Electron-Rich Cavitands via Fourfold Sonogashira Cross-Coupling Reaction of Calix[4]arenes and Bromopyridines – Effect of the Nitrogen Position on Complexation Abilities

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The fourfold Sonogashira cross-coupling reaction is described as efficient synthetic tool for the preparation of calixarenes with relatively deep electron-rich cavities. Reactions of halocalixarenes with terminal alkynes led to coupling products in yields up to 95 %. Two synthetic pathways to the tetraethynylcalixarene **5** were elaborated and their efficencies were compared. This calixarene was used for the synthesis of the three isomeric tetrakis(pyridylethynyl) compounds **10a**–**c**, which were tested as hosts for the binding of pyridinium salts by mass spectrometric and ^{1}H NMR examinations. The effect of the nitrogen position of the host systems revealed an interesting result: calixarene **3** (phenyl), **10a** (2-pyridyl), and **10c** (4-pyridyl) were able to bind NMP$^+$ inside the cavity, calixarene **10b** (3-pyridyl) was not. Association constants were estimated for the complexes in CDCl$_3$/CD$_3$CN (9:1).

Introduction

In biological systems cation-π interactions frequently play an important role in diverse processes e.g. enzyme substrate interactions, acetylcholine receptors or transport through ion channels.[1–4] Theoretical investigations are describing the cation-π interaction as sum of some fundamental, intermolecular forces.[5] For practical considerations, rigid aromatic systems were synthesized as model compounds to study the binding properties of complexes with quaternary compounds like tetramethylammonium or pyridinium salts. For example molecular tweezers,[6] cyclophanes,[7] cyclotriveratrylenes,[8] calixarenes,[9] or resorcinarenes[10] are favourite host molecules because of their definite aromatic binding sites.

It is known, that calix[4]arenes fixed in the *cone* conformation are able to bind quaternary cations in their bowl shaped cavity.[11] Tetrasulfonatocalixarene was one of the first artificial acetylcholine receptors.[12a] Frequently other anionic calix[4]arenes, based on sulfonatocalixarenes are tested as hosts for quaternary cations.[12b–12d] Especially the upper rim is often functionalized to increase the ability of complexing cations.[13] Also some hemicarcerands based on calixarenes are very effective host systems.[14]

We synthesized a set of functionalized *cone*-conformed calixarenes with a relatively deep π-electron-rich cavity by Sonogashira cross-coupling reactions[15] as key steps and examined the influence of the nitrogen position on the ability for binding quaternary compounds.

Results and Discussion

Synthesis and Characterization

Our investigations started with the synthesis of calixarene **3** via a fourfold C–C bond formation by Sonogashira coupling reaction (Scheme 1).[15,16] Fixation of the *cone* conformation was achieved by a sodium templated *O*-alkylation to get calixarene **1**. This rigidified molecule was functionalized at the upper rim by brominating with NBS to give bromocalixarene **2a**. Both synthetic steps were carried out under conditions described in the literature and are achieved in good yields.[17,18] We examined the fourfold Sonogashira coupling of **2a** with phenylacetylene as model reaction: first we tried special conditions with THF as solvent and less triethylamine as usual;[19] as determined by ^{1}H NMR spectroscopy of the crude product, only one- and twofold coupling reactions occurred. Variation of the reaction conditions, such as copper-free methods with (phenylethynyl)magnesium bromide or DMF as solvent under elevated temperature also failed to give the fourfold product.[20,21] With "classical" conditions,[15] triethylamine as base, Pd(PPh$_3$)$_2$Cl$_2$ as catalyst and CuI as co-catalyst at 90 °C, we finally obtained calixarene **3** in 95% yield after column chromatography. Recrystallization from CHCl$_3$/MeOH gave 60% of analytical pure substance.

The Glaser product diphenylbutadiyne was not easy to be removed during the purification of calixarene **3**. There-

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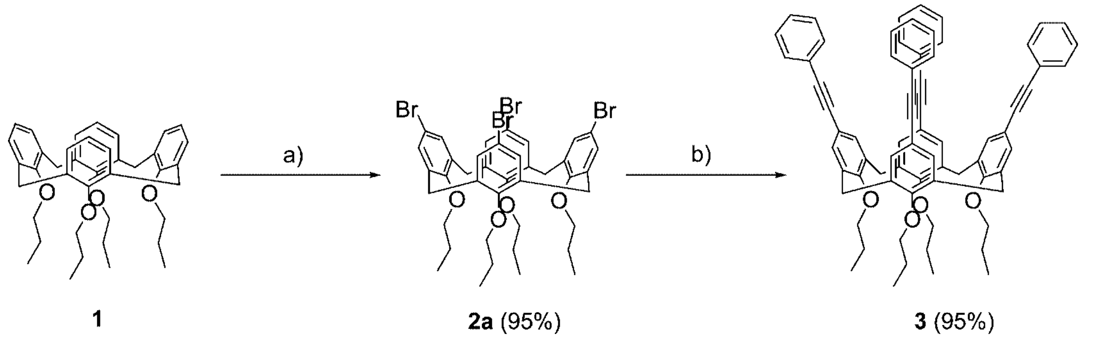
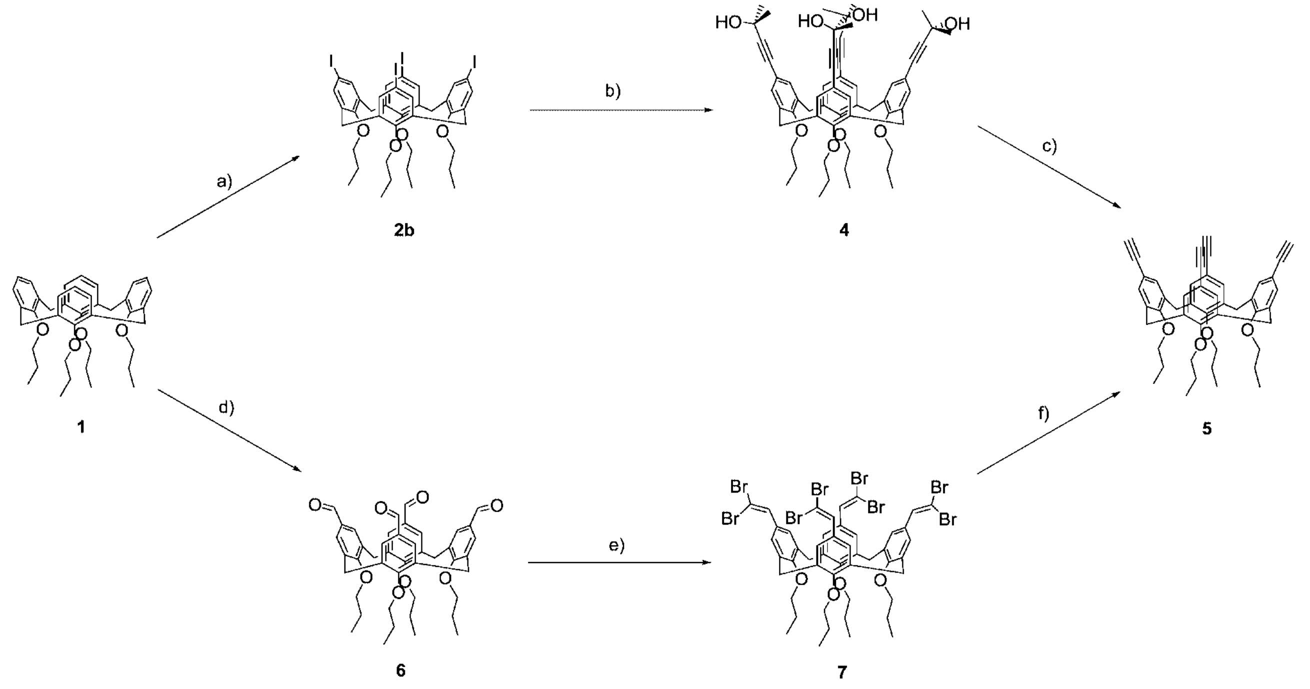


