Unsymmetrical O-bridged calixarenes derived from ^{t}Bu-calix[4]arene and *p*-benzylcalix[4]arene

Mohamed Makha,[a] Peter J. Nichols,[a] Michaele J. Hardie[b] and Colin L. Raston*[b]

[a] *School of Chemistry, Monash University, Clayton, Melbourne, Victoria 3800, Australia*
[b] *School of Chemistry, University of Leeds, Leeds, UK LS2 9JT.*
E-mail: c.l.raston@chemistry.leeds.ac.uk; Fax: +44 0113 233 6401; Tel: +44 0113 233 6555

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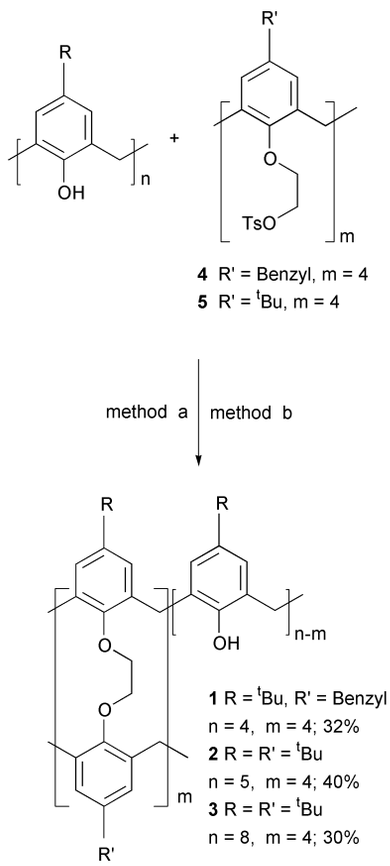
Bis-calixarenes derived from linking *p*-^{t}Bu-calix[4]arene with *p*-^{t}Bu-calix[*n*]arenes (*n* = 5, 8) *via* ethylene linkages have been prepared and structural authentication in the solid state for the compound with *p*-^{t}Bu-calix[4]arene linked to *p*-^{t}Bu-calix[5]arene has been carried out. The bis-calixarene derived from linking *p*-^{t}Bu-calix[4]arene with *p*-benzylcalix[4]arene and its related chemistry are also reported.

Introduction

The ready availability of calixarene macrocycles[1] and their ability to be functionalised at the lower rim has led to the development of new classes of macrocycles such as calix-crowns[2] and fused calixarenes.[3] Calixarenes can be covalently attached through the lower rims with a variety of linkers.[4] Most of these so called bis-calixarenes are attached through one or two moieties.[5] Systems with more linkers form barrel type structures,[6] and include the use of oligoethyl ether bridges.[7] In the case of the oligoethyl ether bridges, a cage-like central core is present which is capable of binding metal ions, and has implications in biomimetic cation transport through cell membranes.[7] Beer *et al.* have reported the synthesis of a symmetrical quadruply-linked bis-^{t}Bu-calix[4]arene ('calix[4]tube') with ethylene linkers, which shows remarkable affinity for potassium ions.[7] The aryl groups radiating from the central core in these tubular receptors are also of importance in the control of metal ion selectivity, behaving as filtering gates by way of cation-π interactions.[8]

Herein we report the first example of an unsymmetrical fused calixarene, derived from *p*-benzylcalix[4]arene linked to ^{t}Bu-calix[4]arene through four ethyl linkers. In addition, in order to understand the factors controlling covalently attaching calixarenes bearing different cavity sizes, we have prepared unsymmetrical bis-calixarenes, using ^{t}Bu-calix[4]arene as the primary building component. The syntheses of *p*-^{t}Bu-calix[4]arene linked to (i) *p*-^{t}Bu-calix[5]arene, (ii) *p*-^{t}Bu-calix[8]arene and (iii) *p*-^{t}Bu-calix[6]arene are also possible. Our endeavours in building up larger bis-calixarenes based on the rather conformationally flexible calix[5]arene (unlike calix[4]arene)[1] and another calix[5]arene or higher order calixarenes are also reported.



Scheme 1 General synthesis methodologies in preparing bis-calixarenes.

Results and discussion

The methodology used is an adaptation of previously reported procedures,[9] consisting of complete esterification of a calix[4]-arene, followed by reduction forming the hydroxyethyloxy analogue and tosylation prior to the condensation reaction with calix[*n*]arenes to form bis-calixarenes,[7] which presumably is driven by steric and proximity effects, Scheme 1.

Bis-calixarene **1** was prepared in 32% yield, by condensation of *p*-^{t}Bu-calix[4]arene and the pertosylated derivative of *p*-benzylcalix[4]arene, **4**, under an inert atmosphere and high dilution in acetonitrile in the presence of K_2CO_3 for 3 days. Moreover, under similar reaction conditions, bis-calixarenes **2** and **3** were prepared in 40% and 30% yields respectively, by condensing *p*-^{t}Bu-calix[*n*]arene (*n* = 5, 8) and the pertosylated derivative of *p*-^{t}Bu-calix[4]arene, **5**.[9] Considering the cone conformation requirement to build tubular bis-calixarenes, we have synthesised *p*-benzylcalix[4]arene derivatives **4**, **6** and **7** as precursors to bis-calixarene, **1**, Scheme 2.

