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Synthesis, solid state structures and interfacial properties of new *para*-phosphonato-*O*-alkoxy-calix[8]arene derivatives

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The synthesis of six *para*-phosphonato-alkoxy-calix[8]arene derivatives are described. Here, a total of 24 intermediates have been isolated, and X-ray structures of the octabromo-octamethoxy-calix[8]arene and octabromo-octabutoxy-calix[8]arene have been resolved. The interfacial properties of the *para*-phosphonato-alkoxy-calix[8]arene derivatives and their di-*iso*-propoxy-protected analogues have been determined.

Introduction

Calix[*n*]arenes[1] are a class of widely studied macrocyclic organic host compounds. The differing chemistries between the *para*-position of the aromatic rings and the pendant phenolic groups has allowed their modification to serve as complexants for a large range of ions and small organic molecules. Interest in their biological properties has grown strongly in recent years. Activity as amphiphilic derivatives or assemblies, notably the work of Schrader *et al.* on protein complexation to monolayers of such molecules,[2,3] as peptido mimetics, as exemplified by the work of Hamilton,[4–6] or, as observed by Schneider[7] and Schrader,[8] as complexing agents for DNA, demonstrates the breadth of their biological properties. In the case of the water soluble *para*-sulfonato derivatives, their direct action as biologically active molecules,[9] in particular their ability to complex and amplify the detection of the prion protein, has been demonstrated by ourselves.[10] Other work on these molecules has shown that they have activity as ion channel blockers,[11–13] enzyme inhibitors[14,15] and as antiviral drugs.[16,17]

In parallel with the above work, the interactions of calix[*n*]arenes with the building blocks of biomacromolecules, including amino acids[18–23] and nucleotides,[24] have been studied in depth. Studies on the complexation of amino acids by the *para*-sulfonato-calix[*n*]arenes have been carried out in solution by Arena[18,19] and ourselves.[20–23] Complementary studies on the solid-state complexes have been undertaken by ourselves[25,26] and the group of Raston.[27]

In the case of the *para*-sulfonato-calix[*n*]arenes, the strength of interaction with both amino acids and proteins generally increases with the size of the macrocycle, with the strongest binding occurring for the calix[8]arene derivatives.[20] For example, the association constants between the basic amino acid arginine and *para*-sulfonato-calix[*n*]arenes varies from 1546 M^{-1} for *para*-sulfonato-calix[4]arene through 3090 M^{-1} for *para*-sulfonato-calix[6]arene to 10083 M^{-1} for *para*-sulfonato-calix[8]arene.[20] A similar increase in binding was observed for interactions with the prion protein.[10]

The phosphonato-calix[*n*]arenes represent a second group of water soluble anionic calix[*n*]arenes. Here, the phosphate function may be introduced at either the *para*-aromatic position or coupled to the phenolic group. In the case of calix[*n*]arenes bearing phosphonate groups on the upper rim, recent work by Kalchenko *et al.* has demonstrated their ability to bind nucleobases[28] and amino acids.[29,30] Work by our group has shown that calix[4]arene-diphosphonic acid possesses an interesting anti-tumor activity.[31]

In view of the above results, showing that the phosphonato-calix[*n*]arenes possess biological activity, and that for the *para*-sulfonato-calix[*n*]arenes the activity is maximum for the calix[8]arene derivatives, the synthesis of calix[8]arene derivatives carrying phosphonic acid groups at the upper rim and alkyl functions at the lower rim (so as to modulate the hydrophilic–hydrophobic balance) is of considerable interest.†

In this paper we report the synthesis of a series of such molecules, as well as the solid-state structures of two intermediate molecules along the synthetic pathway. The formation of stable monolayers at the air–water interface has been observed for *para*-phosphonato-alkoxy-calix[8]arene derivatives having at least three carbon atoms present at the ether functions, while for the di-*iso*-propyl-*P*-protected analogues, at least six carbon atoms are required for the formation of stable monolayers.

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† As the pK_a values of the phosphonic acid derivatives are unknown, uncertainty exists about whether or not they are partially ionised at neutral pH values.

Results and discussion

Synthesis

The synthetic route to the series of *para*-phosphonato-*O*-alkoxy-calix[8]arenes, is shown in Fig. 1.

Total alkylation of calix[8]arene with the required iodoalkane was carried out in DMF using sodium hydride as the base. The obtained yields were good, varying from 66 to 92%.

The *para*-bromo derivatives, **3a–f**, were obtained as per the method of Lamartine *et al.*,[32] using bromine and metallic iron as a dispersion in a chloroform–acetic acid mixture.

The protected di-*iso*-propyl-*para*-phosphonato derivatives, **4a–f**, were obtained by an Arbusov substitution reaction using tri-*iso*-propyl phosphite and nickel(II) bromide. It proved generally useful to use an EDTA extraction to remove residual nickel salts from **4a–f**. While suitable samples for full characterisation have been obtained, generally these derivatives were used without isolation, and the final deprotected phosphonic acid derivatives **5a–f** were obtained by treatment of **4a–f** with trimethylbromosilane at room temperature followed by solvolysis with methanol at 50 °C. Total deprotection was often difficult in a single step, yielding incompletely deprotected mixtures with up to four *iso*-propyl moieties remaining at the phosphonate functions. Re-treatment with trimethylbromosilane, followed by a second methanolysis step, often proved necessary to yield the desired completely deprotected derivatives.

All compounds were characterised by either electrospray mass spectrometry or MALDI mass spectrometry to determine that full substitution had occurred. In the case of the phosphonic acid derivatives **5a–f**, the MALDI spectra showed that some *in situ* degradation occurs, with formation of metaphosphate esters. Similar formation of meta-phosphate esters has previously been reported by Regnouf-de-Vains *et al.* for calix[6]arene-*O*-phosphonic acids.[33] However, subsequent HPLC analysis of **5a–f** showed them to be pure single compounds.

^{31}P NMR analysis showed single peaks at 16.6 ppm for the protected derivatives **4a–f** and single peaks at 16.5 ppm for **5a–f**. These values are in accordance with values of 17.2 and 17.3 ppm observed by Houel *et al.* for the tetra-*O*-alkyl-calix[4]arene analogues.[34]

^{1}H NMR of the methylenic CH_2 bridge hydrogen atoms showed sharp singlet peaks near 4 ppm, meaning a high degree of conformational mobility at room temperature for all the compounds.