Scheme 1. a) NBS, butanone, room temp., 3 d. b) 5 mol-% $Pd(PPh_3)_2Cl_2$, 10 mol-% CuI, phenylacetylene, triethylamine, 90 °C, 3 d.

fore we decided to synthesize the tetraethynylcalixarene **5** as relay substrate for the coupling reaction with bromopyridines in order to minimize by-products.

Two independent pathways to calixarene **5** were tested (Scheme 2). The first one contains the C–C bond formation of tetraiodated compound **2b**[13c,22] with butynol **12** in piperidine at 70 °C and subsequent deprotection to the terminal alkyne groups, which succeeded with 58% yield. We preferred butynol **12** rather than (trimethylsilyl)acetylene as reactant, because the intrinsic polar hydroxyl groups of tetrabutynol **4** simplify the purification by column chromatography. Deprotection by refluxing compound **4** in 2-propa-



Scheme 2. a) 1. CF_3COOAg, $CHCl_3$, 15 min reflux; 2. I_2, 20 min reflux. b) 5 mol-% $Pd(PPh_3)_2Cl_2$, 10 mol-% CuI, 2-methylbut-3-yn-2-ol (**12**), piperidine, 70 °C, 3 d. c) KOH, 2-propanol, 4 h reflux. d) 1. HMTA, CF_3COOH, 4 h, 130 °C; 2. 1 molar HCl_{aq}, CH_2Cl_2, 3 h. e) 1. zinc, CBr_4, PPh_3 (each 12 equivalents), 22 h at room temperature; 2. adding **6**, 3 h at room temperature. f) 8 equivalents *n*BuLi, THF, 1 h at –78 °C, 1 h at room temperature.

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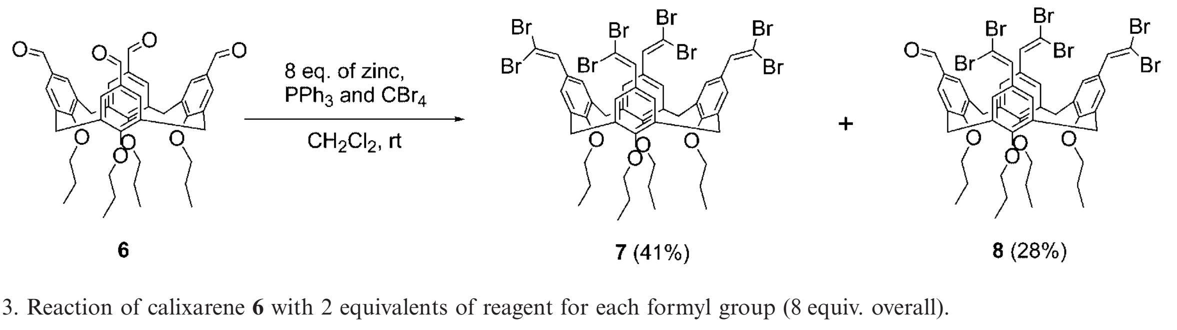


Scheme 3. Reaction of calixarene **6** with 2 equivalents of reagent for each formyl group (8 equiv. overall).

nol in the presence of KOH for 4 hours gave 44% of the desired tetraethynylcalixarene **5,** besides roughly 15% of not fully deprotected material.

Unfortunately, upscaling the Sonogashira reaction of tetraiodated calixarene **2a** with butynol **12** significantly decreased the yield. Therefore, we tried an alternative non-catalytic route (Scheme 2). Beginning with a formylation of **1** with HMTA in trifluoro acetic acid the tetraaldehyde **6** was obtained in 58% yield.[23] However, in several attempts we were unable to achieve the somewhat higher yield reported in literature. The transformation to the tetrakisalkyne was achieved by the general applicable method of Corey and Fuchs,[24] based on the Wittig-type reaction of the tetraaldehyde **6** with a pregenerated reagent from equal amounts of tetrabromomethane, triphenylphosphane and zinc dust in dichloromethane. If two equivalents of the reagent for each formyl group were used, the reaction did not run to completion. Trisalkene **8** was isolated as by-product in 28% yield besides 41% of the tetrabromoalkene **7** as main fraction (Scheme 3). A stoichiometry of 3 equivalents of the reagent gave exclusively tetrabromoalkene **7** in 74% yields. Transformation of compound **7** to the tetraethynylcalixarene **5** was successfully achieved by treatment with two equivalents of *n*-butyllithium for each dibromoethenyl group.[24]

The non-catalytic route achieved an overall yield of 33% compared to the "catalytic" one with 25%.

Because of the higher overall yield and the non-problematic upscaling, the "non-catalytic" route obviously is to be preferred in this case. Other advantages of this pathway are the simple purification of each compound and less overall reaction time.

