Conformationally Mobile Wide Rim Carbamoylmethylphosphine Oxide (CMPO)-Calixarenes

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Received January 12th, 1999

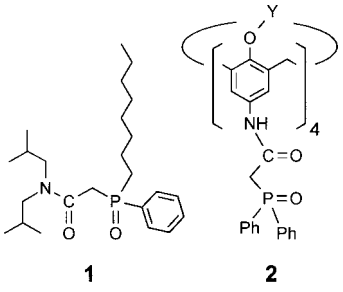
Dedicated to Prof. Fritz Vögtle on the Occasion of his 60th Birthday

Keywords: Actinides, Calixarenes, Extraction, Lanthanides, Carbamoylmethylphosphine Oxides

Abstract. Six new calix[4]arene derivatives **2a**–**f** have been synthesised, bearing CMPO-like functions (-NH–C(O)–CH_2–P(O)Ph_2) at their wide rim. They differ by their alkoxy groups at the narrow rim, comprising all possible combinations of methoxy and *syn*-propoxy groups including the conformationally mobile tetramethyl ether **2e** and the tetrapropyl ether **2f** fixed in the cone conformation. Their extraction behaviour for thorium(IV) and several lanthanides(III) from 1M HNO_3 to dichloromethane has been studied and compared also to non cyclic calixarene analogues **6a**–**e**. Surprisingly the best extraction results were found for the 1,2-dimethoxy-3,4-dipropoxy derivative **2c** among the calixarenes and for the tetramer **6d** among the linear compounds. Extraction of americium(III) in comparison to curium(III) and various lanthanides(LaIII), Ce(III), Nd(III), Sm(III), Eu(III)) from 0.1 – 3M HNO_3 to NPHE (*o*-nitrophenyl hexyl ether) was most effective again for **2c**. Among these cations, the highest distribution coefficients were found for Am(III) and the lowest for Ce(III) with a maximum generally in the range of 1–2M HNO_3.

Nuclear waste reprocessing is a current topic of great importance. Presently plutonium and uranium are effectively removed from nuclear waste streams by the PUREX process [1]. This leaves a waste stream containing long lived radio-nuclides which are both β and γ emitters as well as α emitters. The latter class of compounds includes the actinides which, if efficiently removed, can be transmuted to non-radioactive or short lived nuclides.

Separation of lanthanides and actinides from nuclear waste is presently achieved using the TRUEX process [2] which utilises CMPO **1** (octyl phenyl *N*,*N*- diisobutyl carbamoylmethyl phosphine oxide) as the extractant. Although this is rather efficient it shows little discrimination between lanthanides and actinides. We have previously shown that the attachment of four CMPO-like moieties to the wide rim of a calix[4]arene not only greatly enhances extraction [3], but also imparts a selectivity for actinides and lighter lanthanides [4]. This increase in extraction for molecules of type **2** is believed to be due to the co-operative action of the ligating functions, since studies on CMPO **1** have shown three ligands to be required per cation [5]. However, to date the actual composition and conformation of the extracted species are unknown [6].



1 **2**

Calix[4]arenes [7, 8] are macrocycles which have been used in numerous ways as a platform for the design of ligands [9]. They contain hydroxyl groups at the narrow rim which are small enough to pass through the annulus. Tetra-*O*-alkylation with residues greater than ethyl blocks this rotation and fixes the molecule in a certain conformation. However, the tetramethyl ether(s) show a flexibility similar to the parent calix[4]arenes and can assume all four possible conformers (”cone”, ”partial cone”, ”1,2 alternate”, ”1,3 alternate”). In contrast to the parent calix[4]arenes which exist exclusively in the cone-conformation, due to intramolecular hydrogen bonding between their hydroxy groups, the tetramethyl ethers exist as a mixture of conformers where the partial cone is usually preferred [10].

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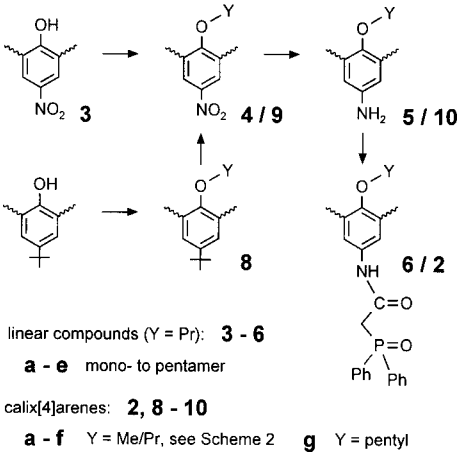
Whilst the first wide rim CMPO-calixarenes were derived from tetraethers fixed in the cone conformation, we found serendipitously that the extraction properties are significantly changed if larger alkoxy groups are partly replaced by methoxy groups. Such mixed ethers can adopt a number of conformations depending on the substitution pattern. In this study we describe the preparation of a complete series of mixed propyl methyl ether extractants and investigate the influence of their structure on extraction. Results for the corresponding linear oligomers are also included for comparison.

Results and Discussion

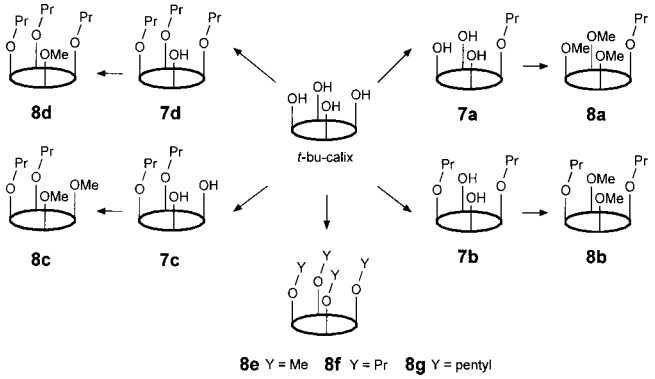
Syntheses

The preparation of the linear CMPO oligomers starts with *p*-nitrophenol (**3a**) and its linear oligomers **3b**–**e** previously described (bisbromomethylation of the n-mer and subsequent condensation with excess *p*-nitrophenol gives the (n+2)-mer) [11]. These oligomers were alkylated with propyl bromide in refluxing acetone in the presence of potassium carbonate. Catalytic hydrogenation (H_2/Pd/C) furnished the amines **5a**–**e** which were efficiently acylated with *p*-nitrophenyl (diphenylphosphoryl)acetate, an active ester described before [3], to give the five novel ligands **6a**–**e**. These synthetic steps are illustrated for a single phenolic unit in Scheme 1.

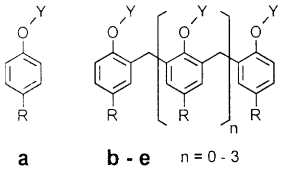
In contrast, the synthetic strategy for the calix[4]arene derivatives was based upon *ipso*-nitration of the corresponding tetraethers of *t*-butylcalix[4]arene, which were obtained in one or two steps from *t*-butyl-calix[4]arene. Exhaustive alkylation of *t*-butyl-calix[4]arene proceeded under mild conditions (8 mol NaH per mol calixarene, *r.t.*) leading to the known tetraalkyl ethers **8e**–**g**. Partial *O*-alkylation of calix[4]arene with propyl bromide was achieved *via* three procedures [12]. Alkylation using a large excess of NaH as base and a slight excess (2.2 mol) of propylbromide at room temperature furnished the 1,2-diether **7c** [13]. From the complex reaction mixture the tripropyl ether **7d** could also be isolated [14]. The monopropyl ether **7a**, in contrast, was obtained using the very weak base (or hydrogen bond acceptor) CsF (1.2 mol) and 1.1 mol of propyl bromide at 40 °C [15]. The 1,3-diether **7b** was efficiently prepared under well known standard conditions using K_2CO_3 as base (2.2 mol) and 2.2 mol of propylbromide [16]. These partial ethers were exhaustively alkylated on treatment with methyl iodide using a modification of our published procedure [3]. These synthetic steps are summarised in Scheme 2. The composition and the structure of the partially propylated compounds **7a**–**d**



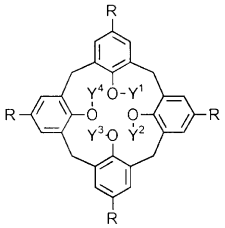
Scheme 1 Synthetic strategies for the preparation of CMPO-calixarenes (**2**) and their non cyclic analogs **6**, shown for a single phenolic unit.



Scheme 2 Synthesis of mixed methyl/propyl ethers **8a**–**d** of *t*-butyl calix[4]arene and of tetraethers with identical alkoxy groups **8e**–**g**. (The characterization by letters **a**–**g** holds also for the subsequent reaction steps **8** → **9** → **10** → **2**, compare Scheme 1.)



