth phenolic oxygens.



**Figure 2.** Structures of new tri-ionizable *p*-*tert*-butylcalix[4]arene ligands.

## Results and Discussion

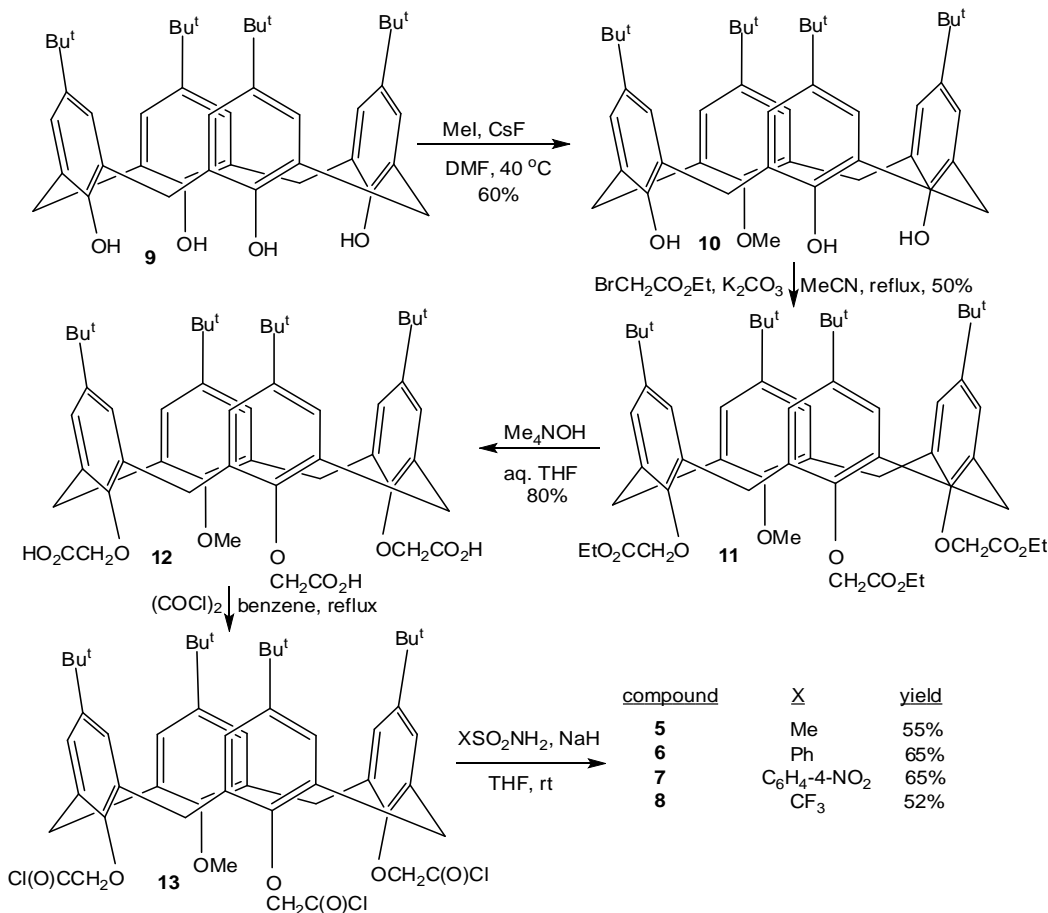
### Ligand synthesis

The synthetic route to the tri-ionizable calix[4]arene ligands **5-8** is shown in Scheme 1.

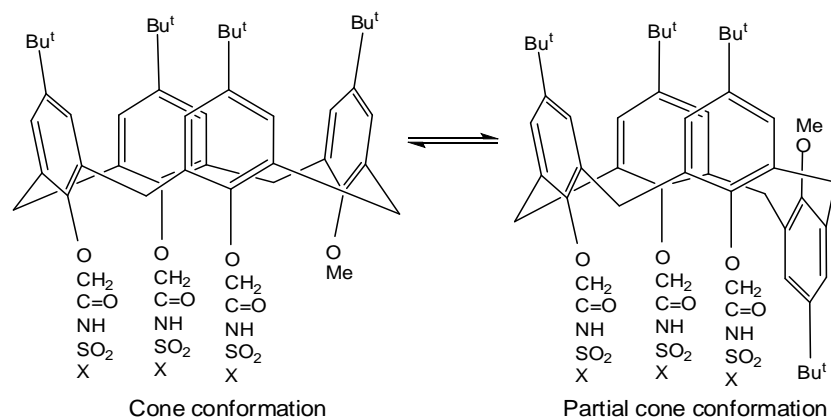
The initial attempt to monomethylate *p*-*tert*-butylcalix[4]arene **9** by its reaction with  $\text{K}_2\text{CO}_3$  and MeI in MeCN at reflux<sup>13</sup> gave mostly dimethylated product. Subsequently, the monomethyl ether **10** was realized in 60% yield by reaction of **9** with CsF and MeI in DMF at 40 °C.<sup>13</sup> The reported reaction of **10** with  $\text{K}_2\text{CO}_3$  and ethyl bromoacetate in MeCN at reflux<sup>14</sup> gave a 50% yield of triester **11**. The IR spectrum of **11** showed two different carbonyl absorptions at 1741

