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Self-organised nano-arrays of *p*-phosphonic acid functionalised higher order calixarenes†

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Water-soluble *p*-phosphonic acid calix[*n*]arenes ($n = 5$, 6 or 8) have been synthesized in five steps in overall 68, 66, 67% yield, respectively, by the recently developed procedure for *p*-phosphonic acid calix[4]arene. The hydrogen bonding prowess of the phosphonic acids dominates their self assembly into nano-arrays in both solution and the gas phase. In DMSO, nano-arrays of *p*-phosphonic acid calix[6]arene are stable for over 24 h, with the solvent molecules slowly disrupting the hydrogen bonded network affording solvated monomeric units. In the gas phase, nano-arrays of around 20 calixarene units were observed for the *p*-phosphonic acid calix[*n*]arenes using MALDI-TOF-MS, and ESI-MS revealed the presence of heteroleptic nano-arrays for a 1 : 1 mixture of *p*-phosphonic acid calix[4,5]arenes.

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Introduction

Water-soluble calixarenes have a range of applications in catalysis, for example, as well as acting as surfactants and host molecules.[1] Water solubility can be imparted by suitable modification of the calixarene skeleton at either the upper or lower rim with polar functionality such as dialkylamino,[1e] carboxylic,[2] sulfonic[3] and phosphonic acid groups.[4] *p*-Sulfonato-calixarenes are the most widely studied class of water-soluble calixarene due to their facile synthesis, high solubility in aqueous media and their potential role in a number of biological applications. For example, they have been shown to be active ion-channel blockers,[5] possess anti-thrombotic and anti-viral activity,[6] and solubilise a variety of otherwise non-soluble drugs.[7]

Studies on the related *p*-phosphonatocalixarenes are limited mainly due to the more challenging synthetic procedures required to gain access to such compounds.[8] Nevertheless, there has been growing interest in the supramolecular chemistry of *p*-phosphonatocalixarenes. This relates to the increased potential of self association of the conjugate acid through hydrogen bonding of the diprotic phosphonic acid groups relative to the monoprotic sulfonic acid groups of the corresponding sulfonatocalixarenes, and also to the greater range of charge that the phosphonated calixarenes can build up relative to the sulfonatocalixarenes. Moreover, they have potential to forming nanoscale capsular assemblies *via* hydrogen or coordination bonding, and possibly acting as nano-reaction vessels or selective carriers of guest molecules, as established for other systems.[9]

A tetra-*p*-phosphonatocalix[4]arene has been shown to form discrete 1 : 1 molecular capsules with complementary tetra-cationic calixarenes.[10] The larger the pK_a difference between the two pre-organized building blocks, the larger the binding constant observed, up to 10^5 M^{-1}. Unfortunately no guest inclusion was seen for any of the molecular capsules, which have an internal volume capacity of 170–230 $Å^3$, and this is possibly a consequence of the high stability of the capsule.[11] There has also been much interest in the use of calix[4]arene tetraphosphonates as amphiphilic receptor molecules for the detection of proteins or cations at the air/water interface[12] and for the recognition of amino alcohols or uracil derivatives in aqueous medium.[13]

We recently reported the five-step synthesis of *p*-phosphonic acid calix[4]arene free of any lower rim substitution, and its self assembly into remarkably stable nano-rafts.[14] Using spinning disc processing (SDP), we formed 3.0(3) and 20(2) nm nano-rafts in water using acetonitrile as a stabilizer, whilst clusters of up to 20 calixarenes are observed in the gas phase using MALDI-TOF mass spectrometry. The assignment of nano-rafts relates mainly to the ability to form bilayer structures, either with or without a layer of water molecules interposed between such layers. We now report the synthesis of the higher order calixarenes, namely *p*-phosphonic acid calix[*n*]arenes ($n = 5$, 6 or 8), thereby demonstrating the versatility of the synthetic protocol that was established for the sibling calix[4]arene analogue.[14] We also report the self-assembly of the calixarenes into nano-arrays in the gas and solution phase, along with structural authentication using X-ray diffraction of some of the intermediates *en route* to the formation of the *p*-phosphonic acid calixarenes.