	Y	R
3	H	NO_2
4	C_3H_7	NO_2
5	C_3H_7	NH_2
6	C_3H_7	NH–C(=O)–CH(P(=O)(C_6H_5)$_2$)–



7	Y^1	Y^2	Y^3	Y^4
a	H	H	H	C_3H_7
b	H	C_3H_7	H	C_3H_7
c	H	H	C_3H_7	C_3H_7
d	H	C_3H_7	C_3H_7	C_3H_7

7,8	R = $C(CH_3)_3$
9	R = NO_2
10	R = NH_2
2	R = NH–C(=O)–CH(P(=O)(C_6H_5)$_2$)–

2,8-10	Y^1	Y^2	Y^3	Y^4
a	CH_3	CH_3	CH_3	C_3H_7
b	CH_3	C_3H_7	CH_3	C_3H_7
c	CH_3	CH_3	C_3H_7	C_3H_7
d	CH_3	C_3H_7	C_3H_7	C_3H_7
e	CH_3	CH_3	CH_3	CH_3
f	C_3H_7	C_3H_7	C_3H_7	C_3H_7
g	C_5H_{11}	C_5H_{11}	C_5H_{11}	C_5H_{11}

was proved by their mass and ^{1}H NMR spectra which confirm also the *syn* arrangement of the propylether groups in **7b**–**d**. In contrast to the mixed ethers **8a**–**d** [17] these partial ethers assume a cone conformation due to intramolecular hydrogen bonding which enables an unambiguous NMR analysis. For this reason it is also important to introduce the propyl ether residues first to ensure their *syn* arrangement.

All tetraethers **8a**–**g** were efficiently *ipso*-nitrated (fuming HNO_3/glacial acetic acid in dichloromethane at *r.t.*) to furnish the tetranitro compounds **9a**–**g**. Reduction to the desired amines **10a**–**g** was achieved by hydrazine in the presence of Raney nickel, apart from the reduction of the nitro compound **9e** which proved possible only with $SnCl_2$. Acylation with *p*-nitrophenyl (diphenylphosphoryl)acetate finally gave the ligands **2a**–**g**. Scheme 1 summarises these reaction steps for a single phenolic unit.

All the conformationally mobile compounds gave highly complex ^{1}H NMR spectra, but could be identified conclusively from their FD-mass spectra. For **8**, **9** and **10** the M^+ peak was found in high abundance as the only peak in this mass region. An M^+ peak was also observed for the tetra-CMPO calix[4]arenes **2**, which, however, showed appreciable fragmentation like their non cyclic analogues **6**. Their purity was confirmed by TLC analysis.

Extraction studies

All the ligands synthesised (**2**, **6**) were studied as extractants of thorium(IV) and lanthanide(III) nitrates from an aqueous acidic solution ($c_M = 10^{-4}$ M, $c(HNO_3)$ = 1M) into dichloromethane. The extraction results for **2a**–**g** are collected in Table 1. In addition to the conformationally fixed tetrapropyl ether **2f** the tetrapentyl CMPO-calix[4]arene **2g** was used as a standard for comparative purposes like in similar studies [9]. As described previously calix[4]arenes of type **2** are highly efficient extractants for lanthanides which require concentrations of 1/100 or less in comparison to CMPO **1** to reach the same extraction levels [3]. We have chosen a concentration of $c_L = 10^{-3}$ M which leads to reasonable extraction values for europium, allowing to distinguish between the different ligands, while lanthanum is nearly quantitatively extracted (%E = 98–100) and ytterbium only sparingly, due to the strong preference for the light lanthanides [4]. Meaningful extraction values for thorium could be obtained only when c_L was lowered to 10^{-4} M.

Table 1 Extraction Percentages of lanthanide and thorium nitrates ($c_M = 10^{-4}$ M) by CMPO calix[4]arenes **2a**–**g** from 1M HNO_3 aqueous solution into dichloromethane (t = 20 °C).

Ligands	$La(NO_3)_3$ $c_L = 10^{-3}$ M	$Eu(NO_3)_3$ $c_L = 10^{-3}$ M	$Yb(NO_3)_3$ $c_L = 10^{-3}$ M	$Th(NO_3)_4$ $c_L = 10^{-4}$ M
2a	98 ± 1	45 ± 1	< 2	69 ± 1
2b	99.4 ± 0.2	48 ± 2	5 ± 1	66 ± 2
2c	100	73 ± 1	3.4 ± 0.7	70 ± 1
2d	100	60 ± 1	< 2	66 ± 2
2e	99 ± 1	35 ± 2	3 ± 2	60 ± 1
2f	98 ± 1	64 ± 1	6.6 ± 0.4	61.8 ± 0.4
2g [a])	98	58	3	61

[a]) Values from ref. [9]

Under these conditions all the CMPO calix[4]arenes **2e**–**g** with identical ether groups show the same extraction (60–62%) for Th^{4+} while the mixed ethers **2a**–**f** show slightly but still significantly higher values of 66–70%. Stronger differences are found for Eu^{3+}, where the tetramethyl ether **2e** shows the lowest (35%) and the 1,2-diether **2c** the highest extraction ability (73%). This means, that the distribution coefficient D = %E/(100-%E) is higher by a factor of 5. But also the tetrapropyl ether shows good extraction (64%), and all the other calixarenes are found inbetween. No easy explanation is evident for these results.

For the ligands **2c**, **2e**, and **2f** the extraction of Eu^{3+} was studied also as a function of c_L. Fig. 1 shows plots of log D *vs.* log c_L which are linear with slopes close to two (**2c** : 1.89, **2e** : 1.97, and **2f** : 1.89) suggesting that the cation is probably extracted as a 1:2 complex (metal:ligand). This is in agreement with former studies on similar compounds [3] while calix[4]arenes bearing CMPO-functions on the narrow rim gave a slope close to one under analogous conditions [9]. Although a 1:2 complex is difficult to envisage with these rather bulky ligands of the podand type, it is not impossible according to CPK-models.

Table 2 contains selected values for the extraction of Eu^{3+} and Th^{4+} with the linear oligomers **6a**–**f**. As expected, their extraction ability increases from the monomer to the tetramer (for **6a**,**b** the ligand concentration c_L had to be increased by a factor of 10, to get meaningful extraction), but it decreases again for the pentamer **6f**. In comparison to the calixarenes **2a**–**f** the tetramer **6d** shows a similar extraction ability for Eu^{3+} (56% *versus* 35–73%) but is distinctly less effective for Th^{4+} (35% *vs.* 60–70%).

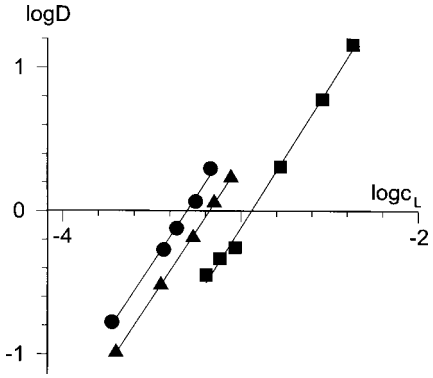


Fig. 1 Plot of log D versus log c_L for the extraction of Eu^{3+} from 1M HNO_3 ($c_M = 10^{-4}$ M) to dichloromethane by CMPO-calixarenes **2c** (●), **2e** (■), and **2f** (▲).

Table 2 Extraction percentages of europium and thorium nitrates by linear CMPO compounds **6a**–**e** from 1M HNO_3 aqueous solution into dichloromethane (T = 20 °C).

Ligands	$Eu(NO_3)$ $c_L = 10^{-2}$ M	$c_L = 10^{-3}$ M	$Th(NO_3)_4$ $c_L = 10^{-3}$ M	$c_L = 10^{-4}$ M
6a	4 ± 2	–	6 ± 2	–
6b	24 ± 1	–	18 ± 2	–
6c	–	23 ± 2	–	6 ± 2
6d	–	56.5 ± 0.3	–	35 ± 2
6e	–	38.1 ± 0.8	–	31 ± 2

For the calix[4]arenes **2a**–**f** the extraction of actinides (^{241}Am, ^{244}Cm, about 1 000–1 500 kBq/l) and lanthanides (La, Ce, Nd, Sm, Eu, $c_M = 10^{-5}$ M)) with *o*-nitrophenyl hexyl ether ($c_L = 10^{-3}$ M) was also studied for different concentrations of nitric acid ($c(HNO_3)$ = 0.01–4M). For all compounds and for all cations the distribution coefficient ($D = \Sigma\, c(M)_{org}/\Sigma\, c(M)_{aq}$) at the lowest concentration is very small (partly < 1), reaches a maximum for $c(HNO_3)$ = 1– 2M and decreases again for the higher concentrations of HNO_3. Some typical examples are shown in Fig. 2. In Fig. 3 the extraction abilities of the different calixarenes for the different cations are compared for $c(HNO_3)$ = 3M, since most interesting from a technical point of view is the extraction from highly acidic solutions.