Compound **1** was isolated by triturating the crude reaction mixture in a hot ethanol–water mixture to remove unreacted

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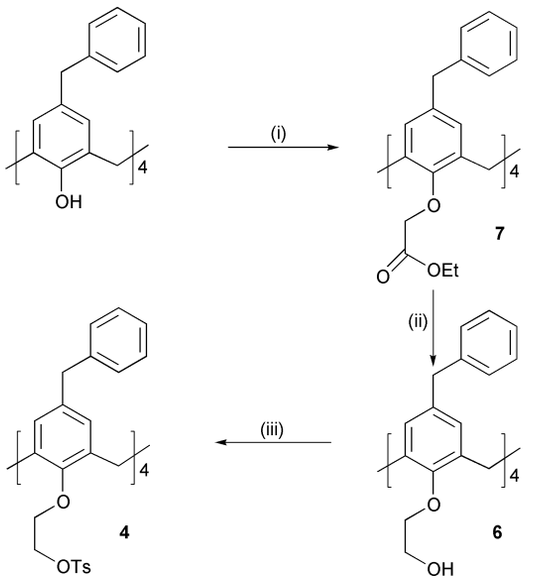


Scheme 2 *Reagents and conditions*: (i) K_2CO_3, $BrCH_2CO_2Et$, CH_3CN, 24 h, reflux. (ii) $LiAlH_4$, $(C_2H_5)_2O$, 24 h, RT. (iii) TsCl, pyridine, 2 days, 0 °C. (iv) K_2CO_3, $ClCH_2CH_2OTs$, CH_3CN, 48 h, reflux.

starting materials, filtration followed by chromatography of the resulting solid, using 1 : 1 dichloromethane–hexane, enabled compound **1** to be isolated from the first and second fractions. Bis-calixarene **2** was produced as a single product and was easily isolated from the crude mixture by first heating the mixture in an ethanol–water mixture and filtering it hot to remove unreacted materials, followed by flash chromatography. In general, the good solubility of the new bis-calixarenes in organic solvents impeded their isolation by crystallisation methods. However, the unreacted starting materials can be removed and recycled if desired, by heating the crude reaction mixture in an appropriate solvent mixture. For instance, unreacted *t*Bu-calix[8]arene in the preparation of bis-calixarene **3** was precipitated using ethyl acetate–hexane mixture and the remaining crude material was subjected to chromatography on a silica gel column using dichloromethane–hexane 1 : 1 to isolate the bis-calixarene, made easy by the high polarity of the pertosylated derivative of *p*-*t*Bu-calix[4]arene, **5**. ^{1}H NMR data is in agreement with their tubular structures showing several doublet AB spin resonances which are symptomatic of fixed conformations of the calixarenes.

It is noteworthy that bis-calixarene, **3** was formed as two isomers in a 1 : 1 ratio (NMR integrations) but their separation was unsuccessful. NMR data is consistent with the presence of a symmetrical isomer A with two sets of AB spin systems from fixed conformations for *p*-*t*Bu-calix[4]arene and *p*-*t*Bu-calix[8]arene units in the macrocycle, and a lower symmetry isomer B with broad peaks. The hydroxy region of the spectrum provides additional structural information; isomer A has a broad singlet for the free hydroxys at 8.80 ppm in contrast to isomer B with four singlets at 9.25, 9.35, 9.40, 9.45, suggestive of the existence of a strong hydrogen bonding array, Fig. 1. Moreover, there are other possible structures for isomer B, also with four different environments for the unbound hydroxy groups. However, in considering the pleated loop conformation of *p*-*t*Bu-calix[8]arene, the proximity effect factor and the relatively short length of the ethyl linkages, in addition to the high values observed for chemical shifts for the unbound hydroxys, which are within range of the chemical shift for hydroxys of *p*-*t*Bu-calix[8]arene (*cf.* 9.6 ppm), the most likely structure for isomer B is that shown in Fig. 1.

From the NMR characterization of bis-calixarene **2** it proved difficult to assign the structure of **2** unambiguously because of the large number of the protons with overlapping regions. However, along with mass spectrometry and microanalyses,

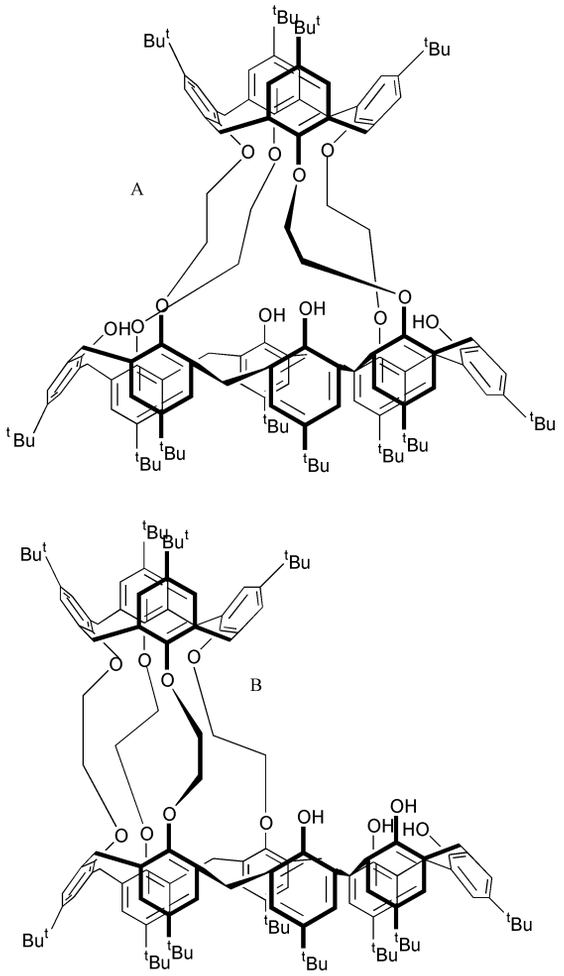


Fig. 1 Structural representation of the isomers of bis-calixarene **3**.

the presence of several doublets between 2.5 and 5.5 ppm, five singlets for the *tert*-butyl groups and four broad doublets and a multiplet for the aromatic protons, the bis-calixarene **2** can be assigned a C_2 symmetry. The ^{1}H NMR was also consistent with the structural rigidity of the molecule with both calixarene moieties in the bis-calixarene adopting the cone conformation, having fewer multiplets arising from the protons of the ethylene bridging linkers in addition to one singlet for the remaining unbound hydroxy proton. Fortunately, the compound has been structurally authenticated (Fig. 2) in the solid state confirming

