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### Synthesis, structural characterisation and metal ion-binding properties of a new *p-tert*-butyldihomooxalix[4]crown-6

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## Synthesis, structural characterisation and metal ion-binding properties of a new *p*-*tert*-butyldihomooxalix[4]crown-6

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1,3-Diethoxy-*p*-*tert*-butyldihomooxalix[4]arene-crown-6 (**3**) was synthesised for the first time. Compound **3** was isolated in a partial cone A conformation in solution at room temperature, as established by NMR measurements (<sup>1</sup>H, <sup>13</sup>C and NOESY). The assignment of both proton and carbon NMR spectra was achieved by a combination of COSY and HSQTOCSY experiments. The binding affinities of ligand **3** for alkali, alkaline earth, transition and heavy metal cations have been assessed by phase transfer and proton NMR titration experiments. Compound **3** is a reasonable extractant for the alkali cations and also for Ag<sup>+</sup>, showing preference for Cs<sup>+</sup>. Ligand **3** forms 1:1 complexes with K<sup>+</sup>, Ca<sup>2+</sup>, Ag<sup>+</sup> and Pb<sup>2+</sup>, as determined by proton NMR titrations, which also indicated that these cations should be encapsulated into the cavity defined by the crown ether unit, the ethoxy group and the inverted aryl ring.

**Keywords:** calixcrowns; dihomooxalix[4]crown-6; conformational analysis; metal cation extraction; <sup>1</sup>H NMR titration

### Introduction

The continuous use of calixarenes (1–3) in numerous and new fields of research, as recently in nanochemistry (4), makes them a unique class of synthetic macrocycles. This evidence is mainly due to the fact that the parent compounds are easily available and can be further functionalised on the lower and upper rims to give a variety of derivatives, which can become versatile building blocks for the construction of highly complex host molecules.

In particular, the calixcrowns (5), where a poly(oxyethylene) chain links two phenolic oxygens of the calixarene framework, have shown remarkable ionophoric properties. Depending on the crown size, on the macrocycle conformation (especially for calix[4]arenes) and on the substituents at the upper and lower rims, calixcrowns exhibit highly selective metal ion recognition. Thus, partial-cone and cone 1,3-dialkoxycalix[4]-crowns-4 show very high selectivity for Na<sup>+</sup> (6), partial-cone and 1,3-alternate calix[4]-crowns-5 are selective for K<sup>+</sup> (7) and 1,3-alternate calix[4]-crowns-6 are selective for Cs<sup>+</sup> (8). Moreover, the exceptional selectivity towards Cs<sup>+</sup> shown by some calix[4]-crown-6 derivatives, has led to their applications as ion-selective electrodes (9) and mainly as selective carriers in the treatment of radioactive liquid wastes (10).

These important results have kept the design and synthesis of new calixcrowns in different conformations (11), as well as the study of their potential applications,

in a high level of development. Examples of recent work show calixcrowns as fluorescent chemosensors (12), on self-assembled monolayers (SAM) (13), as selective electrode for determination of dopamine (14) and in chromatographic partitioning processes (15).

Following our previous studies on the synthesis and metal cation-binding properties of dihomooxalix[4]-crowns-6 (16, 17), we obtained a new 1,3-dialkoxycalix-crown derivative. This paper reports the synthesis, the conformational features in solution and the binding properties towards alkali, alkaline earth, transition and heavy metal cations of the 1,3-diethoxy-*p*-*tert*-butyldihomooxalix[4]arene-crown-6 (**3**). These properties have been assessed by extraction studies of metal picrates from an aqueous solution into dichloromethane and by proton NMR titrations. The results are discussed in the light of those obtained with other dihomooxalix[4]crowns-6 (Figure 1) and also with closely related calix[4]crown derivatives.

### Results and discussion

#### Synthesis and NMR conformational analysis

Calixcrown **3** was synthesised by the reaction of *p*-*tert*-butyldihomooxalix[4]arene-crown-6 (**1**) (18) with iodoethane and NaH in THF/DMF at reflux for 3 h. Proton, carbon-13, COSY, NOESY and HSQTOCSY NMR experiments were carried out in chloroform at room temperature to establish its conformation.