Within the lanthanides Nd^{3+}, Sm^{3+}, Eu^{3+} the usually observed decrease of D with decreasing ion radius is found [4], which means the lighter Nd^{3+} is better extracted than the heavier Eu^{3+}. La^{3+} has in some cases slightly lower D-values than Nd^{3+}, but striking are the very low distribution coefficients of Ce^{3+}. In contrast to the other lanthanides cerium may be oxidised to Ce^{4+}, but considering the results described above for Th^{4+}, this does not necessarily offer an appropriate explanation although the ionic radius of Ce^{4+} is distinctly smaller than that of Ce^{3+}.

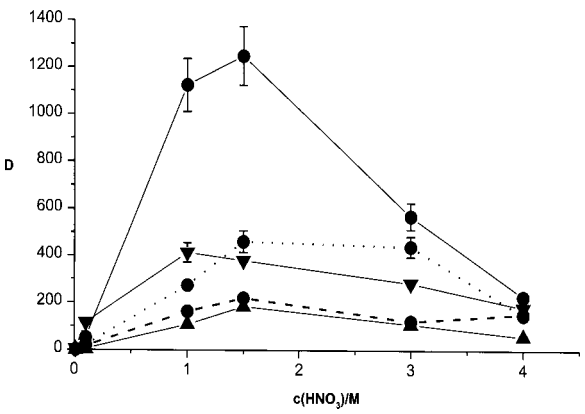


Fig. 2 Distribution coefficient D as function of $c(HNO_3)$ for the extraction of different cations (Am^{3+} (●), Eu^{3+} (▲), La^3 (▼) *o*-nitrophenyl hexyl ether to (NPHE) by different ligands (**2b** ••••, **2c** ——, **2f** - - - -). Estimated errors are indicated by bars only where they are distinctly larger than the symbol.

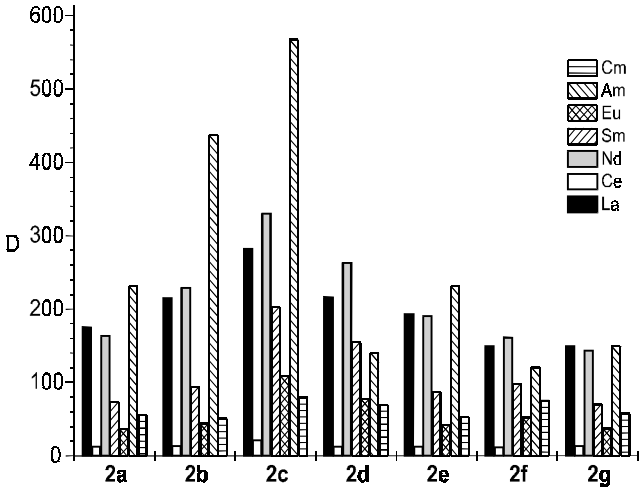


Fig. 3 Extraction of different cations, expressed by the distribution coefficient D, from 1M HNO_3 to *o*-nitrophenyl hexyl ether (NPHE) by different CMPO-calixarenes **2a**–**g**

In general, the 1,2-di-propyl ether **2c** is again the best extractant for all cations, showing a D_{Am} which is nearly five-times higher than that of **2f**. The ratio is even higher (up to nine-times) for $c(HNO_3)$ = 1.5–2 M). The 1,3-di-propyl ether **2b** still extracts Am^{3+} best, while Nd^{3+} is best extracted by **2d** and **2f**. Thus there are differences, not only in the extraction ability (expressed by D) but also in its selectivity.

Often the ratio D_{Am}/D_{Eu} is taken to characterise the selectivity of actinides over lanthanides. This value, which generally decreases with increasing concentration of HNO_3 shows small variations from compound to compound. The highest value at $c(HNO_3)$ = 0.1M is obtained for **2a** (12.5), and at $c(HNO_3)$ = 4M for **2b** (8.4). CMPO **1** itself, which has to be applied in a concentration of 0.25M to obtain distribution coefficients of nearly the same size, has ratios D_{Am}/D_{Eu} between 2 and 1.4.

Conclusion

The substitution pattern at the narrow rim clearly has a significant influence on the extraction efficiency of wide rim CMPOs, but it is difficult to propose a convincing explanation. A complete rotation of an anisol unit (to form the partial cone or an alternate conformation) has not necessarily to occur. The different sizes of the ether residues may also allow a more subtle distortion of the cone conformation to adopt the best fit for a given cation. Furthermore differences in the lipophilicity of the calixarene **2a**–**f** cannot be entirely ruled out. There are also differences in the extraction selectivity, however, the preference for actinides over lanthanides (D_{Am}/D_{Eu}), although distinctly higher than for **1**, could not be increased much in mixed ethers **2a**–**d** in comparison to compounds **2e**–**g** with identical ether residues.

These studies were supported by the Commission of the European Communities (contract F12W-CT96-0022).

Experimental

Syntheses

General remarks. Melting points were determined on Dr. Tottoli´s (Büchi) melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC200 at 200 MHz, unless otherwise stated. FD mass spectra were recorded on a Finnigan MAT 8230 spectrometer (5 kV, 10 mA/min).

Linear Compounds

4,4'-dinitro-2,2'-methanediyl-diphenol (or 2-(2-hydroxy-5-nitrobenzyl)-4-nitrophenol) (**3b**) and *2,6-Bis-(2-hydroxy-5-nitrobenzyl)-4-nitrophenol* (**3c**) were prepared in 90 and 72% yield according to literature procedures [3, 11] using the *bis*-bromomethylated instead of the *bis*-chloromethylated derivative for the synthesis of **3c**.

6,6'-Bis-(2-hydroxy-5-nitrobenzyl)-4,4'-dinitro-2,2'-methanediyl-diphenol (**3d**)

(a) *Bromomethylation*. A stirred mixture of dimer **3b** (10 g, 34 mmol), paraformaldehyd (2.25 g, 75 mmol), $ZnCO_3$ (0.7 g), 33% HBr in glacial acetic acid (50 ml) and acetic anhydride (1.37 ml) was heated to 70 °C for 20 min. After 4 h reflux, petroleum ether (80–100 °C) was added, the precipitate was filtered and dried over KOH. Recrystallisation from ethyl acetate/petroleum ether (80–100 °C) gave the bis-bromomethylated dimer as white powder (11 g, 68%). *m.p.* 235 °C. – ^{1}H NMR (acetone-d_6): δ/ppm = 4.28 (s, 2H, $ArCH_2Ar$), 4.85 (s, 4H, $ArCH_2Br$), 8.01 (d, 2H, ^4J = 2.9, ArH), 8.30 (d, 2H, ^4J = 2.8, ArH).

(b) *Condensation.* The *bis*-bromomethylated dimer (3 g, 6.32 mmol) was dissolved in molten *p*-nitrophenol (22.4, 160 mmol). $ZnCl_2$ (2 g, 20 mmol) was added to the solution, and the mixture was kept at 120–130 °C under nitrogen for 4 h. Hot water was added, and the greenish yellow precipitate was isolated and dissolved in 5% NaOH solution. The tetramer **3d** was obtained by dropping the brownish alkaline solution after filtration into an excess of diluted HCl. The precipitate was filtered, dried over KOH and recrystallised from acetone to obtain **3d** as a white solid (2 g, 53%). *m.p.* 255 °C. – ^{1}H NMR (acetone-d_6): δ/ppm = 4.02 (s, 4H, $ArCH_2Ar$), 4.12 (s, 2H, $ArCH_2Ar$), 7.12 (d, 2H, ^3J = 9.1, ArH), 7.86 (d, 4H, ^4J = 2.7, ArH), 8.16–7.95 (m, 4H, ArH).

2,6-bis-(2-hydroxy-3-(2-hydroxy-5-nitrobenzyl)-5-nitrobenzyl)-4-nitrophenol (**3e**) was prepared using the same procedure described for **3d**.

(a) *Bromomethylation*. Yield 72%; *m.p.* 190 °C. – ^{1}H NMR (acetone-d_6): δ/ppm = 4.26 (s, 4H, $ArCH_2Ar$), 4.83 (s, 4H, $ArCH_2Br$), 7.95 (d, 2H, ^4J = 2.9, ArH), 8.03 (s, 2H, ArH), 8.26 (d, 2H, ^4J = 2.9, ArH).
(b) *Condensation*. Yield of **3e** 80%; *m.p.* 269 °C. – ^{1}H NMR (acetone-d_6): δ/ppm = 4.18 (s, 4H, $ArCH_2Ar$), 4.24 (s, 4H, $ArCH_2Ar$), 7.10 (d, 2H, ^3J = 9.1, ArH), 7.99–7.93 (m, 4H, ArH), 8.02 (d, 2H, ^4J = 2.9, ArH), 8.07 (d, 2H, ^4J = 2.9, ArH), 8.15 (d, 2H, ^3J = 9.0, ArH).

