Calix[5]- and Calix[8]arenes Bridged with Heterocycles[‡]

Serge Konrad,[a] Christian Näther,[b] and Ulrich Lüning*[a]

Keywords: Bridges / Calixarenes / Heterocycles / Macrocycles / Supramolecular chemistry

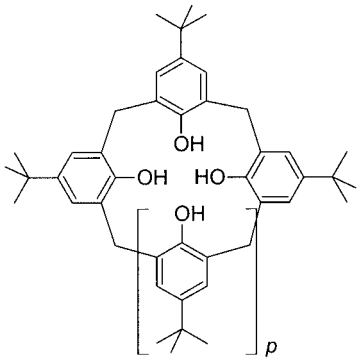
Calix[5]arene (**2**) and calix[8]arene (**4**) reacted with bis(bromomethyl)-substituted heterocycles such as pyridine and 1,10-phenanthroline to give [1+1] condensation products **10** and **16–18** (bridged bimacrocycles) and [2+1] dicalixarenes **11**, **13** and **14**, all of which were fully characterized. Although the bridging capability of both bridging units **5** and **6** is surprisingly similar, calix[5]arene (**2**) could only be bridged with the pyridine derivatives **5**. With calix[8]arene (**4**), the 1,10-phenanthroline bridging reagent **6** gave a cleaner product spectrum than the pyridine reagent **5**. The 1,10-phenanthroline-bridged calix[8]arene **16** was characterized by X-ray analysis.

Introduction

Calixarenes are an easily accessible class of macrocycles. Owing to the remarkable optimization carried out by Gutsche and co-workers,[1–3] three calixarenes, calix[4]arene (**1**), calix[6]arene (**3**) and calix[8]arene (**4**), can be synthesized in excellent yields, and a huge number of derivatives have been synthesized in the past few decades.[4–8] Many of these derivatives, especially the calix[4]arenes, have rigid geometries with functional groups well-defined in space. For this reason, some people call calix[4]arene the "three-dimensional benzene ring".

Calixarene macrocycles can also be bridged,[6,9–13] and remarkable regioselectivities have been observed in bridging reactions. If the bridge contains a functional group, then sterically shielded reagents are accessible. In particular, heterocycles have been exploited as reactive centers in congested environments,[14,15] and calix[4]- and calix[6]arenes have been found to react with appropriate building blocks like 2,6-disubstituted pyridines **5**[10] or 2,9-disubstituted 1,10-phenanthrolines **6**.[11]

The lengths of these bridges match the diameter of calix[6]arene (**3**), and they can bridge calix[6]arene[10,11] from the A to the D ring (we prefer to label the aryl rings by letters[10] because the systematic numbers would be 37 through 42 for calix[6]arene). The resulting heterocycle-bridged calixarenes are interesting compounds. For instance, the 1,10-phenanthroline-bridged compound **8** is a good ligand for copper(I) ions and shows remarkable *syn* selectivity in the copper(I)-catalyzed cyclopropanation of alkenes.[16,17]



p	Calix[*n*]arene	
1	[4]	**1**
2	[5]	**2**
3	[6]	**3**
5	[8]	**4**

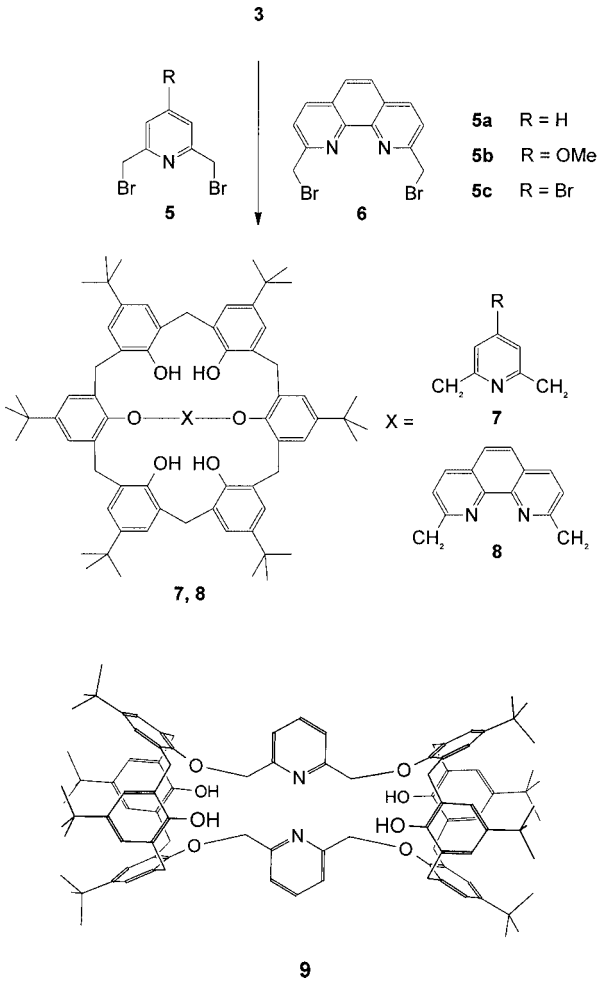
With calix[4]arene (**1**), the "bite angle" of the bridging unit does not match the distance between ring A and C. No pyridine-bridged bimacrocyclic [1+1] calixarene could be isolated, but a [2+2] trimacrocycle **9** was produced.[10]

Results and Discussion

These findings raise the question as to whether calix[5]arene (**2**)[18] can be bridged by 2,6-bis(bromomethyl)pyridines **5** or 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**). Only a few bridged calix[5]arenes are known.[19–21] With calix[5]arene (**2**), the longest possible connection is an A,C bridge as envisioned with calix[4]arene (**1**), however, owing

[‡] Concave Reagents, 44. Part 43: Ref.[22]

[a] Institut für Organische Chemie der Christian-Albrechts-Universität zu Kiel,
Olshausenstr. 40, 24098 Kiel, Germany
Fax: +49-(0)431-880-1558
E-mail: luening@oc.uni-kiel.de
[b] Institut für Anorganische Chemie der Christian-Albrechts-Universität zu Kiel,
Olshausenstraße 40, 24098 Kiel, Germany
Fax: +49-(0)431-880-1520
E-mail: cnaether@ac.uni-kiel.de

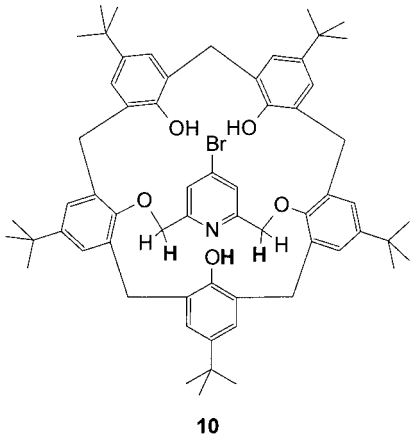


to the larger size of the calix[5]arene macrocycle, the oxygen atoms in position A and C are further apart.

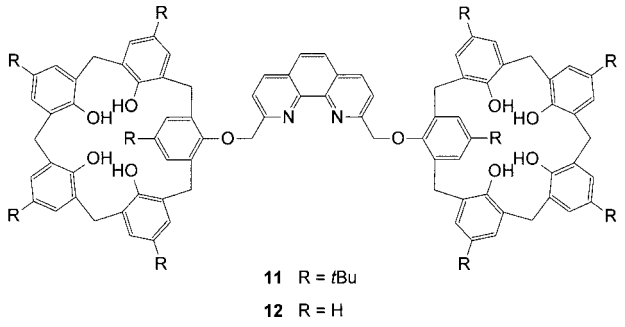
The resulting bridged calix[5]arene possesses less symmetry than an A,D-bridged calix[6]arene such as **7** or **8**. However, the conformations of these bridged calix[6]arenes do not possess the highest possible symmetry. X-ray analyses[22] have shown that the bridge bends to one side and this is why line broadening is observed in their NMR spectra at lower temperatures, especially, when metal ions such as copper(I) are bound to the 1,10-phenanthroline unit in **8**.[17]

Thus, calix[5]arene (**2**) was treated with 4-bromo-2,6-bis-(bromomethyl)pyridine (**5c**) in acetone in the presence of caesium carbonate. After work up and chromatography, 12% of a pyridine-bridged calix[5]arene **10** was isolated and characterized. This new bridged calix[5]arene **10** was found to adopt a conformation in which the pyridine bridge is not perpendicular to the plane of the calixarene macrocycle but is at an angle. The hydrogen atoms that exhibit NOE effects are printed in bold in the structure of **10**.