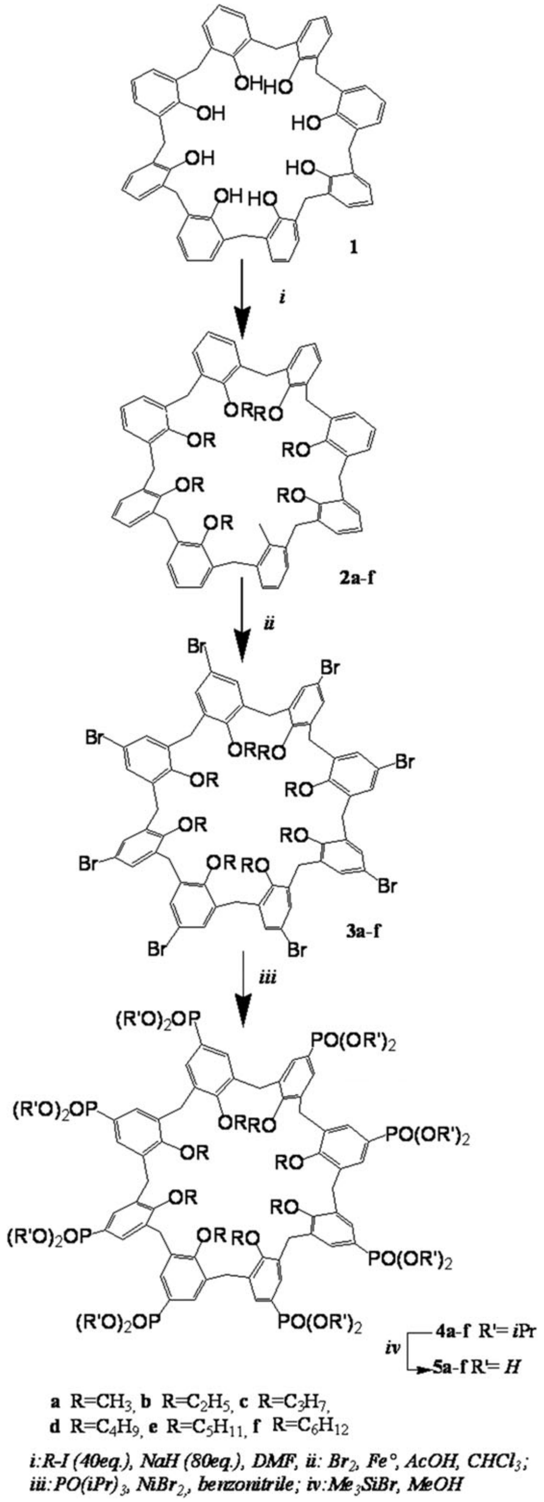

Fig. 1 Schematic route for the synthesis of calix[8]arene derivatives.

Solid-state structures

In the case of **3a** and **3d**, suitable crystals for X-ray diffraction were grown by recrystallisation from chloroform–methanol solutions. The molecular structures and packing diagrams are shown in Fig. 2a and 2b, and Fig. 3a and 3b, respectively. Both molecules **3a** and **3d** are located at the crystallographic centre of symmetry.

para-Octabromo-octamethoxy-calix[8]arene (**3a**) crystallises in a flattened cone conformation, with the methoxy groups alternating 2 up : 2 inside : 2 down : 2 inside the pseudo cavity, with one disordered (standard occupancy factor = 0.5) water molecule also inside. The calixarene macrocyclic rings are stacked one on top of another, forming molecular channels ‘filled’ with water molecules. The conformation of this calix[8]arene molecule differs considerably from that obtained by Lamartine *et al.*[32] for the same compound, in which they found that two methoxy groups pointed outside the cavity, while the six others were inside. Aromatic rings bearing O5,

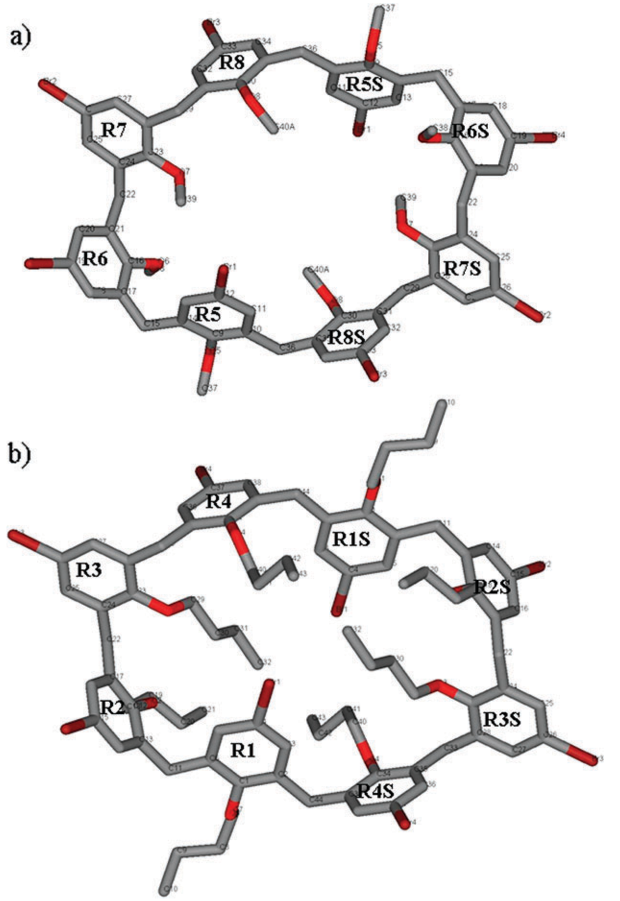

Fig. 2 Molecular structure of (a) **3a** and (b) **3d** showing the annotations of the aromatic rings.

O6, O7 and O8 are called R5, R6, R7 and R8, respectively. The same rings deduced by the inversion center are called R5S, R6S, R7S and R8S, respectively (Fig. 2a). The distances between the centroids of the aromatic rings are 10.25 Å for R5–R5S, 14.85 Å for R6–R6S, 13.76 Å for R7–R7S and 10.99 Å for R8–R8S, which are quite different to the values of Lamartine *et al.*[32] obtained for the same compound. Angles between the neighbouring rings R5 and R6, R6 and R7, R7 and R8, and R8 and R5S are 112.1, 113.8, 113.8 and 115.9°, respectively.

The butoxy analogue **3d** crystallises in a completely different non-solvated form. Two symmetrically independent molecules were found on each crystallographic center of symmetry; in one of them, the disorder of one of the alkyl ether groups over two positions is observed. In both molecules, the alkyl ether groups are pointing in a 3 : 1 : 3 : 1 sequence towards the interior : the exterior : the interior : the exterior (Fig. 2b). Among the triple units pointing inside, for one unit, one is pointing down and two are pointing down; on the opposite side, one is pointing down and two are pointing up. The distances between the centroids of the aromatic rings for the two independent molecules are 8.40 and 8.60 Å for R1–R1S, 13.91 and 12.28 Å for R2–R2S, 15.22 and 15.15 Å for R3–R3S, and 11.67 and 10.99 Å for R4–R4S. In this structure, angles between neighbouring rings R1–R2, R2–R3, R3–R4 and R4–R1S are 113.5 and 106.3°, 114.1 and 94.4°, 114.8 and 91.9°, and 115.7 and 91.4°, respectively.