Alkylation (General Procedure)

A suspension of 4-nitrophenol (**3a**) or one of its linear oligomers **3b**–**e** (1 mmol) was dissolved in acetone (2 ml) under argon. K_2CO_3 (1.5 mol per OH) was added followed, after 30 min, by propyl bromide (2 mol per OH). The suspension was stirred at room temperature for 3d. The solvent was removed under reduced pressure and the residue partitioned between water and dichloromethane. The organic layer was extracted twice with 15% NaOH solution, washed with water and dried over sodium sulphate.

4-Nitrophenyl propyl ether (**4a**)

[18] Transparent oil. Yield 92%. – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.05 (t, 3H, ^3J = 6.4 Hz, CH_3), 1.95–1.70 (m, 2H, CH_2),.4.03 (t, 2H, ^3J = 6.5 Hz, CH_2), 6.95 (d, 2H, ^3J = 9.2 Hz, ArH), 8.20 (d, 2H, ^3J = 9.2 Hz, ArH).

$C_9H_{11}NO_3$	Calcd.:	C 59.66	H 6.12	N 7.73
(181.19)	Found:	C 59.56	H 6.22	N 7.70.

2-(2-Propoxy-5-nitrobenzyl)-4-nitrophenyl propyl ether (**4b**)

White solid (recrystallised from MeOH). Yield 51%; *m.p.* 165–166 °C. – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.05 (t, 6H, ^3J = 6.0 Hz, CH_3), 2.01–1.80 (m, 4H, $ArOCH_2C\underline{H}_2$), 4.02–3.90 (m, 6H, $ArCH_2Ar$ + OCH_2), 6.69 (d, 2H, ^3J = 8.0 Hz, ArH), 8.28–7.95 (m, 4H, ArH).

$C_{19}H_{22}N_2O_6$	Calcd.:	C 60.94	H 5.93	N 7.49
(374.39)	Found:	C 60.49	H 5.91	N 7.39.

2,6-Bis-(2-propoxy-5-nitrobenzyl)-4-nitrophenyl propyl ether (**4c**)

White solid (recrystallised from MeOH). Yield 52%; *m.p.* 149–150 °C. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.91 (t, 6H, ^3J = 6.1 Hz, CH_3), 1.03 (t, 3H, ^3J = 6.0 Hz, CH_3), 1.92–1.68 (m, 6H, $ArOCH_2C\underline{H}_2$), 3.84 (t, 2H, ^3J = 6.6 Hz, $ArOCH_2$) 4.04 (t, 4H, ^3J = 6.4 Hz, $ArOCH_2$), 4.07 (s. 4H, $ArCH_2Ar$), 6.91 (d, 2H, ^3J = 8.0 Hz, ArH), 7.82 (s, 2H, ArH), 8.00 (d, 2H, ^4J = 2.8 Hz, ArH), 8.15 (d, 2H, ^3J = 8.0 Hz, ArH). – FD-MS (*m/z*): 567.3 (M^+).

$C_{29}H_{33}N_3O_9$	Calcd.:	C 61.35	H 5.86	N 7.41
(567.2)	Found:	C 61.05	H 6.01	N 7.38.

6,6'-Bis-(2-propoxy-5-nitrobenzyl)-4,4'-dinitro-2,2'-methanediyl-di(phenyl propyl ether) (**4d**)

White solid (recrystallised from MeOH). Yield 56%; *m.p.* 130–131 °C. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.93 (t, 6H, ^3J = 6.1 Hz, CH_3), 0.99 (t, 6H, ^3J = 6.0 Hz, CH_3), 1.87–1.73 (m, 8H, CH_2), 3.79 (t, 4H, ^3J = 6.1, $ArOCH_2$), 4.00 (t, 4H, ^3J = 6.1, $ArOCH_2$), 4.08 (s, 4H, $ArCH_2Ar$), 4.15 (s, 2H, $ArCH_2Ar$), 6.91 (d, 2H, ^3J = 8.0 Hz, ArH), 7.77 (d, 2H, ^4J = 2.9 Hz, ArH), 7.86 (d, 2H, ^4J = 2.9 Hz, ArH), 8.03 (d, 2H, ^4J = 2.9 Hz, ArH), 8.13 (d, 1H, ^4J = 2.4 Hz, ArH), 8.18 (d, 1H, ^4J = 2.5 Hz, ArH).

$C_{39}H_{44}N_4O_{12}$	Calcd.:	C 61.57	H 5.83	N 7.36
(760.80)	Found:	C 61.84	H 5.75	N 7.38.

2,6-Bis-(2-propoxy-3-(2-propoxy-5-nitrobenzyl)-5-nitrobenzyl)-4-nitrophenyl propyl ether (**4e**)

White solid (recrystallised from MeOH). Yield 58%; *m.p.* 99–100 °C. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.98 (t, 6H, ^3J = 6.1 Hz, CH_3), 1.01 (t, 9H, ^3J = 6.0 Hz, CH_3), 1.86–1.73 (m, 10H, CH_2), 3.87–3.78 (m, 6H, $ArOCH_2$), 4.01 (t, 4H, ^3J = 6.1, $ArOCH_2$), 4.12 (s, 4H, $ArCH_2Ar$), 4.17 (s, 4H, $ArCH_2Ar$),

6.91 (d, 2H, ^3J = 8.0 Hz, ArH), 7.76 (d, 2H, ^4J = 2.9 Hz, ArH), 7.81 (s, 2H, ArH), 7.86 (d, 2H, ^4J = 2.9 Hz, ArH), 8.03 (d, 2H, ^4J = 2.9 Hz, ArH), 8.13 (d, 1H, ^4J = 2.4 Hz, ArH), 8.18 (d, 1H, ^4J = 2.5 Hz, ArH).

$C_{49}H_{55}N_5O_{15}$	Calcd.:	C 61.68	H 5.81	N 7.34
(954.00)	Found:	C 61.58	H 5.72	N 7.21.

Hydrogenation of the Nitro Compounds 4a–e (General Procedure)

A catalytic amount of Raney nickel (washed with EtOH) was added to a solution of **4a–e** (1 mmol) in dry toluene (100 ml) and the mixture stirred at room temperature under H_2. Filtration and evaporation of the solvent gave the corresponding amino compounds **5a–e** as transparent oils which could be used for the next step without further purification.

4-Aminophenyl propyl ether (**5a**)

Yield 82%. – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.01 (t, 3H, ^3J = 6.1 Hz, CH_3), 1.81–1.67 (m, 2H, CH_2), 3.15 (br s, 2H, NH_2), 3.85 (t, 2H, ^3J = 6.1 Hz, $ArOCH_2$), 6.61 (d, 2H, ^3J = 8.1 Hz, ArH), 6.78 (d, 2H, ^3J = 8.1 Hz, ArH).

2-(2-Propoxy-5-aminobenzyl)-4-aminophenyl propyl ether (**5b**)

Yield 95%. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.96 (t, 6H, ^3J = 6.1 Hz, CH_3) 1.89–1.56 (m, 4H, CH_2), 3.14 (br s, 4H, $ArNH_2$), 3.97–3.73 (m, 6H, $ArCH_2Ar$ + $ArOCH_2$), 6.54–6.34 (m, 4H, ArH), 6.67 (d, 2H, ^3J = 4.0 Hz, ArH).

2,6-Bis-(2-propoxy-5-aminobenzyl)-4-aminophenol propyl ether (**5c**)

Yield 80%. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.96 (t, 9H, ^3J = 6.1 Hz, CH_3), 1.90–1.56 (m, 6H, CH_2), 3.06 (br s, 6H, $ArNH_2$), 3.93–3.70 (m, 10H, $ArCH_2Ar$ + $ArOCH_2$), 6.66 (d, 2H, ^3J = 4.0 Hz, ArH), 6.60–6.30 (m, 6H, ArH).

6,6'-Bis-(2-propoxy-5-aminobenzyl)-4,4'-diamino-2,2'-methanediyl-di(phenyl propyl ether) (**5d**)

Yield 92%. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.87 (m, 12H, CH_3), 1.70 (m, 8H, CH_2), 3.11 (br s, 8H, $ArNH_2$), 3.68 (t, 4H, ^3J = 6.2 Hz, OCH_2), 3.86 (t, 4H, ^3J = 6.5 Hz, OCH_2), 3.88 (s, 4H, $ArCH_2Ar$), 3.92 (s, 2H, $ArCH_2Ar$), 6.22 (s, 4H, ArH), 6.41 (d, 2H, ^4J = 2.7 Hz, ArH), 6.48 (d, 2H, ^3J = 8.5 Hz, ArH), 6.68 (d, 2H, ^3J = 8.5 Hz, ArH).