Next, an analogous bridging experiment was tried with 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**) but only a [2+1] compound, **11**, could be isolated in which the 1,10-phenanthroline unit connects two calix[5]arenes. When this bridging experiment was carried out with a 2:1 stoichiometry of the building blocks, 34% of the dimer **11** was isolated

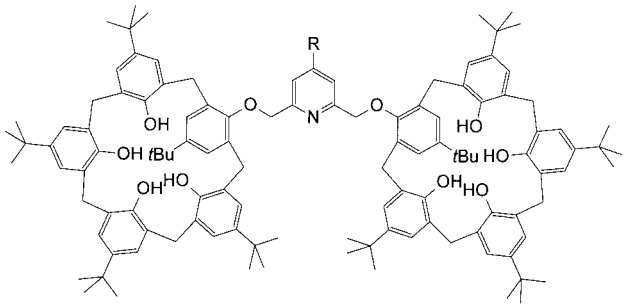


and characterized. Reaction of **6** with a calix[5]arene without the *tert*-butyl groups at the wide rim gave the analogous [2+1] product **12** according to spectroscopic analysis.



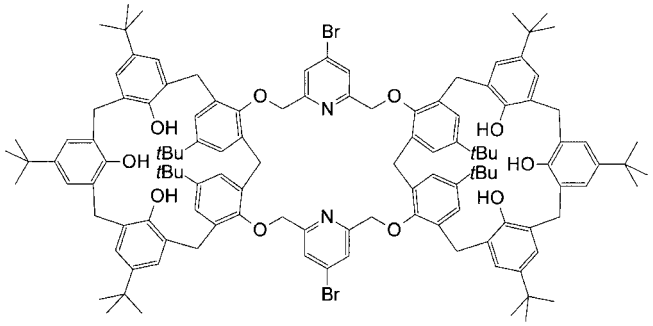
Analogous [2+1] products were also synthesized with 2,6-bis(bromomethyl)pyridines **5** although the chosen stoichiometries of these reactions were originally aimed at the synthesis of the bridged [1+1] compounds and therefore the bridging pyridine units **5** had been used in 10–20% excess. Nevertheless, a 2,6-dimethylene-4-methoxypyridine-connected calix[5]arene dimer **13** and the analogous 4-chloro-substituted compound **14** were obtained in 20 and 34% yields, respectively, and characterized. By chance, the 4-chloro-substituted compound **14** was synthesized even though 4-bromo-2,6-bis(bromomethyl)pyridine (**5c**) was used as the alkylating reagent. The conditions used for the work up were responsible for the halogen exchange. Hydrochloric acid was used to neutralize the solution, and an excess of chloride led to *ipso*-substitution of the bromine atom. This exchange reaction was verified by MALDI-MS analysis. When analyzing the bridging reaction, the initial MALDI mass spectra showed incomplete exchange of the bromine atom. Only continuous stirring with hydrochloric acid for 15 h gave the fully exchanged 4-chloro-substituted compound **14**. Related [2+1] products with xylylene bridges have been described previously.[23]

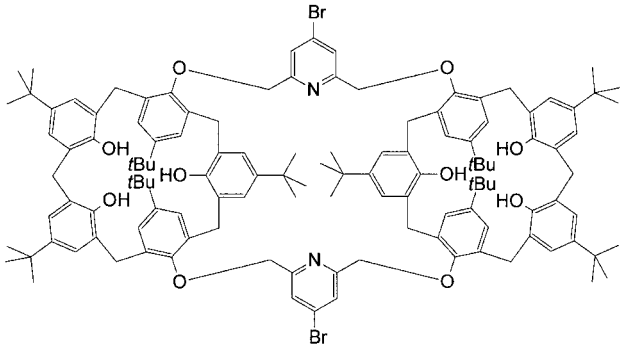
The reaction of calix[5]arene (**2**) with 4-bromo-2,6-bis-(bromomethyl)pyridine (**5c**) as bridging unit led to a third class of pyridine-connected calix[5]arene **15** after repeated chromatography. According to the NMR and mass spectra, two calix[5]arenes (**2**) (Figure 1) were connected by two dimethylenepyridine bridges. This is the same connecting mo-



13: R = OMe, **14**: R = Cl

tif as that found in **9** formed from the reaction of calix[4]-arene (**1**) with bis(bromomethyl)pyridines **5**.[10] The high symmetry of the NMR signals is in accord with a more symmetrical addition product like A,A′:B,B′ or A,A′:C,C′. The third conceivable product A,A′:B,C′ (not shown) is less symmetric and accordingly there should be more signals in the NMR spectrum.



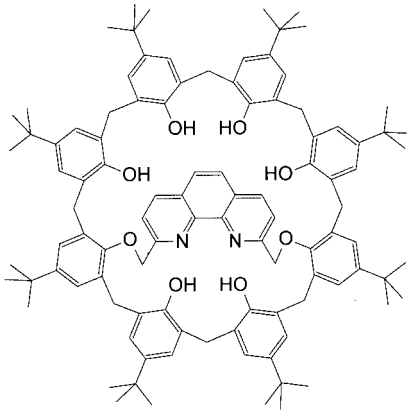


15

Figure 1. Possible connection patterns for the [2+2] product **15** resulting from the reaction of calix[5]arene (**2**) with the pyridine building block **5c**.

Finally, the largest, easily accessible calixarene, calix[8]-arene (**4**), was also used as a substrate in the bridging experiments. Here, the diameter of the macrocycle is definitively large enough for bridging to occur. Many examples of bridged and multiply bridged calix[8]arenes are known.[13] In contrast with earlier experiments, the question now arises as to whether the ring is too large, and therefore whether too many isomers may form when bis(bromomethyl)pyridines **5** and 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**) are used as bridges:[24] bridged, doubly or multiply bridged, connected macrocycles, and their regioisomers, oligomers and polymers.

With both bridging reagents, bridged [1+1] bimacrocycles **16**–**18** were isolated and characterized. The 1,10-phenanthroline bridge gave the best result: 60% of the A,D-bridged calix[8]arene **16** and no other regioisomer could be isolated.



16

Crystals of **16** were obtained from dichloromethane/acetonitrile, and an X-ray analysis was carried out. The structure proves the existence of a [1+1] bimacrocycle and the A,D bridging (Figure 2). In contrast to many other calix[8]-arene derivatives, the conformation of the calixarene macrocycle is an almost perfect circle with most OH groups pointing inwards. This arrangement is stabilized by a hydrogen-bonding network between the phenolic OH groups. The 1,10-phenanthroline bridge, however, does not span the

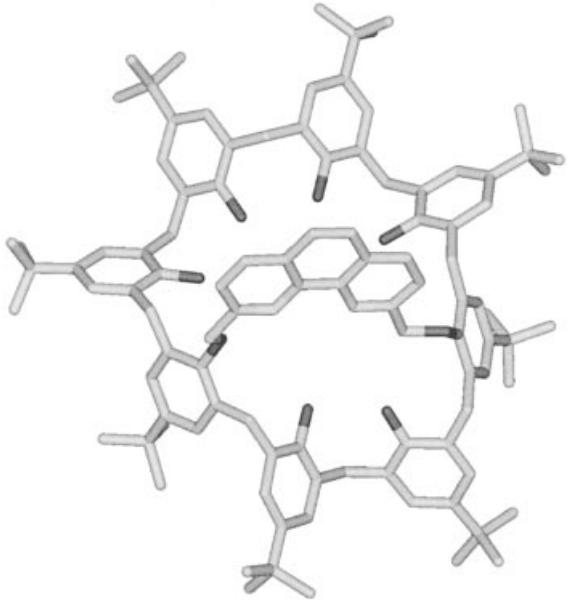
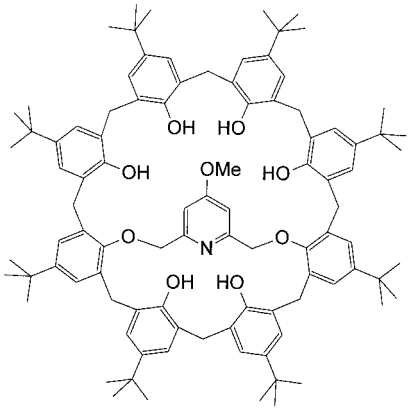