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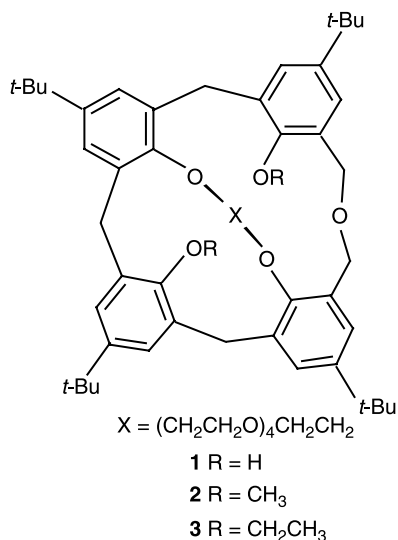
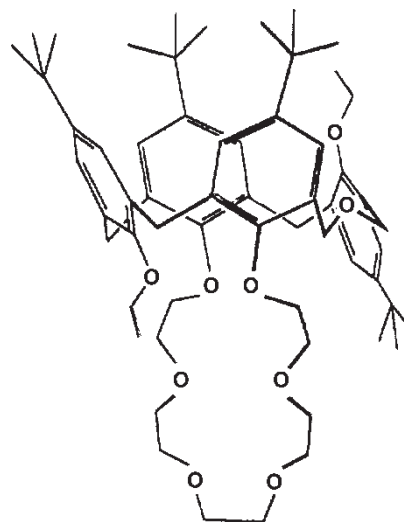


Figure 1. Structural formulae of calixarenes.

The  $^1\text{H}$  NMR spectrum displays four singlets for the *tert*-butyl groups, five AB quartets (one of them overlapped) for the  $\text{CH}_2$  bridge protons, a complex multiplet for the polyether chain protons and four pairs of doublets for the aromatic protons. In addition, the  $\text{OCH}_2\text{CH}_3$  groups exhibit two triplets and three multiplets for the  $\text{CH}_3$  and  $\text{CH}_2$  protons, respectively. The upfield shifts experienced by both the methyl triplet ( $\delta -0.07$  ppm) and the methylene multiplets ( $\delta 1.86$  and  $2.26$  ppm) of one ethoxy group indicate a shielding effect for these protons due to the aromatic rings, and consequently that the phenol unit bearing that substituent group is inverted. Moreover, those signals are broadened and the  $\text{CH}_2$  protons are non-equivalent, contrary to those of the other ethoxy group, suggesting some constraint to the rotation of that group.

Due to the overlapping of signals in the  $^{13}\text{C}$  NMR spectrum, fewer lines than expected were obtained. Thus, this spectrum shows a pattern containing 21 of the 24 expected downfield resonances arising from the aromatic carbon atoms, 10 of the 14 expected midfield resonances arising from the methylene carbon atoms of the  $\text{CH}_2\text{OCH}_2$  and  $\text{OCH}_2\text{CH}_3$  groups and crown moiety, and 12 of the 13 upfield resonances arising from the quaternary carbon atoms ( $\text{C}(\text{CH}_3)_3$ , three of the four lines), the methyl carbon atoms of the *tert*-butyl ( $\text{C}(\text{CH}_3)_3$ , four lines) and ethoxy groups (two lines), and the methylene carbon atoms  $\text{ArCH}_2\text{Ar}$  (three lines, two of them partly hidden under the *t*-Bu signals). All resonances were assigned by DEPT experiments. The three  $\text{ArCH}_2\text{Ar}$  resonances appear at 31.2, 31.5 and 38.4 ppm, indicating a partial cone A (*19*) conformation (Figure 2) for calixcrown **3**. This conformation was further confirmed by proton–proton correlations observed in a NOESY spectrum. The more relevant NOE enhancements are shown in Figure 3. The preferential formation of the partial

Figure 2. Partial cone A conformation for calixcrown **3**.

cone A conformation over the partial cone B (the other possible partial cone conformation for dihomooxalix[4]-arenes) should be mainly due to steric hindrance effects. The former conformation allows a better accommodation of the inverted *t*-Bu group than the latter, providing a more stable conformer. The assignment of both proton and carbon spectra (Table 1) was obtained from cross-peak correlations in a COSY spectrum and by the analysis of a HSQCTOCSY spectrum, which correlates directly bonded  $^1\text{H}$  and  $^{13}\text{C}$  nuclei.