and  $1758\text{ cm}^{-1}$ . Basic hydrolysis of triester **11** followed by acidification gave an 80% yield of tri(carboxylic acid) **12**. Refluxing **12** with an excess of oxalyl in benzene gave tri(acid chloride) **13**, which was used directly in the next step. In the IR spectrum of **13**, the carbonyl and O-H stretching absorptions of **12** were replaced by a new carbonyl absorption at  $1809\text{ cm}^{-1}$ . From reactions of tri(acid chloride) **13** with the sodium salts of commercially available sulfonamides in THF, the tri-ionizable calix[4]arene ligands **5-8** were obtained in 52-65% overall yields from tri(carboxylic acid) **12**. Structures of new compounds **5-8** and **12** were verified by IR and NMR spectroscopy and confirmed by combustion analysis.

Attachment of groups larger than ethyl to the lower-rim oxygens of calix[4]arenes restricts oxygen-through-the-annulus rotation of the arene units.<sup>14</sup> Therefore, ligands **5-8** have one mobile arene unit with two possible limiting conformations: cone and partial cone (paco). The broadened signals observed in the  $^1\text{H-NMR}$  spectra for the  $\text{OCH}_3$  group (e.g., at 3.52 ppm in **7**) indicate that conformational interconversions are taking place in  $\text{CDCl}_3$ .



**Scheme 1.** Synthesis of tri-ionizable *p*-*tert*-butylcalix[4]arene ligands **5-8**.



**Figure 3.** Limiting conformations of tri-ionizable calix[4]arene ligands **5-8**.

The  $^1\text{H-NMR}$  spectra of ligands **5-8** feature two pairs of doublets for the methylene groups that bridge the arene units ( $\text{ArCH}_2\text{Ar}$ ) (in **7** at 3.20 and 3.33 ppm for the pseudo equatorial protons and 4.11 and 4.29 ppm for the pseudoaxial protons). A pair of doublets for the diastereotopic protons in the two equivalent  $\text{OCH}_2\text{C}(\text{O})$  groups (in **7** at 4.47 and 4.58 ppm) and a singlet for the nonequivalent  $\text{OCH}_2\text{C}(\text{O})$  group (in **7** at 4.56 ppm) are also observable. Two nonequivalent N-H groups appears as a pair of broad singlets at 9.60–10.00 ppm, except for compound **8** due to the stronger acidic character when  $\text{X} = \text{SO}_2\text{CF}_3$ .