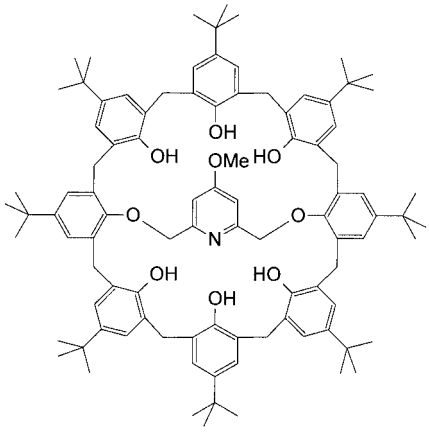
Figure 2. X-ray structure of the bimacrocyclic calix[8]arene derivative **16** with a 1,10-phenanthroline-2,9-bismethylene bridge connecting the phenol rings A and D.

macrocycle symmetrically. As observed with the calix[6]arene derivative **8**, the 1,10-phenanthroline bridge is shifted along the A,D axis and the orientations of the CH_2–O connections between the calixarene macrocycle and the 1,10-phenanthroline bridge are different. In solution, however, there are fast equilibrating processes that give 1,10-phenanthroline a symmetric orientation on the NMR timescale.

The selectivity that led to the formation of only one bimacrocycle in the case of the 1,10-phenanthroline bridge was not observed in the analogous pyridine experiment. Two regioisomeric [1+1] products **17** and **18** were isolated from the reaction mixture by a tedious chromatographic procedure and characterized: an A,D-bridged macrocycle **17** and an A,E-bridged compound **18** were formed in 12 and 10% yields, respectively. Remarkably, experiments involving the related 1,3-xylylene bridge have been described in which either A,E (Neri and co-workers,[25] 80%) or A,D (Shinkai and co-workers,[26] 20%)-bridged compounds were found. The main difference between these bridging experiments seems to be in the metal ion (Na^+[26] and Cs^+[25]) of the base employed. In this work, potassium was used as the counterion in both bridging experiments. The difference observed between the pyridine and the 1,10-phenanthroline experiments must therefore be caused by the nature of the bridge. MALDI mass spectra also show that doubly bridged [1+2] products were formed but owing to the multiplicity and the similarity of the possible (regio)isomers none of them could be isolated.



17



18

Conclusions

2,6-Bis(bromomethyl)pyridines **5** and 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**) react with different calixarenes to give bimacrocyclic [1+1] compounds, and also [2+2] and [2+1] products. The similarity in the bridging capability of the two bridges **5** and **6** is a surprise at first glance because 1,10-phenanthroline is much larger than pyridine, but the angles between the two axes, defined by the bromomethyl groups and the carbon atoms they are connected to, are different too. Therefore both bridges can span a similar distance.[27] Thus, calix[6]arene can react with both heterocycles to form the [1+1] bimacrocycles **7** and **8** in good yields, but the two bridges behave differently with other calixarenes. The pyridine bridge **5** is able to span a slightly smaller gap than the 1,10-phenanthroline bridge **6**: a pyridine-bridged calix[5]arene **10** was isolated whilst the analogous 1,10-phenanthroline compound could not be found. Comparing calix[4]- through calix[6]arene, calix[4]arene (**1**) cannot be spanned by either of the bridges, calix[5]arene (**2**) is spanned by the pyridine bridge, and calix[6]arene (**3**) can be bridged by both bridges.

Not surprisingly, calix[8]arene (**4**) can be spanned by both bridges **5** and **6**. But also with this calixarene, a distinct difference is observed between the two bridges. By using the same base counterion (K^+), two pyridine-bridged calix[8]arenes **17** and **18** were found while with the 1,10-phenanthroline bridge **6**, only one product **16** was isolated and in a remarkable yield. This reflects the higher flexibility of the pyridine bridging unit **5** compared with the tricyclic 1,10-phenanthroline.

Experimental Section

General Remarks: The following chemicals were obtained commercially and were used without further purification: potassium *tert*-butoxide (Fluka), potassium trimethylsilanolate (Aldrich), *N*,*N*-dimethylformamide (Fluka), caesium carbonate (Acros). 4-Chloropyridine-2,6-dimethanol,[28] *p*-*tert*-butylcalix[5]arene (**2**),[18] *p*-*tert*-butylcalix[6]arene (**3**),[2] *p*-*tert*-butylcalix[8]arene (**4**),[3] 2,6-bis(bromomethyl)-4-methoxypyridine (**5b**)[29] and 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**)[30] were prepared according to literature procedures. Tetrahydrofuran was dried by distillation from lithium aluminium hydride and dry acetone was prepared by distillation from phosphorus pentoxide. Column chromatography was carried out on neutral alumina (Macherey–Nagel, activity I) or silica gel (Macherey–Nagel, activity I). The chromatotron used was model 7924T from Harrison Research. The layer of silica gel used in the chromatotron was prepared with silica gel Merck $60PF_{254}$ (with gypsum). ^1H and ^{13}C NMR spectra were recorded with a Bruker AV 200, ARX 300 or DRX 500 instrument (200–500 MHz and 50–125 MHz, respectively). Owing to slow interconversions of conformers, some NMR spectra were measured at an elevated temperature (75 °C) and reduced magnetic field strength (e.g. 200 MHz) resulting in sharper signals (for example, see Figure 3). In a number of cases, the phenolic hydrogen atoms could not be

found under any circumstances. IR spectra were recorded with a Perkin–Elmer Paragon 1000 machine. MALDI mass spectra were recorded with a Bruker Biflex III instrument. Elemental analyses were carried out with a Euro Vector "Euro-EA, Elemental Analyzer" machine.

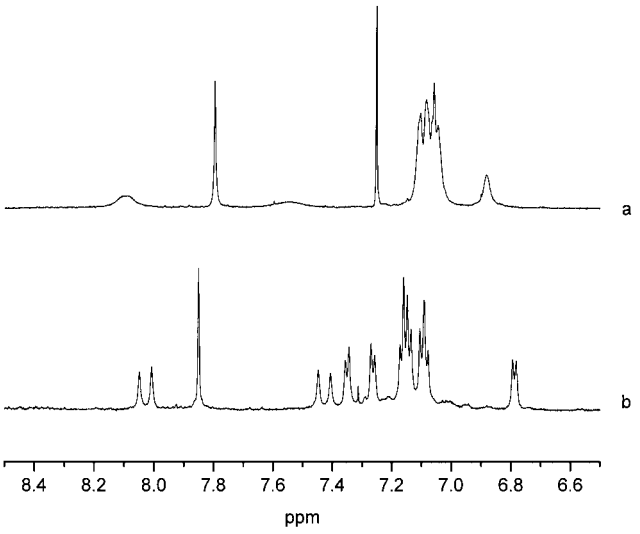


Figure 3. Comparison of the ^{1}H NMR spectra of **16** measured at a) 25 °C, 300 MHz, b) 75 °C, 200 MHz.