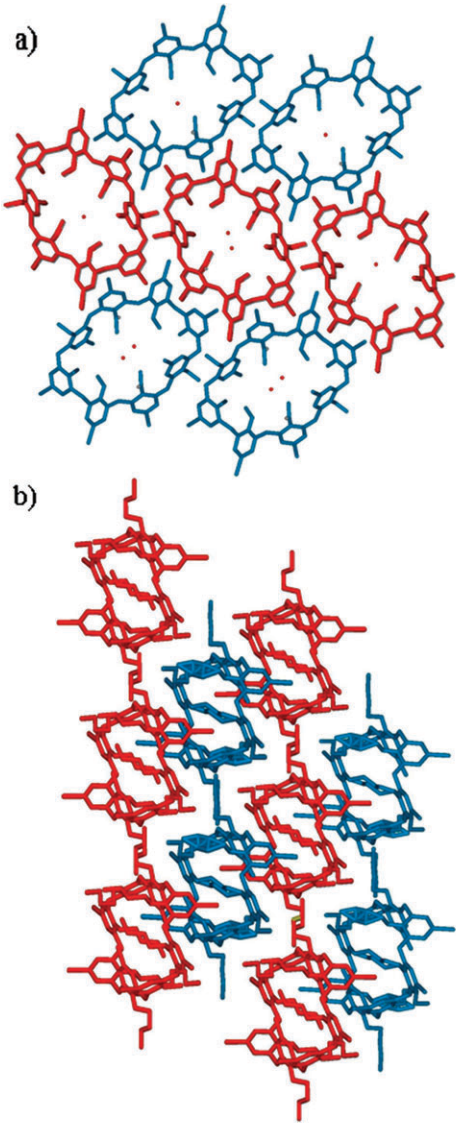

Fig. 3 Structural packing motifs for (a) **3a** and (b) **3d**. Alternating layers are shown in red and blue for clarity.

The differences in the calixarene structures lead to quite different packing architectures: a closely packed "herring bone"-like structural motif for **3a** and a less densely packed system of parallel chains for **3d** (Fig. 3), where the butoxy groups link adjacent molecules in the chains and also traverse between the parallel chains.

For both cases, the packing is mainly assured by Br π-interactions (3.349 and 3.339 Å for **3a** and **3d**, respectively), C–C short contacts between pairs of aromatic units (3.636, 3.751 and 3.785 Å for **3a**, 3.606 and 3.823 Å for **3d**) and a short chain carbon atom to aromatic ring distance of 3.688 Å (for **3d** only).

Furthermore, for the butoxy derivative **3d**, short contacts between *para*-Br and oxygens of the alkyl chains of another calixarene (Br_6–O_3 = 3.265 Å, Br_3–O_7 = 3.282 Å), and *para*-Br and carbon atoms of the phenyl rings of another molecule (Br_8–C_{25} = 3.338 Å, Br_8–C_{24} = 3.368 Å) occur.

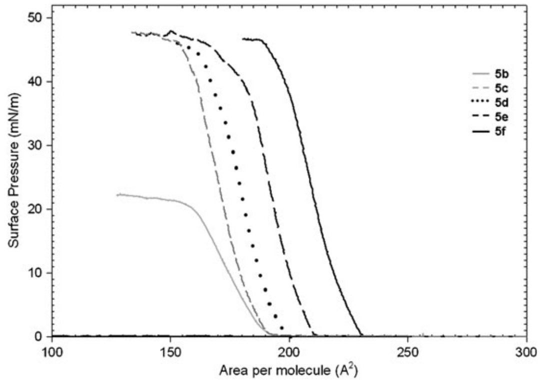

Fig. 4 Compression isotherms for **5b** to **5f**.

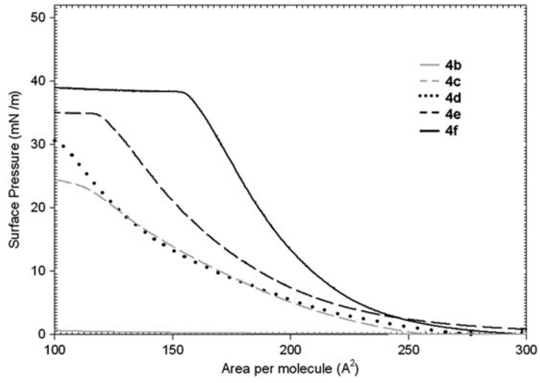

Fig. 5 Compression isotherms of **4b** to **4f**.

It is important to note that, in both cases, no hydrogen bonding is observed in the molecular packings of the structures.

Interfacial properties

The compression isotherms for **5a–f** on a pure water surface are presented in Fig. 4, and the characteristic values are summarised in Table 1.

From the crystallographic data obtained for **3a** and **3d**, it can be postulated that an approximate molecular area in the range 140–160 $Å^2$ is expected for the calix[8]arene-alkoxy ether core if all the *O*-alkoxy groups are aligned perpendicular to the air–water interface. The observed collapse areas for **5b–5e** all lie in this range, increasing from 150 $Å^2$ for **5b** to 160 $Å^2$ for **5e**. For **5f**, the collapse area is 190 $Å^2$. Thus, whilst there are small effects for the shorter chain lengths, in the case of the *O*-hexyl derivative, the alkyl chains play a much greater role in determining the molecular area at collapse. The above results can be compared to the collapse molecular area of *para-tert*-butyl-calix[8]arene of 151 $Å^2$ [35] and to the limiting molecular area, A_0, of 200 $Å^2$ [35] or 180 $Å^2$.[36]

The collapse pressure values of around 47 mN m^{-1} for the phosphonic acid derivatives (**5c–5f**) are similar to that observed by Houel *et al.* for *para*-phosphonato-*O*-decyl-calix[4]-arene,[35] and are effectively independent of chain length. However, for the *O*-ethoxy ether **5b**, there is a steep decrease in the collapse pressure, which is now 21 mN m^{-1}. In the case of the *O*-methoxy ether **5a**, the observed pressure is zero throughout the compression range.

Table 1 Isotherm data for **5a–f** on pure water[a]

Compound	$A_0/Å^2$	$A_1/Å^2$	$A_m/Å^2$	$A_c/Å^2$	π_c/mN m^{-1}	Cs^{-1}/mN m^{-1}
5f	231	229	223	190	47	336
5e	216	210	205	160	47	244
5d	199	197	193	159	46	226
5c	198	190	185	153	46	206
5b	195	190	188	150	21	113
5a	—	—	—	—	—	—

[a] A is the area all along the experiment, π is the pressure all along the experiment, A_0 is the apparent molecular area at $\pi = 0$, A_1 is the apparent molecular area at $\pi = 1$ mN m^{-1}, A_m is the extrapolated molecular area, A_c is the apparent molecular area at the collapse point and π_c is the collapse pressure. Cs^{-1} is the compressibility modulus.

The compressibility modulus, Cs^{-1} (eqn. (1)),[37] reflects the behaviour and state of the monolayer at the air–water interface.

$$Cs^{-1} = -A(\delta\pi/\delta A) \qquad (1)$$

Cs^{-1} varies from 206 to 336 mN m^{-1} for **5c** to **5f**. These values are typical of condensed liquid phase monolayers.[37] In the case of **5b**, this value decreases to 113 mN m^{-1}, a value that is in the range of an expanded liquid phase monolayer.