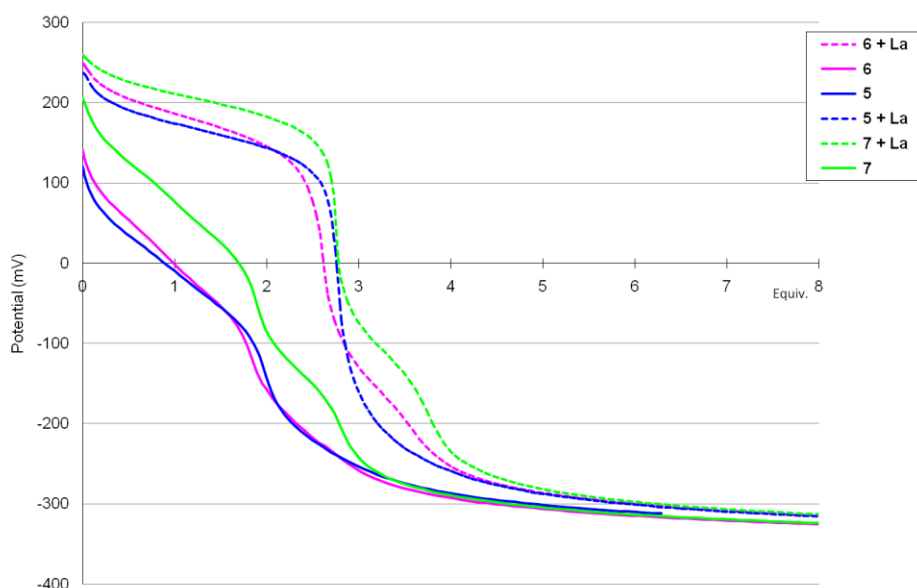
The new tri-ionizable calix[4]arenes are conformationally flexible. When the  $^1\text{H-NMR}$  spectrum of compound **6** was taken in  $\text{CDCl}_3$  at 23  $^\circ\text{C}$ , no signal was observed for the  $\text{OCH}_3$  protons. When the temperature was increased to 45  $^\circ\text{C}$ , a broad peak at 3.53 ppm was seen. When the temperature was equal to or below 0  $^\circ\text{C}$ , a broad peak emerged at 3.76 ppm. This behavior is interpreted in terms of a cone conformation that interconverts to a partial cone conformation slowly on the NMR time scale at lower temperature but rapidly at higher temperature. The resonances arising from the bridge methylene protons appear as two pairs of doublets at 45  $^\circ\text{C}$  in the region of 3.00–4.50 ppm. The higher field pair of doublets corresponds to the pseudo-equatorial protons (closer to aromatic rings) and the lower field pair of doublets to the pseudo-axial protons (closer to the ether linkage). The closest pseudo-equatorial protons to the  $\text{OCH}_3$  group are strongly affected by variations in temperature. At 45  $^\circ\text{C}$ , they appeared as a sharp doublet at 3.24 ppm, but when the temperature was decreased the peaks become broader and almost collapse into the other pseudo-equatorial protons peak at  $-20$   $^\circ\text{C}$ . This is explained in terms of the conformationally mobile character of the aromatic ring holding the  $\text{OCH}_3$  group in compound **6**.

### Complexation of trivalent lanthanides

Since the new ligands **5-8** (Figure 2) behave as acidic ligands ( $\text{LH}_3$ ), the first estimation of their binding properties towards some lanthanide ions was obtained potentiometrically. Stability constants  $\beta_{xyz}$  of the complexes, corresponding to the overall equation  $\text{xLn}^{3+} + \text{yL}^{3-} + \text{zH}^+ \leftrightarrow$

$\text{Ln}_x\text{L}_y\text{H}_z^{(3x-3y+z)+}$  (1) were determined in MeOH in the presence of  $10^{-2}$  M  $\text{Et}_4\text{NCl}$  as the background electrolyte using a competitive method with the protons. The experimental procedure has been previously described in detail.<sup>15</sup>

In a first step, the acid-base behavior of ligands **5-8** was investigated. Interpretation of the titration curves for ligands **5-7** (Figure 4) confirmed their tri-acidic character leading to the values of the ionization constants,  $\text{pK}_{\text{a},n}$ , given in Table 1. The  $\text{pK}_{\text{a},n}$  values for ligands **5** and **6** are nearly the same due to the similarity of the electron-withdrawing abilities of the X groups in the  $\text{OCH}_2\text{C}(\text{O})\text{NHSO}_2\text{X}$  side arms.<sup>16</sup> Due to stronger electron-withdrawal when  $\text{X} = \text{C}_6\text{H}_4\text{-4-NO}_2$  than Me and Ph, the  $\text{pK}_{\text{a},n}$  values shift appreciably lower. Ligand **8** behaved quite differently. The titration curve showed a drop of potential (*i.e.*, an increase in pH) from the beginning with no inflexion points. We are unable to interpret this behavior at present.



**Figure 4.** Potentiometric titration curves for ligands **5-7** in MeOH in the absence and presence of  $\text{La}^{3+}$