4-Bromo-2,6-bis(bromomethyl)pyridine (5c): 4-Bromo-2,6-bis(bromomethyl)pyridine (**5c**)[31] was not synthesized according to the literature procedure: Under reflux, 4-chloropyridine-2,6-dimethanol[28] (1.69 g, 9.74 mmol) was stirred in hydrobromic acid (30 mL, 48%) for 8 h. After neutralizing the solution with sodium carbonate, dichloromethane (100 mL) and water (50 mL) were added and the organic layer was washed with water (2 × 30 mL). The organic layer was evaporated to dryness and the residue was once again stirred under reflux in hydrobromic acid (30 mL, 48%) for 10 h. The hydrobromic acid was neutralized with sodium carbonate. The insoluble residue was filtered off and dried in vacuo. Filtration through a short silica gel column with dichloromethane resulted in the pure white product **5c** (1.81 g, 54%). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 4.49 (s, 4 H, CH_2), 7.56 (s, 2 H, Ar-H) ppm.

5,11,17,23,29-Penta-*tert*-butyl-32,34,35-trihydroxy-31,33-[4-bromopyridine-2,6-diylbis(methyleneoxy)]calix[5]arene (10): Under nitrogen, *p*-*tert*-butylcalix[5]arene (**2**) (466 mg, 575 μmol) and caesium carbonate (1.31 g, 4.03 mmol) as base were refluxed in dry acetone (150 mL). After 1.5 h, 4-bromo-2,6-bis(bromomethyl)pyridine (**5c**) (217 mg, 632 μmol) in acetone (30 mL) was added dropwise over 30 min and then the mixture was refluxed for 6 h. The solution was evaporated to dryness and 0.2 M hydrochloric acid (40 mL) was added to the crude yellow material to form a slurry. After extraction with dichloromethane (3 × 40 mL) the organic layer was washed with water (2 × 40 mL), dried with magnesium sulfate, evaporated to dryness and filtered through a short silica gel column with dichloromethane/methanol (10:1). The product was purified by chromatography using a chromatotron (silica gel, 2 mm). Initially dichloromethane/cyclohexane (1:3) was used as eluent and two fractions containing starting material were collected. The polarity was then increased by using dichloromethane/cyclohexane (1:1) and the two main fractions were collected. The less polar one contained the [2+1] product **14** (55 mg, 11%) and the more polar one contained the bridged [1+1] product **10** (65 mg, 12%, based on the calixarene). To increase the purity of the products, each main fraction was subjected to chromatography again. M.p. 190–210 °C (decomp.). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 0.99 [s, 9 H, 23-C$(CH_3)_3$], 1.16 [s, 18 H, 5-C$(CH_3)_3$, 11-C$(CH_3)_3$], 1.40 [s, 18 H, 17-C$(CH_3)_3$, 29-C$(CH_3)_3$], 3.25 (d, $^2J_{H,H}$ = 13.9 Hz, 1 H, 8-H), 3.40 (d, $^2J_{H,H}$ = 13.8 Hz, 2 H, 20-H, 26-H), 3.43 (d, $^2J_{H,H}$ = 13.6 Hz, 2 H, 2-H, 14-H), 3.75 (br. s, 1 H, 8-H), 4.27 (d, $^2J_{H,H}$ = 13.9 Hz, 2 H, 2-H, 14-H), 5.00 (d, $^2J_{H,H}$ = 13.6 Hz, 2 H, 20-H, 26-H), 5.04 (br. d, $^2J_{H,H} \approx$ 10 Hz, 2 H, O-CH_2-Py), 5.75 (d, $^2J_{H,H}$ = 10.6 Hz, 2 H, O-CH_2-Py), 6.33 (br. s, 2 H, OH), 6.87 (br. s, 2 H, 22-H, 24-H), 6.98 (d, $^4J_{H,H}$ = 2.4 Hz, 2 H, 6-H, 10-H), 7.09 (d, $^4J_{H,H}$ = 2.4 Hz, 2 H, 4-H, 12-H), 7.38 (d, $^4J_{H,H}$ = 2.4 Hz, 2 H, 18-H, 28-H), 7.40 (br. s, 2 H, 16-H, 30-H), 7.83 (br. s, 2 H, Py-H), 9.78 (br. s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 30.4 (C-2, C-14), 31.0 [23-C($CH_3)_3$], 31.1 (C-8), 31.2 (C-20, C-26), 31.4 [17-C($CH_3)_3$, 29-C($CH_3)_3$], 32.5 [5-C($CH_3)_3$, 11-C($CH_3)_3$], 33.8 [5-$C(CH_3)_3$, 11-$C(CH_3)_3$], 33.9 [23-$C(CH_3)_3$], 34.3 [17-$C(CH_3)_3$, 29-$C(CH_3)_3$], 73.3 (O-CH_2-Py), 124.1 (C-22, C-24), 125.3 (C-4, C-12), 125.5 (C-6, C-10), 126.4 (C-16, C-30), 126.6 (Py C-3, C-5), 127.2 (C-7, C-9), 127.8 (C-3, C-13, C-18, C-28), 131.6 (C-21, C-25), 134.2 (C-1, C-15), 134.7 (Py C-4), 135.5 (C-19, C-27), 143.4 (C-5, C-11), 143.8 (C-23), 148.0 (C-17, C-29), 148.2 (C-32), 148.3 (C-34, C-35), 151.1 (C-31, C-33), 157.0 (Py C-2, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 873 (w), 1200 (s), 1362 (m), 1482 (s), 1578 (m), 2959 (s), 3421 (s) cm^{-1}. MALDI-MS: *m*/*z* = 994 [M + H]$^+$, 1016 [M + Na]$^+$, 1032 [M + K]$^+$. $C_{62}H_{74}BrNO_5 \cdot 0.5H_2O$ (1002): calcd. C 74.30, H 7.54, N 1.40; found C 74.12, H 7.68, N 1.40.

2,9-Bis(5,11,17,23,29-penta-*tert*-butyl-32,33,34,35-tetrahydroxycalix[5]aren-31-yloxymethyl)-1,10-phenanthroline (11): Under nitrogen, *p*-*tert*-butylcalix[5]arene (**2**) (2.20 g, 2.71 mmol) and caesium carbonate (2.65 g, 8.15 mmol) as base were stirred in refluxing dry acetone (300 mL). After 1 h, 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**) (490 mg, 1.34 mmol) in acetone (100 mL) was added dropwise over 30 min and then refluxed for 4 h. At room temp., the solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving in dichloromethane (200 mL), the organic layer was washed with water (3 × 80 mL) and the aqueous layer was extracted with dichloromethane (50 mL). The organic layer was dried with magnesium sulfate, evaporated to dryness and filtered through a short silica gel column with dichloromethane/methanol (10:1) as eluent. The product was purified by chromatography using a chromatotron (silica gel, 4 mm). Initially dichloromethane/cyclohexane (1:1) was used before the polarity was increased by addition of small amounts of ethyl acetate to give crude **11** (852 mg, 34%). M.p. 221 °C (decomp.). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 1.08 [s, 18 H, C$(CH_3)_3$], 1.24 [s, 36 H, C$(CH_3)_3$], 1.27 [s, 36 H, C$(CH_3)_3$], 3.41 (d, $^2J_{H,H}$ = 14.1 Hz, 4 H, Ar-CH_2-Ar), 3.46 (d, $^2J_{H,H}$ = 13.9 Hz, 4 H, Ar-CH_2-Ar), 3.49 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, Ar-CH_2-Ar), 4.10 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, Ar-CH_2-Ar), 4.11 (d, $^2J_{H,H}$ = 14.1 Hz, 4 H, Ar-CH_2-Ar), 4.55 (d, $^2J_{H,H}$ = 13.9 Hz, 4 H, Ar-CH_2-Ar), 5.62 (s, 4 H, OCH_2), 7.12 (s, 4 H, Ar-H), 7.17 (d, $^4J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.18 (d, $^4J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.20 (d, $^4J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.21 (d, $^4J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.95 (s, 2 H, Phen 5-H, 6-H), 8.06 (br. s, 8 H, OH), 8.58 (s, 4 H, Phen 3-H, 4-H, 7-H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 30.5 (Ar-CH_2-Ar), 31.2 [C($CH_3)_3$], 31.4 (Ar-CH_2-Ar), 31.5, 31.6 [C($CH_3)_3$], 33.8, 33.9, 34.2 [$C(CH_3)_3$], 77.5 (OCH_2), 121.4 (Phen C-3, C-8), 125.3, 125.4, 125.7, 126.0, 126.3 (arom. C-H), 126.4 (arom. C_q), 126.6 (Phen C-5, C-6), 126.8, 127.0 (arom. C_q), 128.6 (Phen C-4a, C-6a), 132.1 (arom. C_q), 137.8 (Phen C-4, C-7), 142.7, 143.9 (arom. C_q), 145.1 (Phen C-10a, C-10b), 147.3, 147.5 (arom. C_q), 147.6, 149.1 (C-OH), 150.2 (C-OCH_2), 157.9 (Phen C-2, C-9) ppm. IR (KBr): $\tilde{\nu}$ = 1203 (m), 1362 (m), 1484 (s), 2960 (s), 3423 (m) cm^{-1}.