Thus for the *para*-phosphonato-alkoxy-calix[8]arene derivatives, highly stable monolayers are formed at the air–water interface when the alkoxy ether chain length is three carbon atoms or greater, a much less stable monolayer is observed for a chain length of two carbon atoms, and for a chain length of one carbon atom, no stable monolayer is observed. This is in agreement with the much higher solubility of this compound in methanol and ethanol, and its observed partial solubility in water.

For the di-*iso*-propyl-*para*-phosphonato derivatives **4a–f**, the compression isotherms are given in Fig. 5 and the isotherm data are summarised in Table 2.

The observed compression isotherms are clearly different from those observed for the phosphonic acid derivatives **5a–f**. Firstly, they are characterised by very much higher A_0 and A_1 values, all observed values being greater than 250 $Å^2$, which would seem to imply that the molecules form a flattened structure at the air–water interface and that the *iso*-propyl groups have a strong geometric influence. Similarly, the Cs^{-1} values are much lower than those observed for the phosphonic acid analogues, implying lower cohesion at the water surface.

For this series, the collapse pressures decline from 39 mN m^{-1} for **4f** to 26 mN m^{-1} for **4c**, and to zero for both **4a** and **4b**. Only for **4f** is a collapse area, 160 $Å^2$, observed in the range corresponding to the supposed "core" molecular area, the

Table 2 Isotherm data for **4a** to **4f** on pure water

Compound	$A_0/Å^2$	$A_1/Å^2$	$A_m/Å^2$	$A_c/Å^2$	π_c/mN m^{-1}	Cs^{-1}/mN m^{-1}
4f	294	267	245	160	39	118
4e	355	288	218	122	35	72
4d	275	254	198	105	30	49
4c	254	240	—	113	26	42
4b	—	—	—	—	—	—
4a	—	—	—	—	—	—

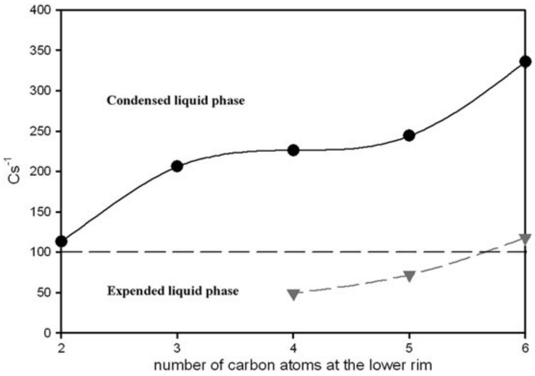

Fig. 6 Plot of Cs^{-1} against chain length at the lower rim for derivatives **5** (▲) and **4** (▼).

observed collapse areas for **4c–e** being lower and decreasing with decreasing chain length. This certainly arises from the loss of material at the air–water interface and most probably by the formation of bi- or multilayers due to lower polarity, and hence the cohesion between the *iso*-propyl-phosphonato head groups and water.

Fig. 6 summarises the behaviour of all the compounds studied at the air–water interface, with Cs^{-1} plotted as a function of the chain length. It can be clearly seen that Cs^{-1} increases with the chain length. For **5b**, an expanded liquid phase is observed, for compounds **5c–e**, a plateau in the Cs^{-1} value is observed at approximately 250 mN m^{-1}, and for **5f**, a much higher compressibility index occurs. In the case of the protected derivatives **4**, only expanded liquid phases are observed, with a small increase in Cs^{-1} with increasing chain length.

Experimental

General

Iodoalkanes, $NiBr_2$, bromotrimethylsilane and benzonitrile were purchased from Sigma-Aldrich. Tri-*iso*-propylphosphite, Br_2, Fe° and NaH 60% were purchased from Acros Organics and used without further purification. All reactions were carried out under nitrogen.

^{1}H and ^{13}C NMR spectra were recorded at 25 °C on a Varian® operating at 500 and 121.5 MHz. The chemical shifts are reported from internal tetramethylsilane standards. ^{31}P NMR spectra were recorded on a Bruker Avance DPX200 at 81.0 MHz with external 85% H_3PO_4 standards.

ESI-MS experiments were performed on a Perkin-Elmer Sciex API 165, and MALDI-TOF on a Voyager-DE PRO (Applied Biosystems).

Melting point determinations were performed on a Stuart Scientific SMP1 apparatus and are uncorrected.

General procedure for the preparation of 40,50,51,52,53, 54,55,56-octaalkoxy-calix[8]arenes 2a–f. These derivatives were synthesized by following the procedure described by Gutsche *et al.*[1] for the methylation of calix[8]arene:

To a mixture containing 1 g (1.18 mmol) of calix[8]arene and 3.78 g (94.4 mmol, 80 equiv.) of NaH 60% in mineral oil in 100 mL of DMF, was added 40 equiv. of iodoalkane. The mixture was refluxed overnight and then worked up by extraction with water. The organic layer was dried over $MgSO_4$, concentrated *in vacuo* and precipitated with EtOH. The white solid was dried *in vacuo* to give the pure compounds in good yield.

2a yield: 89%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 3.53 (s, 24H, OCH_3), 4.06 (s, 16H, Ar–CH_2–Ar), 6.90 (bs, 24H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 30.4 (Ar–CH_2–Ar), 61.2 (OCH_3), 124.1 (C_{para}, Ar), 130.1 (C_{meta}, Ar), 134.6 (C_{ortho}, Ar), 157.0 ($COCH_3$, Ar); ESI-MS for $C_{64}H_{56}O_8$ (960.53) m/z = 961.5 [M + H^+], 983.3 [M + Na^+].

2b yield: 71%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 1.23 (s, 24H, CH_3), 3.66 (t, 16H, OCH_2), 4.05 (s, 16H, Ar–CH_2–Ar), 6.89 (bs, 24H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.3 (CH_3), 30.7 (Ar–CH_2–Ar), 73.9 (OCH_2), 124.3 (C_{para}, Ar), 129.5 (C_{meta}, Ar), 134.7 (C_{ortho}, Ar), 156.1 ($COCH_2$, Ar); ESI-MS for $C_{72}H_{80}O_8$ (1072.6) m/z = 1096.1 [M + Na^+].

2c yield: 78%. Mp: 240 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.88 (t, 24H, CH_3), 1.66 (m, 16H, OCH_2CH_2), 3.60 (t, 16H, OCH_2), 4.06 (s, 16H, Ar–CH_2–Ar), 6.84 (d, 8H, ArH_{para}), 6.89 (s, 16H, ArH_{meta}); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 10.9 (CH_3), 23.9 (OCH_2CH_2), 30.3 (Ar–CH_2–Ar), 75.1 (OCH_2), 124.0 (C_{para}, Ar), 129.3 (C_{meta}, Ar), 134.6 (C_{ortho}, Ar), 155.9 ($COCH_2$, Ar); ESI-MS for $C_{80}H_{96}O_8$ (1184.7) m/z = 1185.6 [M + H^+], 1207.6 [M + Na^+].