Some low-temperature  $^1\text{H}$  NMR experiments were also done with compound **3**. The temperature was lowered until  $-50^\circ\text{C}$  in  $\text{CDCl}_3$  and  $-80^\circ\text{C}$  in  $\text{CD}_2\text{Cl}_2$ , but the analysis of these spectra showed no evidence for the

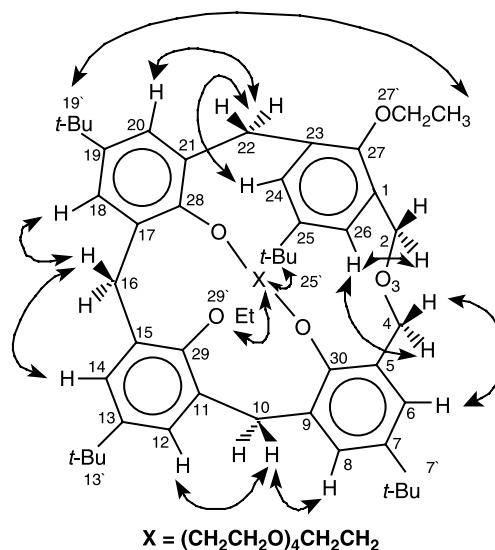
Figure 3. Relevant NOE enhancements used to confirm the partial cone conformation A of calixcrown **3**.

Table 1. Chemical shifts ( $\delta$ , ppm) of protons and carbons of calixcrown **3**.

Atom	$\delta_C$	$\delta_H$ (eq), (ax)
2	64.5	4.22; 4.37
4	66.4	4.20; 4.90
10	31.5	3.28; 4.41
16	31.2	3.32; 4.41
22	38.4	3.84
6	125.2	7.13
8	126.6	7.10
12	127.5	7.08
14	125.9	7.14
18	126.3	7.16
20	126.1	7.06
24	127.2	7.27
26	125.3	7.11
7'	31.4	1.21
13'	31.7	1.28
19'	31.5	1.24
25'	31.6	1.33
27'	68.7 (CH <sub>2</sub> )	1.86, 2.26
27'	15.7 (CH <sub>3</sub> )	-0.07
29'	69.0 (CH <sub>2</sub> )	3.77
29'	15.2 (CH <sub>3</sub> )	1.04

presence of conformations other than that found at room temperature.

### Extraction studies

The ionophoric properties of dihomooxalixcrown **3** towards alkali, alkaline earth, transition and heavy metal cations were evaluated by the standard picrate extraction method (20). The results, expressed as a percentage

of cation extracted (% *E*), are reported in Tables 2 and 3. The corresponding values for calixcrown **1** and **2** are included for comparison.

The data reveal that calixcrown **3** displays low to reasonably high extraction levels towards the alkali cations (% *E* ranges from 3.8 to 47). Compound **3** shows a preference for Cs<sup>+</sup> (47%), as does the majority of the calix[4]-crown-6 derivatives. Comparing with calixcrown **2** and the analogue 1,3-diethoxy-*p*-*tert*-butylcalix[4]-crown-6 (Et[4]-C6) (11a), both in a partial cone conformation as well, **3** exhibits a higher extraction efficiency, mainly for Cs<sup>+</sup>. A similar situation is found when the comparison is done with the unsubstituted calixcrown **1**, in the cone conformation. The binding efficiency of this type of compounds is strongly conformationally dependent. Among 1,3-dialkoxycalix[4]-crowns-5 and crowns-6, the partial cone conformation is preferred over the cone conformation (21, 22). The former conformation is less polar and less solvated than the cone, and the bound cations can interact not only with the crown ether moiety, but also with one rotated aromatic nucleus (cation/ $\pi$  interaction) of the partial cone conformation. Within the alkaline earth series, **3** is a very poor phase transfer agent, as was already observed with calixcrown **2** and other calix[4]crown derivatives.

In the case of the transition and heavy metal cations, **3** is also a weak extractant, except for Ag<sup>+</sup> (18% *E*). Although this cation is a soft Lewis acid (23), ligands bearing hard oxygen donor atoms (like calixcrowns) show usually a clear affinity for it, as has been observed by us for other derivatives (24, 25).

Table 2. Percentage extraction of alkali and alkaline earth metal picrates into CH<sub>2</sub>Cl<sub>2</sub> at 25°C<sup>a</sup>.