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† Electronic supplementary information (ESI) available: A full description of the methods used, synthetic procedures for *p*-phosphonic acid calix[6,8]arenes and crystal/refinement details for compounds **3c**, **3d** and **4d**. CCDC reference numbers 669055–669059. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b801256c

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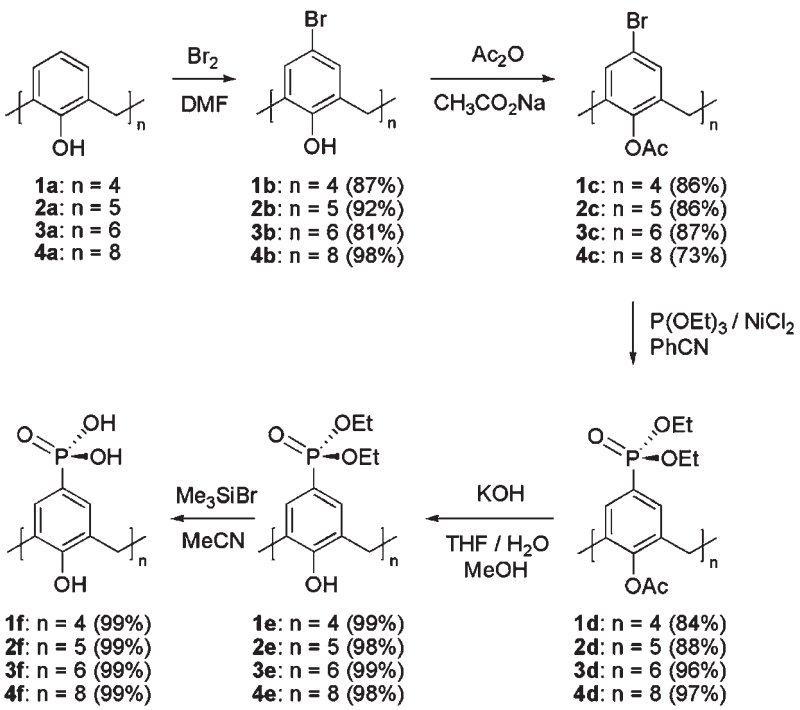
Results and discussion

The synthesis of *p*-phosphonic acid calix[4]arene, **1f**, has previously been accomplished in five steps in 62% overall yield from the commercially available *p*-H-calix[4]arene, **1a**.[14] The key development involved the use of a tetraacetoxy-*p*-bromocalix[4]arene precursor, **1c**, for the nickel-catalyzed Arbuzov reaction[8] to effect the aryl C–P bond formation. This precursor was synthesized from a modified literature procedure for octa-acetoxy-*p*-bromocalix[8]arene, **4c**, which involved bromination of *p*-H-calix[8]arene, **4a**, using elemental bromine followed by acetylation using acetic anhydride.[15] It was anticipated that the same procedure could be applied to any of the *p*-H-calix[4,5,6,8]arenes, **1a–4a**, respectively, to produce the corresponding acetylated *p*-bromocalix-[4,5,6,8]arenes, **1c–4c**, respectively. Indeed this was the case and the nickel-catalyzed Arbuzov reaction proceeded smoothly with any of the acetylated *p*-bromocalix[4,5,6,8]-arenes, **1c–4c**, respectively, in excellent yield. The acetyl groups were then removed quantitatively using potassium hydroxide, and subsequent de-esterification of the phosphonate esters using bromotrimethylsilane (BTMS) was also effected in quantitative yield. The yield over five steps for preparing *p*-phosphonic acid calix[*n*]arenes (n = 5, 6 or 8), **2f–4f**, were 68, 66 and 67%, respectively. It is noteworthy that the earlier protocol *en route* for the synthesis of *p*-phosphonic acid calix[4]arene[8] is not applicable for higher-order calixarenes because of solubility issues (Scheme 1).[14]

The nickel catalyzed Arbuzov reaction was sensitive to the concentration of the reaction mixture with more concentrated solutions producing higher yields. This can be seen for the higher calix[6,8]arenes, **3c** and **4c**, respectively, which are the least soluble in benzonitrile, with calix[8]arene, **4c**, being only sparingly soluble at the reaction temperature of 180 °C. The only purification required throughout the synthesis was a simple flash chromatography on the crude phosphonate esters, **2d–4d**. The phosphonic acids **2f–4f** are highly soluble in water and dimethyl sulfoxide (DMSO), moderately soluble in alcohols such as methanol and insoluble in common non-polar organic solvents. Structure authentication by means of single-crystal X-ray diffraction was performed on calixarenes **2c**, **3c**, **2d**, **3d** and **4d**.[16]

The calix[8]arene, **4d**, was recrystallized by slow evaporation of a pure saturated solution from ethyl acetate–dichloromethane to afford colourless single crystals suitable for X-ray diffraction studies. This yielded a solvent-free structure in the space group $P\bar{1}$ (Z = 1), albeit with substantial disorder of the phosphonate groups. The calix[8]arene molecule adopts a very compact spatial arrangement resulting from the orientation of the aromatic rings relative to the bridging methylenes whereby two acetyl and ethoxy groups occupy the available space within the molecular cavity, Fig. 1(A).