2d yield: 75%. Mp: 185 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.86 (t, 24H, CH_3), 1.41 (m, 16H, CH_2CH_3), 1.67 (m, 16H, OCH_2CH_2), 3.68 (t, 16H, OCH_2), 4.07 (s, 16H, Ar–CH_2–Ar), 6.84 (s, 8H, ArH_{para}), 6.88 (s, 16H, ArH_{meta}); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.4 (CH_3), 19.7 (CH_2CH_3), 30.1 (Ar–CH_2–Ar), 32.8 (OCH_2CH_2), 73.6 (OCH_2), 124.1 (C_{para}, Ar), 129.3 (C_{meta}, Ar), 134.7 (C_{ortho}, Ar), 155.9 ($COCH_2$, Ar); ESI-MS for $C_{88}H_{112}O_8$ (1297.8) m/z = 1298.7 [M + H^+], 1319.7 [M + Na^+].

2e yield: 92%. Mp: 115 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.86 (t, 24H, CH_3), 1.30 (m, 16H, CH_2CH_3), 1.40 (m, 16H, $CH_2CH_2CH_3$), 1.70 (m, 16H, OCH_2CH_2), 3.69 (t, 16H, OCH_2), 4.08 (s, 16H, Ar–CH_2–Ar), 6.84 (s, 8H, ArH_{para}), 6.88 (s, 16H, ArH_{meta}); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.4 (CH_3), 23.1 (CH_2CH_3), 28.7 ($CH_2CH_2CH_3$), 30.2 (Ar–CH_2–Ar), 30.5 (OCH_2CH_2), 73.8 (OCH_2), 124.1 (C_{para}, Ar), 129.3 (C_{meta}, Ar), 134.7 (C_{ortho}, Ar), 155.9 ($COCH_2$, Ar); ESI-MS for $C_{96}H_{128}O_8$ (1410.0) m/z = 1410.8 [M + H^+], 1432.8 [M + Na^+].

2f yield: 66%. Mp: 110 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.87 (t, 24H, CH_3), 1.28 (m, 32H, $CH_2CH_2CH_3$), 1.41 (m, 16H, $OCH_2CH_2CH_2$), 1.70 (m, 16H, OCH_2CH_2), 3.69 (d, 16H, OCH_2), 4.01 (s, 16H, Ar–CH_2–Ar), 6.85 (s, 8H, ArH_{para}), 6.89 (s, 16H, ArH_{meta}); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.4 (CH_3), 22.9 (CH_2CH_3), 26.5 ($CH_2CH_2CH_3$), 30.3 ($OCH_2CH_2CH_2$), 30.5 (Ar–CH_2–Ar), 32.1 (OCH_2CH_2), 74.1 (OCH_2), 123.6 (C_{para}, Ar), 130.2 (C_{meta}, Ar), 135.2 (C_{ortho}, Ar), 155.5 ($COCH_2$, Ar); ESI-MS for $C_{104}H_{144}O_8$ (1521.1) m/z = 1592.9 [M + H^+], 1614.7 [M + Na^+].

General procedure for the preparation of 5,11,17,23,29, 35,41,47-octabromo-octaalkoxy-calix[8]arenes 3a–f. These derivatives were synthesised by following the procedure described by Baudry *et al.*[32]

To a cooled (0 °C) solution of octa-alkoxy-calix[8]arene **2** (2.08 mmol) in 100 mL of $CHCl_3$ containing a catalytic amount of Fe metal, was added, with stirring, 2.2 mL (42 mmol, 20 equiv.) of Br_2 in 20 mL of acetic acid over a period of 30 min. The mixture was stirred at 0 °C for 1 h and then at room temperature until TLC analysis (SiO_2, hexane/AcOEt 7 : 3) indicated the disappearance of the starting material. The reaction was then quenched by pouring it into 50 mL of 10% $NaHSO_3$. The organic layer was separated, concentrated by steam distillation and then stirred again in 100 mL of 10% $NaHSO_3$. The precipitate was filtered off, washed 3 times with water and 30 mL of acetone to afford a white pure powder.

3a yield: 71%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 3.67 (s, 24H, CH_3), 3.95 (s, 16H, Ar–CH_2–Ar), 7.01 (s, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 30.3 (Ar–CH_2–Ar), 61.2 (OCH_3), 117.7 (Br–*C*, Ar), 132.2 (C_{meta}, Ar), 135.5 (C_{ortho}, Ar), 156.9 ($COCH_3$), Ar); ESI-MS for $C_{64}H_{56}O_8Br_8$ (1592.3) *m/z* = 1592.9 [M + H$^+$], 1614.7 [M + Na$^+$].

3b yield: 88%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 1.23 (t, 24H, CH_3), 3.67 (d, 16H, OCH_2), 3.99 (s, 16H, Ar–CH_2–Ar), 7.03 (s, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.5 (CH_3), 30.4 (Ar–CH_2–Ar), 72.7 (OCH_2), 117.8 (Br–*C*, Ar), 132.2 (C_{meta}, Ar), 135.5 (C_{ortho}, Ar), 155.2 ($COCH_2$), Ar); ESI-MS for $C_{72}H_{72}O_8Br_8$ (1704.6) *m/z* = 1705.4 [M + H$^+$], 1727.3 [M + Na$^+$].

3c yield: 56%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.84 (t, 24H, CH_3), 1.59 (m, 16H, OCH_2CH_2), 3.56 (t, 16H, OCH_2), 3.93 (s, 16H, Ar–CH_2–Ar), 7.04 (s, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 13.5 (CH_3), 24.0 (OCH_2CH_2), 30.4 (Ar–CH_2–Ar), 74.2 (OCH_2), 117.6 (Br–*C*, Ar), 131.9 (C_{meta}, Ar), 136.1 (C_{ortho}, Ar), 155.7 ($COCH_2$), Ar); ESI-MS for $C_{80}H_{88}O_8Br_8$ (1816.8) *m/z* = 1840.4 [M + Na$^+$].

3d yield: 71%. Mp: 235 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.85 (t, 24H, CH_3), 1.36 (m, 16H, CH_2CH_3), 1.64 (m, 16H, OCH_2CH_2), 3.64 (d, 16H, OCH_2), 3.95 (s, 16H, Ar–CH_2–Ar), 7.02 (s, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.3 (CH_3), 20.1 (CH_2CH_3), 30.3 (Ar–CH_2–Ar), 33.1 (OCH_2CH_2), 74.0 (OCH_2), 117.3 (Br–*C*, Ar), 131.8 (C_{meta}, Ar), 136.2 (C_{ortho}, Ar), 156.0 ($COCH_2$, Ar); ESI-MS for $C_{88}H_{104}O_8Br_8$ (1929.0) *m/z* = 1929.4 [M + H$^+$], 1951.2 [M + Na$^+$].