MALDI-MS: *m/z* = 1827 [M + H]$^+$, 1849 [M + Na]$^+$, 1865 [M + K]$^+$. $C_{124}H_{148}N_2O_{10}$ (1826): calcd. C 81.54, H 8.17, N 1.53; found C 81.40, H 8.28, N 1.56.

2,9-Bis(32,33,34,35-tetrahydroxycalix[5]aren-31-yloxymethyl)-1,10-phenanthroline (12): Under nitrogen, calix[5]arene[32] (211 mg, 398 μmol) and caesium carbonate (1.30 g, 3.98 mmol) as base were stirred in refluxing dry acetone (100 mL). After 2 h, 2,9-bis(bromomethyl)-1,10-phenanthroline (**6**) (160 mg, 438 μmol) in dry acetone (50 mL) was added dropwise over 30 min and then refluxed for 4 h. At room temp., the solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving in chloroform (100 mL), the organic layer was washed with water (3 × 30 mL) and the aqueous layer was extracted with chloroform (30 mL). The organic layer was dried with magnesium sulfate, evaporated to dryness and filtered through a short silica gel column with dichloromethane/methanol (10:1) as eluent. The product was purified by chromatography using a chromatotron (silica gel, 2 mm) with dichloromethane as eluent to give the only isolated compound **12** (6 mg, 2%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.44 (br. d, $^2J_{H,H}$ = 14.1 Hz, 4 H, Ar-CH_2-Ar), 3.51 (br. d, $^2J_{H,H}$ = 14.3 Hz, 4 H, Ar-CH_2-Ar), 3.53 (br. d, $^2J_{H,H}$ = 14.4 Hz, 2 H, Ar-CH_2-Ar), 3.93 (br. d, $^2J_{H,H}$ = 14.4 Hz, 2 H, Ar-CH_2-Ar), 4.07 (br. d, $^2J_{H,H}$ = 14.1 Hz, 4 H, Ar-CH_2-Ar), 4.61 (br. d, $^2J_{H,H}$ = 14.3 Hz, 4 H, Ar-CH_2-Ar), 5.42 (br. s, 4 H, OCH_2), 6.75–7.20 (m, 30 H, Ar-H), 7.91 (br. s, 2 H, Phen 5-H, 6-H), 8.21 (br. d, $^3J_{H,H}$ = 8.3 Hz, 2 H, Phen 3-H, 8-H), 8.48 (br. d, $^3J_{H,H}$ = 8.3 Hz, 2 H, Phen 4-H, 7-H).

2,6-Bis(5,11,17,23,29-penta-*tert*-butyl-32,33,34,35-tetrahydroxycalix[5]aren-31-yloxymethyl)-4-methoxypyridine (13): Under nitrogen, *p-tert*-butylcalix[5]arene (**2**) (466 mg, 575 μmol) and caesium carbonate (1.31 g, 4.03 mmol) as base were stirred in dry acetone (100 mL). After 30 min, 2,6-bis(bromomethyl)-4-methoxypyridine (**5b**) (186 mg, 632 μmol) in acetone (30 mL) was added dropwise over 10 min and then the mixture was refluxed for 5 h. The solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving in chloroform (80 mL), the organic layer was washed with water (3 × 30 mL) and the aqueous layer was extracted with chloroform (30 mL). The organic layer was dried with magnesium sulfate, evaporated to dryness and filtered through a short silica gel column with dichloromethane/methanol (10:1) as eluent. The product was purified by chromatography using a chromatotron (silica gel, 2 mm). Initially dichloromethane/cyclohexane (1:2) was used and then the polarity was increased by addition of small amounts of ethyl acetate to give crude **13** (119 mg, 20%, based on the calixarene). M.p. 198 °C (decomp.). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 54 °C): δ = 1.17 [s, 18 H, 29-C(CH_3)$_3$, 29′-C(CH_3)$_3$], 1.31 [s, 36 H, 11-C(CH_3)$_3$, 17-C(CH_3)$_3$, 11′-C(CH_3)$_3$, 17′-C(CH_3)$_3$], 1.33 [s, 36 H, 5-C(CH_3)$_3$, 23-C(CH_3)$_3$, 5′-C(CH_3)$_3$, 23′-C(CH_3)$_3$], 3.45 (d, $^2J_{H,H}$ = 14.1 Hz, 4 H, 8-H, 20-H, 8′-H, 20′-H), 3.49 (d, $^2J_{H,H}$ = 13.9 Hz, 4 H, 2-H, 26-H, 2′-H, 26′-H), 3.50 (d, $^2J_{H,H}$ = 14.1 Hz, 2 H, 14-H, 14′-H), 4.12 (d, $^2J_{H,H}$ = 14.0 Hz, 2 H, 14-H, 14′-H), 4.16 (d, $^2J_{H,H}$ = 13.9 Hz, 4 H, 8-H, 20-H, 8′-H, 20′-H), 4.34 (s, 3 H, O-CH_3), 4.52 (d, $^2J_{H,H}$ = 13.7 Hz, 4 H, 2-H, 26-H, 2′-H, 26′-H), 5.44 (s, 4 H, O-CH_2), 7.24 (d, $^4J_{H,H}$ = 2.5 Hz, 8 H, 4-H, 12-H, 16-H, 24-H, 4′-H, 12′-H, 16′-H, 24′-H), 7.25 (s, 4 H, 28-H, 30-H, 28′-H, 30′-H), 7.27 (d, $^4J_{H,H}$ = 2.5 Hz, 8 H, 6-H, 10-H, 18-H, 22-H, 6′-H, 10′-H, 18′-H, 22′-H), 7.71 (s, 2 H, Py-H), 7.8–8.3 (br. s, 8 H, OH) ppm. ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 54 °C): δ = 31.0 [29-C(CH_3)$_3$, 29′-C(CH_3)$_3$], 30.3 (C-2, C-26, C2′, C-26′), 31.1 (C-8, C-14, C-20, C-8′, C-14′, C-20′), 31.4 [5-C(CH_3)$_3$, 23-C(CH_3)$_3$, 5′C(CH_3)$_3$, 23′C(CH_3)$_3$], 31.3 [11-C(CH_3)$_3$, 17-C(CH_3)$_3$, 11′-C(CH_3)$_3$, 17′-C(CH_3)$_3$], 33.6 [5-*C*(CH_3)$_3$, 11-*C*(CH_3)$_3$, 17-*C*(CH_3)$_3$, 23-*C*(CH_3)$_3$, 5′*C*(CH_3)$_3$, 11′-*C*(CH_3)$_3$, 17′-*C*(CH_3)$_3$, 23′-*C*(CH_3)$_3$], 33.9 [29*C*(CH_3)$_3$, 29′-*C*(CH_3)$_3$], 55.8 (O-CH_3), 77.1 (O-*C*H_2-Py), 107.5 (Py C-3, C-5), 125.5 (C-12, C-16, C-12′, C-16′), 125.6 (C-28, C-30, C-28′, C-30′), 125.2, 125.9 (C-4, C-6, C-22, C-24, C-4′, C-6′, C-22′, C-24′), 126.1 (C-10, C-18, C-10′, C-18′), 126.2 (C-3, C-25, C-3′, C-25′), 126.3 126.7, 127.1 (C-7, C-9, C-13, C-15, C-19, C-21, C-7′, C-9′, C-13′, C15′, C-19′, C-21′), 132.2 (C-1, C-27, C-1′, C-27′), 142.8 (C-5, C-23, C-5′, C-23′), 143.8 (C-11, C-17, C-11′, C-17′), 147.3 (C-33, C-34, C-33′, C34′), 147.4 (C-29, C-29′), 148.6 (C-32, C-35, C-32′, C-35′), 150.3 (C-31, C-31′), 158.0 (Py C-2, C-6), 168.0 (Py C-4) ppm. IR (KBr): $\tilde{\nu}$ = 1203 (m), 1362 (m), 1486 (s), 1604 (m), 2960 (s), 3356 (s) cm^{-1}. MALDI-MS: *m/z* = 1756 [M + H]$^+$, 1778 [M + Na]$^+$, 1794 [M + K]$^+$. $C_{118}H_{147}NO_{11}{\cdot}H_2O$ (1771): calcd. C 79.91, H 8.47, N 0.79; found C 79.83, H 8.56, N 0.82.