2,6-Bis-(2-propoxy-3-(2-propoxy-5-aminobenzyl)-5-aminobenzyl)-4-aminophenyl propyl ether (**5e**)

Yield 91%. – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.88 (m, 15H, CH_3), 1.72 (m, 10H, CH_2), 2.65 (br s, 10H, $ArNH_2$), 3.68 (t, 6H, ^3J = 6.6 Hz, OCH_2), 3.86 (t, 4H, ^3J = 6.4 Hz, OCH_2), 3.88 (s, 4H, $ArCH_2Ar$), 3.92 (s, 4H, $ArCH_2Ar$), 6.22 (s, 6H, ArH), 6.41 (d, 2H, ^4J = 2.4 Hz, ArH), 6.49 (d, 2H, ^3J = 8.5 Hz, ArH), 6.67 (d, 2H, ^3J = 8.4 Hz, ArH).

Preparation of the Linear CMPO Compounds 6a–e (General Procedure)

Amino compound **5a–e** (1mmol) and *p*-nitrophenyl(diphenylphosphoryl)acetate (1.5 mmol per free NH_2) were suspended in toluene (20 ml) containing triethylamine (10 mmol).The mixture was stirred at room temperature for 24h. The solvent was evaporated and the residue dissolved in dichloromethane. The organic layer was washed repeatedly with 10% NaOH, subsequently with brine, dried and the solvent evaporated. Precipitation from chloroform/methanol gave the desired product.

4-Diphenylphosphoryl-acetamidophenyl propyl ether (**6a**)

White solid. Yield 68%; *m.p.* 181–183 °C. – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.03 (t. 3H, ^3J = 6.3 Hz, CH_3), 1.92–1.65 (m, 2H, CH_2), 3.46 (d, 2H, ^2J = 13 Hz, $POCH_2$), 3.85 (t, 2H, ^3J = 6.4 Hz, $ArOCH_2$), 6.75 (d, 2H, ^3J = 8.5 Hz, ArH), 7.60–7.30 (m. 8H, ArH + POArH), 7.85–7.65 (m, 4H, POArH), 9.45 (s, 1H, ArNH). – FD-MS (*m/z*): 393.1 (M^+).

$C_{23}H_{24}NPO_3$	Calcd.:	C 70.20	H 6.15	N 3.56
(393.4)	Found:	C 70.22	H 6.28	N 3.56.

2-(2-Propoxy-5-diphenylphosphoryl-acetamidobenzyl)-4-(diphenylphosphoryl-acetamido)phenyl propyl ether (**6b**)

White solid. Yield 79%; *m.p.* 100–101 °C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.96 (t, 6H, ^3J = 6.0 Hz, CH_3), 1.72–1.64 (m, 4H, CH_2), 3.52 (d, 4H, ^2J = 13.0 Hz, $POCH_2$), 3.72 (s, 2H, $ArCH_2Ar$), 3.77 (t, 4H, ^3J = 6.0 Hz, $ArOCH_2$), 6.54 (d, 2H, ^3J = 8.0 Hz, ArH), 6.70 (s, 2H, ArH), 7.32 (d, 2H, ^3J = 8.1 Hz, ArH), 7.49–7.35 (m, 12H, POArH), 7.85–7.70 (m, 8H, POArH), 9.73 (s, 2H, ArNH),. – FD-MS (*m/z*): 799.1 (M^+).

$C_{47}H_{48}N_2P_2O_6 \cdot 2H_2O$	Calcd.:	C 67.62	H 6.28	N 3.36
(798.6)	Found:	C 67.59	H 6.50	N 3.29:

2,6-Bis-(2-propoxy-5-diphenylphosphorylacetamidoben-zyl)-4-diphenylphosphorylacetamidophenyl propyl ether (**6c**)

White solid. Yield 53%; *m.p.* 130–133 °C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.90 (m, 9H, CH_3), 1.72–1.64 (m, 6H, CH_2), 3.56–3.40 (m, 6H, $POCH_2$), 3.72 (s, 4H, $ArCH_2Ar$), 3.77 (t, 6H, ^3J = 6.0 Hz, $ArOCH_2$), 6.62 (d, 2H, ^3J = 8.0 Hz, ArH), 6.76 (br s, 2H, ArH), 6.85 (br s, 2H, ArH), 7.35 (m, 20H, ArH and PArH), 7.65–7.85 (m, 12H, PArH), 9.35 (br s, 1H, ArNH), 9.47 (br s, 2H, ArNH). – FD-MS (*m/z*): 1205.5 (M^+).

$C_{71}H_{72}N_3P_3O_9 \cdot 2H_2O$	Calcd.:	C 68.75	H 6.18	N 3.39
(1204.2)	Found:	C 68.95	H 6.44	N 3.37.

6,6'-Bis-(2-propoxy-5-diphenylphosphoryl-acetamidobenzyl)-4,4'-bis-(diphenylphosphoryl-acetamido)-2,2'-methanediyl-di(phenyl propyl ether) (**6d**)

Yellow powder. Yield 68%; *m.p.* 140–144 °C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ/ppm = 0.85 (t, 12H, ^3J = 6.0 Hz, CH_3), 1.72–1.48 (m, 8H, CH_2), 3.75–3.44 (m, 12H, $POCH_2$ + $ArOCH_2$), 3.96–3.77 (m, 10H, $ArCH_2Ar$ + $ArOCH_2$), 6.67 (d, 2H, ^3J = 8.2 Hz, ArH), 6.73 (d, 2H, ^4J = 2.0 Hz, ArH), 6.86 (d, 2H, ^4J = 2.0 Hz, ArH), 7.01 (d, 2H, ^4J = 2.0 Hz, ArH), 7.47–7.28 (m, 26H, POArH and ArH), 7.78–7.62 (m, 16H, POArH), 9.69 (s, 2H, ArNH), 9.70 (s, 2H, ArNH). – FD-MS (*m/z*): 1609.1 (M^+).

$C_{95}H_{96}N_4P_4O_{12}$	Calcd.:	C 70.88	H 6.01	N 3.48
(1609.7)	Found:	C 70.76	H 5.96	N 3.32.

2,6-Bis-(2-propoxy-3-(2-propoxy-5diphenylphosphoryl-acetamidobenzyl)-5-diphenylphosphoryl-acetamidobenzyl)-4-diphenylphosphoryl-acetamidophenyl propyl ether (**6e**)

White solid. Yield 60%; *m.p.* 149–150 °C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ/ppm = 0.96–0.73 (m, 15H, CH_3), 1.77–1.47 (m, 10H, CH_2), 3.73–3.42 (m, 16H, $ArOCH_2$ + $POCH_2$), 4.01–3.74 (m, 12H, $ArCH_2Ar$ + $ArOCH_2$), 7.10–6.74 (m,

8H, ArH), 7.56–7.33 (m, 34H, POArH + ArH), 7.99–7.66 (m, 20H, POArH), 9.80 (s, 5H, ArNH). – FD-MS (*m/z*): 2015.7 (M^+).

$C_{119}H_{120}N_5P_5O_{15}\cdot 2H_2O$ (2015.1)	Calcd.: C 69.68	H 6.09 N 3.41
	Found: C 69.26	H 6.56 N 3.54.

Calix[4]arenes

5,11,17,23-Tetra-tert-butyl-25,26,27-trihydroxy-28-propoxy-calix[4]arene (**7a**)

p-tert-Butylcalix[4]arene (5.00 g, 7.69 mmol) was suspended with CsF (1.39 g, 9.23 mmol) in DMF (130 ml). Propyl bromide (7 ml, 7.72 mmol) was then added and the mixture taken to 40 °C. The mixture was stirred for 72 h and then cooled. 2M HCl (200 ml) was added and the mixture extracted with dichloromethane. The organic layer was dried and the solvent evaporated. The residue was dissolved in a mixture of dichloromethane/methanol (1:1) and filtered. Column chromatography (chloroform) gave a white solid (3.14 g, 59%). *m.p.* 234–236 °C (ref. *m.p.* 238–239 °C [19]). R_f = 0.63 (chloroform/hexane 1:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.19 (s, 9H, *t*-Bu), 1.20 (s, 18H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 1.23 (m, 3H, $CH_2C\underline{H}_3$), 2.18 (sext, 2H, ^3J = 7.3 Hz, $OCH_2C\underline{H}_2$.), 3.40 (d, 2H, ^2J = 12.7 Hz, $ArCH_2Ar$), 3.43 (d, 2H, ^2J = 13.7 Hz, $ArCH_2Ar$), 4.09 (t, 2H, ^3J = 7.1 Hz, OCH_2), 4.27 (d, 2H, ^2J = 13.7 Hz, $ArCH_2Ar$), 4.36 (d, 2H, ^2J = 12.7 Hz, $ArCH_2Ar$), 6.84 (s, 4H, ArH), 6.98 (s, 2H, ArH), 7.03 (s, 4H, ArH), 7.08 (s, 2H, ArH), 9.61 (s, 2H, OH), 10.2 (s, 1H, O$\underline{H}$). – FD-MS (*m/z*): 690.8 (M^+).