3e yield: 51%. Mp: 230 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.84 (m, 24H, CH_3), 1.26 (m, 16H, CH_2CH_3), 1.37 (m, 16H, $OCH_2CH_2CH_2$), 1.68 (m, 16H, OCH_2CH_2), 3.67 (d, 16H, OCH_2), 3.97 (s, 16H, Ar–CH_2–Ar), 6.99 (s, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.4 (CH_3), 23.3 (CH_2CH_3), 29.0 ($CH_2CH_2CH_3$), 30.3 (Ar–CH_2–Ar), 30.6 (OCH_2CH_2), 73.9 (OCH_2), 117.4 (Br–*C*, Ar), 131.7 (C_{meta}, Ar), 136.1 (C_{ortho}, Ar), 155.9 ($COCH_2$), Ar); ESI-MS for $C_{96}H_{120}O_8Br_8$ (2041.2) *m/z* = 2063.4 [M + Na$^+$], 2079.4 [M + K$^+$].

3f yield: 71%. Mp: 215 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.84 (t, 24H, CH_3), 1.26 (m, 32H, $CH_2CH_2CH_3$), 1.37 (m, 16H, $OCH_2CH_2CH_2$), 1.68 (m, 16H, OCH_2CH_2), 3.67 (d, 16H, OCH_2), 3.97 (s, 16H, Ar–CH_2–Ar), 6.99 (s, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.4 (CH_3), 22.8 (CH_2CH_3), 26.2 ($CH_2CH_2CH_3$), 30.4 ($OCH_2CH_2CH_2$), 30.5 (Ar–CH_2–Ar), 32.1 (OCH_2CH_2), 74.2 (OCH_2), 117.6 (Br–*C*, Ar), 132.1 (C_{meta}, Ar), 136.0 (C_{ortho}, Ar), 155.1 ($COCH_2$, Ar); ESI-MS for $C_{104}H_{136}O_8Br_8$ (2153.4) *m/z* = 2154.9 [M + H$^+$], 2175.5 [M + Na$^+$].

General procedure for the preparation of calix[8]arene phosphonates 4a–f. Tri-*iso*-propyl phosphite (9.9 mmol, 30 equiv.) was added dropwise to a solution of the relevant octabromo-octaalkoxy-calix[8]arene **3a–f** (0.33 mmol, 1 equiv.) in benzonitrile (100 mL) in the presence of $NiBr_2$ (0.37 mmol, 1.1 equiv.) at 170 °C. The resulting solution was refluxed for 1 h. The reaction mixture was evaporated *in vacuo* (0.05 mmHg) to give a brown oil. The oil was dissolved in dichloromethane and washed with NH_4OH solution, EDTA solution and then water in order to extract the nickel. The organic phase was dried over $MgSO_4$. The organic solvent was then evaporated, and the resulting compound was purified by crystallization from hexane. Yield: 45–74%.

4a yield: 70%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 1.25–1.30 (m, 96H, $(CH_3)_2CHO$), 3.41–3.59 (two s, 24H, OCH_3), 3.97 (s, 16H, Ar–CH_2–Ar), 4.56 (m, 16H, $CHOP$), 7.39 (m, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 23.4 ($POCH(CH_3)_2$), 30.3 (Ar–CH_2–Ar), 42.3 ($POCH(CH_3)_2$), 61.2 (OCH_3), 117.3 (C_{para}, Ar), 132.1 (C_{meta}, Ar), 135.9 (C_{ortho}, Ar), 156.5 ($COCH_3$, Ar); ^{31}P NMR (δ/ppm): 16.9; ESI-MS for $C_{112}H_{168}O_{32}P_8$ (2272.9) *m/z* = 2296.3 [M + Na$^+$], 1159.8 [(M + 2Na$^+$)/2].

4b yield: 68%. Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.80 (t, 24H, CH_2CH_3), 1.12–1.30 (m, 96H, $(CH_3)_2CHO$), 3.60 (m, 16H, OCH_2), 4.00 (s, 16H, Ar–CH_2–Ar), 4.58 (m, 16H, $CHOP$), 7.38 (m, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.5 (CH_3), 23.2 (($POCH(CH_3)_2$), 30.4 (Ar–CH_2–Ar), 42.3 ($POCH(CH_3)_2$), 69.7 (OCH_2), 117.2 (C_{para}, Ar), 131.7 (C_{meta}, Ar), 136.2 (C_{ortho}, Ar), 154.9 ($COCH_2$, Ar); ^{31}P NMR (δ/ppm): 16.9; ESI-MS for $C_{120}H_{184}O_{32}P_8$ (2385.1) *m/z* = 2386.3 [M + H$^+$], 2408.1 [M + Na$^+$], 1215.7 [(M + 2Na$^+$)/2].

4c yield: 56%. Mp: 180 °C, ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.74 (t, 24H, CH_2CH_3), 1.12–1.29 (m, 96H, $(CH_3)_2CHO$), 1.52 (m, 16H, CH_2CH_3), 3.50 (t, 16H, OCH_2), 3.99 (s, 16H, Ar–CH_2–Ar), 4.57 (m, 16H, $CHOP$), 7.40 (m, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.5 (CH_3), 23.2 ($POCH(CH_3)_2$), 23.7 (OCH_2CH_2), 30.4 (Ar–CH_2–Ar), 42.3 ($POCH(CH_3)_2$), 74.8 (OCH_2), 117.2 (C_{para}, Ar), 131.7 (C_{meta}, Ar), 136.2 (C_{ortho}, Ar), 154.9 ($COCH_2$, Ar); ^{31}P NMR (δ/ppm): 17.0; ESI-MS for $C_{128}H_{200}O_{32}P_8$ (2497.2) *m/z* = 2498.3 [M + H$^+$] 2520.4 [M + Na$^+$] 1260.7 [(M + H$^+$ + Na$^+$)/2], 1271.7 [(M + 2Na$^+$)/2].

4d yield: 74%. Mp: 145 °C. ^{1}H NMR ($CDCl_3$, 25 °C) (δ/ppm): 0.77 (br s, 24H, CH_3), 1.10–1.27 (m, 96H, $(CH_3)_2CHO$), 1.48 (m, 16H, CH_2CH_3), 1.81 (m, 16H, OCH_2CH_2), 3.57 (d, 16H, OCH_2), 3.98 (s, 16H, Ar–CH_2–Ar), 4.56 (m, 16H, $CHOP$), 7.34 (m, 16H, Ar*H*); ^{13}C NMR ($CDCl_3$, 25 °C) (δ/ppm): 14.1 (CH_3), 19.8 (CH_2CH_3), 24.2 ($POCH(CH_3)_2$), 30.1 (Ar–CH_2–Ar), 32.4 (OCH_2CH_2), 70.8 ($POCH(CH_3)_2$), 73.6 (OCH_2), 117.1–123.7 (C_{para}, Ar), 133.3 (C_{meta}, Ar), 136.3 (C_{ortho}, Ar), 154.4 ($COCH_2$, Ar); ^{31}P NMR (δ/ppm): 17.0; ESI-MS for $C_{136}H_{216}O_{32}P_8$ (2609.3) *m/z* =

2610.5 [M + H$^+$], 2633.1 [M + Na$^+$], 1305.7 [(M + 2H$^+$)/2], 1316.7 [(M + H$^+$ + Na$^+$)/2], 1327.6 [(M + 2Na$^+$)/2].