	Li <sup>+</sup>	Na <sup>+</sup>	K <sup>+</sup>	Rb <sup>+</sup>	Cs <sup>+</sup>	Mg <sup>2+</sup>	Ca <sup>2+</sup>	Sr <sup>2+</sup>	Ba <sup>2+</sup>
Ionic radius <sup>b</sup> (Å)	0.78	0.98	1.33	1.49	1.65	0.78	1.06	1.27	1.43
<b>1</b> <sup>c</sup>	4.4	4.4	3.6	5.8	6.1	4.8	4.8	3.7	5.8
<b>2</b> <sup>c</sup>	5.4	12	22	36	40	1.0	3.0	3.3	2.5
<b>3</b>	3.8	8.3	25	38	47	3.1	4.8	2.3	4.5
Et[4]-C6 <sup>d</sup>	–	1.7	2.8	3.3	3.3	–	–	–	–

<sup>a</sup> Values with uncertainties less than 5%.

<sup>b</sup> Goldschmidt, V. M. *Skrifter Norske Videnskaps-Akad. Oslo, I, Mat.-Naturv. Kl.*, **1926**; data quoted in Marcus, I. *Ion Properties*, Marcel Dekker: New York, 1997; pp 46–47.

<sup>c</sup> Data taken from Ref. (16).

<sup>d</sup> Data taken from Ref. (11a).

Table 3. Percentage extraction of transition and heavy metal picrates into CH<sub>2</sub>Cl<sub>2</sub> at 25°C<sup>a</sup>.

	Mn <sup>2+</sup>	Fe <sup>2+</sup>	Co <sup>2+</sup>	Ni <sup>2+</sup>	Cu <sup>2+</sup>	Zn <sup>2+</sup>	Ag <sup>+</sup>	Cd <sup>2+</sup>	Pb <sup>2+</sup>
Ionic radius <sup>b</sup> (Å)	0.83	0.78	0.75	0.69	0.73	0.75	1.15	0.95	1.18
<b>1</b> <sup>c</sup>	5.8	1.7	1.4	2.5	2.2	2.2	1.5	1.5	2.5
<b>2</b> <sup>c</sup>	7.9	1.3	1.6	3.2	9.6	4.6	18	3.2	7.3
<b>3</b>	3.7	6.8	5.4	8.7	5.1	3.5	18	3.6	5.8

<sup>a</sup> Values with uncertainties less than 5%.

<sup>b</sup> Shannon, R.D.; Prewitt, C.T. *Acta Cryst.* **1969**, B25, 925; **1970**, B26, 1046; data quoted in Marcus, I. *Ion Properties*, Marcel Dekker: New York, 1997; pp 46–47.

<sup>c</sup> Data taken from Ref. (17).

### Proton NMR studies

To obtain further information on the cation-binding behaviour of calixcrown **3**, specifically concerning the binding sites, proton NMR studies were performed. The cations studied were  $K^+$ ,  $Ca^{2+}$ ,  $Zn^{2+}$ ,  $Ag^+$  and  $Pb^{2+}$ . Variable amounts of the salts were added to compound **3** and the proton spectra recorded after each addition.

Different situations were found after the addition of the salts to ligand **3**. The titration of **3** with  $K^+$  cation shows that with [salt]/[ligand] ratios lower than 1 both signals of the complexed and uncomplexed ligands are present in the spectra, indicating that on the NMR time scale the exchange rate between the two species is slow, at room temperature. This behaviour reflects a high affinity of ligand **3** towards  $K^+$ , which is consistent with the extraction results. Upon reaching a 1:1 ratio, all signals for the free ligand disappear and those of the complexed ligand remain unaltered after subsequent additions of the salt, indicating a 1:1 metal-to-ligand stoichiometry. By contrast, very small changes were observed in the case of  $Zn^{2+}$ , indicating a very weak affinity of **3** towards this cation, as previously observed in extraction. A third situation is observed for  $Ca^{2+}$ ,  $Ag^+$  and  $Pb^{2+}$ . Titrations of ligand **3** with these salts initially induce broadening of the signals until the [salt]/[ligand] ratio reaches the unity value, when the signals become sharper. Addition of a slight excess of salt completes the sharpening of the peaks. This indicates a fast exchange rate between the two species on the NMR time scale, at room temperature, and consequently a weak affinity of ligand **3** towards those cations. This is in agreement with the extraction results, mainly for  $Ca^{2+}$  and  $Pb^{2+}$ . The proton NMR titration experiments suggest a 1:1 metal-to-ligand stoichiometry, since all signals remain unchanged after subsequent additions of the salts.