The compact organisation of **4d** based on the intramolecular interactions of the acetyl and the ester ethoxy groups involves two short $H_3C\cdots O{=}C$ distances of 3.44 and 3.70 Å. There is also a short $H_3C\cdots O{=}C$ distance of 3.04 Å, and a short $H_3C\cdots O{=}P$ distance of 3.86 Å which is between adjacent aromatic moieties. The dihedral angles between the plane of the methylene bridges and bonded aromatic rings are 29.5 and 123.0° (Ph1–C1–Ph2), 74.1 and 75.8° (Ph2–C2–Ph3), 130.1 and 66.3° (Ph3–C3–Ph4), 67.4 and 124.7° (Ph4–C4–Ph1a) and 58.7 and 106.4° (Ph4a–C4a–Ph1). The molecules pack together into a complex layered arrangement in the extended structure parallel to the *bc* plane with numerous short contacts between



Scheme 1 Synthesis of *p*-phosphonic acid calix[4,5,6,8]arenes, **1f–4f**, starting from *p*-H-calix[4,5,6,8]arenes, **1a–4a**. DMF = dimethylformamide, Ac = acetyl, Et = ethyl, Ph = phenyl, THF = tetrahydrofuran, Me = methyl.

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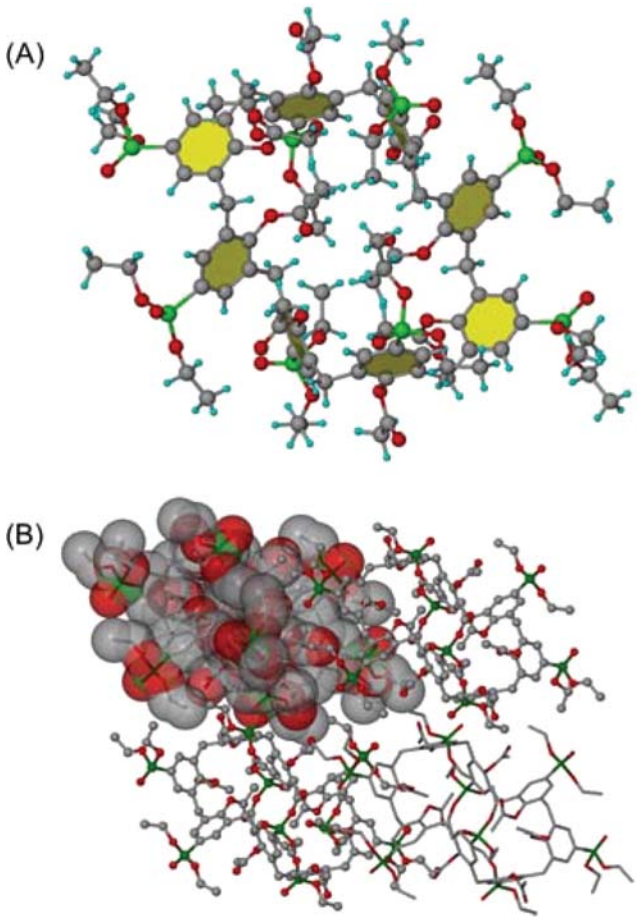

Fig. 1 X-Ray crystal structure of phosphonate ester calix[8]arene, **4d**. (A) Compact packing of the acetyl and ethoxy groups in the molecular cavity associated with inversion of the aromatic rings relative to the bridging methylenes. (B) Partial packing of **4d** within a layered arrangement viewed down the *a* axis and depicted with different atomic style for clarity. The following colour scheme is used: carbon atoms – grey, oxygen atoms – red and phosphorus atoms – green. Disordered phosphonate groups, and hydrogens have been removed for clarity.

neighbouring calixarenes, $H_2C\cdots O{=}C$ 3.38 Å, $HC_{Ar}\cdots O{=}C$ 3.29 Å, $C_{centroid}\cdots CH_2$ 2.93 Å, $H_2C\cdots O{=}P$ 3.65 Å and $H_3C\cdots O{=}P$ 3.30, 3.43 and 3.59 Å, Fig. 1(B).