4e yield: 45%. Mp: 140 °C, ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 0.72 (br s, 24H, CH_3), 1.13–1.30 (m, 96H, $(CH_3)_2$CHO), 1.50 (m, 16H, CH_2CH$_3$), 1.90 (m, 16H, OCH$_2$CH$_2$CH_2), 2.10 (m, 16H, OCH$_2$CH_2), 3.61 (br s, 16H, OCH_2), 3.98 (s, 16H, Ar–CH_2–Ar), 4.59 (m, 16H, CHOP), 7.31 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 25 °C) (δ/ppm): 14.4 (CH$_3$), 22.8 (CH$_2$CH$_3$), 24.2 (POCH(CH$_3$)$_2$), 28.4 (OCH$_2$CH$_2$$CH_2$), 30.2 (Ar–$CH_2$–Ar), 32.4 (OCH$_2$$CH_2$), 70.8 (PO$C$H(CH$_3$)$_2$), 73.8 (O$CH_2$), 117.0–117.4 ($C_{\mathrm{para}}$, Ar), 133.1 ($C_{\mathrm{meta}}$, Ar), 135.5 ($C_{\mathrm{ortho}}$, Ar), 153.9 ($COCH_2$, Ar); ^{31}P NMR ($\delta$/ppm): 16.9; ESI-MS for $C_{144}H_{232}O_{32}P_8$ (2723.2) m/z = 2723.6 [M + H$^+$], 2745.5 [M + Na$^+$], 1362.57 [(M + 2H$^+$)/2], 1384.5 [(M + 2Na$^+$)/2].

4f yield: 51%. Mp: 140 °C. ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 0.74 (br s, 24H, CH_3), 1.12–1.26 (m, 96H, (CH_3)$_2$CHO), 1.50–1.62 (m, 32H, CH_2CH_2CH$_3$), 1.85 (m, 16H, OCH$_2$CH$_2$CH_2), 2.12 (m, 16H, OCH$_2$CH_2), 3.50 (br s, 16H, OCH_2), 3.99 (s, 16H, Ar–CH_2–Ar), 4.57 (m, 16H, CHOP), 7.37 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 25 °C) (δ/ppm): 14.4 (CH$_3$), 22.9 (CH$_2$CH$_3$), 24.4 (POCH(CH$_3$)$_2$), 26.7 (CH$_2$CH$_2$CH$_3$), 30.2 (OCH$_2$CH$_2$$CH_2$), 30.4 (Ar–$CH_2$–Ar), 32.1 (OCH$_2$$CH_2$), 70.6 (PO$C$H(CH$_3$)$_2$), 73.6 (O$CH_2$), 117.2 ($C_{\mathrm{para}}$, Ar), 133.3 ($C_{\mathrm{meta}}$, Ar), 135.6 ($C_{\mathrm{ortho}}$, Ar), 154.2 ($COCH_2$, Ar); ^{31}P NMR ($\delta$/ppm): 16.9; ESI-MS for $C_{152}H_{248}O_{32}P_8$ (2833.6) m/z = 2834.5 [M + H$^+$], 2826.6 [M + Na$^+$], 1417.7 [(M + 2H$^+$)/2], 1428.4 [(M + H$^+$ + Na$^+$)/2], 1439.8 [(M + 2Na$^+$)/2].

General procedure for the synthesis of calix[8]arene phosphonic acids 5a–f. To a solution of protected octaphosphorylated calix[8]arene **4a–f** (0.8 mmol) in 30 mL of dry chloroform was added bromotrimethylsilane (40 mmol, 50 equiv.). The reaction mixture was stirred at room temperature for 48 h. The reaction mixture was then evaporated under reduced pressure and an excess of absolute methanol added to the residue. The methanol solution was heated at 50 °C for 2 h and then stood overnight at room temperature. The solvent was evaporated, the solid residue concentrated *in vacuo* (0.05 mmHg), precipitated in 1 M HCl, filtered, and then dried *in vacuo*. A yellow-brown powder was obtained.

5a yield: 69%. Mp: >250 °C. ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 3.52 (s, 24H, OCH_3), 4.04 (s, 16H, Ar–CH_2–Ar), 7.43 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 10% pyridine-d_5, 25 °C) (δ/ppm): 30.2 (Ar–CH$_2$–Ar), 62.1 (OCH$_3$), 117.0 (C_{para}, Ar), 132.9 (C_{meta}, Ar), 136.1 (C_{ortho}, Ar), 156.4 (COCH$_3$, Ar); ^{31}P NMR (δ/ppm): 16.1; MALDI-TOF (−) MS for $C_{64}H_{72}O_{32}P_8$ (1600.2) m/z = 1599.3 [M − H$^+$], 1623.2 [M + Na − H$^+$], 1585.3 [M − CH$_3$$^+$].

5b yield: 88%. Mp: >250 °C. ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 1.01 (t, 24H, CH$_2$CH_3), 3.18 (m, 16H, OCH_2), 3.92 (s, 16H, Ar–CH_2–Ar), 7.37 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 10% pyridine-d_5, 25 °C) (δ/ppm): 14.4 (CH$_3$), 30.5 (Ar–CH$_2$–Ar), 70.0 (OCH$_2$), 116.9 (C_{para}, Ar), 133.8 (C_{meta}, Ar), 136.4 (C_{ortho}, Ar), 154.8 (COCH$_2$, Ar); ^{31}P NMR (δ/ppm): 16.3; MALDI-TOF (−) MS for $C_{72}H_{88}O_{32}P_8$ (1713.2) m/z = 1712.0 [M − H$^+$], 1695.1 [M − H$_2$O$^+$].

5c yield: 56%. Mp: >250 °C. ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 0.74 (t, 24H, CH$_2$CH_3), 1.52 (m, 16H, CH_2CH$_3$), 3.50 (t, 16H, OCH_2), 3.99 (s, 16H, Ar–CH_2–Ar), 7.65 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 10% pyridine-d_5, 25 °C) (δ/ppm): 14.5 (CH$_3$), 23.7 (OCH$_2$$CH_2$), 30.4 (Ar–$CH_2$–Ar), 74.8 (O$CH_2$), 117.1 ($C_{\mathrm{para}}$, Ar), 132.6 ($C_{\mathrm{meta}}$, Ar), 136.4 ($C_{\mathrm{ortho}}$, Ar), 154.8 ($COCH_2$, Ar); ^{31}P NMR ($\delta$/ppm): 16.5; MALDI-TOF (−) MS for $C_{80}H_{104}O_{32}P_8$ (1816.8) m/z = 1840.4 [M + Na$^+$].