5,11,17,23-Tetra-tert-butyl-25,27-dihydroxy-26,28-dipropoxy-calix[4]arene- (**7b**)

A suspension of *p-tert*-butylcalix[4]arene (8.00 g, 12.4 mmol) and K_2CO_3 (3.73 g, 27 mmol) in acetonitrile (300 ml) was heated at reflux under argon for 1 h. The solution was cooled and then propyl bromide (2.46 ml, 27 mmol) added. The mixture was kept at 70 °C for 2 days. The solvent was evaporated and the residue taken up in a mixture of chloroform (200 ml)/water (200 ml). The organic layer was separated, washed with water (30 ml), brine (30 ml) and dried. Evaporation of the solvent and precipitation from chloroform/methanol gave 4.62 g (51%) of the title compound as a white solid; *m.p.* 245–246 °C (ref. *m.p.* 247–249 °C [20]. R_f = 0.31 (hexane/chloroform 2:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.99 (s, 18H, *t*-Bu), 1.25 (m, 24H, *t*-Bu + $CH_2C\underline{H}_3$), 2.02 (sext, 4H, ^3J = 6.8 Hz, $OCH_2C\underline{H}_2$.), 3.29 (d, 4H, ^2J = 14.1 Hz, $ArCH_2Ar$), 3.93 (t, 4H, ^3J = 6.4 Hz, OCH_2), 4.29 (d, 4H, ^2J = 13.2 Hz, $ArCH_2Ar$), 6.84 (s, 4H, ArH), 7.02 (s, 4H, ArH), 7.89 (s, 2H, O$\underline{H}$). – FD-MS (*m/z*): 732.9 (M^+).

5,11,17,23-Tetra-tert-butyl-25,26-dihydroxy-27,28-dipropoxy-calix[4]arene (**7c**)

p-tert-butylcalix[4]arene (10.0 g, 15.4 mmol) was suspended in dry DMF (300 ml) under argon. NaH (1.71 g, 67.7 mmol) was added followed, after 30 min, by propyl bromide (3.08 ml, 33.9 mmol). The suspension was stirred for 24 h at room temperature. Water (50 ml) was added and the resulting precipitate collected and dried. Column chromatography (hexane/chloroform 1:1) gave the title compound as a white solid (3.34 g, 30%); *m.p.* 108–110 °C (ref. *m.p.*119–121 °C [19]). R_f = 0.17 (chloroform/hexane 1:4). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.10 (m, 27H, *t*-Bu + $CH_2C\underline{H}_3$), 1.20 (s, 18H, *t*-Bu), 1.22 (s, 9H, *t*-Bu), 2.08 (sext, 2H, ^3J = 7.3 Hz, $OCH_2C\underline{H}_2$), 3.29–3.36 (m, 4H, $ArCH_2Ar$), 3.78–4.10 (m, 2H, OCH_2), 4.29 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 4.31 (d, 2H, ^2J = 13.2 Hz, $ArCH_2Ar$), 4.48 (d, 1H, ^3J = 12.2 Hz, $ArCH_2Ar$), 6.89 (m, 2H, ArH), 6.95–7.03 (br m, 6H, ArH), 8.91 (br s, 2H, O$\underline{H}$). – FD-MS (*m/z*): 733.4 (M^+).

5,11,17,23-Tetra-tert-butyl-25-hydroxy-26,27,28-tripropoxy-calix[4] arene- (**7d**) (as a by-product of **7c**)

The precipitate obtained in an experiment described above (starting with 5.00 g *p-tert*-butylcalix[4]arene) was dissolved in chloroform, washed with 10% HCl (30 ml) and brine (30 ml) and dried. Evaporation of the solvent gave a crude solid. Gradient column chromatography (hexane/chloroform 4:1, 3:1, 2:1) gave first 1.61 g (27%) of the trialkylated product **7d** (while later fractions contained **7c**); *m.p.* 193–196 °C (ref. *m.p.* 194–196 [20]) R_f = 0.53 (hexane/chloroform 4:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.81 (s, 18H, *t*-Bu), 0.94 (t, 3H, ^3J = 7.5 Hz, $CH_2C\underline{H}_3$), 1.08 (t, 6H, ^3J = 7.3 Hz, $CH_2C\underline{H}_3$), 1.31 (s, 9H, *t*-Bu), 1.33 (s, 9H, *t*-Bu), 1.89 (m, 4H, $OCH_2C\underline{H}_2$.), 2.35 (m, 2H, $OCH_2C\underline{H}_2$), 3.15 (d, 2H, ^2J = 12.7 Hz, $ArCH_2Ar$), 3.22 (d, 2H, ^2J = 13.7 Hz, $ArCH_2Ar$), 3.70–3.87 (m, 6H, OCH_2), 4.32 (d, 2H, ^2J = 13.2 Hz, $ArCH_2Ar$), 4.35 (d, 2H, ^2J = 12.7 Hz, $ArCH_2Ar$), 5.60 (s, 1H, OH), 6.49 (s, 4H, ArH), 7.03 (s, 2H, ArH), 7.13 (s, 2H, ArH). – FD-MS (*m/z*): 774.8 (M^+).

Exhaustive *O*-Methylation of Partial Ethers (General Procedure)

The partially *O*-alkylated compound (1.00 mmol) was dissolved in DMF (20 ml) under argon. NaH (1.5 mol per mol OH) was added followed, after 30 min, by methyl iodide (2 mol per mol OH). The suspension was stirred at room temperature for 2 d. Water (30 ml) was added and the resulting precipitate collected. It was dissolved in chloroform, washed with water and brine and dried. Evaporation of the solid followed by precipitation from chloroform/methanol gave the desired compounds as chromatographically pure white solids. Only **8a** was purified by column chromatography.

5,11,17,23-Tetra-tert-butyl-25,26,27-trimethoxy-28-propoxy-calix[4]arene (**8a**)

Column chromatography (chloroform/hexane 1:1) Yield 71%; *m.p.* 193–196 °C. R_f = 0.74 (chloroform/hexane 1:1). – FD-MS (*m/z*): 732.8 (M^+).

5,11,17,23-Tetra-tert-butyl-25,27-dimethoxy-26,28-dipropoxy-calix[4]arene (**8b**)

Yield 92%; *m.p.* 208–210 °C. R_f = 0.2 (hexane/chloroform 4:1). – FD-MS (*m/z*): 760.8 (M^+).

5,11,17,23-Tetra-tert-butyl-25,26-dimethoxy-27,28-dipropoxy-calix[4]arene (**8c**)

Yield 90%; *m.p.* 178–181 °C. R_f = 0.31 (chloroform/hexane 1:4). – FD-MS (*m/z*): 761.5 (M^+).

5,11,17,23-Tetra-tert-butyl-25-methoxy-26,27,28-tripropoxy-calix[4]arene (**8d**)

Yield 95%; *m.p.* 202–204 °C. R_f = 0.84 (chloroform/hexane 1:1). – FD-MS (*m/z*): 789.1 (M^+).