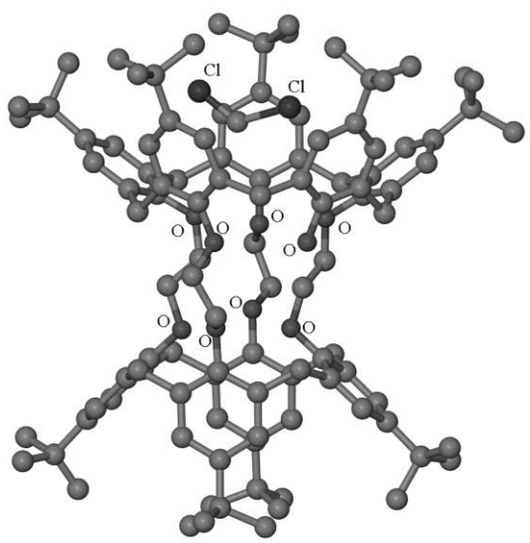


Fig. 2 Molecular structure of *t*Bu-calix[4]arene linked to *t*Bu-calix[5]-arene, bis-calixarene **2** and a molecule guest of CH_2Cl_2.

the NMR prediction and serves as a guide to establish the structures of the other fused calixarenes in conjunction with mass spectrometry and microanalyses.

Bis-calixarene **2** crystallises in a triclinic, $P\bar{1}$ space group. A dichloromethane molecule is included in the cavity of the calix[5]arene moiety, with both C–H bonds directed towards the centres of two aromatic rings (1,3). The short C–H ··· Aryl centroid distances are 2.96 Å and 2.87 Å, indicating that the dichloromethane molecule is tightly bound within the cavity. The calix[5]arene has a distorted cone conformation with tilt angles relative to the plane of the phenolic oxygens of 28.99°, 93.74°, 25.09°, 89.35° and 72.36°. In contrast, the calix[4]arene moiety retains a symmetrical cone conformation similar to that in the bis-calix[4]arene reported by Beer *et al.*,[7] with tilt angles of 39.82°, 68.91°, 35.69° and 84.91°. The crystal packing shows the bis-calixarene forms an infinite linear array with calix[5]arene and calix[4]arene moieties in a head to head arrangement at the van der Waals limit and packing of adjacent linear arrays gives an overall honeycomb arrangement, Fig. 3.

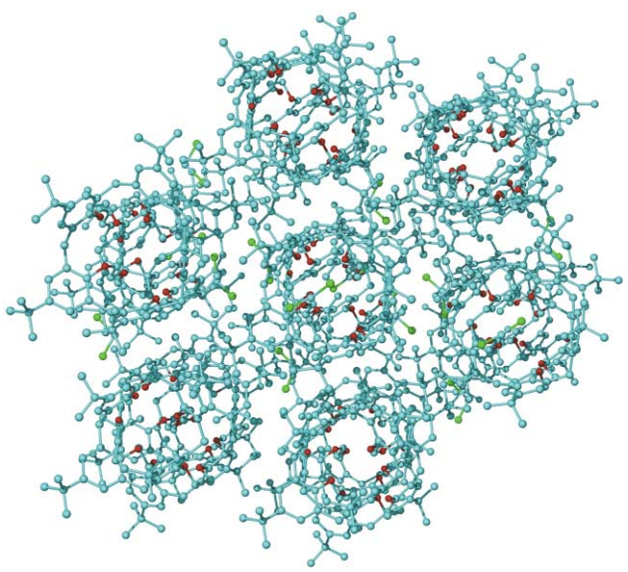


Fig. 3 Crystal packing diagram for stacked bis-calixarenes **2** forming tubular arrays within the crystal lattice (hydrogens and solvent molecules are removed for clarity).

To complete our investigation into the condensation reaction of the pertosylated derivative of *p*-^{t}Bu-calix[4]arene with different ring sizes of *p*-^{t}Bu-calix[*n*]arene (*n* = 4, 5, 6, 8), we have attempted the condensation reaction of the pertosylated derivative, **5** with *p*-^{t}Bu-calix[6]arene under the previously outlined reaction conditions. However, this resulted in the formation of the tris-calixarene **8** isolated in 26% yield, consisting of two ^{t}Bu-calix[6]arenes joined to a ^{t}Bu-calix[4]arene base by ethylene linkages. The ESI-MS analysis shows the presence of the molecular ions $[M + H]^+$ and $[M + Na]^+$ of the tris-calixarene **8**. However, the ^{1}H NMR experiment proved inconclusive in assigning the structure. The presence of several AB spin system resonances and a single broad singlet at 8.6 ppm accounts for the eight free hydroxy protons (with strong hydrogen bonding engagement) suggesting that both *p*-^{t}Bu-calix[6]arenes are connected to *p*-^{t}Bu-calix[4]arene in a similar fashion. Hence, the proposed mode of attachment of the *p*-^{t}Bu-calix[6]arene units to *p*-^{t}Bu-calix[4]arene is **I** or **II**, presented in Fig. 4. It is likely that the *p*-^{t}Bu-calix[6]arenes are in the 'pinched' cone conformation, linked *via* ethylene linkers to *p*-^{t}Bu-calix[4]arene, and forced to adopt the 1,3-alternate conformation to overcome the steric hindrance, *i.e.* structure **I**.