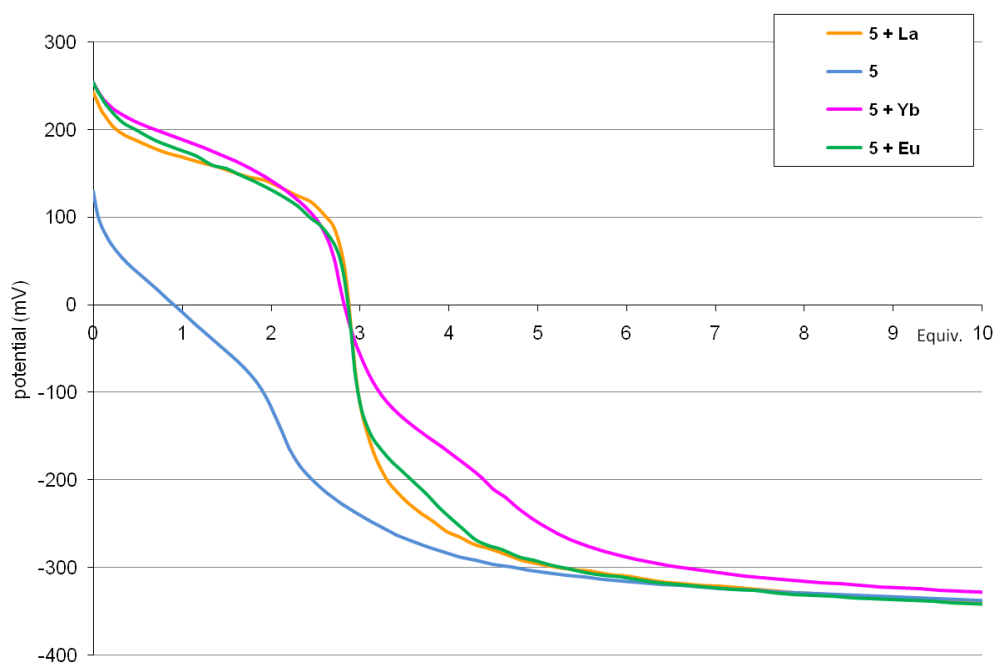
Titration curves for ligand **5** in the presence of one equivalent of  $\text{La}^{3+}$ ,  $\text{Eu}^{3+}$  and  $\text{Yb}^{3+}$  (Figure 5) and of the three ligands **5-7** in the presence of  $\text{La}^{3+}$  (Figure 4) showed equivalence points near three equivalents of base, consistent with the participation of the three *N*-(X)sulfonyl carboxamide groups to the complexation and the formation of 1:1 ( $\text{Ln}:\text{L}$ ) complexes and possibly the corresponding protonated species. After these equivalences, the shape of the titration curves suggested the formation of methoxy species. The simplest models fitting satisfactorily the experimental data are given in Table 2. However, it must be said that certainly additional methoxy species should form besides the  $\text{LnL}(\text{MeO})^-$  complex, since the fit in this region still has to be improved. The results show no important selectivity of ligand **5** in the series. Lanthanum complexes with ligand **7** are the least stable. This is in agreement with the acidity of

this ligand, as shown by linear correlation between  $\log \beta_{110}$  and  $\Sigma(\text{p}K_{\text{a},n})$  (Figure 6) and confirms the predominance of electrostatic interactions in the stability of these complexes.

**Table 1.** Values of  $\text{p}K_{\text{a},n}$  for ligands **5-7** in MeOH at 25 °C

Ligand			
n	5	6	7
1	8.00±0.01 <sup>a</sup>	7.80±0.06	6.49±0.01
2	9.70±0.06	9.85±0.08	8.36±0.01
3	13.3±0.2	13.0±0.1	11.59±0.03

<sup>a</sup>Confidence intervals:  $\pm\sigma_{n-1}$ , with  $\sigma_{n-1}$  being the standard deviation on mean values of  $n$  experiments ( $n \geq 3$ ).

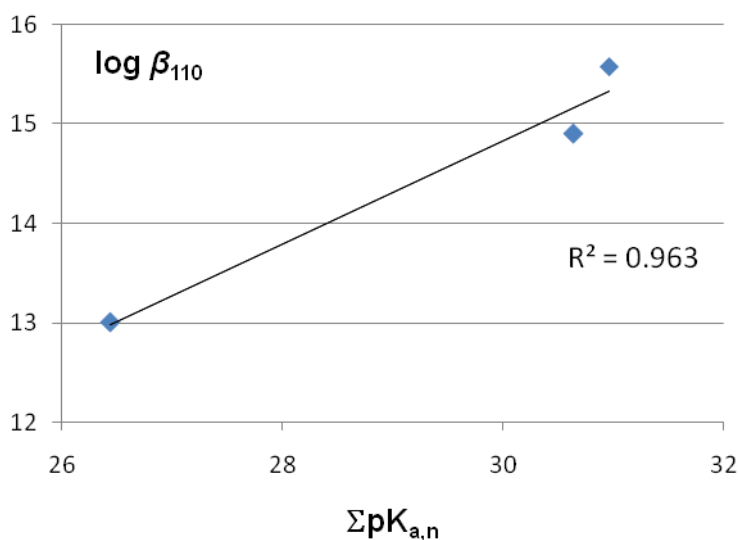


**Figure 5.** Potentiometric titration curves corresponding to the complexation of  $\text{La}^{3+}$ ,  $\text{Eu}^{3+}$ , and  $\text{Yb}^{3+}$  by ligand **5** in MeOH.