Tetra-*O*-Alkylation of *t*-Butylcalix[4]arene (General Procedure)

NaH (3.12 g, 0,124 mol) and DMF (200 ml) were added to a suspension of *p-tert*-butylcalix[4]arene (10.0 g, 15.4 mmol) in DMF (300 ml) under argon. The suspension was stirred for 1 h, and then the alkylating agent (0.124 mol) was added. Stirring was continued at room temperature for 2 d. Water (100 ml) was added and the precipitate formed collected by filtration. The solid was dissolved in chloroform and washed with 15% HCl and water. The organic layer was dried and the solvent evaporated. Precipitation from chloroform/methanol gave the desired compounds as white solids with sufficient purity.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-methoxy-calix[4] arene (**8e**)

Yield 63%; *m.p.* 244–246 °C (ref. *m.p.* 226.5–228 [21]), R_f = 0.34 (chloroform/hexane 1:1). – FD-MS (*m/z*): 704.7 (M^+).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-propoxy-calix[4]arene (**8f**)

Yield 37%; *m.p.* 236–237 °C (ref. *m.p.* 246–247 °C. [20]) R_f = 0.78 (chloroform/hexane 4:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.97 (t, 12H, ^3J = 7.6 Hz, $CH_2C\underline{H}_3$), 1.06 (s, 36H, *t*-Bu), 2.00 (sext, 8H, ^3J = 7.8 Hz, $OCH_2C\underline{H}_2$.), 3.09 (d, 4H, ^2J = 12.2 Hz, $ArCH_2Ar$), 3.79 (t, 8H, ^3J = 7.6 Hz, OCH_2), 4.40 (d, 4H, ^2J = 12.7 Hz, $ArCH_2Ar$), 6.75 (s, 8H, ArH). – FD-MS (*m/z*): 817.1 (M^+).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-pentoxy-calix[4] arene (**8g**)

Yield 77%; *m.p.* 145–147 °C (ref. *m.p.* 147–148 °C [22]). R_f = 0.66 (hexane/chloroform 4:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.94 (t, 12H, ^3J = 6.6 Hz, $CH_2C\underline{H}_3$), 1.06 (s, 36H, *t*-Bu), 1.39 (m, 16H, $C\underline{H}_2C\underline{H}_2CH_3$), 2.00 (quin, 8H, ^3J = 7.3 Hz, $OCH_2C\underline{H}_2$.), 3.09 (d, 4H, ^2J = 12.2 Hz, $ArCH_2Ar$), 3.83 (t, 8H, ^3J = 7.6 Hz, OCH_2), 4.40 (d, 4H, ^2J = 12.2 Hz, $ArC\underline{H}_2Ar$), 6.76 (s, 8H, $Ar\underline{H}$). – FD-MS (*m/z*): 929.4 (M^+).

***Ipso*-Nitration (General Procedure)**

A mixture of glacial acetic acid (15 ml) and fuming nitric acid (15 ml) was added to a solution of fully alkylated calix[4]arene (2.81 mmol) in dichloromethane (90 ml). After 1.5 h the solution turned from a deep black colour to orange. Water was added and the mixture stirred for 10 min. The water was decanted, and the organic layer washed with water (6 × 30 ml), dried and the solvent evaporated. Precipitation from chloroform/methanol gave the desired compounds as pale yellow solid of sufficient purity.

5,11,17,23-Tetra-nitro-25,26,27-trimethoxy-28-propoxy-calix[4]arene (**9a**)

Yield 74%; *m.p.* 309–311 °C. R_f = 0.26 (chloroform). – FD-MS (*m/z*): 688.3 (M^+).

5,11,17,23-Tetra-nitro-25,27-dimethoxy-26,28-dipropoxy-calix[4]arene (**9b**)

Yield 84%; *m.p.* 282–285 °C. R_f = 0.33 (chloroform). – FD-MS (*m/z*): 716.5 (M^+).

5,11,17,23-Tetra-nitro-25,26-dimethoxy-27,28-dipropoxy-calix[4]arene (**9c**)

Yield 83%; *m.p.* 300–303 °C. R_f = 0.38 (chloroform). – FD-MS (*m/z*): 716.9 (M^+).

5,11,17,23-Tetra-nitro-25-methoxy-26,27,28-tripropoxy-calix[4]arene (**9d**)

Yield 74%; *m.p.* 288–291 °C. R_f = 0.27 (chloroform). – FD-MS (*m/z*): 744.6 (M^+).

5,11,17,23-Tetra-nitro-25,26,27,28-tetra-methoxy-calix[4]-arene (**9e**)

Yield 85%; *m.p.* 316–318 °C (ref. *m.p.* >300 °C [23]). R_f = 0.31 (chloroform). – FD-MS (*m/z*): 660.4 (M^+).

5,11,17,23-Tetra-nitro-25,26,27,28-tetra-propoxy-calix[4]-arene (**9f**)

Yield 76%; *m.p.* > 300 °C (ref. *m.p.* > 300 °C [23]). R_f = 0.36 (chloroform). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.00 (t, 12H, ^3J = 7.3 Hz, $CH_2C\underline{H}_3$), 1.89 (sext, 8H, ^3J = 7.6 Hz, $OCH_2C\underline{H}_2$.), 3.38 (d, 4H, ^2J = 14.2 Hz, $ArCH_2Ar$), 3.94 (t, 8H, ^3J = 7.6 Hz, OCH_2), 4.50 (d, 4H, ^2J = 14.2 Hz, $ArCH_2Ar$), 7.56 (s, 8H, ArH). – FD-MS (*m/z*): 772.8 (M^+).

5,11,17,23-Tetra-nitro-25,26,27,28-tetra-pentoxy-calix[4]-arene (**9g**)

Yield 77%; *m.p.* 246–248 °C (ref. *m.p.* 251–253 [22]. R_f = 0.87 (chloroform/methanol 30:1). – ^{1}H NMR (DMSO-d_6): δ/ppm = 0.90 (br t, 12H, $CH_2C\underline{H}_3$), 1.36 (m, 16H, $C\underline{H}_2C\underline{H}_2CH_3$), 2.00 (br s, 8H, $OCH_2C\underline{H}_2$.), 3.68 (d, 4H, ^2J = 14.2 Hz, $ArCH_2Ar$), 3.97 (t, 8H, ^3J = 7.1 Hz, OCH_2), 4.35 (d, 4H, ^2J = 13.7, Hz $ArCH_2Ar$), 7.63 (s, 8H, ArH). – FD-MS (*m/z*): 885.1 (M^+).

Reduction of Nitro-calixarenes by Hydrazine (General Procedure)

Hydrazine hydrate (10.5 ml, 216 mmol) was added to a suspension of a tetranitro calix[4]arene (1.94 mmol) and a catalytic amount of Raney nickel in methanol (90 ml). The mixture was heated at reflux for 4 h and then filtered, whilst hot, through Celite®. The filtrate was diluted with water and then extracted with dichloromethane (2 × 50 ml). The organic layer was dried and the solvent evaporated. The resulting tetraamines, characterised by FD-MS, were normally used without further purification.

5,11,17,23-Tetra-amino-25,26,27-trimethoxy-28-propoxy-calix[4]arene (**10a**)

Yield 94%; R_f = 0.37 (chloroform/methanol 5:1). – FD-MS (*m/z*): 568.3 (M^+).

5,11,17,23-Tetra-amino-25,27-dimethoxy-26,28-dipropoxy-calix[4]arene (**10b**)

Yield 84%; R_f = 0.13 (chloroform/methanol 5:1). – FD-MS (*m/z*): 596.6 (M^+).

5,11,17,23-Tetra-amino-25,26-dimethoxy-27,28-dipropoxy-calix[4]arene (**10c**)

Yield 93%; R_f = 0.24 (chloroform/methanol 9:1). – FD-MS (*m/z*): 596.9 (M^+).

5,11,17,23-Tetra-amino-25-methoxy-26,27,28-tripropoxy-calix[4]arene (**10d**)

Yield 90%; R_f = 0.36 (chloroform/methanol 5:1). – FD-MS (*m/z*): 624.3 (M^+).

5,11,17,23-Tetra-amino-25,26,27,28-tetra-propoxy-calix[4]-arene (**10f**)

The product was obtained as a white solid by precipitation from dichloromethane/hexane Yield 90%; *m.p.* 320–321 °C. R_f = 0.20 (chloroform/methanol 9:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.92 (t, 12H, ^3J = 7.6 Hz, $CH_2C\underline{H}_3$), 1.83 (sext, 8H, ^3J = 7.6 Hz, $OCH_2C\underline{H}_2$.), 2.89 (d, 4H, ^2J = 13.7 Hz, $ArCH_2Ar$), 3.43 (br s, 8H, NH_2), 3.69 (t, 8H, ^3J = 7.3 Hz, OCH_2), 4.28 (d, 4H, ^2J = 13.2 Hz, $ArCH_2Ar$), 6.06 (s, 8H, ArH). – FD-MS (*m/z*): 652.6 (M^+).

5,11,17,23-Tetra-amino-25,26,27,28-tetra-pentoxy-calix[4]-arene (**10g**)

Yield 85% after precipitation from dichloromethane/hexane; *m.p.* 135–137 °C (dec) (ref. *m.p.* 136–137 °C [22]. R_f = 0.22 (chloroform/methanol 9:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.89 (br s, 12H, $CH_2C\underline{H}_3$), 1.31 (br s, 16H $C\underline{H}_2C\underline{H}_2CH_3$), 1.80 (br s, 8H, $OCH_2C\underline{H}_2$.), 2.87 (d, 4H, ^2J = 13.7 Hz, $ArCH_2Ar$), 3.58 (br s, 8H, NH_2), 3.71 (t, 8H, ^3J = 7.1 Hz, OCH_2), 4.26 (d, 4H, ^2J = 13.2 Hz $ArCH_2Ar$), 6.07 (s, 8H, ArH). – FD-MS (*m/z*): 765.0 (M^+).