Self-assembled nano-rafts of *p*-phosphonic acid calix[4]-arene, **1f**, have remarkable stability in DMSO at room temperature, slowly dissociating over the course of 36 h into solvated monomeric units.[14] This behaviour is also observed for the calix[6]arene analogue, **3f**, which is in contrast to tetra-urea-calixarene dimers, which "denature' within seconds upon addition of a few mol% of DMSO.[17] The ^{1}H NMR spectrum of a freshly prepared solution of **3f** in d_6-DMSO gave a broad singlet and two doublets for the two equivalent aromatic protons which are split by coupling to the single phosphorus atom, Fig. 2(A)–(C). The broad singlet can be attributed to conformationally flexible monomeric units of **3f** on the NMR time scale. The doublets are reminiscent of the those seen for the analogous protons of the conformationally restricted calix[4]arene, **1f**. Thus the doublets herein can be attributed to nano-arrays of **3f** whereby the conformation of **3f** is locked

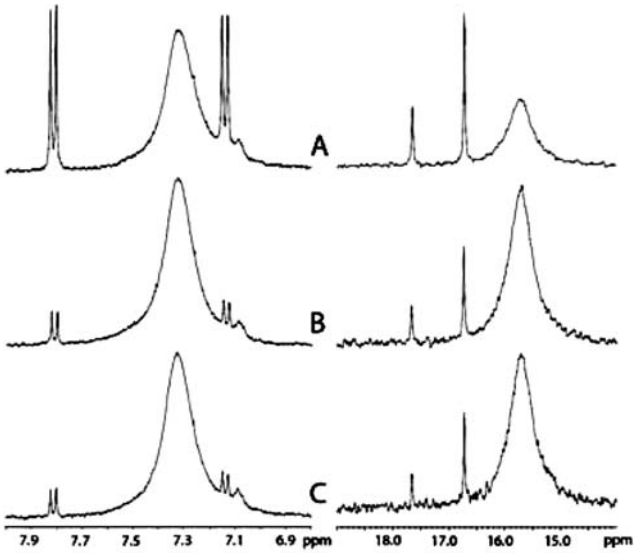

Fig. 2 ^{1}H NMR (left) and ^{31}P NMR (right) expansions between 8.0–6.8 and 19.0–14.0 ppm, respectively, for calix[6]arene **3f** in d_6-DMSO: (A) 0 h, (B) 7 h, (C) 24 h.

due to aggregation thereby reducing the broad nature of the signal. These nano-arrays take over 24 h to slowly dissociate into solvated monomeric units. This is also confirmed by ^{31}P NMR, which shows one broad singlet increasing in intensity and two sharp singlets decreasing in intensity over time. The nano-array behaviour is attributed to residual acetonitrile from the synthetic procedure orchestrating the nano-array assembly by participating in hydrogen bonding and also by acting as a stabilizer on the surface of the nano-arrays with the non-polar methyl groups directed into the cavities of the calixarenes.

Previously calix[4]arene, **1f**, was shown to form stable nano-rafts in the gas phase using MALDI-TOF-MS with up to 20 calixarene units per raft.[14] The assignment of nano-rafts in this case comes from the availability of crystal structure data on the extended structure, revealing a bi-layer arrangement which is most likely prevalent in the gas phase. Hence the assignment of the aggregates of the calixarene as nano-rafts is justified. For the MALDI-TOF-MS studies herein, using the acidic matrix, 2,5-dihydroxybenzoic acid (2,5-DHB), successive peaks out to 20-mer and beyond were also observed for **2f–4f**, Fig. 3(A)–(C). This equates to nano-arrays of around 18–30 kDa for **2f–4f**.

The nano-arrays for calix[5]arene, **2f**, are likely to have similar packing as that deduced for calix[4]arene, **1f**, whereby the calixarenes take on a bilayer arrangement within the nano-rafts.[18] This is reasonable as both calixarenes, **1f** and **2f**, adopt the locked-cone conformation (^{1}H NMR), and analogously *p*-sulfonatocalix[5]arenes were shown to form bilayers in the solid state.[19] However, assignment of the nano-rafts comprised of bi-layer organisation for **3f** and **4f** is not substantiated.

ESI-MS on a 1 : 1 mixture of **1f** and **2f** revealed the existence of hetero-nano-arrays with mixed dimers, trimers and tetramers being observed, Fig. 4(A)–(D).