**Table 2.** Overall stability constants of some lanthanide complexes in MeOH at 25 °C

log $\beta_{xyz\pm\sigma_{n-1}}$ for ligand					
cation	xyz	species	5	6	7
La <sup>3+</sup>	110	LnL	15.6±0.2	14.9±0.3	13.0±0.1
	111	LnLH <sup>+</sup>	22.27±0.02	22.03±0.03	19.0±0.2
		LnLH <sub>2</sub> <sup>2+</sup>	27.1±0.2	-	-
	11-1	LnL(OMe) <sup>-</sup>	2.8±0.3	3.2±0.5	2.3±0.1
Eu <sup>3+</sup>	110	LnL	16.2±0.3		
	111	LnLH <sup>+</sup>	22.9±0.2		
		LnLH <sub>2</sub> <sup>2+</sup>	28.1±0.2		
	11-1	LnL(OMe) <sup>-</sup>	4.3±0.4		
Yb <sup>3+</sup>	110	LnL	15.62±0.01		
	111	LnLH <sup>+</sup>	22.87±0.01		
		LnLH <sub>2</sub> <sup>2+</sup>	27.1±0.1		
	11-1	LnL(OMe) <sup>-</sup>	4.65±0.01		

<sup>a</sup>Confidence intervals:  $\pm\sigma_{n-1}$ , with  $\sigma_{n-1}$  being the standard deviation on mean values of n experiments ( $n\geq 3$ ).

**Figure 6.** Plot of  $\log \beta_{110}$  (La<sup>3+</sup>) versus  $\Sigma pK_{a,n}$  for ligands 5-7.

## Experimental Section

**General.** Reagents were purchased from commercial suppliers and used as received unless otherwise indicated. Tetrahydrofuran (THF) was dried over sodium with benzophenone as an

indicator and distilled immediately before use. Dimethylformamide (DMF), benzene, and acetonitrile were stored over 4 Å molecular sieves. Potassium carbonate and cesium fluoride were activated by heating at 120 °C under oil pump vacuum overnight just before use. Melting points were determined with a Mel-Temp melting point apparatus. Infrared (IR) spectra were recorded with a Perkin-Elmer Model 1600 FT-IR spectrometer on a NaCl plate (film deposited from CH<sub>2</sub>Cl<sub>2</sub> solution) and are reported in wavenumbers (cm<sup>-1</sup>). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded with a Varian Unity Inova FT-500 spectrometer at 499.7 and 125.7 MHz, respectively, in CDCl<sub>3</sub>. The <sup>1</sup>H-NMR chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane (TMS). Splitting patterns in the NMR spectra are identified as: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; br s, broad singlet; and m, multiplet. Elemental analysis was performed by Desert Analytics Laboratory (now Columbia Analytical Services) of Tucson, Arizona.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-28-methoxycalix[4]arene (10).** To a solution of CsF (0.18 g, 1.2 mmol) in DMF (20 mL) was added *p*-*tert*-butylcalix[4]arene (**9**; toluene complex 1:0.8, 0.72 g, 1.0 mmol)<sup>17</sup> and MeI (0.62 mL, 10 mmol). The mixture was stirred at 40 °C for 26 h and then quenched by addition of 2 N HCl (40 mL). The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 20 mL). The combined organic layers were washed with water (2 x 25 mL) and dried over MgSO<sub>4</sub>. After evaporation of the solvent *in vacuo*, the residue was treated with MeOH (20 mL) and CH<sub>2</sub>Cl<sub>2</sub> (20 mL). The solution was filtered to remove unreacted *p*-*tert*-butylcalix[4]arene. The filtrate was evaporated *in vacuo* and chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/petroleum ether (3:1) as eluent to give 0.40 g (60 %) of **2**: mp 206-208 °C (lit<sup>13</sup> 203-204 °C). IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 3325, 3212, 3189 (OH), 1261 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 1.16-1.25 (m, 36H), 3.43 (d, 4H, *J* 13.0 Hz), 4.12 (s, 3H), 4.27 (d, 2H, *J* 14.0 Hz), 4.36 (d, 2H, *J* 13.0 Hz), 6.99 (d, 2H, *J* 2.5 Hz), 7.02-7.03 (m, 4H), 7.10 (s, 2H), 9.55 (s, 2H), 10.16 (s, 1H).