Our pursuit in building larger tubular structures has focused on *p*-^{t}Bu-calix[5]arene as the basic building block. Hence, the penta-ester **9**,[10] pentakis-hydroxyethyloxy **10** and pentakis-tosyloxyethyloxy **11** derivatives were prepared and structurally

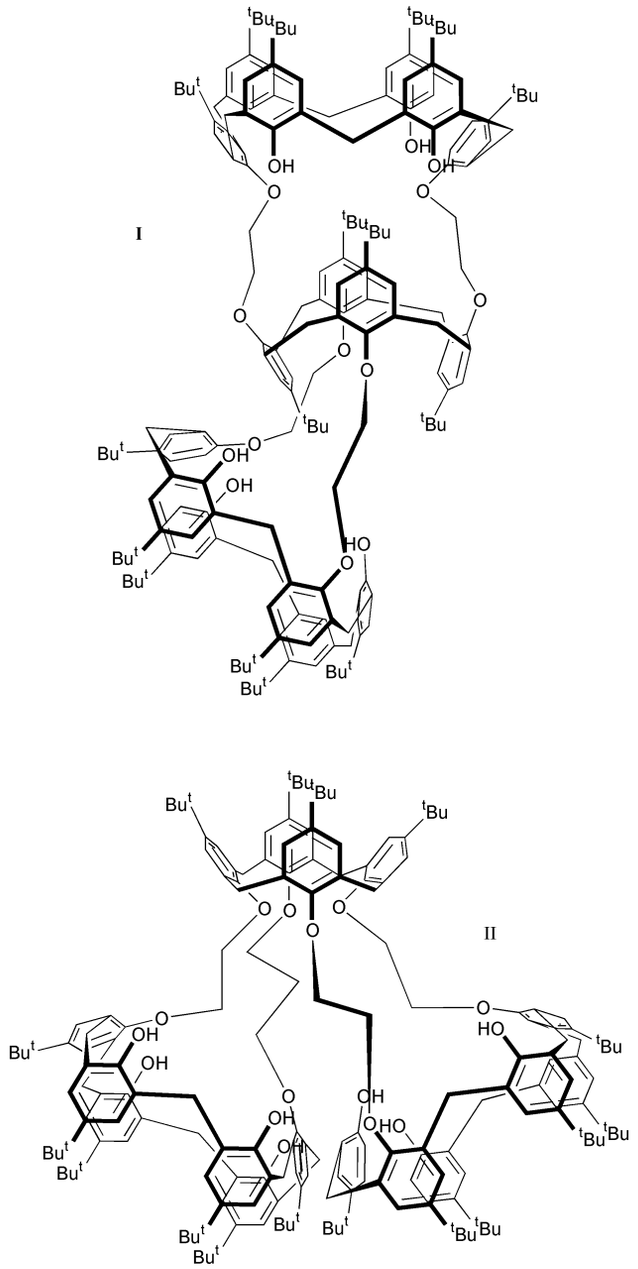
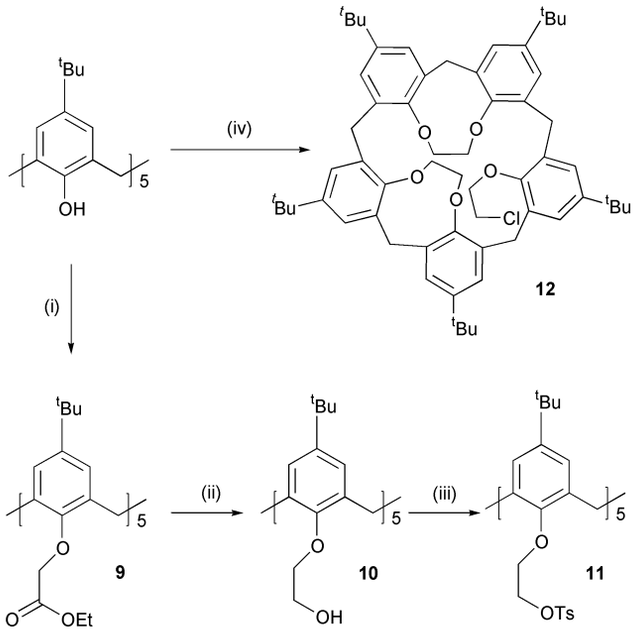


Fig. 4 The two possible isomeric structures for tris-calixarene **8**.

authenticated, with all derivatives shown to be in the cone conformation, an ideal prerequisite to the formation of bis-calix[5]arene (Scheme 3).

Unlike the advances in functionalising calix[4]arene where derivatives in particular conformations can be prepared (cone, 1,2-alternate or 1,3-alternate), calix[5]arene with its larger cavity and greater number of possible conformations results in an unpredictable mixture of conformers. In this instance, we have anticipated the importance of the first derivatisation as a deciding step for the preparation of derivatives in the desired cone conformation. The penta-ester derivative of *p*-^{t}Bu-calix-[5]arene was prepared using a large excess of K_2CO_3 and bromoethyl acetate in a concentrated solution of acetonitrile, and was obtained as a single conformer.

The syntheses of compounds **10** and **11** were adapted from literature procedures,[9] with their structures established in the solid state. The reduction of the ester groups yielded compound **10** crystallising as a potassium complex, with inclusion of a methanol molecule in the cavity, Fig. 5. The potassium is septa-coordinated, involving only four phenoxy oxygens, two of the terminal OH groups which are associated with five membered chelate rings, and the oxygen of methanol included



Scheme 3 *Reagents and conditions*: (i) K_2CO_3, $BrCH_2CO_2Et$, CH_3CN, 24 h, reflux. (ii) $LiAlH_4$, $(C_2H_5)_2O$, 24 h, RT. (iii) TsCl, pyridine, 2 days, 0 °C. (iv) K_2CO_3, $ClCH_2CH_2OTs$, CH_3CN, 48 h, reflux.