It can be seen that mixed dimers comprised of one **1f** and one **2f** with charges ranging from −1, −2 and −3 are observed at *m*/*z* 1673, 836 and 557, respectively, Fig. 4(A). Mixed trimers composed of two **1f** and one **2f** with charges −2 and

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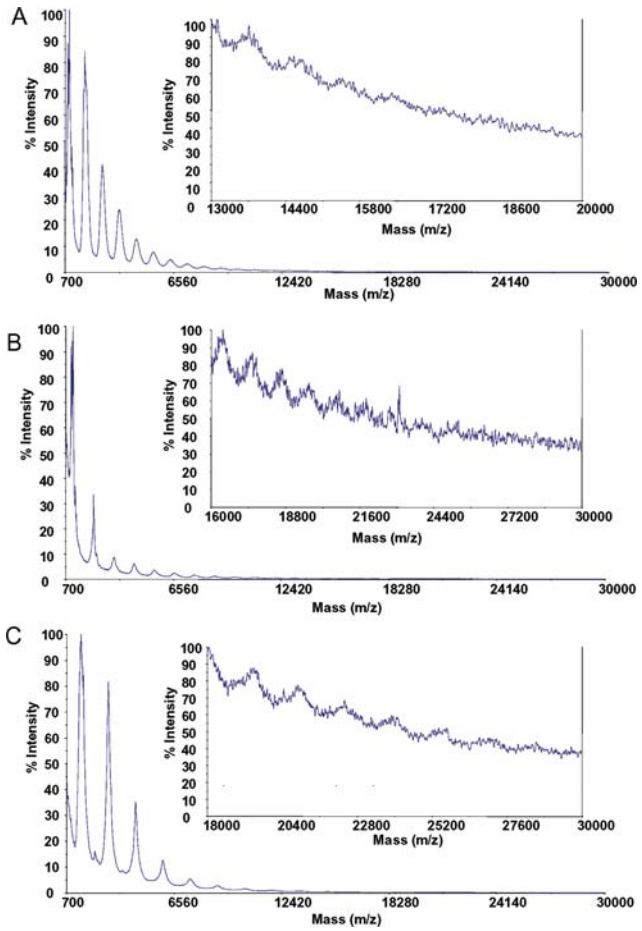

Fig. 3 MALDI-TOF spectra showing nano-assemblies in the gas phase for the *p*-phosphonic acids of (A) calix[5]arene, **2f**, (B) calix[6]-arene, **3f**, and (C) calix[8]arene, **4f**.

−3 are observed at *m*/*z* 1208 and 805, respectively, Fig. 4(B), and one **1f** and two **2f** with charges −2 and −3 are observed at *m*/*z* 1301 and 867, respectively, Fig. 4(C). Finally a mixed tetramer with composition of two **1f** and two **2f** of charge −3 is also observed at *m*/*z* 1115, Fig. 4(D).

Experimental

All starting materials and solvents were obtained from commercial suppliers and used without further purification except otherwise noted. Acetonitrile was dried over 4 Å molecular sieves for 24 h and $NiCl_2{\cdot}6H_2O$ was dried at 180 °C *in vacuo* for 8 h before use. All moisture-sensitive reactions were performed under a positive pressure of nitrogen. *p*-Phosphonic acid calix[4]arene,[14] *p*-H-calix[5]arene,[20] *p*-H-calix[6]arene[21] and *p*-H-calix[8]arene[21] were prepared as described previously in the literature.

5, 11, 17, 23, 29-Pentabromo-31,32,33,34,35-pentahydroxycalix[5]-arene (2b)

3.62 mL (70.73 mmol) of bromine in 50 mL of DMF was added dropwise with stirring to a solution of 5.00 g (9.43 mmol) of calix[5]arene, **2a**, in 200 mL of DMF. The solution was stirred for 4 h and the volatiles were removed under reduced pressure. After addition of 250 mL of methanol the precipitate was filtered off and washed with methanol (3 × 40 mL) to yield 8.01 g (92%) of **2b** as a pale brown solid. ^{1}H NMR ($CDCl_3$, 25 °C, 250 MHz) δ 8.77 (s, 5H, O*H*), 7.31 (s, 10H, Ar*H*), 3.75 (br s, 10H, ArCH_2Ar).

5,11,17,23,29-Pentabromo-31,32,33,34,35-pentaacetoxycalix[5]-arene (2c)

A mixture of 7.03 g (7.64 mmol) of **2b** and 4.70 g (57.28 mmol) of anhydrous sodium acetate in 60 mL of acetic anhydride was refluxed for 4 h. After cooling to RT the solution was slowly quenched with 80 mL of water. The precipitate was collected by filtration and washed with methanol (3 × 30 mL) to yield 7.43 g (86%) of **2c** as a light green solid. Recrystallisation from dichloromethane yielded X-ray quality single crystals, **2c**·$3CH_2Cl_2{\cdot}2{,}25H_2O$, which were also submitted for microanalysis; mp >270 °C (decomp.); IR (KBr) 2932 (w), 1764 (s), 1574 (m), 1458 (s), 1369 (m), 1208 (s), 1173 (s), 873 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 25 °C, 500 MHz) δ 7.76–6.68 (m, 10H, Ar*H*), 4.02–3.02 (m, 10H, ArCH_2Ar), 2.74–1.10 (m, 15H, CH_3); ^{13}C NMR ($CDCl_3$, 25 °C, 126 MHz) δ168.80–167.81 (m), 147.72–145.06 (m), 135.88–130.24 (m), 119.91–118.36 (m), 34.91–33.09 (m), 31.69–29.89 (m), 20.99–18.61 (m); HRMS (FAB) *m*/*z* calc. for $[C_{45}H_{35}Br_5O_{10} - H]^-$ 1132.8028, found 1132.7952. Elemental analysis. Calc. (%) for $C_{45}H_{35}Br_5O_{10}$: C 47.61, H 3.11. Found: C 47.41, H 3.02.