In the case of  $Ag^+$ , besides those signals, another set of peaks of much lower intensity (around 30%, as estimated from the spectral data) can be seen in the spectra after the addition of 1 equiv of the salt, indicating the presence of a second species. Such an observation is hampered by some broadening of the spectra for [salt]/[ligand] ratios lower than unity. Furthermore, the intensity of this set of signals only slightly increases, as the addition of the salt proceeds (up to 5 equiv). From a detailed analysis of the spectra it is possible to see two methyl triplets, corresponding to the minor species, at 1.49 and 1.73 ppm. A COSY experiment further indicated the correlations of these triplets with two  $CH_2$  multiplets at 4.36 and 4.39 ppm, respectively. Therefore, both ethoxy groups of this minor species present downfield chemical shifts, indicating that no aromatic unit is inverted. This suggests a slow interconversion to a cone conformation, as is evidenced by the exchange peaks present in the NOESY spectrum. A similar observation has been made for a related

calix[4]crown-6 derivative with  $Cs^+$  (8) and a calix[4]-arene with  $Ag^+$  (26). Moreover, each aromatic proton of the minor species has only one NOE effect on each equatorial methylene proton of the  $CH_2$  bridges, further supporting that conformation.

Proton NMR data of the free and complexed ligand **3** are collected in Table 4. The complete interpretation of the spectra, even with additional COSY and NOESY experiments, was not possible due to overlapping of peaks, mainly in the  $CH_2$  region. Nevertheless, the more relevant protons could be assigned. Complexation of the cations (except  $Zn^{2+}$ ) affects all the proton chemical shifts in the ligand, although the *tert*-butyl groups undergo very small variations. The largest upfield variations are observed for the methyl protons of the ethoxy group attached to the inverted aromatic moiety, and it is maximum for  $K^+$  ( $\Delta\delta = 1.37$  ppm). Moreover, in the case of  $Pb^{2+}$  complexation, there is a clear NOE effect of those methyl protons on both aromatic protons of the opposite ring. This suggests that the ethoxy group moves inside the hydrophobic cavity generated by the other three phenol units. This situation should indicate some minor conformational rearrangements of the calixarene upon complexation and not an interaction with the cations, as the hydrophobic cavity will not participate in the complexation.

The methyl and methylene protons of the non-inverted ethoxy group, the crown moiety protons and the aromatic protons show the largest downfield shift variations. However, a closer examination of the spectral changes of the crown unit upon complexation indicates, besides the large downfield shifts already mentioned, also upfield shifts of its protons. In fact, upon complexation, the range of chemical shifts among the crown ether protons increases significantly, being maximum for the  $Pb^{2+}$ ,  $Ag^+$  and  $K^+$  cations. Identical situations were observed among the eight aromatic protons, with  $\Delta\delta$  being after complexation double and even triple (in the case of  $Pb^{2+}$ ) of the value of the free ligand.

The large shift variations shown by the crown ether protons indicate the participation of the crown unit in cation complexation, and the deshielding effect observed for the aromatic protons indicates the involvement of the phenolic oxygens in complexation, as reported previously (27). This suggests that the cations must be inside the cavity defined by the crown ether unit, the ethoxy group and the inverted aryl ring. The cations should be bound into that cavity through metal–oxygen electrostatic interactions. Ikeda and Shinkai (28) reported that the large downfield shifts of aromatic protons in inverted rings of calix[4]arenes indicate  $\pi$ -donor participation in cation complexation. In the present study, although it is possible to observe NOE effects between both aromatic protons of the inverted ring and some crown ether protons, the downfield shifts experienced by those aromatic protons are

Table 4. Relevant proton chemical shifts ( $\delta$ , ppm) of ligand **3** and its 1:1 metal complexes.