2,6-Bis(5,11,17,23,29-penta-*tert*-butyl-32,33,34,35-tetrahydroxycalix[5]aren-31-yloxymethyl)-4-chloropyridine (14): Under nitrogen, *p-tert*-butylcalix[5]arene (**2**) (1.01 g, 1.25 mmol) and caesium carbonate (2.44 g, 7.49 mmol) as base were refluxed in a mixture of dry tetrahydrofuran (100 mL) and dry *N,N*-dimethylformamide (10 mL). After 1 h, 4-bromo-2,6-bis(bromomethyl)pyridine (**5c**) (516 mg, 1.50 mmol) in tetrahydrofuran (70 mL) was added dropwise over 30 min and the mixture was refluxed for 3 h. The solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving the residue in dichloromethane (80 mL), the organic layer was washed with water (3 × 30 mL) and the aqueous layer was extracted with chloroform (30 mL). The organic layer was dried with magnesium sulfate, evaporated to dryness and purified by chromatography on a silica gel column (0.04–0.063 mm) with chloroform as the eluent. Two fractions were collected, a less polar one containing starting material and the more polar product **14** (417 mg, 34%). M.p. 197–212 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.08 [s, 18 H, C(CH_3)$_3$], 1.23 [s, 36 H, C(CH_3)$_3$], 1.28 [s, 36 H, C(CH_3)$_3$], 3.35–3.50 (m, 10 H, Ar-CH_2-Ar), 4.00–4.20 (m, 6 H, Ar-CH_2-Ar), 4.43 (d, $^2J_{H,H}$ = 13.7 Hz, 4 H, Ar-CH_2-Ar), 5.34 (br. s, 4 H, OCH_2), 7.14 (br. s, 4 H, Ar-H), 7.17 (br. s, 8 H, Ar-H), 7.19 (br. s, 8 H, Ar-H), 7.87 (br. s, 8 H, OH), 8.20 (s, 2 H, Py-H) ppm. ^{13}C NMR (50 MHz, $C_2D_2Cl_4$, 75 °C): δ = 29.9, 30.2, 30.3 [C(*C*H_3)$_3$], 32.6, 32.6, 32.9 [*C*(CH_3)$_3$],[33] 73.0 (O-CH_2), 124.3, 124.4, 124.4, 124.6, 124.6, 124.9 (arom. C-H), 125.2, 125.3, 125.5, 125.5, 125.8 (arom. C_q), 131.2 (Py C-4), 141.9, 142.7 (arom. C_q), 146.4 (C-OH), 146.8 (arom. C_q), 147.7 (C-OH), 149.3 (*C*-OCH_2), 156.9 (Py C-2, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 872 (w), 1203 (s), 1362 (m), 1485 (s), 1579 (m), 2960 (s), 3384 (s) cm^{-1}. MALDI-MS: *m/z* = 1761 [M + H]$^+$, 1784 [M + Na]$^+$, 1799 [M + K]$^+$. $C_{117}H_{144}ClNO_{10}{\cdot}C_6H_{12}{\cdot}H_2O$ (1862): calcd. C 79.33, H 8.50, N 0.83; found C 79.34, H 8.55, N 0.75.

Compound 15: Under nitrogen, *p-tert*-butylcalix[5]arene (**2**) (400 mg, 493 μmol) and potassium *tert*-butoxide (221 mg, 1.97 mmol) as base were stirred in dry tetrahydrofuran (150 mL). After 20 min, 4-bromo-2,6-bis(bromomethyl)pyridine (**5c**) (186 mg, 542 μmol) in tetrahydrofuran (80 mL) was added dropwise within 2 h and then the mixture was stirred for another 48 h. The turbid solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving in chloroform (80 mL), the organic layer was washed with water (30 mL) and brine (30 mL) once and dried with magnesium sulfate. After evaporation to dryness the crude material was purified by chromatography on a silica gel column with dichloromethane and recrystallized from dichloromethane/methanol. ^{1}H NMR analysis showed several compounds. The only one separated was the [2+2] calixarene compound **15** (8 mg). It was separated by HPLC on a reversed phase silica gel column with dichloromethane/methanol as the solvents. ^{1}H NMR (500

MHz, $CDCl_3$, 25 °C): δ = 1.19 [s, 36 H, $C(CH_3)_3$], 1.27 [s, 36 H, $C(CH_3)_3$], 1.35 [s, 18 H, $C(CH_3)_3$], 3.40 (d, $^2J_{H,H}$ = 14.0 Hz, 2 H, Ar-CH_2-Ar), 3.46–3.54 (m, 8 H, Ar-CH_2-Ar), 4.13 (d, $^2J_{H,H}$ = 14.0 Hz, 2 H, Ar-CH_2-Ar), 4.40 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, Ar-CH_2-Ar), 4.52 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, Ar-CH_2-Ar), 5.31 (d, $^2J_{H,H}$ = 13.7 Hz, 4 H, OCH_2), 5.42 (d, $^2J_{H,H}$ = 13.7 Hz, 4 H, OCH_2), 7.18 (d, $^2J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.25 (d, $^2J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.31 (s, 4 H, Ar-H), 7.34 (s, 8 H, Ar-H), 7.74 (br. s, 4 H, OH), 7.89 (s, 2 H, OH), 9.16 (s, 4 H, Py-H) ppm. MALDI-MS: *m*/*z* = 1987 $[M + H]^+$, 2009 $[M + Na]^+$, 2025 $[M + K]^+$.