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26,27-tris(ethoxycarbonylmethoxy)-28-methoxycalix[4]arene (11).** To **10** (0.25 g, 0.38 mmol) in MeCN (30 mL) was added K<sub>2</sub>CO<sub>3</sub> (0.83 g, 6.0 mmol) and ethyl bromoacetate (0.51 mL, 4.6 mmol). The mixture was refluxed for 6 h and the solvent was removed *in vacuo*. To the solid residue were added CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and 2 N HCl (50 mL). The organic phase was separated, extracted with water (2 x 50 mL), and dried over MgSO<sub>4</sub>. After evaporation *in vacuo*, the residue was recrystallized from EtOH to give 0.17 g (50 %) of triester **11**: mp 167-170 °C (lit<sup>14</sup> 171-172 °C). IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 1758, 1741 (C=O), 1182 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 0.86 (br s, 18 H), 1.22-1.36 (m, 27 H), 3.20 (m, 4H), 3.90-5.15 (m, 19H), 6.52 (m, 4H), 7.06 (br s, 4H).

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-26,27,28-tris(hydroxycarbonylmethoxy)-25-methoxycalix[4]arene (12).** To triester **11** (1.68 g, 1.83 mmol) in THF (75 mL) was added Me<sub>4</sub>NOH (80 mL of 7.8 % aq solution) and the mixture was refluxed for 30 h. The THF was evaporated *in vacuo* and the residue was acidified to pH<1 (8 mL of conc HCl). After extraction with CH<sub>2</sub>Cl<sub>2</sub> (75 mL), the aqueous phase was back-extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL).



The combined organic extracts were washed with water (50 mL) and dried over MgSO<sub>4</sub>. Evaporation *in vacuo* gave 1.22 g (80 %) of **12** as a white solid: mp 248-251 °C (lit<sup>14</sup> 243-245 °C). IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 2800-3600 (OH), 1751 (C=O), 1194 (C-O) cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 0.86 (s, 9H), 0.87 (s, 9H), 1.32 (s, 18H), 3.25 (dd, 4H, *J* 13.0 Hz), 3.80 (s, 3H), 4.28 (d, 2H, *J* 13.0 Hz), 4.56 (br s, 2H), 4.81 (br s, 6H), 6.63 (d, 4H, *J* 12.0 Hz), 7.15 (s, 4H).

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-26,27,28-tris(chloridocarbonyl-methoxy)-25-methoxycalix[4]arene (13).** To triacid **12** (1.20 g, 1.44 mmol) in benzene (40 mL) under nitrogen in an oil bath at 60 °C, oxalyl chloride (0.77 mL, 6 eq) was added. The mixture was stirred at 60 °C for 17 h. The solution was evaporated *in vacuo* and 1.28 g (100 %) of a waxy solid was obtained. IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 1807 (C=O) cm<sup>-1</sup>.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-26,27,28-tris[*N*-(X)sulphonyl carboxamidomethoxy]-25-methoxycalix[4]arenes (5-8).** The sulfonamide salt was prepared under argon by adding THF (20 mL) to a flask containing NaH (0.41 g, 17.08 mmol). A solution of the appropriate sulfonamide (7.20 mmol) in THF (40 mL) was added over a 10-min period. The mixture was stirred at room temperature for 1.5 hour followed by the dropwise addition of a solution of the tri(acid chloride) **13** (1.30 g, 1.44 mmol) in THF (20 mL). The mixture was stirred at room temperature for 14 h. Water (5.0 mL) was added slowly to destroy the residual NaH. The organic phase was washed with 10 % aq K<sub>2</sub>CO<sub>3</sub> (2 x 40 mL). The solvent was evaporated *in vacuo*. The residue was dissolved in MeOH-CH<sub>2</sub>Cl<sub>2</sub> (1:9) and chromatographed on silica gel with MeOH-CH<sub>2</sub>Cl<sub>2</sub> (1:9) as eluent. The resultant solid was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and washed with 1 M HCl (10 mL) and distilled water (10 mL). The organic solution was dried over MgSO<sub>4</sub> and evaporated *in vacuo*.