In the case of the octabromo compound **7** suitable single crystals for X-ray analysis were obtained by the work up procedure (Figure 1).[25] The molecules crystallized in the polar space group *Cc*, with every single molecule as a chiral unit. The molecules are fixed in a *pinched cone* conformation. Two opposite aryl groups are roughly coplanar with a negative angle of –12(1)° and a dihedral angle of 88(1)° of the other two aryl cores.

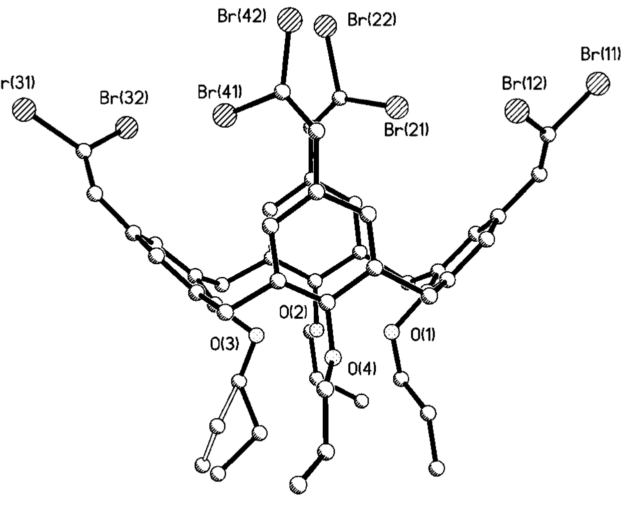


Figure 1. Crystal structure of compound **7**.

Diffraction-quality single crystals of tetraethynyl **5** were grown by slow evaporation of a saturated ethyl acetate solution (Figure 2).[25] In the solid state calixarene **5** is fixed in a *pinched cone* conformation, with a dihedral angle of 116.3(8)° of two opposite phenyl rings and a negative angle of –18.2(8)° of the almost coplanar rings. Two of the alkyne-bonds are slightly distorted with observed angles of 173.4(4)° (C27) and 175.9(4)° (C17). In the elemental cell no included solvent molecules were found. Also C–H-π in-

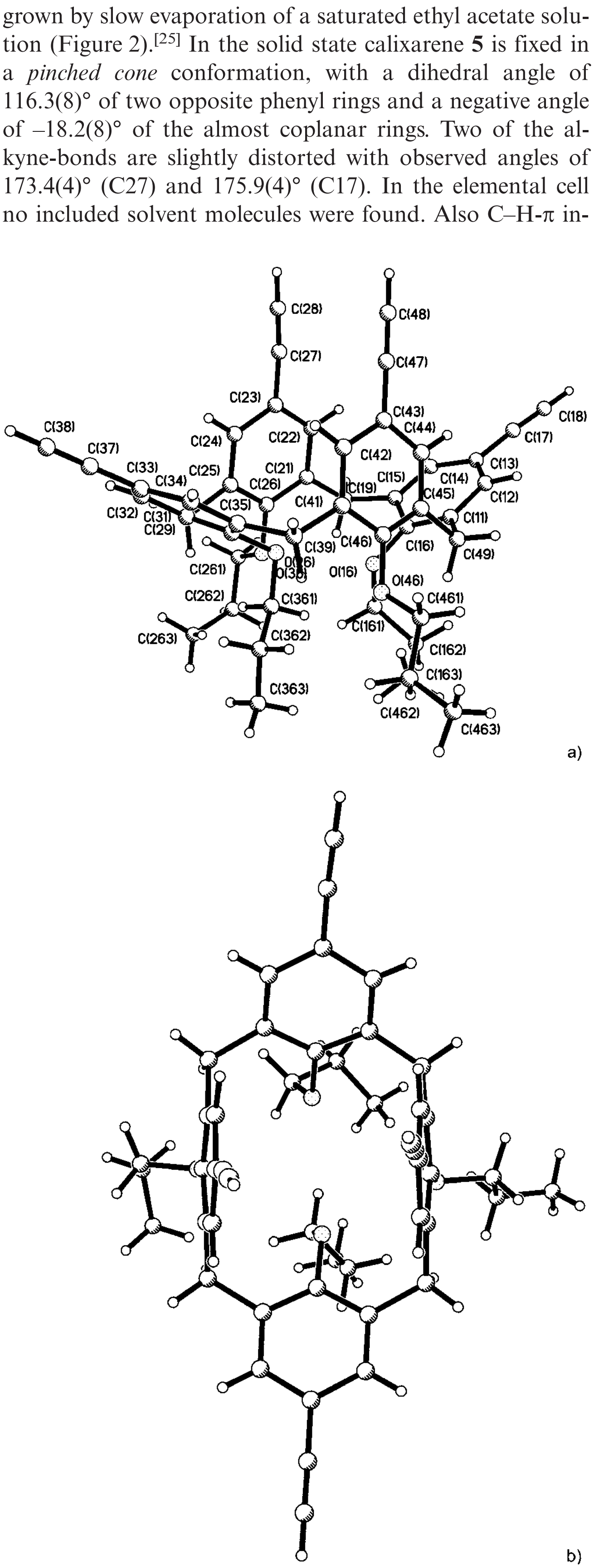
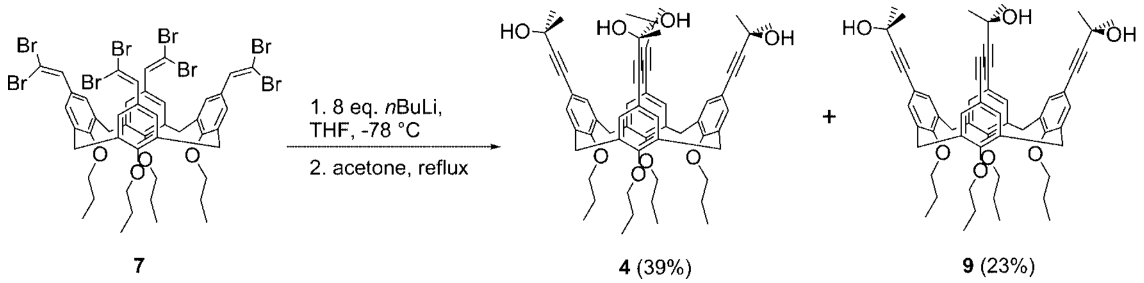
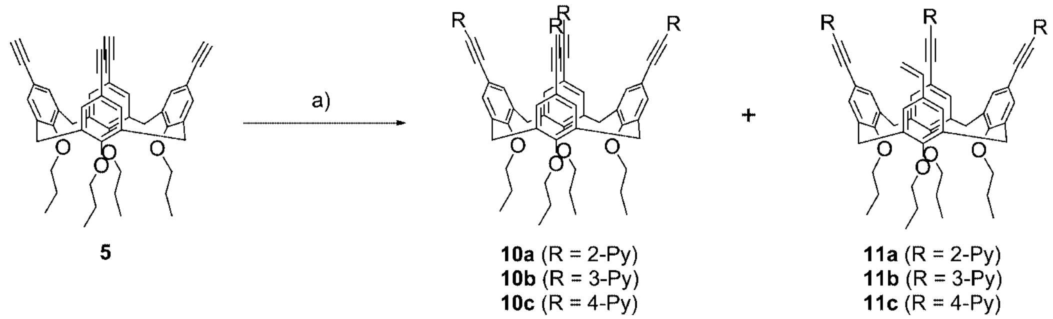


Figure 2. Crystal structure of calixarene **5**.