5,11,17,23,29,35,41,47-Octa-*tert*-butyl-50,51,53,54,55,56-hexahydroxy-49,52-[1,10-phenanthroline-2,9-diylbis(methyleneoxy)]calix[8]arene (16): Under nitrogen, *p*-*tert*-butylcalix[8]arene (**4**) (648 mg, 500 μmol) and potassium carbonate (2.00 g, 15.5 mmol) as base were stirred under reflux in a mixture of dry tetrahydrofuran (100 mL) and dry *N*,*N*-dimethylformamide (10 mL). After 30 min, the mixture was allowed to cool to room temperature and 2,9-bis-(bromomethyl)-1,10-phenanthroline (**6**) (220 mg, 600 μmol) in tetrahydrofuran (50 mL) was added dropwise over 30 min, and the mixture was stirred for 15 h. The yellow turbid solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving in dichloromethane (100 mL), the organic layer was washed with water (4 × 30 mL) and the aqueous layer was extracted with dichloromethane (30 mL). The organic layer was dried with magnesium sulfate and the solvents evaporated to dryness. Chromatography on a silica gel column (0.04–0.063 mm) with dichloromethane/ethyl acetate (20:1) as eluent led to the only isolated compound **16** (447 mg, 60%), m.p. 254 °C (decomp.). Analytical samples were recrystallized from cyclohexane or dichloromethane/acetonitrile to give single crystals. ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 75 °C): δ = 1.27 [s, 18 H, $C(CH_3)_3$], 1.28 [s, 18 H, $C(CH_3)_3$], 1.32 [s, 18 H, $C(CH_3)_3$], 1.33 [s, 18 H, $C(CH_3)_3$], 2.67 (br. s, 1 H, Ar-CH_2-Ar), 3.13 (br. d, $^2J_{H,H}$ = 14.9 Hz, 1 H, Ar-CH_2-Ar), 3.51 (d, $^2J_{H,H}$ = 13.5 Hz, 1 H, Ar-CH_2-Ar), 3.67 (br. s, 4 H, Ar-CH_2-Ar), 3.82 (d, $^2J_{H,H}$ = 13.5 Hz, 1 H, Ar-CH_2-Ar), 4.1–4.4 (m, 8 H, Ar-CH_2-Ar), 5.31 (d, $^2J_{H,H}$ = 12.1 Hz, 2 H, Phen-CH_2-O), 5.43 (d, $^2J_{H,H}$ = 12.1 Hz, 2 H, Phen-CH_2-O), 6.83 (br. s, 2 H, Ar-H), 7.09 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.11 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.13 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.15 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.16 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.22 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.29 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, Ar-H), 7.49 (br. s, 2 H, Phen 3-H, 8-H), 7.87 (s, 2 H, Phen 5-H, 6-H), 8.09 (br. s, 2 H, Phen 4-H, 7-H) ppm. ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 75 °C): δ = 30.1, 32.1, 32.7 (Ar-*C*H_2-Ar), 31.2, 31.3, 31.3, 31.5, [C(*C*H_3)$_3$], 32.1, 32.7 (Ar-*C*H_2-Ar), 33.6, 33.7, 33.8, 34.0 [*C*$(CH_3)_3$], 74.7 (OCH_2), 121.9 (Phen C-3, C-8), 125.0, 125.0, 125.2, 125.2 (arom. C-H), 125.3 (arom. C_q), 125.5, 125.6, 126.1 (arom. C-H), 126.3 (Phen C-5, C-6), 127.0 (arom. C-H), 127.1, 127.3, 127.8, 127.8, 127.9 (arom. C_q), 128.2 (Phen C-4a, C-6a), 132.7, 133.1 (arom. C_q), 136.8 (Phen C-4, C-7), 142.6, 143.4, 143.6 [*C*-C$(CH_3)_3$], 145.1 (Phen C-10a, C-10b), 147.1 [*C*-C$(CH_3)_3$], 147.9, 148.1, 148.7 (C-OH), 150.9 (*C*-OCH_2), 157.4 (Phen C-2, C-9) ppm. IR (KBr): $\tilde{\nu}$ = 1203 (m), 1362 (m), 1483 (s), 2959 (s), 3385 (m) cm^{-1}. MALDI-MS: *m*/*z* = 1502 $[M + H]^+$, 1524 $[M + Na]^+$, 1540 $[M + K]^+$. $C_{102}H_{120}N_2O_8{\cdot}H_2O{\cdot}C_6H_{12}$ (1604): calcd. C 80.86, H 8.42, N 1.75; found C 80.95, H 8.60, N 1.85.

X-ray Crystal Structure Determination of 16: Empirical formula $C_{102}H_{120}N_2O_8$, *MW* = 1502.00 g mol^{-1}, *a* = 17.4905(15), *b* = 18.6998(19), *c* = 20.502(2) Å, α = 95.450(9), β = 108.620(8), γ = 107.510(10)°, *V* = 5923.3(10) Å^3, *T* = 170 K, $\rho_{calcd.}$ = 0.842 g cm^{-3}, μ = 0.052 mm^{-1}, triclinic, space group $P\bar{1}$ (No. 2), *Z* = 2, STOE imaging plate diffraction system (IPDS), $Mo_{K\alpha}$ (λ = 0.71073 Å), 33713 measured reflections in the range of 5° ≤ 2θ ≤ 56°, 23893 independent reflections used for refinement and 13827 reflections with $I \geq 2\sigma(I)$, R_{int} = 0.0462. Structure solution was performed using SHELXS-97 whilst structure refinement against F^2 was carried out using SHELXL-97. 1010 refined parameters, R_1 for all reflections with $I \geq 2\sigma(I)$ = 0.1075, wR_2 for all reflections = 0.3310, *GOF* = 1.114, residual electron density = 1.084/–0.718 e Å^{-3}. All non-hydrogen atoms were refined using anisotropic displacement parameters. The C–H hydrogen atoms were positioned with idealized geometry and refined with isotropic displacement parameters using a riding model. The O–H hydrogen atoms were located in a difference map and refined isotropically with ideal bond lengths using the riding model. The crystal contained disordered solvent for which no reasonable structure model was found and therefore the data were corrected for disordered solvent using the "Squeeze" option in Platon.

CCDC-253474 (for **16**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

5,11,17,23,29,35,41,47-Octa-*tert*-butyl-50,51,53,54,55,56-hexahydroxy-49,52-[4-methoxypyridin-2,6-diylbis(methyleneoxy)]calix[8]arene (17): Under nitrogen, *p*-*tert*-butylcalix[8]arene (**4**) (1.02 g, 786 μmol) and potassium trimethylsilanolate (805 mg, 6.29 mmol) as base were stirred in a mixture of dry tetrahydrofuran (200 mL) and dry *N*,*N*-dimethylformamide (20 mL). After 45 min, 2,6-bis-(bromomethyl)-4-methoxypyridine (**5b**) (278 mg, 942 μmol) in tetrahydrofuran (70 mL) was added dropwise over 1 h and then the mixture was stirred for another 18 h. The yellow turbid solution was neutralized with 1 M hydrochloric acid and the solvents were evaporated to dryness. After dissolving in dichloromethane (100 mL), the organic layer was washed with water (3 × 30 mL) and the aqueous layer was extracted with dichloromethane (30 mL). The organic layer was dried with magnesium sulfate, evaporated to dryness and filtered through a short silica gel column using dichloromethane/methanol (10:1) as eluent. Thin-layer chromatography [silica gel, cyclohexane/ethyl acetate (4:1)] showed that the crude product consisted of at least four compounds including the starting material. The compounds were separated by chromatography using a chromatotron (silica gel, 4 mm) and dichloromethane as the solvent. Two fractions were isolated: the first consisted of the A,D-bridged calixarene **17** (131 mg, 12%) and the A,E-bridged calixarene **18** (107 mg, 10%), which were separated by a second chromatography with chloroform/cyclohexane (1:2) as the eluent. The second fraction consisted of several doubly bridged calixarene isomers which could not be separated.

Calixarene **17**: M.p. > 290 °C. ^{1}H NMR (200 MHz, $C_2D_2Cl_4$, 75 °C): δ = 1.28 [s, 18 H, $C(CH_3)_3$], 1.30 [s, 18 H, $C(CH_3)_3$], 1.34 [s, 18 H, $C(CH_3)_3$], 1.35 [s, 18 H, $C(CH_3)_3$], 3.53 (s, 3 H, CH_3), 4.00–4.56 (m, 8 H, Ar-CH_2-Ar), 4.03 (br. s, 4 H, Ar-CH_2-Ar), 4.11 (br. s, 4 H, Ar-CH_2-Ar), 5.10 (br. s, 4 H, OCH_2), 7.07–7.12 (m, 4 H, Ar-H), 7.15 (br. d, $^4J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.20 (br. s, 6 H, Ar-H), 7.27 (br. d, $^4J_{H,H}$ = 2.4 Hz, 2 H, Ar-H), 7.38 (br. d, $^4J_{H,H}$ = 2.4 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $C_2D_2Cl_4$, 75 °C, selected signals[34]): δ = 30.2, 30.3, 30.4, 32.6, 32.7, 32.8, 33.0, 73.0, 124.0, 124.1, 124.5, 124.7, 125.5, 125.8, 126.3, 126.6, 127.3, 131.6, 132.2, 142.0, 142.8, 143.0, 146.7, 147.0, 147.6, 149.9, 156.9 ppm. IR (KBr): $\tilde{\nu}$ = 873 (m), 1203 (s), 1362 (m), 1483 (s), 1605 (m), 2956 (s), 3316 (s) cm^{-1}. MALDI-MS: *m*/*z* = 1432 $[M + H]^+$, 1454 $[M + Na]^+$, 1470 $[M + K]^+$. $C_{96}H_{119}NO_9{\cdot}2CH_2Cl_2$ (1601): calcd. C 73.53, H 7.75, N 0.88; found C 73.42, H 7.92, N 0.98.