**5,11,17,23-Tetrakis(1,1-dimethylethyl)-26,27,28-tris(*N*-methanesulfonyl carboxamidomethoxy)-25-methoxycalix[4]arene (5)** was obtained as 0.85 g (55 %) of white solid: mp 287-290 °C. IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 3240 (N-H), 1720 (C=O), 1348, 1185 (SO<sub>2</sub>) cm<sup>-1</sup>. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ 1.02 (s, 18H), 1.10 (s, 9H), 1.16 (s, 9H), 3.34 (d, 2H, *J* 13.0 Hz), 3.38-3.44 (m, 14H), 4.17 (d, 2H, *J* 13.0 Hz), 4.47 (d, 2H, *J* 13.0 Hz), 4.54 (d, 2H, *J* 15.0 Hz), 4.61 (s, 2H), 4.67 (d, 2H, *J* 15.5 Hz), 6.79 (s, 2H) 6.85 (s, 2H), 6.94 (br s, 2H), 6.96 (br s, 2H), 9.70 (br s, 2H), 9.75 (br s, 1H). <sup>13</sup>C NMR (500 MHz, CDCl<sub>3</sub>): δ 30.7, 31.0, 32.0, 32.2, 32.3, 33.1, 35.2, 35.3, 54.4, 74.0, 74.2, 125.4, 125.8, 125.9, 126.2, 131.7, 132.2, 133.4, 134.1, 145.1, 147.8, 147.8, 152.2, 152.6, 168.2, 168.3. Anal. Calcd. for C<sub>54</sub>H<sub>73</sub>N<sub>3</sub>O<sub>13</sub>S<sub>3</sub>: C, 60.74; H, 6.84; N, 3.94; Found C, 60.50; H, 7.01; N, 3.86.

**5,11,17,23-Tetrakis(1,1-dimethylethyl)-26,27,28-tris[*N*-benzenesulfonyl carboxamidomethoxy]-25-methoxycalix[4]arene (6)** was realized as 1.19 g (65 %) of white solid: mp 256-258 °C. IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 3240 (N-H), 1720 (C=O), 1348, 1186 (SO<sub>2</sub>) cm<sup>-1</sup>. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ 0.96 (s, 18H) 1.16 (s, 9H), 1.20 (s, 9H), 3.13 (d, 2H, *J* 13.0 Hz), 3.24 (br d, 2H, *J* 12.5 Hz), 3.52 (br s, 3H), 4.08 (d, 2H, *J* 13.0 Hz), 4.21 (d, 2H, *J* 13.0 Hz), 4.30-4.42 (m, 4H), 4.58 (s, 2H), 6.63 (br s, 2H), 6.65 (br s, 2H), 6.88 (s, 2H), 6.95 (s, 2H), 7.50 (t, 2H, *J* 7.5 Hz), 7.55 (t, 4H, *J* 7.5 Hz), 7.59-7.67 (m, 3H), 8.03 (d, 2H, *J* 8.0 Hz), 8.17

(d, 4H, *J* 8.0 Hz), 9.68 (s, 2H), 9.75 (s, 1H). <sup>13</sup>C NMR (500 MHz, CDCl<sub>3</sub>): δ 31.1, 31.4, 31.4, 33.8, 34.0, 34.1, 53.4, 73.8, 74.0, 125.4, 125.8, 125.9, 126.2, 128.6, 128.7, 129.0, 129.1, 131.5, 132.1, 133.0, 133.7, 134.1, 134.1, 138.3, 138.4, 145.8, 146.2, 146.6, 151.9, 152.5, 167.6, 168.2. Anal. Calcd. for C<sub>69</sub>H<sub>79</sub>N<sub>3</sub>O<sub>13</sub>S<sub>3</sub>: C, 66.06; H, 6.35; N, 3.35; Found C, 66.37; H, 6.15; N, 3.44.

**5,11,17,23-Tetrakis(1,1-dimethylethyl)-26,27,28-tris[*N-p*-nitrobenzenesulfonyl carboxamidomethoxy]-25-methoxycalix[4]arene (7)** was obtained as 1.31 g (65 %) of white solid: mp 186-189 °C. IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 3259 (N-H), 1720 (C=O), 1348, 1162 (SO<sub>2</sub>) cm<sup>-1</sup>. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ 1.07 (s, 18H), 1.12 (s, 18H), 3.20 (d, 2H, *J* 13.0 Hz), 3.33 (d, 2H, *J* 13.5 Hz), 3.52 (br s, 3H), 4.11 (d, 2H, *J* 13.5 Hz), 4.29 (d, 2H, *J* 13.0 Hz), 4.47 (d, 2H, *J* 15.5 Hz), 4.56 (s, 2H), 4.58 (d, 2H, *J* 15.0 Hz), 6.77-6.81 (m, 4H), 6.83 (d, 2H, *J* 2.0 Hz), 6.86 (s, 2H), 8.29 (d, 2H, *J* 9.0 Hz), 8.32 (d, 4H, *J* 9.0 Hz), 8.34-8.42 (m, 6H), 9.91 (s, 2H), 9.96 (s, 1H). <sup>13</sup>C NMR (500 MHz, CDCl<sub>3</sub>): δ 31.6, 32.0, 32.5, 33.1, 33.6, 34.1, 53.3, 73.8, 75.0, 125.3, 125.4, 125.8, 125.9, 128.8, 129.7, 131.0, 132.1, 133.8, 133.0, 133.6, 135.6, 135.9, 144.7, 145.0, 145.8, 146.8, 152.0, 152.2, 167.5, 167.8. Anal. Calcd. for C<sub>69</sub>H<sub>76</sub>N<sub>6</sub>O<sub>19</sub>S<sub>3</sub>: C, 59.67; H, 5.47; N, 6.05; Found C, 59.88; H, 5.48; N, 5.95.