Scheme 4. Transformation of calixarene **7** to tetrabutynol **4** by subsequent treatment with 8 equiv. *n*BuLi and acetone.



Scheme 5. Sonogashira cross-coupling reaction of calixarene **5** with bromopyridines. a) 5 mol-% $Pd(PPh_3)_2Cl_2$, 10 mol-% CuI, bromopyridine, base; for reaction conditions and yields see Table 1.

Table 1. Conditions and yields of the Sonogashira cross-coupling of calixarene **5** with bromopyridines.

	Conditions				Products and yields			
Entry	Solvent	Temp.	Time	R–Br				
1	NEt_3	60 °C	14 h	2-Py	**10a**	61%	11a	25%
2	NEt_3	70 °C	3 d	3-Py	**10b**	43%	11b	–[a]
3	Hünig base	50–60 °C	2 d	4-Py (HCl salt)	**10c**	27%	11c	–[a]

[a] Not isolated and purified.

Table 2. Characteristic spectroscopic data of synthesized calixarenes. All NMR spectroscopic data were recorded in $CDCl_3$ as solvent. ^1H NMR spectra were measured at 500.1 MHz or 400.1 MHz, ^{13}C NMR spectroscopic data were collected at 125.8 MHz or 100.6 MHz.

		^1H-NMR data, δ in ppm (*J* in Hz)			^{13}C-NMR data, δ in ppm		IR data (in cm^{-1})
Entry	Calixarene	Ar–CH_2–Ar	Selected diagnostic signals	Ar–H	Ar–CH_2–Ar	Alkyne-C	Alkyne
1	**3**	3.23 (13.3) 4.48 (13.2)	–	7.02	30.8	88.1, 89.8	2202
2	**4**	3.08 (13.3) 4.36 (13.2)	–	6.81	30.8	82.4, 92.4	2220
3	**5**	3.10 (13.5) 4.37 (13.4)	2.88[a]	6.83	30.7	75.9, 84.0	2105
4	**7**	3.16 (13.4) 4.43 (13.3)	7.18[b]	6.89	31.0	–	–
5	**8**	3.17 (13.6) 3.25 (13.5) 4.43 (13.5) 4.47 (13.4)	7.05[b], 7.19[b]	6.83, 6.88, 6.93, 7.19	30.9, 31.0	–	–
6	**9**	3.08 (13.6) 3.09 (13.6) 4.35 (13.0) 4.36 (13.5)	3.00[a]	6.73, 6.74, 6.86, 6.92	30.8	76.0, 82.3, 82.6, 84.3, 92.3	2219
7	**10a**	3.17 (13.4) 4.43 (13.4)	7.02[c] (d, 4.0), 7.40[c] (m), 8.43[c] (d, 4.6)	7.00	30.7	87.6, 90.0	2210
8	**10b**	3.23 (13.5) 4.48 (13.6)	7.11[c] (br., s), 7.67[c] (d, 8.0), 8.44[c] (br., s), 8.67[c] (br., s)	6.99	30.9	84.8, 93.3	2210
9	**10c**	3.20 (13.6) 4.46 (13.4)	7.23[c] (d, 4.8), 8.43[c] (br., s)	6.97	30.8	85.7, 94.8	2209
10	**11a**	3.18 (13.6) 4.45 (13.5)	4.76[b], 5.31[b], 6.40[b], 7.12–7.17[c], 7.45[c], 7.53[c], 7.64[c], 8.50[c], 8.57[c]	6.56, 6.83, 7.12–7.17	30.7, 30.9	87.3, 90.6	2209

[a] Terminal alkyne protons. [b] Alkene protons. [c] Pyridyl protons.

teractions of the alkyne hydrogen atoms with the aromatic rings were not observed.[26]

An alternative route to tetrabutynol **4** was achieved by reaction of bromoalkene **7** with *n*BuLi and subsequent quenching of the intermediate lithiathed calixarene with acetone (Scheme 4). However, this reaction took place with 39% yield; in addition the trisacetone adduct **9** was formed as by-product in an amount of 23%.

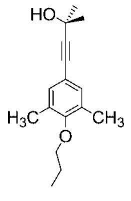
In order to study the influence of the pyridinic nitrogen atom, especially the positional effect on the ability of binding pyridinium ions, we synthesized the host molecules **10a**–**c** by Sonogashira reaction of calixarene **5** with an excess of bromopyridines (Scheme 5, Table 1). The fully coupled products **10a**–**c** were isolated in a range of 27–61% yield. The appearance of the by-products **11a**–**c** in relative high yields is worth mentioning: three alkyne moieties undergo the Pd-catalyzed coupling reaction and one ethynyl group surprisingly is hydrated to an olefin. The calixarenes **11a** to **11c** were identified by their typical alkene signals in the ^{1}H NMR spectra, but only by-product **11a** was exemplarily purified for full characterization.

Structures and conformations of all calixarenes were confirmed by NMR spectroscopy, mass spectroscopy and IR spectroscopy (for diagnostic spectroscopic data see Table 2). All calixarenes are in the *cone* conformation, which was verified by the ^{1}H NMR signals of the methylene protons, appearing as two doublets with a geminal coupling in the case of the fourfold products and the ^{13}C NMR shifts of the methylene carbon at roughly 31 ppm.[9,27] It is worth mentioning that all pyridine protons gave relative broad signals in fact of a possible slow rotation of the pyridine groups around the C_{py}–C_{sp} bond on the NMR time scale.

Complexation Studies

Calixarenes **3**, **4**, **10a**, **10b**, and **10c** were tested as host molecules for quaternary cations: *N*-methylpyridinium (NMP^+) as a nearly planar aromatic cation and tetramethylammonium (TMA^+) as a more globular one were tested.