Crystal/refinement details for 2c·$3CH_2Cl_2{\cdot}2.25H_2O$. $C_{48}H_{45.5}Br_5Cl_6O_{12.25}$, M = 1430.59, F(000) = 5668 *e*, monoclinic, *C*2/*c*, Z = 8, T = 100(2) K, a = 37.319(8), b = 15.438(5), c = 21.720(6) Å, β = 115.70(10)°, V = 11 276(5) Å^3, D_c = 1.685 g cm^{-3}, μ_{Mo} = 3.906 mm^{-1}, $\sin(\theta/\lambda_{max})$ = 0.6427, N(unique) = 12 406 (merged from 38 911, R_{int} = 0.0723, R_{sig} = 0.0839), N_o ($I > 2\sigma(I)$) = 7523, R = 0.0710, $wR2$ = 0.1600 (A, B = 0.06, 121.8), GOF = 1.034, $|\Delta\rho_{max}|$ = 0.9(1) e Å^{-3}. CCDC 669055.

5,11,17,23,29-Penta(diethoxyphosphoryl)-31,32,33,34,35-pentaacetoxycalix[5]arene (2d)

A solution of 3.87 g (3.43 mmol) of **2c** and 0.56 g (4.28 mmol) of $NiCl_2$ in 20 mL of benzonitrile was treated dropwise with 7.34 mL (42.83 mmol) of $P(OEt)_3$ under nitrogen at 190 °C. The solution was stirred for 0.5 h and the volatiles removed under reduced pressure to leave an orange residue. The residue was purified by flash chromatography to yield 5.21 g of a light yellow solid. Recrystallisation from toluene–hexane yielded 4.30 g (88%) of **2d** as a white solid. Further recrystallisation from toluene yielded X-ray quality single crystals, **2d**, which were also submitted for microanalysis. R_f = 0.43 (1 : 4 methanol–ethyl acetate); mp 253–255 °C; IR (KBr) 2985 (m), 2911 (w), 1763 (s), 1653 (w), 1457 (m), 1373 (m), 1272 (m), 1020 (s), 966 (s), 796 (w), 605 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 25 °C, 500 MHz) δ8.12–7.01 (m, 10H, Ar*H*), 4.46–3.24 (m, 30H, ArCH_2Ar and POCH_2), 2.82–0.87 (m, 45H, CH_3 and POCH_2CH_3); ^{13}C NMR ($CDCl_3$, 25 °C, 126 MHz) δ 167.93, 151.95–148.10 (m), 135.35–130.04 (m), 128.38–124.95 (m), 62.36 (d, $^2J_{P-C}$ = 3.6 Hz), 35.69–33.91 (m), 31.54–30.32 (m), 21.53–18.15 (m), 16.32