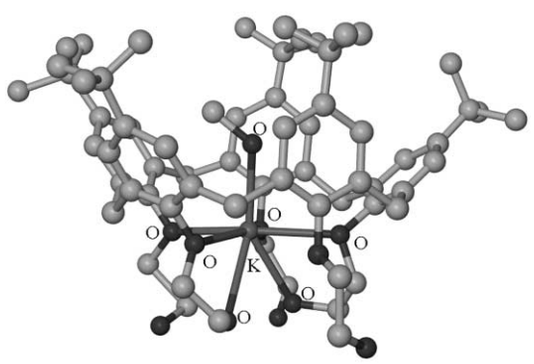


Fig. 5 Molecular structure of the potassium complex of ^{t}Bu-calix[5]-arene derivative **10**, enforced in the cone conformation.

in the cavity. Hence, the potassium is offset relative to the centroid of the phenoxy oxygens, showing that the ion is too small to involve the fifth hydroxyethoxy group in its coordination sphere. Consequently, compound **10** has a distorted cone conformation which is quantified by the tilt angles of the aryl moieties relative to the plane formed by the phenoxy oxygens of the calix[5]arene, which are 40.41°, 93.19°, 53.41°, 59.85° and 91.76°, Fig. 5.

The structure of the pentakis-tosyloxyethyloxy derivative of *p*-^{t}Bu-calix[5]arene, **11**, also shows a distortion of the cone conformation with self-inclusion of one *para-tert*-butyl substituent leaning towards the cavity, with a tilt angle of the phenol plane with respect to the phenoxy oxygens plane of 115.05°, with the lower rim tosyloxyethyloxy group protruding out. The remaining four phenolic moieties have tilt angles of 47.62°, 79.15°, 83.44° and 37.38° indicating that the aryls are in an alternating in-and-out arrangement, Fig. 6.

The coupling reaction of the pentakis-tosyloxyethyloxy derivative of *p*-^{t}Bu-calix[5]arene with another calix[5]arene to form the target compound bis-calix[5]arene was unsuccessful, even with the coupling reaction being performed under high dilution, with different reaction conditions, different temperatures, and using metal templates. For instance, the use of NaH or K-Selectride as the base instead of K_2CO_3 followed by addition of **11** at low temperature prior to reflux only resulted in recovering the starting materials.

A more direct approach involving *p*-^{t}Bu-calix[5]arene and chloroethyltoluene-*p*-sulfonate with K_2CO_3 produced a rather

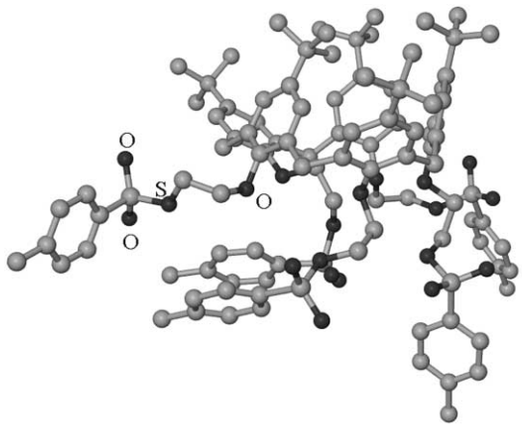


Fig. 6 Molecular structure of the pertosylated derivative of ^{t}Bu-calix-[5]arene, **11** in a distorted cone conformation.

unexpected compound, 1,2–3,5 proximal *p*-^{t}Bu-calix[5]di-crown, **12** in good yield (60%), with the remaining hydroxy bearing a chloroethyl functionality set up for further elaboration, but no presence of bis-calixarenes (Scheme 2). This is presumably a consequence of the higher reactivity of the carbon bearing the tosyl group compared to the carbon bearing a chlorine in the chloroethyltoluene-*p*-sulfonate reagent. The former carbon centres react in the first instance to form the intermediate tris-chloroethyloxy of ^{t}Bu-calix[5]arene, which undergoes self condensation. Also, the 1,3-alternate conformation can be accounted for by the involvement of the tosyl groups in the reaction, as for the behaviour established in calix[4]arene chemistry.[12] Finally, the favoured proximal conformation can be explained by the short length of the ethylene spanner, generating a non-cone immobilised 1,2–3,5 proximal ^{t}Bu-calix[5]di-crown, Fig. 7.

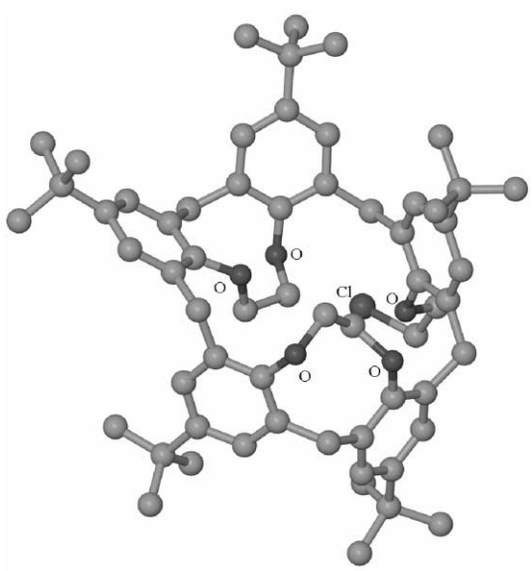


Fig. 7 Molecular structure of 1,2–3,5 proximal ^{t}Bu-calix[5]di-crown, **12** from the X-ray structure of $(\mathbf{12})_4(\text{propan-2-ol})_{6.5}(H_2O)_2$.

In conclusion, we have demonstrated the preparation of novel bis-calixarenes **1**, **2**, **3** and tris-calixarene **8**, with the solid state authentication of *p*-^{t}Bu-[4]arene linked to *p*-^{t}Bu-calix[5]-arene. The synthesis and structural elucidation of precursors **10** and **11** as a potassium complex for **10** and a novel di-crown of calix[5]arene, **12**, are significant advances in calix[5]arene chemistry. The new chemistry for *p*-benzylcalix[4]arene is noteworthy in calix[4]arene chemistry in general. Our current efforts are directed towards the investigation of inclusion properties of these receptors and in the derivatisation of these novel classes of bridged calixarenes.