5,11,17,23-Tetra-amino-25,26,27,28-tetra-methoxy-calix[4]-arene (**10e**)

5,11,17,23-tetranitro-25,26,27,28-tetramethoxy-calix[4]arene (600 mg, 0.91 mmol) and $SnCl_2$ (4.26 g) were suspended in ethanol (25 ml) and heated at reflux for 18 h. The hot mixture was poured onto ice and diluted with ethylacetate (200 ml). After 1 h of stirring, 1M HCl (200 ml) was added and the mixture stirred for a further 30 min. The organic layer was then separated and washed with water and brine. The solution was dried and the solvents evaporated to give a brown glass (420 mg, 86%). R_f = 0.18 (chloroform/methanol 9:1). FD-MS (*m/z*): 540.3 (M^+).

(Diphenylphosphoryl)acetamido calix[4]arenes 2a–g

were prepared in the same way as described for **6a–e** by heating the reactants at 50 °C for 18 h. Precipitation from chloroform/hexane gave the desired product which was additionally purified by column chromatography as indicated.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25,26,27-trimethoxy-28-propoxy-calix[4]arene (**2a**)

Column chromatography (chloroform/methanol 30:1). Yield 91%; *m.p.* 176–180 °C. R_f = 0.45 (chloroform/methanol 9:1). – FD-MS (*m/z*): 1537.6 (M^+).

$C_{90}H_{84}N_4P_4O_{12}\cdot 3H_2O$	Calcd.:	C 67.92	H 5.70	N 3.52
(1537.5)	Found:	C 67.72	H 6.58	N 3.29.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25,27-dimethoxy-26,28-dipropoxy-calix[4]arene (**2b**)

Column chromatography (chloroform/methanol 30:1). Yield 95%; *m.p.* 184–188 °C. R_f = 0.37 (chloroform/methanol 9:1). – FD-MS (*m/z*): 1566.2 (M^+).

$C_{92}H_{88}N_4P_4O_{12}\cdot 3H_2O$	Calcd.:	C 68.22	H 5.85	N 3.46
(1565.5)	Found:	C 68.32	H 6.03	N 3.36.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25,26-dimethoxy-27,28-dipropoxy-calix[4]arene (**2c**)

Yield 90%; *m.p.* 184–189 °C. R_f = 0.45 (chloroform/methanol 9:1). – FD-MS (*m/z*): 1567.4 (M^+).

$C_{92}H_{88}N_4P_4O_{12}\cdot 3H_2O$	Calcd.:	C 68.22	H 5.85	N 3.46
(1565.5)	Found:	C 68.27	H 6.19	N 3.28.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25-methoxy-26,27,28-tripropoxy-calix[4]arene (**2d**)

Column chromatography (chloroform/methanol 30:1). Yield 95%; *m.p.* 185–190 °C. R_f = 0.49 (chloroform/methanol 9:1). – FD-MS (*m/z*): 1595.4 (M^+).

$C_{94}H_{92}N_4P_4O_{12}\cdot 3H_2O$	Calcd.:	C 68.52	H 5.99	N 3.40
(1593.6)	Found:	C 68.58	H 6.26	N 3.14.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25,26,27,28-tetra-methoxy-calix[4]arene (**2e**)

Column chromatography (chloroform/methanol 30:1). Yield 56%; *m.p.* 191–196 °C (dec). R_f = 0.41 (chloroform/methanol 9:1). – FD-MS (*m/z*): 1510.6 (M^+).

$C_{88}H_{80}N_4P_4O_{12}\cdot 3H_2O$	Calcd.:	C 67.51	H 5.67	N 3.58
(1509.5)	Found:	C 67.49	H 5.94	N 3.47.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25,26,27,28-tetra-propoxy-calix[4]arene (**2f**)

Column chromatography (chloroform/methanol 30:1). Yield 85 %; *m.p.* 196–199 °C. R_f = 0.33 (chloroform/methanol 9:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.91 (t, 12H, ^3J = 7.1 Hz, $CH_2C\underline{H}_3$), 1.79 (m, 8H, $OCH_2C\underline{H}_2$.), 3.01 (d, 4H, ^2J = 13.2 Hz, $ArCH_2Ar$), 3.71 (m, 16H, $COCH_2PO + OCH_2$), 4.25 (d, 4H, ^2J = 12.7 Hz, $ArCH_2Ar$), 6.66 (s, 8H, ArH), 7.46–7.79 (m, 40H, P–ArH), 9.55 (4H, s, NH). – FD-MS (*m/z*): 1622.6 (M^+).

$C_{96}H_{96}N_4P_4O_{12}$	Calcd.:	C 71.10	H 5.97	N 3.45
(1621.6)	Found:	C 70.95	H 5.83	N 3.28.

5,11,17,23-Tetra-(diphenylphosphoryl)acetamido-25,26,27,28-tetra-pentoxy-calix[4]arene (**2g**)

Yield 83%; *m.p.* 206–211 °C. R_f = 0.39 (chloroform/methanol 9:1). – ^{1}H NMR (DMSO-d_6): δ/ppm = 0.87 (br s, 12H, $CH_2C\underline{H}_3$), 1.32 (br s, 16H, $C\underline{H}_2C\underline{H}_2CH_3$), 1.78 (br s, 8H, $OCH_2C\underline{H}_2$.), 3.01 (d, 4H, ^2J = 13.2 Hz, $ArCH_2Ar$), 3.71 (br m, 16H, OCH_2 + $COCH_2PO$), 4.23 (d, 4H, ^2J = 13.2 Hz $ArCH_2Ar$), 6.66 (s, 8H, ArH), 7.47–7.79 (m, 40H, P–ArH), 9.56 (s, 4H, NH). – FD-MS (*m/z*): 1734.5 (M^+).

$C_{104}H_{112}N_4P_4O_{12}\cdot 3H_2O$	Calcd.:	C 69.86	H 6.65	N 3.13
(1733.7)	Found:	C 69.91	H 6.30	N 3.08.

Extraction Studies

Extraction to Dichloromethane

Solvents (dichloromethane [Carlo Erba, max 0.02% water, stabilised with ethyl alcohol] and methanol [Carlo Erba, 99.9%]) were used without further purification. Thorium(IV) and lanthanum(III) were used as the nitrates: $Th(NO_3)_4\cdot 5H_2O$ and $La(NO_3)_3\cdot H_2O$ (Merck p.a.) as purchased, while $Eu(NO_3)_3\cdot xH_2O$ and $Yb(NO_3)_3\cdot xH_2O$ were prepared by reaction of the corresponding carbonates with a nitric acid solution (Carlo Erba, 65% for analysis) following the literature procedure [24].

Stock solutions were standardised by complexometric titrations with EDTA in the presence of the appropriate indicator. Arsenazo(III) (Aldrich) was used for the spectrophotometric determination of Ln(III) and Th(IV) during extraction experiments.

The percentage extraction of cations (%E) from a 1M HNO_3 solution of lanthanide and thorium nitrates (10^{-4} M) into a dichloromethane solution containing the ligand at various concentrations (10^{-2} – 10^{-4} M) has been determined at 20 °C analysing the aqueous phase before and after extraction. The conditions of a standard experiment have been previously reported in detail [3], as well as the determination of $\%E = 100\ (A_1–A)/(A_1–A_0)$ and $D = \%E/(100-\%E)$ and the theoretical background of the log-log plot analysis.

Extraction to o-Nitrophenyl hexyl ether (NPHE)

Organic phases were prepared by dissolving a weighed amount of extractant in NPHE ($c_L = 10^{-3}$ M), aqueous phases accordingly by dissolving a weighed amount of lanthanide nitrate ($c_M = 10^{-5}$ M) in nitric acid solutions ranging from 10^{-2} M to 4M. Actinides (Am, Cm) were used at trace level ($c_M = 10^{-8}$ – 10^{-9} M corresponding to an activity of about 1500 kBq/l) Equal volumes of organic and aqueous phases were shaken for one hour and then separated by centrifugation. The initial and final concentrations of lanthanides and americium in the aqueous phases were determined by ICP-MS (Inductively Coupled Plasma Mass Spectrometry). The activity of curium in aqueous and organic phases was measured by liquid scintillation.

The distribution coefficient is defined as $D = \Sigma\, c(M)_{org}/\Sigma\, c(M)_{aq}$ (where $\Sigma\, c(M)_{org}$ and $\Sigma\, c(M)_{aq}$ symbolise the sum of the concentrations of all metal cation species in the organic and in the aqueous phase). Values for D were calculated directly from the activity of both phases (case of Cm) or from the concentrations in the aqueous phases before (c_0) and after extraction (c) as $D = (c_0 - c)/c$ (all other cations). An accuracy of ± 5% for $D = 0.01$ to 100 and ±10% for $D > 100$ (or < 0.01) is estimated.

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