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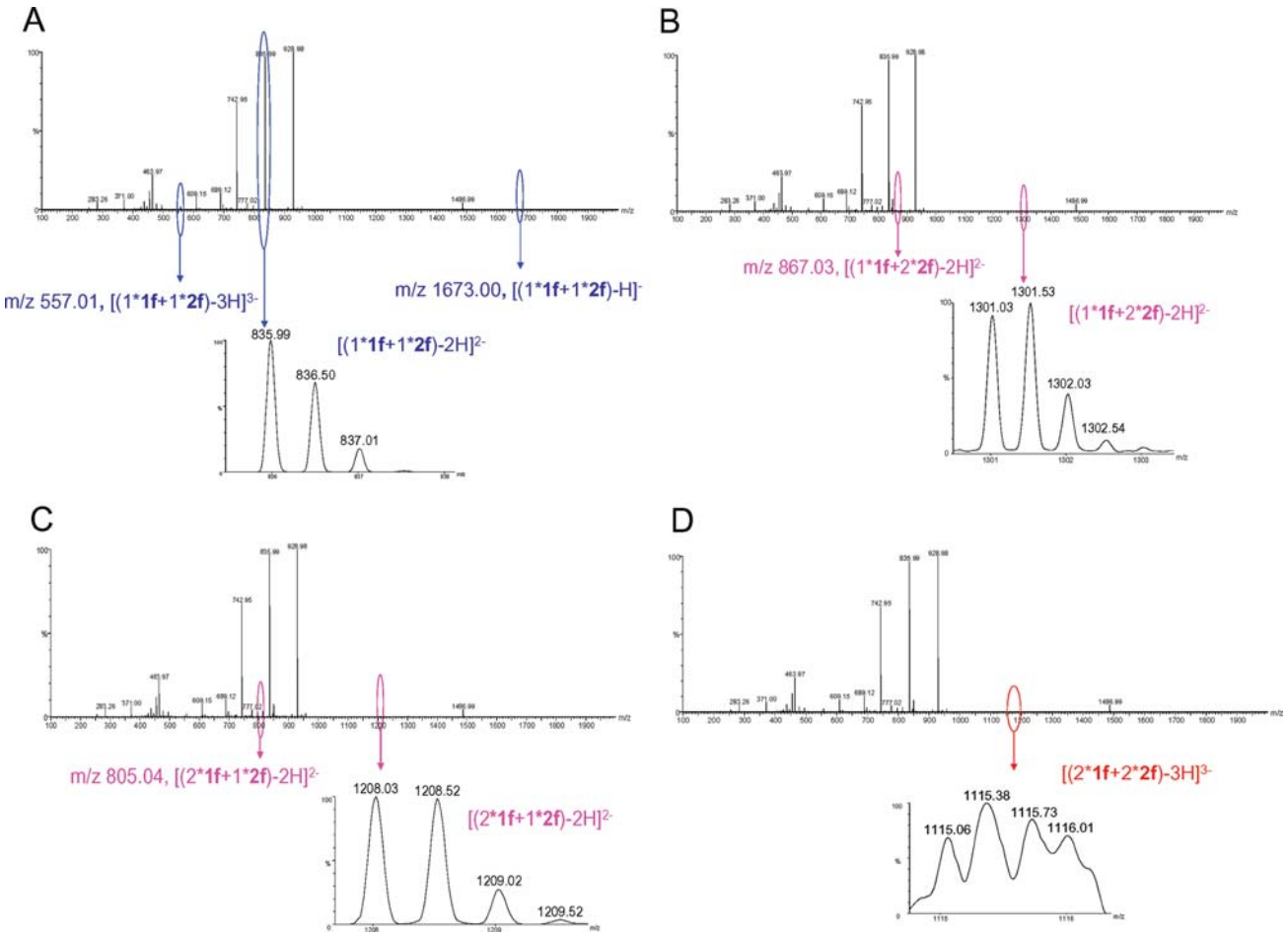

Fig. 4 ESI mass spectra showing hetero-nano-arrays in the gas phase between **1f** and **2f**. (A) Hetero-dimer formation, **1f**·**2f**. (B) Hetero-trimer formation, (**1f**)$_2$·**2f**. (C) Hetero-trimer formation, **1f**·(**2f**)$_2$. (D) Hetero-tetramer formation, (**1f**)$_2$·(**2f**)$_2$.

(d, $^3J_{P-C}$ = 4.2 Hz); ^{31}P NMR ($CDCl_3$, 25 °C, 101 MHz) δ 17.71; MS (ESI) m/z calc. for $[C_{65}H_{85}O_{25}P_5 + Na]^+$ 1443.3966, found 1443.4003. Elemental analysis. Calc. (%) for $C_{65}H_{85}O_{25}P_5 \cdot 0.65H_2O$: C 54.48, H 6.07. Found: C 54.21, H 5.78.

Crystal/refinement details for 2d. $C_{65}H_{85}O_{25}P_5$, M = 1421.18, $F(000)$ = 1500 e, triclinic, $P\bar{1}$, Z = 2, T = 100(2) K, a = 12.9938(4), b = 16.3618(5), c = 18.4136(6) Å, α = 100.825(3), β = 94.164(3), γ = 112.261(3)°, V = 3513.2(7) Å^3, D_c = 1.343 g cm^{-3}, μ_{Cu} = 1.873 mm^{-1}, $\sin(\theta/\lambda_{max})$ = 0.5970, N(unique) = 12 348 (merged from 41 009, R_{int} = 0.0483, R_{sig} = 0.0599), N_o ($I > 2\sigma(I)$) = 7153, R = 0.0731, $wR2$ = 0.1995 (A, B = 0.145, 0), GOF = 1.008, $|\Delta\rho_{max}|$ = 1.63(9) e Å^{-3}. CCDC 669056.