Experimental

General

Derivatives of *p*-benzylcalix[4]arene and ^{t}Bu-calix[5]arene were prepared using adapted procedures similar to those employed for converting ^{t}Bu-calix[4]arene.[9] Compounds **5** and **9** were prepared as previously described in the literature.[9,10] Compounds **10** and **11** were prepared by an adaptation of literature procedures.[9] *p*-Benzylcalix[4]arene was prepared using our recently reported procedure.[11]

General procedure for preparing bis-calixarenes, 1, 2 and 3

The pertosylated derivative of ^{t}Bu-calix[4]arene, **5** or the pertosylated derivative of *p*-benzylcalix[4]arene, **4** (in the case of preparing **1**) in acetonitrile was added dropwise to a stirred suspension of ^{t}Bu-calix[*n*]arene (n = 4, 5, 8) with potassium carbonate, in dry acetonitrile under nitrogen and the reaction mixture was heated at reflux for 3 days. Acetonitrile was evaporated and the residue was heated in either ethanol–water for **1** and **2** or ethyl acetate–hexane for **3** and filtered hot. The crude mixture was then dissolved in chloroform, washed successively with 1 M HCl, brine solution, water and dried over Na_2SO_4. Filtration followed by evaporation of the solvent yielded a solid which was subjected to a silica gel column using dichloromethane–hexane 1 : 1 as eluent to isolate the bis-calixarenes.†

Compound 1. Yield 32%, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (s, 36H, CH_3), 3.20 (d, 4H, Ar-CH_2-Ar), 3.28 (d, 4H, Ar-CH_2-Ar, J_{AB} 15 Hz), 3.92 (s, 8H, Ar-CH_2-Ph), 4.43 (s, 8H, O-CH_2-), 4.55 (d, 4H, Ar-CH_2-Ar), 4.56 (d, 4H, Ar-CH_2-Ar, J_{AB} 15 Hz), 6.33 (s, 8H, O-CH_2-), 6.54 (s, 8H, Ar-H), 6.88 (s, 8H, Ar-H), 7.01–7.30 (m, 20H, Ph); MS (ESI$^+$) *m*/*z*: 1559.8 [M + Na]$^+$, 1575.8 [M + K]$^+$; $C_{108}H_{112}O_8$ (1561.06): calcd C 84.33, H 7.34%; found C 84.30, H 7.80%.

Compound 2. Yield (40%), ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 (s, 18H, CH_3), 1.14 (s, 18H, CH_3), 1.19 (s, 9H, CH_3), 1.23 (s, 18H, CH_3), 1.24 (s, 18H, CH_3), 3.00 (d, 1H), 3.23 (d, 2H), 3.33 (d, 4H), 3.43 (d, 2H), 3.74 (m, 2H), 3.95 (d, 2H), 4.28 (d, 4H), 4.36 (d, 2H), 4.48 (d, 2H), 4.63(d, 4H), 4.79 (d, 4H), 4.83 (d, 2H), 5.06 (d, 1H), 6.80 (s, 2H, Ar-H), 6.90 (s, 8H, Ar-H), 7.03 (s, 2H, Ar-H), 7.05 (s, 2H, Ar-H), 7.10 (s, 2H, Ar-H), 7.24 (s, 2H, Ar-H), 7.90 (s, 1H, ArOH); MS (ESI$^+$) *m*/*z*: 1565.0 [M + H]$^+$, 1583.01 [M + Na]$^+$, 1597.02 [M + K]$^+$; $C_{107}H_{134}O_9$ (1564.2): calcd C 82.16, H 8.63%; found C 81.95, H 9.23%.

Compound 3 (isomer A). Yield (*ca.* 15%), ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 36H, CH_3), 1.24 (s, 36H, CH_3), 1.26 (s, 36H, CH_3), 3.19 (d, 4H, Ar-CH_2-Ar, J_{AB} 13.6 Hz), 3.51 (d, 4H, Ar-CH_2-Ar, J_{AB} 15.6 Hz), 3.70 (br m, 4H, Ar-CH_2-Ar), 4.30 (br s, 8H, ArO-CH_2-), 4.51 (d, 4H, Ar-CH_2-Ar, J_{AB} 13.6 Hz), 4.70 (br m, 4H, Ar-CH_2-Ar), 4.90 (d, 4H, Ar-CH_2-Ar, J_{AB} 15.6 Hz), 5.30 (s, 8H, ArO-CH_2-), 7.14 (s, 8H, Ar-H), 7.40 (s, 18H, Ar-H), 7.15 (s, 8H, Ar-H), 8.80 (br s, 4H, ArOH); MS (ESI$^+$) *m*/*z*: 1559.8 [M + Na]$^+$, 1575.81 [M + K]$^+$; $C_{140}H_{176}O_{12}$ (2049.3): calcd C 81.98, H 8.66%; found C 81.25, H 9.47%.

Compound 3 (isomer B). Yield (*ca.* 15%), ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80–1.35 (m, 108H, CH_3), 3.18 (br d, 4H, Ar-CH_2-Ar), 3.60–4.40 (br m, 16H, Ar-CH_2-Ar; 16H, ArO-CH_2-CH_2-OAr), 4.65 (br d, 4H, Ar-CH_2-Ar), 6.30–7.30 (m, 72H, Ar-H), 9.25 (s, 1H, ArOH), 9.35 (s, 1H, ArOH), 9.40 (s, 1H, ArOH), 9.45 (s, 1H, ArOH).

† The ^{13}C NMR of the bis-calixarenes were very complex especially at the aromatic region (overlapping peaks).