5d yield: 71%. Mp: 200 °C. ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 0.90 (br s, 24H, CH$_2$CH_3), 1.26 (m, 16H, CH_2CH$_3$), 1.60 (m, 16H, OCH$_2$CH_2), 3.47 (d, 16H, OCH_2), 4.01 (d, 16H, Ar–CH_2–Ar), 7.80 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 10% pyridine-d_5, 25 °C) (δ/ppm): 13.4 (CH$_3$), 19.3 (CH$_2$CH$_3$), 30.1 (Ar–CH$_2$–Ar), 32.3 (OCH$_2$$CH_2$), 73.6 (O$CH_2$), 116.8 ($C_{\mathrm{para}}$, Ar), 134.4 ($C_{\mathrm{meta}}$, Ar), 136.5 ($C_{\mathrm{ortho}}$, Ar), 154.8 ($COCH_2$, Ar); ^{31}P NMR ($\delta$/ppm): 16.6; MALDI-TOF MS for $C_{88}H_{120}O_{32}P_8$ (1936.6) m/z = 1934.9 [M − H$^+$], 1918.1 [M − H$_2$O − H$^+$], 1900.6 [M − 2H$_2$O − H$^+$].

5e yield: 65%. Mp: 170 °C. ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 0.72 (br s, 24H, CH_3), 1.50 (m, 16H, CH_2CH$_3$), 1.90 (m, 16H, OCH$_2$CH$_2$CH_2), 2.10 (m, 16H, OCH$_2$CH_2), 3.61 (br s, 16H, OCH_2), 3.98 (s, 16H, Ar–CH_2–Ar), 7.31 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 10% pyridine-d_5, 25 °C) (δ/ppm): 14.4 (CH$_3$), 21.9 (CH$_2$CH$_3$), 28.0 (OCH$_2$CH$_2$$CH_2$), 30.2 (Ar–$CH_2$–Ar), 32.4 (OCH$_2$$CH_2$), 73.9 (O$CH_2$), 116.9 ($C_{\mathrm{para}}$, Ar), 134.9 ($C_{\mathrm{meta}}$, Ar), 136.0 ($C_{\mathrm{ortho}}$, Ar), 154.5 ($COCH_2$, Ar); ^{31}P NMR ($\delta$/ppm): 16.6; MALDI-TOF (−) MS for $C_{96}H_{136}O_{32}P_8$ (2049.9) m/z = 2049.1 [M − H$^+$], 2071.2 [M + Na − H$^+$], 2031.8 [M − H$_2$O − H$^+$], 2031.8 [M − 2H$_2$O − H$^+$].

5f yield: 71%. Mp: 172 °C, ^{1}H NMR (CDCl$_3$, 25 °C) (δ/ppm): 0.72 (br s, 24H, CH_3), 1.47–1.62 (m, 32H, CH_2CH_2CH$_3$), 1.85 (m, 16H, OCH$_2$CH$_2$CH_2), 2.12 (m, 16H, OCH$_2$CH_2), 3.61 (br s, 16H, OCH_2), 4.05 (s, 16H, Ar–CH_2–Ar), 7.28 (m, 16H, ArH); ^{13}C NMR (CDCl$_3$, 10% pyridine-d_5, 25 °C) (δ/ppm): 14.4 (CH$_3$), 22.5 (CH$_2$CH$_3$), 26.6 (CH$_2$CH$_2$CH$_3$), 30.1 (OCH$_2$CH$_2$$CH_2$), 30.4 (Ar–$CH_2$–Ar), 32.1 (OCH$_2$$CH_2$), 73.8 (O$CH_2$), 116.8 ($C_{\mathrm{para}}$, Ar), 134.7 ($C_{\mathrm{meta}}$, Ar), 136.4 ($C_{\mathrm{ortho}}$, Ar), 154.5 ($COCH_2$, Ar); ^{31}P NMR ($\delta$/ppm): 16.5; MALDI-TOF (−) MS for $C_{104}H_{152}O_{32}P_8$ (2162.1) m/z = 2160.9 [M − H$^+$], 2184.3 [M + Na − H$^+$], 2143.3 [M − H$_2$O − H$^+$], 2125.4 [M − 2H$_2$O − H$^+$].

Crystal data

3a ($C_{64}H_{56}Br_8O_8 \cdot H_2O$), M_r = 1626.37; colorless, 0.20 × 0.22 × 0.38 mm, monoclinic, $P2_1/n$, a = 8.7192(7), b = 26.300(1), c = 15.251(2) Å, β = 91.521(6)°, V = 3496.1(6) Å^3, Z = 2, ρ_{calc} = 1.528 Mg m^{-3}, $\theta_{\max}$ = 23.3°, μ(Mo-K$_\alpha$) = 4.637 mm^{-1}, T = 293 K, 4980 independent reflections, 2800 [$I > 2\sigma(I)$], R_{int} = 0.080, R = 0.085, wR = 0.237 (R = 0.147, wR = 0.269 for all data), GOF = 1.03. CCDC 637889.

3d ($C_{88}H_{104}Br_8O_8$), M_r = 1928.99; colorless, 0.04 × 0.12 × 0.20 mm, triclinic, P-1, a = 15.8507(3), b = 16.6896(3), c = 18.4507(4) Å, α = 107.078 (1), β = 90.820(1), γ = 114.725(1)°, V = 4184.8 (2) Å^3, Z = 2, ρ_{calc} = 1.530 Mg m^{-3}, $\theta_{\max}$ = 27.5°, μ(Mo-K$_\alpha$) = 3.876 mm^{-1}, T = 100 K, 18835 independent reflections, 13533 [$I > 2\sigma(I)$], R_{int} = 0.093, R = 0.079, wR = 0.164 (R = 0.119, wR = 0.181 for all data), GOF = 1.07. CCDC 637890.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b616480n

Langmuir experiments

Langmuir film measurements were carried out in a 400 mL Teflon trough. 4 mg mL^{-1} calix[8]arene solutions were spread at appropriate volumes at the air–water interface with a Micropipetman (Gilson). 30 min were allowed for solvent evaporation and equilibration. Isotherms were carried out on a Langmuir type balance (NIMA Technology). Compressions were performed continuously at a rate of 25 cm^2 min^{-1} from 510 to 50 cm^2. Each sample was run at least three times to ensure the reproducibility of results (deviation of area and pressure were less than 3%).

Conclusions

The synthesis, four steps from calix[8]arene, of a series of *para*-phosphonato-*O*-alkoxy-calix[8]arenes has been achieved in reasonable overall yields. The crystal structures of two of the intermediate molecules reveal them to be in an ovoid cone conformation. The *para*-phosphonato-*O*-alkoxy-calix[8]arene alkoxy ether derivatives form stable monolayers at the air–water interface with chain lengths greater than two carbon atoms. In the case of the corresponding *iso*-propoxy-protected compounds, a chain length of at least six carbon appears necessary for the formation of stable monolayers at the air–water interface.

Work is currently under way to determine the biological activities of these molecules.

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