**5,11,17,23-Tetrakis(1,1-dimethylethyl)-26,27,28-tris[*N*-trifluoromethanesulfonyl carboxamidomethoxy]-25-methoxycalix[4]arene (8)** was obtained as 0.93 g (52 %) of white solid: mp 317-320 °C. IR (deposit on NaCl plate from CH<sub>2</sub>Cl<sub>2</sub> solution): 1615 (C(O)N<sup>-</sup>), 1311, 1190 (SO<sub>2</sub>) cm<sup>-1</sup>. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ 1.11 (s, 9H), 1.14 (s, 9H), 1.16 (s, 18H), 3.37 (d, 2H, *J* 12.5 Hz), 3.42 (d, 2H, *J* 12.5 Hz), 3.87 (s, 3H), 4.10 (d, 2H, *J* 12.5 Hz), 4.14 (d, 2H, *J* 12.5 Hz), 4.36 (s, 2H), 4.38 (d, 2H, *J* 17.0 Hz), 4.58 (d, 2H, *J* 17.0 Hz), 7.09 (br s, 2H), 7.10 (br s, 2H), 7.13 (s, 4H). <sup>13</sup>C NMR (500 MHz, CDCl<sub>3</sub>): δ 31.0, 31.5, 31.6, 33.2, 33.9, 34.5, 54.0, 73.1, 73.8, 125.3, 125.1, 125.5, 125.9, 130.0, 132.0, 133.8, 133.9, 146.2, 145.9, 146.5, 151.7, 152.9, 168.0, 168.33. Anal. Calcd. for C<sub>54</sub>H<sub>64</sub>N<sub>3</sub>O<sub>13</sub>S<sub>3</sub>F<sub>9</sub>: C, 52.67; H, 5.20; N, 3.41; Found C, 52.27; H, 5.42; N, 3.09. (Note: Although the IR and NMR spectra were consistent with the ionized form of **8**, the combustion analysis results agreed with the neutral ligand.)

### Potentiometric titrations

The experiments were performed at 25 °C with a combination glass electrode (Mettler U402/S7/120) connected to an automatic titrator (Metrohm 716 DMS Titrino) at 25 °C. The standard filling solution (saturated aq KCl) of the external reference of the combination glass electrode was replaced by a 10<sup>-2</sup> M solution of Et<sub>4</sub>NCl in MeOH saturated in AgCl. The electrode was calibrated by titration of a 1.0 mM solution of HClO<sub>4</sub> with a 10 mM solution of Me<sub>4</sub>NOH, previously standardized with potassium phthalate. The stability constants of the lanthanide complexes with these ligands were determined by acid-base titration of the *ca.* 1.0 mM ligand solutions containing one equivalent of the metal cation with a concentrated Et<sub>4</sub>NOH solution. The titration data were interpreted using the programs Sirko<sup>18</sup> and Hyperquad.<sup>19</sup> The protonation constants of the L<sup>3-</sup> ligands, previously determined from titrations without the metal ions, were held constant during the refinement procedure. The autoprotolysis constant used for the calculations was pK<sub>MeOH</sub> = 16.7.<sup>20</sup>

The metal salts were the lanthanide chlorides:  $\text{LaCl}_3 \cdot x\text{H}_2\text{O}$ ,  $\text{EuCl}_3 \cdot x\text{H}_2\text{O}$ , and  $\text{YbCl}_3 \cdot x\text{H}_2\text{O}$ , dried at room temperature under vacuum before use. Their stock solutions were titrated by complexometry with EDTA using xylenol orange as an indicator.

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