Synthesis of compound 4. Toluene-*p*-sulfonyl chloride (1.38 g, 7.2 mmol) was added at 0 °C to a solution of the tetrakis-hydroxyethyloxy derivative of *p*-benzylcalix[4]arene (0.58 g, 0.6 mmol) in pyridine (20 ml), whereupon the homogenous solution was stored in the fridge for 2 days. The reaction mixture was poured into ice cold 2 M HCl (100 ml) and the precipitate was collected by filtration. The solid was dissolved in dichloromethane (50 ml), washed successively with HCl, brine and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure, followed by crystallisation from propan-2-ol–methanol affords the pertosylated derivative of *p*-benzylcalix[4]arene, **4**. Yield 72%, mp = 131 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.88 (d, 4H, Ar-CH_2-Ar, J_{AB} 15 Hz), 3.62 (s, 8H, Ar-CH_2-Ph), 4.06 (t, 8H, O-CH_2CH_2OTs, ^3J = 4.3 Hz), 4.18 (d, 1H, Ar-CH_2-Ar), 4.36 (t, 8H, O-CH_2CH_2OTs), 6.42 (s, 8H, Ar-H), 7.0–7.25 (m, 20H, Ph), 7.24 (d, 8H, Ts, J_{AX} 9.3 Hz), 7.72 (d, 8H, Ts); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0 (CH_3), 31.0 (Ar-CH_2-Ar), 41.6 (Ar-CH_2-Ph), 69.9 (O-CH_2CH_2), 72.0 (O-CH_2CH_2), 126.1 (Ar), 128.1 (Ar), 128.5 (Ar), 128.8 (Ar), 129.1 (Ar), 130.1 (Ar), 133.1 (Ar), 134.5 (Ar), 135.1 (Ar), 141.8 (Ar), 144.9 (Ar), 153.6 (Ar); MS (ESI$^+$): *m*/*z*: 1599.5 [M + Na]$^+$; $C_{92}H_{88}O_{16}S_4$ (1576.5): calcd C 70.03, H 5.63%; found C 69.7, H 5.04%.

Synthesis of compound 6. $LiAlH_4$ (0.75 g, 19.8 mmol) was added in small portions at 10 °C to a supension of the tetra-ester of *p*-benzylcalix[4]arene (2.8 g, 2.47 mmol) in diethyl ether (50 ml) and the mixture was stirred overnight at room temperature. 2 M HCl was added in small portions until a firm precipitate had formed which was filtered and the organic layer was dried over $MgSO_4$. The solvent was evaporated, and the crude product was crystallized from dichloromethane–propan-2-ol to give tetrakis-ethoxycarbonylmethoxy of *p*-benzylcalix-[4]arene, **7** as white needle crystals. Yield 42%, mp = 220–222 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.12 (d, 4H, Ar-CH_2-Ar, J_{AB} = 14.6 Hz), 3.65 (s, 8H, Ar-CH_2-Ph), 3.95 (s, 16H, O-CH_2CH_2O-), 4.28 (d, 4H; Ar-CH_2-Ar), 6.55 (s, 8H, Ar-H), 7.01–7.30 (m, 20H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.5 (Ar-CH_2-Ar), 41.6 (Ar-CH_2-Ph), 61.9 (O-CH_2CH_2-), 78.2 (O-CH_2CH_2-), 126.2 (Ar), 128.5 (Ar), 128.8 (Ar), 129.5 (Ar), 134.6 (Ar), 135.7 (Ar), 141.7 (Ar), 153.5 (Ar); MS (ESI$^+$) *m*/*z*: 983.3 [M + Na]$^+$; $C_{64}H_{64}O_8$ (960.5): calcd C 79.96, H 6.72%; found C 81.06, H 6.80%.

Synthesis of compound 7. Anhydrous potassium carbonate (3.4 g, 24.7 mmol), *p*-benzylcalix[4]arene (3.22 g, 4.1 mmol), and bromoethyl acetate (3.6 ml, 32.9 mmol) were heated to reflux in dry acetonitrile (150 ml) under N_2 for 24 hours. The acetonitrile was removed under vacuum and the product extracted into dichloromethane (50 ml), washed with 2 M HCl solution, brine, water and dried with $MgSO_4$ to afford a light amber oil. Addition of warm diethyl ether (50 ml) to the oily residue yielded, upon standing, **6** as a white precipitate (2.8 g, 60%); mp 150 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (m, 12H, -CH_3, ^3J 6 Hz), 2.60–3.80 (br s, 4H, Ar-CH_2-Ar), 3.50–4.30 (br s, 4H, Ar-CH_2-Ar), 4.13 (br s, 16H, Ar-CH_2Ph, -O-CH_2-Me), 4.50 (br s, 8H, ArO-CH_2-R), 6.40–7.10 (br s, 8H, Ar-H), 6.9–7.25 (m, 20H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 14.5 (-CH_3), 31.0 (Ar-CH_2-Ar), 40.8 (Ar-CH_2-Ph), 61.1 (ArO-CH_2-R), 71.2 (O-CH_2-Me), 125.7 (Ar), 128.3 (Ar), 128.7 (Ar), 129.9 (Ar), 133.5 (Ar), 137.6 (Ar), 142.2 (Ar), 154.3 (Ar(C)-OR), 169.9 (C=O); MS (ESI$^+$) *m*/*z*: 1716.8 [M + Na]$^+$; $C_{72}H_{72}O_{12}$ (1128.5): calcd C 76.57, H 6.43%; found C 76.95, H 6.37%.

Compound 8. Yield 26%, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.7–1.40 (m, 144H, CH_3), 2.78 (d, 2H), 3.10 (d, 2H), 3.12 (d, 2H), 3.20 (d, 2H), 3.23 (d, 2H), 3.31 (d, 4H), 3.40 (d, 2H), 3.59 (m, 4H), 3.72 (m, 4H), 3.83 (d, 2H), 3.72 (d, 2H), 4.05 (m, 4H), 4.29 (d, 2H), 4.31 (d, 2H), 4.40 (d, 2H), 4.56 (d, 4H), 4.79 (d, 2H), 4.96 (d, 2H), 4.98 (d, 2H), 7.60–7.20 (m, 32H, Ar-H), 8.60

(br s, 8H, ArOH); MS (ESI$^+$) *m*/*z*: 2700.53 [M + H]$^+$, 2722.6 [M + Na]$^+$, 2755.6 [M(CH_3OH)+Na]$^+$; $C_{184}H_{232}O_{16}$ (2699.8): calcd C 81.86, H 8.66%; found C 79.85, H 9.01%.