For NMP^+ iodide in a solution of $CDCl_3/CD_3CN$ (9:1) we observed a paratropic ^{1}H NMR shift by addition of the hosts **3**, **4**, **10a**, and **10c**. In the case of compound **10b** we detected no significant change in NMR shifts for the NMP^+ signals. However, the relative broad pyridine ^{1}H NMR peaks of all pyridine compounds **10a**–**10c**, became sharp multiplets in the presence of NMP^+ iodide. Therefore we assume, that the 3-pyridylcalixarene **10b** builds an *exo* complex with the NMP^+ cation, where the lone electron pairs of the 3-pyridyl moieties are fixed in the direction of the cation, which is centered above the cavity (Scheme 6). This corresponds to studies on pyridine cation interactions revealing a preference for a binding interaction with the lone electron pair rather than with the aromatic π-system.[1a,28] Concerning the calixarenes **3**, **4**, and **10a** we suggest an *endo* complexation inside the cavity in a 1:1 ratio (Scheme 6). This was also verified by NMR experiments with model compound **13**, representing a part of the macrocyclic structure **4**: no significant changes were observed for NMP^+ upon addition model compound **13** (Scheme 7). Thus, an effect of the functional groups and the aromatic rings building an *exo* complex could be excluded. The 1:1 ratio was determined exemplary by a Job-plot of tetrabutynol **4** with NMP^+ iodide.



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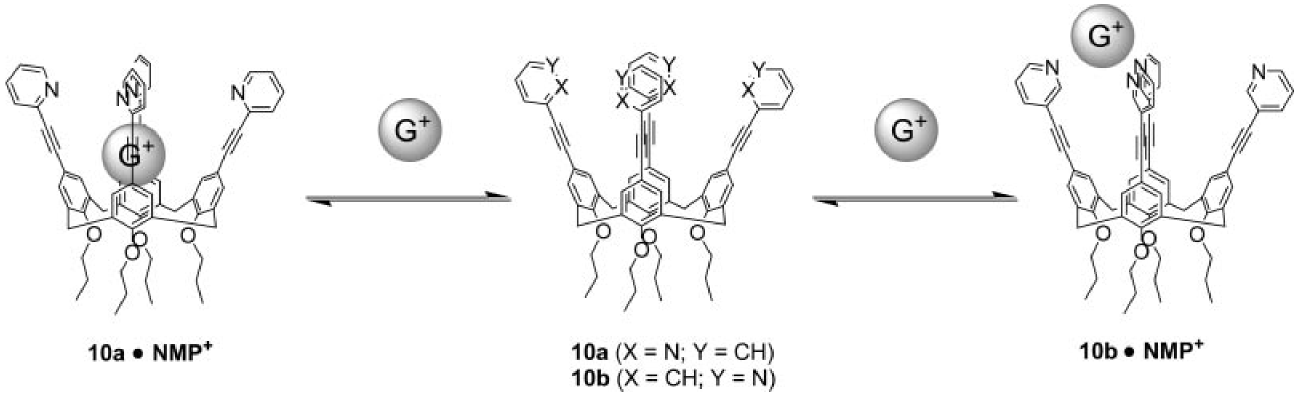
Scheme 7. Structure of model compound **13**.

For the cavitands **3**, **4**, **10a**, and **10c** association constants and $\Delta\delta_{max}$ values were estimated by NMR-titration experiments (Table 3).[29] The values of K_{ass} were in the expected range, compared with those of calixarenes described in the literature.[13,14] For calixarene **3** we estimated a value of 12.8 L·mol^{-1}, for the compounds **4** and **10a** values of 32.5 and 36.8 L·mol^{-1}. The higher complexation energies of **4** and **10a** are explained by the additional electron lone pairs



Scheme 6. Different complexation modes of NMP^+ by calixarenes **10a** and **10b**. Suggested structures of the complexes based on AM1-calculated optimizations (see Supporting Information).

Table 3. Results of the NMR titrations with NMP$^+$ iodide as guest in $CDCl_3/CD_3CN$ (9:1) as solvent.

Calixarene	$\Delta\delta_{max}$ (NCH_3)	$\Delta\delta_{max}$ (Py-2-H)	$\Delta\delta_{max}$ (Py-3-H)	$\Delta\delta_{max}$ (Py-4-H)	K_{ass} (L·mol^{-1})	ΔG (kJ·mol^{-1})
3	–0.61	–0.78	–0.75	–0.74	12.8	–6.4
4	–0.63	–1.61	–1.80	–2.00	32.5	–8.8
10a	–0.43	–0.70	–0.95	–0.93	36.8	–9.1
10b[a]	–	–	–	–	–	–
10c[b]	–0.21	n.d.[c]	–0.22	n.d.[c]	13.4	–6.5

$\Delta\delta_{max}$ in ppm. All data are the average of two runs.

[a] No significant shifts were observed. [b] Results were estimated by a single titration. [c] Could not be determined.

of the hydroxyl or pyridyl groups, directing in a synergetic manner to the centre of the cavity.[30]

In accord with these explanations, the estimated association constant of 13.4 L·mol^{-1} in the case of the 4-pyridylcalixarene **10c** is similar to that of the phenylethynylcalixarene **3**; as anticipated the molecular topology of **10c** with its nitrogen atoms in 4-position has neither an additive "blocking" nor an "binding" effect as it is the case for its isomers **10b** or **10a**. This corroborates the assumption of the strong synergetic effects of the nitrogen lone pairs in calixarenes **10a** and **10c**.

Most interestingly, mass spectroscopy confirms the results obtained by NMR titration: it is known, that calixarene complexes with quaternary cations could be detected in mass spectra.[31] Under common FAB conditions in NBA as matrices of well ground mixtures of the calixarenes and NMP$^+$ iodide, the hosts **3**, **4**, and **10a** (Figure 3) build stable complexes with the NMP$^+$ cation, even in the gas phase. Peaks at m/z = 1090.6 of the complex [**10a**·NMP]$^+$, m/z = 1086.6 of the complex [**3**·NMP]$^+$and m/z = 1014.7 of the complex [**4**·NMP]$^+$ appearing in the spectra. However, the results of the non complexation of calixarene **10b** was also verified by mass spectroscopy (Figure 4). The mixture of NMP$^+$ iodide and **10b** gave only the separate signals of NMP$^+$ at m/z = 94.1 and the [M + H]$^+$-peak of compound **10b** at m/z = 997.5. An additional signal of a complex was not observed.