5,11,17,23,29-Penta(diethoxyphosphoryl)-31,32,33,34,35-pentahydroxycalix[5]arene (2e)

A mixture of 2.04 g (1.44 mmol) of **2d** and 1.01 g (17.98 mmol) of KOH in 50 mL of methanol, 50 mL of tetrahydrofuran and 50 mL of water was stirred for 4 h. The solvents were removed under reduced pressure and the residue treated with 50 mL of dichloromethane and 50 mL of 2 M HCl. The organic layer was separated, washed with 2 M HCl (1 × 25 mL), water (2 × 25 mL), dried over $MgSO_4$ and evaporated under reduced pressure to yield 1.70 g (98%) of **2e** as a white solid. Recrystallisation from ethyl acetate–hexane yielded a white solid suitable for microanalysis; mp 128–130 °C; IR (KBr) 3365 (br), 2984 (m), 2907 (m), 1653 (m), 1473 (m), 1394 (m), 1278 (m), 1022 (s), 966 (s), 795 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 25 °C, 500 MHz) δ 9.03 (br s, 5H, O*H*), 7.66 (d, 10H, Ar*H*, J_{P-H} = 13.0 Hz), 4.28–3.62 (m, 30H, ArCH_2Ar and POCH_2), 1.23 (t, 30H, POCH$_2$CH_3, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 25 °C, 126 MHz) δ 153.73, 133.32 (d, $^2J_{P-C}$ = 10.7 Hz), 126.77 (d, $^3J_{P-C}$ = 14.2 Hz), 121.20 (d, $^1J_{P-C}$ = 190.1 Hz), 62.07 (d, $^2J_{P-C}$ = 5.2 Hz), 30.96, 16.23 (d, $^3J_{P-C}$ = 6.5 Hz); ^{31}P NMR ($CDCl_3$, 25 °C, 101 MHz) δ 19.21; MS (ESI) m/z calc. for $[C_{55}H_{75}O_{20}P_5 + Na]^+$ 1233.3438, found 1233.3505. Elemental analysis. Calc. (%) for $C_{55}H_{75}O_{20}P_5$: C 54.55, H 6.24. Found: C 54.56, H 6.05.

5,11,17,23,29-Penta(dihydroxyphosphoryl)-31,32,33,34,35-pentahydroxycalix[5]arene (2f)

3.53 mL (26.77 mmol) of bromotrimethylsilane was added to 1.62 g (1.34 mmol) of **2e** in 50 mL of dry acetonitrile and the solution was refluxed for 16 h. The volatiles were removed under reduced pressure and the resulting residue was triturated with 40 mL of acetonitrile and 2 mL of water. The precipitate formed was filtered off and washed with aceto-

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nitrile (3 x 20 mL) to yield 1.23 g (99%) of **2f** as a white solid. Purification using the ion exchange resin, Dowex 50W yielded a white solid suitable for microanalysis; mp >280 °C (decomp.); IR (KBr) 3393 (br), 2300 (br), 1597 (m), 1471 (s), 1385 (m), 1280 (m), 1124 (m), 950 (m), 874 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 25 °C, 600 MHz) δ 7.42 (d, 10H, Ar*H*, J_{P-H} = 13.2 Hz), 5.35 (br s, CO*H*/PO*H*, shifts downfield with increasing $[H]^+$), 3.88 (s, 10H, ArCH_2Ar); ^{13}C NMR (DMSO-d_6, 25 °C, 151 MHz) δ 154.14, 131.74 (d, $^{2}J_{P-C}$ = 10.3 Hz), 127.57 (d, $^{3}J_{P-C}$ = 15.4 Hz), 124.58 (d, $^{1}J_{P-C}$ = 186.1 Hz), 30.78; ^{31}P NMR (DMSO-d_6, 25 °C, 243 MHz) δ 15.03; MS (ESI) *m*/*z* calc. for $[C_{35}H_{35}O_{20}P_5 + H]^+$ 931.05, found 931.13. Elemental analysis. Calc. (%) for $C_{35}H_{35}O_{20}P_5 \cdot 1.25H_2O$: C 44.11, H 3.97. Found: C 44.31, H 4.18.

Conclusion

We have successfully applied the synthetic procedure developed for *p*-phosphonic acid calix[4]arene to the higher-order calixarenes, *p*-phosphonic acid calix[*n*]arenes (*n* = 5, 6 or 8) in overall 68, 66 and 67% yield, respectively. These highly water-soluble molecules assemble into nano-arrays both in solution and the gas phase, and most certainly serve as a platform for supramolecular chemistry and materials science, investigations we are currently pursuing.

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