Compound 12. A suspension of ^{t}Bu-calix[5]arene (0.3 g, 0.06 mmol) and potassium carbonate (0.35 g, 2.5 mmol) in dry acetonitrile (30 ml) was heated and stirred under nitrogen for half an hour. Chloroethyltoluene-*p*-sulfonate (0.21 g, 0.89 mmol) was added and the reaction mixture brought to reflux for four days. Acetonitrile was removed *in vacuo* and the crude product was dissolved in chloroform, washed with 2 M HCl solution, brine, water, and dried over $MgSO_4$. Crystallisation from propan-2-ol–dichloromethane afforded 4-chloroethanoxy-1,2–3,5-di-crown ^{t}Bu-calix[5]arene in 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00–1.40 (m, 45H, CH_3), 3.07 (d, 1H, Ar-CH_2-Ar, *J* 15.6 Hz), 3.17 (d, 2H, Ar-CH_2-Ar, *J* 14.3 Hz), 3.24–3.38 (m, 6H, Ar-CH_2-Ar, O-CH_2CH_2-), 3.41 (d, 2H, Ar-CH_2-Ar, *J* 15.6 Hz), 3.84–4.40 (m, 6H, O-CH_2-CH_2-), 4.35 (br d, 1H, Ar-CH_3-Ar), 4.49 (d, 2H, Ar-CH_2-Ar, *J* 15.6 Hz), 4.67 (d, 2H, Ar-CH_2-Ar, *J* 14.3 Hz), 6.30–7.40 (m, 10H, Ar-H); MS (ESI$^+$) *m*/*z*: 947.53 [M + Na]$^+$; $C_{61}H_{77}O_5Cl$ (925.7): calcd C 79.17, H 8.39%; found C 78.53, H 8.10%.

X-Ray crystallography ‡

X-Ray data were collected at 123(1) K on an Enraf–Nonius Kappa CCD single crystal diffractometer with Mo-Kα radiation (λ = 0.71073 Å). The structures were solved by direct methods with SHELXS-97 and refined by full or block matrix least-squares on F^2 using SHELXS-97. Unless otherwise indicated, all non-hydrogen atoms were refined anisotropically, and C–H hydrogen positions included as invariants at geometrically estimated positions.

Compound 2 as 2·(CH_2Cl_2)$_{2.5}$. $C_{109.50}H_{138}Cl_5O_9$, M_r = 1775.45, triclinic, $P\bar{1}$, *a* = 13.239(3), *b* = 20.884(4), *c* = 20.883(4) Å, α = 115.45(3), β = 95.24(3), γ = 97.16(3)°, *V* = 5104.6(2) Å^3, *Z* = 2, ρ = 1.155 g cm^{-1}, μ = 0.197 mm^{-1} (no correction), colourless, 0.15 × 0.15 × 0.10 mm, θ_{max} = 28.04°, 80599 reflections measured, 23329 unique reflections (R_{int} = 0.080), 1148 parameters, R_1 = 0.1511 (on 11664 observed data [$I > 2\sigma(I)$]), wR_2 = 0.4449 (all data), *S* = 1.413. Disordered solvent refined isotropically.

Compound 10 as [K(CH_3OH)(10)]Br·solvent. Crystals diffracted extremely weakly with only *ca.* 25% observed data, hence should be regarded as a preliminary investigation and full details are not presented. Structural detail shown in Fig. 3 is well defined, trigonal (hexagonal), $R\bar{3}$, *a* = *b* = 35.3037(10), *c* = 28.5278(6) Å.

Compound 11. $C_{100}H_{120}O_{20}S_5$, M_r = 1802.26, triclinic, $P\bar{1}$, *a* = 14.154(3), *b* = 19.042(4), *c* = 20.780(4) Å, α = 64.68(3), β = 75.15(3), γ = 72.46(3)°, *V* = 4774.2(2) Å^3, *Z* = 2, ρ = 1.254 g cm^{-1}, μ = 0.190 mm^{-1} (no correction), colourless, 0.15 × 0.15 × 0.12 mm, θ_{max} = 25.0°, 43539 reflections measured, 16683 unique reflections (R_{int} = 0.132), 1216 parameters, R_1 = 0.1185 (on 7671 observed data [$I > 2\sigma(I)$]), wR_2 = 0.3056 (all data), *S* = 1.044. One *t*-Bu and one toluene-*p*-sulfonate group were disordered over two sites with one disordered toluene-*p*-sulfonate site refined isotropically with a rigid body refinement.

Compound 12 as (12)$_4$(propan-2-ol)$_{6.5}$(H_2O)$_2$. $C_{263.5}H_{341.5}Cl_4O_{28.5}$, M_r = 4106.67, triclinic, $P\bar{1}$, *a* = 19.1047(5), *b* = 21.9058(3), *c* = 31.8410(8) Å, α = 90.268(1), β = 91.758(1), γ = 112.179(1)°, *V* = 12331.9(5) Å^3, *Z* = 2, ρ = 1.106 g cm^{-1}, μ = 0.112 mm^{-1} (no correction), colourless, 0.20 × 0.15 × 0.10 mm, θ_{max} = 27.88°, 82575 reflections measured, 53357 unique reflections (R_{int} = 0.061), 2611 parameters, R_1 = 0.1412 (on 25726 observed data [$I > 2\sigma(I)$]), wR_2 = 0.3925 (all data), *S* = 1.026. Solvent propanol and water molecules were refined isotropically. One chloro atom was modelled as disordered over two sites at 80 : 20 occupancy.

‡ CCDC reference number(s) 173080–173082. See http://www.rsc.org/suppdata/p1/b1/b109625g/ for crystallographic files in .cif or other electronic format.

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