	Crown		OCH <sub>2</sub> CH <sub>3</sub>		ArH
	<i>t</i> -Bu	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>2</sub> <sup>a</sup>	
<b>3</b>	1.21, 1.24, 1.28, 1.33	3.49–3.90	–0.07, 1.04	1.86, 2.26, 3.77	7.06, 7.08, 7.10, 7.11, 7.13, 7.14, 7.16, 7.27
<b>3</b> + K <sup>+</sup>	1.22, 1.22, 1.30, 1.31	3.06–3.25, 3.54–4.38	–1.44, 1.60	2.06, 2.18, 4.17	7.05, 7.06, 7.15, 7.23, 7.35, 7.44, 7.45, 7.50
<b>3</b> + Ca <sup>2+</sup>	1.21, 1.25, 1.27, 1.31	3.49, 3.65–4.35, 4.86	–1.39, 1.44	1.85, 4.10	7.02, 7.08, 7.15, 7.16, 7.36, 7.40, 7.42, 7.57
<b>3</b> + Zn <sup>2+</sup>	1.22, 1.24, 1.27, 1.33	3.52–3.92	–0.12, 1.07	1.85, 2.27, 3.78	7.06, 7.09, 7.10, 7.10, 7.16, 7.16, 7.18, 7.26
<b>3</b> + Ag <sup>+</sup>	1.20, 1.21, 1.33, 1.33	3.00, 3.23, 3.32–4.35	–1.28, 1.59	2.26, 2.42, 4.26, 4.44	7.09, 7.10, 7.21, 7.22, 7.34, 7.39, 7.39, 7.44
<b>3</b> + Ag <sup>+</sup> (minor)	0.96, 1.16, 1.26, 1.29	3.30–4.50	1.49, 1.73	4.23, 4.48, 4.29, 4.48	6.80, 6.86, 7.04, 7.09, 7.10, 7.12, 7.28, 7.41
<b>3</b> + Pb <sup>2+</sup>	1.23, 1.28, 1.29, 1.30	3.18, 3.29, 3.39, 3.65–4.25, 4.78	–1.13, 1.45	2.35, 2.48, 4.32, 4.38	7.04, 7.15, 7.24, 7.36, 7.44, 7.51, 7.66

<sup>a</sup>The CH<sub>2</sub> protons of the two ethoxy groups can be non-equivalent.

not the largest ones. The largest shifts are observed for those protons of the non-inverted ring bearing the ethoxy group. Thus, the cation/ $\pi$  interactions in our complexes should be less effective than in those with the calix[4]arenes previously mentioned. A possible reason for that behaviour may be the larger size of the macrocycle dihomooxa compared with that of the calix[4]arene.

Ligand **3** showed a strong discrimination between the smaller and the larger cations. Among the latter, the highest chemical shift variations are displayed for complexation with Pb<sup>2+</sup>, followed by K<sup>+</sup> and Ag<sup>+</sup>. This preference of ligand **3** seems to be the result of the combination of two main factors affecting complexation: size and charge of the cations.

## Conclusions

Diethoxycalixcrown **3** was synthesised and obtained in a partial cone conformation in solution. Extraction studies with metal picrates from an aqueous solution into CH<sub>2</sub>Cl<sub>2</sub> have shown that calixcrown **3** is a reasonable extractant for the alkali cations, showing preference for Cs<sup>+</sup> (47% *E*). Towards the other groups of cations **3** is a weak phase transfer agent, with exception for Ag<sup>+</sup>, to which it exhibits a significant affinity. Ligand **3** forms 1:1 complexes with K<sup>+</sup>, Ca<sup>2+</sup>, Ag<sup>+</sup> and Pb<sup>2+</sup> and no complexation with Zn<sup>2+</sup>. In the case of Ag<sup>+</sup> another 1:1 species, resulting from interconversion of the partial cone conformation to the cone conformation, is also observed. The structures of these complexes deduced from NMR experiments show that the cations should be encapsulated into the cavity defined by the crown ether unit, the ethoxy group and the inverted aryl ring.

## Experimental

### Synthesis

All chemicals were reagent grade and were used without further purification. Melting points were measured on a Stuart Scientific apparatus and are uncorrected. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Varian Inova 300 and Bruker Avance III 500 MHz spectrometers, with TMS as internal reference. The gradient version of the COSY spectrum was collected as 512  $\times$  2K complex points. The phase sensitive NOESY experiment was collected as 256  $\times$  2K complex points with a mixing time of 0.6 s, a delay of 1.5 s and 32 transients. Gradient version of HSQCTOCSY experiment for connecting <sup>1</sup>H and <sup>13</sup>C was run with 32 scans and a delay of 1.5 s. Elemental analysis was determined on a Fisons EA 1108 microanalyser.