TMA$^+$ was also tested as guest molecule. Complexes with the calixarenes **3**, **4** and **10a** were detected by mass spectroscopy. Compound **10b** also failed as host for TMA$^+$; again no additional signal was detected in the mass spectrum. In solution ($CDCl_3/CD_3CN$ = 9:1) the signal of the TMA$^+$ methyl protons of the chloride shifted only about $\Delta\delta$ = –0.05 ppm upon addition of the calixarenes **3**, **4**, and **10a**. Because of the rather small effect, we dispended to measure the association constants through NMR titration. This weak interaction could be explained by the more space-filling globular structure of the cation in comparison to the more planar NMP$^+$ cation.

Initial tests were made with the pair tetrabutynol **4** and choline$^+$: a signal of a host-guest complex was observed by mass spectroscopy.

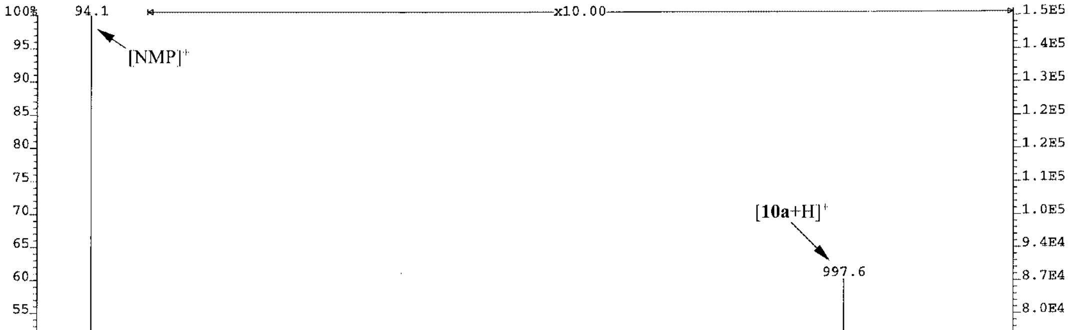


Figure 3. FAB mass spectrum of a ground mixture of calixarene **10a** and NMP$^+$ iodide.

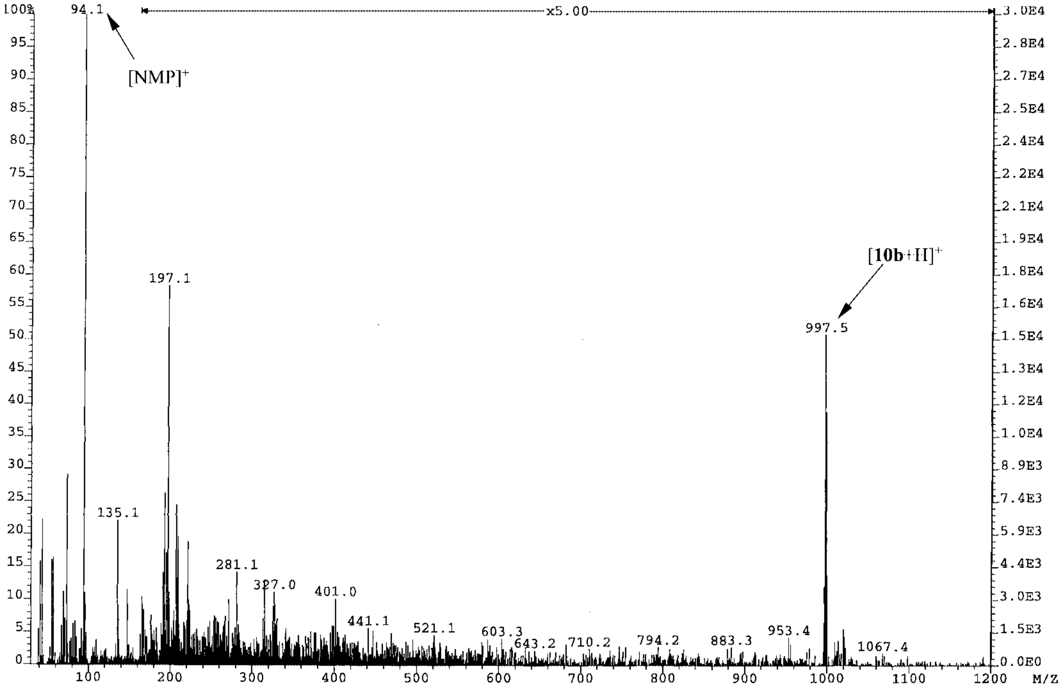


Figure 4. Mass spectrum of a ground mixture of calixarene **10b** and NMP+ iodide.

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Conclusions

Two independent pathways for the synthesis of tetraethynylcalixarene **5** were investigated and evaluated. **5** was used as starting material for Sonogashira cross-coupling reactions with various N-hetarenes. The resulting functionalized compounds **10a**–**10c** were tested as host molecules for the complexation of quaternary cations. **3**, **4**, **10a**, and **10c** are able to bind quaternary cations, compound **10b** not. These results reflect the strong additional influence of the nitrogen lone pairs on complexation. Due to the synergetic effect of the pyridine moieties and the molecular topologies the different values for the determined association constants can be explained.

Currently, we are synthesizing calixarenes with mixed pyridylethynyl substituents on the upper rim, to get more detailed information of the contribution of each pyridyl group to the complexation abilities and stabilities. Furthermore, we are interested on building supramolecular aggregates of the N-hetarene-derived calixarenes **10a**–**c** with palladium or platinum salts.[32]

Experimental Section

General Remarks: Melting points (uncorrected values, °C) were determined with a Kofler Heizmikroskop, Model Reichert Thermovar. Elemental analyses were determined with a Carlo–Erba Elemental Analyser 1106 or with a Vario EL. Infrared spectroscopy was performed with a Bruker Vector 22, a Perkin–Elmer 983G or a Perkin–Elmer 841 (KBr, $\tilde{\nu}$ in cm^{-1}). UV/Vis spectra were recorded with a Perkin–Elmer Lambda 40 apparatus or a Carey Varian 1 ($\lambda_{\text{max.}}$ in nm, ε in cm^2 mmol^{-1}). ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DPX 200, a Bruker WM 300, a Bruker DRX 400 or a Bruker DRX 500. All spectra were calibrated on the internal solvent peak δ (CHCl$_3$) = 7.26 ppm (^{1}H) and 77.05 ppm (^{13}C). Mass spectroscopy was performed with a Varian MAT 311 A, an AMD 604, a Varian MAT CH5 or a VG Autospec. FAB spectra were recorded in NBA as matrix. For TLC SiO$_2$ plates (Polygram SIL G/UV 254) from Macherey–Nagel were used. All compounds were purified by flash chromatography on Kieselgel 60 (Merck, 0.030–0.60 mm). All commercially available products were used without further purification. Solvents were dried with common methods. Calixarenes **1**,[17] **2a**,[18] **2b**[13c] and **6**[23] were synthesized according to the literature.