5,11,17,23,29,35,41,47-Octa-*tert*-butyl-50,51,52,54,55,56-hexahydroxy-49,53-[4-methoxypyridine-2,6-diylbis(methyleneoxy)]calix[8]-

arene (18): For the synthesis of compound **18** and its separation from **17**, see above. M.p. 222 °C. ^{1}H NMR (200 MHz, $C_2D_2Cl_4$, 75 °C): δ = 1.29 [s, 18 H, $C(CH_3)_3$], 1.34 [s, 36 H, $C(CH_3)_3$], 1.49 [s, 18 H, $C(CH_3)_3$], 3.75 (d, $^2J_{H,H}$ = 13.9 Hz, 4 H, Ar-CH_2-Ar), 3.94 (d, $^2J_{H,H}$ = 13.9 Hz, 4 H, Ar-CH_2-Ar), 4.01 (s, 3 H, OCH_3), 4.05 (d, $^2J_{H,H}$ = 14.5 Hz, 4 H, Ar-CH_2-Ar), 4.13 (d, $^2J_{H,H}$ = 14.5 Hz, 4 H, Ar-CH_2-Ar), 5.50 (br. s, 4 H, OCH_2), 7.16 (br. s, 2 H, Py-H), 7.18–7.22 (m, 8 H, Ar-H), 7.25 (d, $^4J_{H,H}$ = 2.4 Hz, 4 H, Ar-H), 7.28 (br. s, 4 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $C_2D_2Cl_4$, 75 °C, selected signals[34]): δ = 30.1, 30.2, 30.3, 30.4, 31.5, 32.7, 33.1, 33.2, 73.0, 124.5, 125.0, 125.1, 126.1, 126.2, 126.3, 126.9, 132.2, 142.4, 147.3, 149.3 ppm. IR (KBr): $\tilde{\nu}$ = 873 (m), 1119 (m), 1202 (s), 1362 (m), 1483 (s), 1604 (m), 2960 (s), 3404 (m) cm^{-1}. MALDI-MS: *m*/*z* = 1432 $[M + H]^+$, 1454 $[M + Na]^+$, 1470 $[M + K]^+$. $C_{96}H_{119}NO_9 \cdot 1.5H_2O \cdot C_6H_{12}$ (1542): calcd. C 79.44, H 8.76, N 0.91; found C 79.58, H 8.77, N 1.04.

[1] C. D. Gutsche, M. Iqbal, *Org. Synth.* **1990**, *68*, 234–237.
[2] C. D. Gutsche, B. Dhawan, M. Leonis, D. Stewart, *Org. Synth.* **1990**, *68*, 238–242.
[3] J. H. Munch, C. D. Gutsche, *Org. Synth.* **1990**, *68*, 243–246.
[4] C. D. Gutsche, *Calixarenes*, The Royal Society of Chemistry, Cambridge, **1989** and **1992**.
[5] C. D. Gutsche, *Calixarenes Revisited*, The Royal Society of Chemistry, Cambridge, **1998**.
[6] Z. Asfari, V. Böhmer, J. M. Harrowfield, J. Vicens (Eds.), *Calixarenes 2001*, Kluwer Academic Publishers, Dordrecht, **2001**.
[7] L. Mandolini (Ed.), *Calixarenes in Action*, Imperial College Press, London, **2000**.
[8] J. Vicens, V. Böhmer, *Calixarenes, A Versatile Class of Macrocyclic Compounds*, Kluwer Academic Press, Dordrecht, **1991**.
[9] Y. Chen, S. Gong, *J. Incl. Phenom. Macrocycl. Chem.* **2003**, *45*, 165–184.
[10] H. Ross, U. Lüning, *Angew. Chem.* **1995**, *107*, 2723–2725; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2555–2557.
[11] H. Ross, U. Lüning, *Tetrahedron Lett.* **1997**, *38*, 4539–4542.
[12] U. Lüning, H. Ross, I. Thondorf, *J. Chem. Soc., Perkin Trans. 2* **1998**, 1313–1317, and references cited therein.
[13] P. Neri, G. M. L. Consoli, F. Cunsolo, C. Geraci, M. Piattelli in *Calixarenes 2001* (Eds.: Z. Asfari, V. Böhmer, J. M. Harrowfield, J. Vicens), Kluwer Academic Publishers, Dordrecht, **2001**.
[14] J. L. Atwood, J. Steed (Eds.) *Encyclopedia of Supramolecular Chemistry*, Marcel Dekker, New York, **2004**.
[15] U. Lüning, M. Hagen, F. Löffler, T. Marquardt, B. Meynhardt, *J. Incl. Phen. Mol. Recogn. Chem.* **1999**, *35*, 381–387.
[16] F. Löffler, M. Hagen, U. Lüning, *Synlett* **1999**, 1826–1828, and references cited therein.
[17] M. Bühl, F. Terstegen, F. Löffler, B. Meynhardt, S. Kierse, M. Müller, C. Näther, U. Lüning, *Eur. J. Org. Chem.* **2001**, 2151–2160.
[18] D. R. Stewart, C. D. Gutsche, *Org. Prep. Proced. Int.* **1993**, *25*, 137–139.
[19] D. Kraft, R. Arnecke, V. Böhmer, W. Vogt, *Tetrahedron* **1993**, *49*, 6019–6024.
[20] S. Pappalardo, M. F. Parisi, *J. Org. Chem.* **1996**, *61*, 8724–8725.
[21] A. Notti, M. F. Parisi, S. Pappalardo in *Calixarenes 2001* (Eds.: Z. Asfari, V. Böhmer, J. M. Harrowfield, J. Vicens), Kluwer Academic Publishers, Dordrecht, **2001**.
[22] J. P. W. Eggert, J. Harrowfield, U. Lüning, B. W. Skelton, A. H. White, F. Löffler, S. Konrad, *Eur. J. Org. Chem.* **2005**, 1348–1353.
[23] D. Garozzo, G. Gattuso, F. H. Kohnke, A. Notti, S. Pappalardo, M. F. Parisi, I. Pisagatti, A. J. P. White, D. J. Williams, *Org. Lett.* **2003**, *5*, 4025−4028.
[24] With an acridone-containing bridge, a mixture of products was obtained from which a [1+1] bridged calix[8]arene and a [2+1] bis-calix[8]arene were isolated in low yields by preparative TLC: Y. S. Tsantrizos, W. Chew, L. D. Colebrook, F. Sauriol, *Tetrahedron Lett.* **1997**, *38*, 5411–5414.
[25] C. Gaeta, L. Gregoli, M. Martino, P. Neri, *Tetrahedron Lett.* **2002**, *43*, 8875–8878.
[26] A. Ikeda, K. Akao, T. Harada, S. Shinkai, *Tetrahedron Lett.* **1996**, *37*, 1621–1624.
[27] U. Lüning, M. Müller, *Liebigs Ann. Chem.* **1989**, 367–374.
[28] U. Lüning, R. Baumstark, M. Müller, *Liebigs Ann. Chem.* **1991**, 987–998.
[29] E. Weber, F. Vögtle, H.-P. Josel, G. R. Newkome, W. E. Pucket, *Chem. Ber.* **1983**, *116*, 1906–1913.
[30] M. A. Masood, D. J. Hodgson, *Inorg. Chem.* **1993**, *32*, 4839–4844.
[31] H. Takalo, P. Pasanen, J. Kankare, *Acta Chem. Scand., Ser. B.* **1988**, *42*, 373.
[32] C. D. Gutsche, L.-G. Lin, *Tetrahedron* **1986**, *42*, 1633–1640.
[33] The underlying Ar-CH_2-Ar signals could not be separated, even by DEPT.
[34] Owing to the very low signal-to-noise ratio in the ^{13}C NMR spectrum even at 75 °C (caused by a high coalescence temperature) the spectrum cannot be interpreted fully.

Received: October 28, 2004