### 7,13,19,25-Tetra-*tert*-butyl-27,29-diethoxy-28,30-crown-6-2,3-dihomo-3-oxacalix[4]arene (**3**)

To a stirred solution of 0.60 g (0.68 mmol) of *p*-*tert*-butyldihomooxalix[4]arene-crown-6 (**1**) in 44 mL of dry

THF/DMF (10:1, v/v) 0.06 g (2 mmol) of sodium hydride (80% oil dispersion) was added, followed by 0.16 mL (2 mmol) of iodoethane. The reaction mixture was refluxed under N<sub>2</sub> for 3 h. Most of the solvent was then evaporated, and a dark orange oily residue was obtained and poured into 60 mL of 0.2 N HCl solution. A dark white precipitate was immediately obtained, filtered, taken up in dichloromethane, washed several times with water and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent gave a white solid, which was recrystallised from acetone/methanol affording 0.38 g (60%) of **3** as white crystals: mp 119–121°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ –0.07, 1.04 (2t, 6H, OCH<sub>2</sub>CH<sub>3</sub>), 1.21, 1.24, 1.28, 1.33 (4s, 36H, C(CH<sub>3</sub>)<sub>3</sub>), 1.86, 2.26 (2bm, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 3.28, 4.41 (ABq, 2H, J = 13.8 Hz, ArCH<sub>2</sub>Ar), 3.32, 4.41 (ABq, 2H, J = 13.5 Hz, ArCH<sub>2</sub>Ar), 3.48–3.90 (m, 20H, crown), 3.77 (m, 2H, OCH<sub>2</sub>CH<sub>3</sub>), 3.84 (m, 2H, ArCH<sub>2</sub>Ar), 4.20, 4.90 (ABq, 2H, J = 12.3 Hz, CH<sub>2</sub>OCH<sub>2</sub>), 4.22, 4.37 (ABq, 2H, J = 12.6 Hz, CH<sub>2</sub>OCH<sub>2</sub>), 7.06, 7.08, 7.10, 7.11, 7.13, 7.14, 7.16, 7.27 (8d, 8H, ArH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 15.2, 15.7 (OCH<sub>2</sub>CH<sub>3</sub>), 31.2, 31.5, 38.4 (ArCH<sub>2</sub>Ar), 31.4, 31.5, 31.6, 31.7 (C(CH<sub>3</sub>)<sub>3</sub>), 34.06, 34.11, 34.19 (C(CH<sub>3</sub>)<sub>3</sub>), 64.5, 66.4 (CH<sub>2</sub>OCH<sub>2</sub>), 68.7, 69.0 (OCH<sub>2</sub>CH<sub>3</sub>), 70.3, 70.7, 70.9, 71.0, 71.5, 72.8 (crown), 125.2, 125.3, 125.9, 126.1, 126.3, 126.6, 127.2, 127.5 (ArH), 130.0, 130.7, 133.3, 133.5, 134.2, 134.6, 144.8, 145.0, 145.3, 153.2, 153.6, 153.9 (Ar). Analysis calculated for C<sub>59</sub>H<sub>84</sub>O<sub>9</sub>: C, 75.60; H, 9.03. Found: C, 75.29; H, 9.20.

### Extraction studies

Equal volumes (5 mL) of aqueous solutions of metal picrates ( $2.5 \times 10^{-4}$  M) and solutions of the calixarenes ( $2.5 \times 10^{-4}$  M) in CH<sub>2</sub>Cl<sub>2</sub> were vigorously shaken for 2 min, and then thermostated in a water bath with mechanical stirring at 25°C overnight. After complete phase separation, the concentration of picrate ion in the aqueous phase was determined spectrophotometrically ( $\lambda_{\text{max}} = 354$  nm). For each cation–calixarene system the absorbance measurements were repeated, at least, four times. Blank experiments showed negligible picrate extraction in the absence of a calixarene. The details of metal picrate preparation have already been described (29, 30).

### Proton NMR titration experiments

Several aliquots (up to 3–5 equiv) of the salt solutions (0.25 M) in CD<sub>3</sub>OD were added to CDCl<sub>3</sub> solutions ( $0.5 \times 10^{-2}$  M) of ligand **3** directly in the NMR tube. The salts used were KSCN, Ag and Zn triflates and Ca and Pb perchlorates. The spectra were recorded on a Bruker Avance III 500 Spectrometer after each addition of the salts. The temperature of the NMR probe was kept constant at 22°C.

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