***cone*-5,11,17,23-Tetrakis(phenylethynyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (3):** To a solution of bromocalixarene **2a** (300 mg, 0.35 mmol) in triethylamine (10 mL) bis(triphenylphosphane)palladium(II) chloride (50 mg, 0.07 mmol) and copper(I) iodide (25 mg, 0.14 mmol) were added and the mixture was degassed with argon for 30 min. Phenylacetylene (820 mg, 7.9 mmol) was added and the reaction mixture was heated 3 days at 90 °C. The reaction mixture was diluted with dichloromethane (35 mL) and filtered through Celite 535. The filtrate was washed 5× with water (20 mL) and solvents were evaporated in vacuo to remain roughly 1 g of a brown solid residue. TLC (light petroleum ether/CH$_2$Cl$_2$, 3:1), R_f = 0.58, 0.48, 0.36, 0.23, 0.15 (**3**), 0.12. The brown residue was separated by column chromatography (PE/CH$_2$Cl$_2$, 3:1) to give 315 mg (95%) of phenylethynylcalixarene **3** as pale yellow solid. Recrystallization from MeOH/CHCl$_3$ gave 200 mg (60%) of **3** as colourless solid. M.p. 310–316 °C. IR (KBr): $\tilde{\nu}$ = 3052 cm^{-1}, 3040, 3019, 3010, 2961, 2933, 2875, 2202, 1700, 1684, 1653, 1559, 1540, 1507, 1492, 1458, 1231, 1201, 1121, 1002, 961, 754, 689. UV/Vis (CH$_3$CN): $\lambda_{\text{max.}}$ (lg ε) = 196 (5.1) nm, 227 (4.8), 286 (4.9), 306 (4.7). ^{1}H NMR (500.1 MHz, CDCl$_3$): δ = 1.05 ppm (t, J = 7.4 Hz, 12 H, OCH$_2$-CH$_2$-CH_3), 1.99 (m, 8 H, OCH$_2$-CH_2-CH$_3$), 3.23 (d, J = 13.3 Hz, 4 H, Ar-CH_2-Ar), 3.94 (t, J = 7.4 Hz, 8 H, Ar-OCH_2-C_2H_5), 4.48 (d, J = 13.2 Hz, 4 H, Ar-CH_2-Ar), 7.02 (s, 8 H, Ar-H), 7.30–7.21 (m, 12 H, Ar′-H), 7.45 (d, J = 7.08 Hz, 8 H, Ar′-H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 10.3 ppm (q, O-CH_2-CH_2-$C$$H_3$), 23.2 (t, O-$CH_2$-$C$$H_2$-$CH_3$), 30.8 (t, Ar-$C$$H_2$-Ar), 77.1 (t, O-$C$$H_2$-$CH_2$-$CH_3$), 88.1 (s, Ar′-C-$C$-Ar), 89.8 (s, Ar′-$C$-C-Ar),117.1 (s, Ar′-CC-ArC), 123.7 (s, Ar′C-CC-Ar), 127.6 (d, ArC-H), 128.1 (d, Ar′C-H), 131.5 (d, Ar′C-H), 131.9 (d, Ar′C-H), 134.7 (s, ArC-CH_2-Ar), 156.9 (s, ArC-O-). MS (EI, 70 eV, 330 °C): m/z (%): 995 (10) [M^+ + 3], 994 (33) [M^+ + 2], 993 (78) [M^+ + 1], 992 (100) [M^+], 44 (21), 42 (5), 41 (9), 40 (11), 39 (5). Elemental analysis calcd. (%) for $C_{72}H_{64}O_4$ (992.48): C: 87.06, H 6.49; found C 86.83, H 6.41.

***cone*-5,11,17,23-Tetrakis(3-hydroxy-3-methylbut-1-ynyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (4). Method A:** To a solution of iodocalixarene **2b** (354 mg, 0.32 mmol) in piperidine (10 mL) bis(triphenylphosphane)palladium(II) chloride (50 mg, 0.07 mmol) and copper(I) iodide (25 mg, 0.14 mmol) were added and the mixture was degassed with argon for 30 min. Butynol **12** (659 mg, 7.8 mmol) was added and the reaction mixture was stirred 3d at 70 °C. To the brown reaction mixture dichloromethane (25 mL) was added and passed through celite 535. The filtrate was washed 5× with water (20 mL), 3× with 1 N aqueous ammonium chloride solution (25 mL) and once with brine (25 mL). The solvents of the organic layer were removed by rotary evaporation and the resulted brown residue purified by flash chromatography. TLC (PE/EA, 1:2), R_f = 0.67, 0.55, 0.27 (**4**), 0.06. The fraction with R_f (PE/EA, 1:2) = 0.27 was dried in vacuo (50 °C, 5.0•10^{-1} mbar) to give 170 mg (58%) of tetrabutynol **4** as pale yellow powder of sufficient purity. 70 mg (24%) of pure compound was obtained by recrystallization from toluene/pentane as colourless solid. M.p. 175–180 °C. IR (KBr): ṽ = 3355 cm^{-1}, 2961, 2978, 2934, 2876, 2220, 1598, 1570, 1462, 1384, 1284, 1229, 1140, 1067, 1003, 953, 875, 560, 498. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 210 (4.8, sh) nm, 224 (4.9), 249 (4.7), 255 (4.7, sh), 283 (3.6, sh), 294 (3.3, sh). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 0.96 ppm (t, J = 7.4 Hz, 12 H, OCH_2-CH_2-CH_3), 1.60 [s, 24 H, (H_3C)$_2$-C(OH)-C], 1.88 (m, 8 H, OCH_2-CH_2-CH_3), 3.08 (d, J = 13.3 Hz, 4 H, Ar-CH_2-Ar), 3.83 (t, J = 7.5 Hz, 8 H, Ar-OCH_2-C_2H_5), 4.36 (d, J = 13.2 Hz, 4 H, Ar-CH_2-Ar), 6.81 (s, 8 H, Ar-H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 10.3 ppm (q, O-CH_2-CH_2-$C$$H_3$), 23.1 (t, O-$CH_2$-$C$$H_2$-$CH_3$), 30.8 (t, Ar-$C$$H_2$-Ar), 31.6 [q, ($C$$H_3$)$_2$C(OH)-C-C-Ar], 65.6 [s, (CH_3)$_2$$C$(OH)-C-C-Ar], 76.8 (t, O-$C$$H_2$-$CH_2$-$CH_3$), 82.4 [s, ($CH_3$)$_2$C(OH)-C-$C$-Ar], 92.4 [s, ($CH_3$)$_2$C(OH)-$C$-C-Ar], 116.4 (s, CC-Ar$C$), 132.0 (d, Ar$C$-H), 134.6 (s, Ar$C$-$CH_2$-Ar$C$), 156.8 (s, Ar$C$-O-). MS (70 eV, 270 °C): m/z (%): 920 (< 2) [M^+], 903 (9), 902 (13), 862 (3), 844 (7), 58 (45), 44 (16), 43 (100), 42 (6), 41 (5). Elemental analysis calcd. (%) for $C_{60}H_{72}O_8$ (921.22): C 78.23, H 7.88; found C 78.20, H 7.84.

Method B: A solution of bromoalkene **7** (844 mg, 0.64 mmol) in dry THF (15 mL) was cooled to –78 °C and 3.6 mL (5.76 mmol) of a *n*-butyllithium solution (1.6 molar in hexane) were added. The reaction mixture was stirred at –78 °C for 1 hour and at room temperature for an additional hour. Dry acetone (10 mL) was added and the reaction mixture was refluxed 3 h. Water (40 mL) was added and the mixture extracted twice with dichloromethane (50 mL). The organic layer was washed twice with water (50 mL), once with brine (50 mL) and dried with magnesium sulfate. Solvents were removed by rotary evaporation. TLC (PE/EA, 1:1): R_f = 0.73, 0.56 (**9**), 0.41 (**4**), 0.22. The residue was separated by column chromatography to give after drying in vacuo: **1. Fraction (R_f = 0.56):** 130 mg (23%) of **9** as colourless crystals. M.p. 140–142 °C. IR (KBr): ṽ = 3312 cm^{-1}, 2976, 2933, 2875, 2219, 1599, 1572, 1461, 1384, 1307, 1278, 1228, 1166, 1139, 1067, 1038, 1003, 960, 876, 589, 562. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 295 nm (3.5), 282 (3.8), 249 (4.8), 231 (4.8). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 0.93–1.00 ppm (m, 12 H, -$OCH_2CH_2C$$H3$), 1.58 [s, 12 H, ($H_3$C)$_2$C(OH)-C-], 1.62 [s, 12 H, (H_3C)$_2$C(OH)-C-], 1.84–1.92 (m, 8 H, OCH_2C$H_2$$CH_3$), 3.00 (s, 1 H, CC-$H$), 3.08 (d, J = 13.6 Hz, 2 H, Ar-CH_2-Ar), 3.09 (d, J = 13.6 Hz, 2 H, Ar-CH_2-Ar), 3.78 (t, J = 7.3 Hz, 4 H, O-C$H_2$$CH_2CH_3$), 3.86 (t, 2 H, O-C$H_2$$CH_2CH_3$), 3.88 (t, 2 H, O-C$H_2$$CH_2CH_3$), 4.35 (d, J = 13.0 Hz, 2 H, Ar-CH_2-Ar), 4.36 (d, J = 13.5 Hz, 2 H, Ar-CH_2-Ar), 6.73 (s, 2 H, Ar-H), 6.74 (s, 2 H, Ar-H), 6.86 (s, 2 H, Ar-H), 6.92 (s, 2 H, Ar-H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 10.19 ppm (q, $OCH_2CH_2$$C$$H_3$), 10.34 (q, $OCH_2CH_2$$C$$H_3$), 23.11 (t, -$OCH_2$$C$$H_2$$CH_3$), 23.18 (t, -$OCH_2$$C$$H_2$$CH_3$), 30.75 (t, Ar-$C$$H_2$–Ar), 31.50, 31.61 [both q, ($C$$H_3$)$_2$C(OH)-CC-Ar], 65.56, 65.68 [both s, (CH_3)$_2$$C$(OH)-CC-Ar], 76.03 (s, H-CC-Ar), 76.92, 77.25 (both t, -O$C$$H_2CH_2CH_3$), 82.28, 82.55 [both s, (CH_3)$_2$C(OH)-CC-Ar], 84.34 (d, H-CC-Ar), 92.33 [two superimposed signals: both s, (CH_3)$_2$C(OH)-CC-Ar], 115.71 (s, ArC-CCH), 116.44 [two superimposed signals: both s, ArC-CC(OH)(CH_3)$_2$], 131.87, 131.94, 132.01, 132.45 (all d, ArC-H), 134.24, 134.31, 134.84, 135.01 (all s, ArC-CH_2-Ar), 156.63, 156.95, 157.43 (all s, all ArC-O-). MS (FAB): m/z (%): 886 (16) [M + Na^+], 862 (10) [M^+], 845 (32) [M – (CH_3)$_2$CO + K^+], 827 (47) [M – (CH_3)$_2$CO + Na^+]. Elemental analysis calcd. (%) for $C_{57}H_{66}O_7$• ½CH_2Cl_2 (905.61): C 76.26, H 7.46, found C 76.28, H 7.45. **2. Fraction (R_f = 0.41):** 230 mg (39%) of tetrabutynol **4** as colourless solid (^{1}H NMR spectroscopic data are in agreement with those in method A).

***cone*-5,11,17,23-Tetraethynyl-25,26,27,28-tetra-*n*-propoxycalix[4]arene (5). Method A:** To a hot solution of potassium hydroxide (130 mg, 2.32 mmol) in 2-propanol (5 mL) a solution of tetrabutynol **4** (200 mg, 0.22 mmol) in 2-propanol (4 mL) was added dropwise and the solution was refluxed for 4 hours. 2-Propanol was removed by rotary evaporation and the residue was suspended with dichloromethane (15 mL). Insoluble materials were filtered off. Dichloromethane was removed in vacuo and 255 mg of crude solid was obtained. TLC (PE/EA, 3:1), R_f = 0.60 (**5**), 0.42. The residue was separated by flash chromatography (PE/EA, 3:1) to give after drying in vacuo (50 °C, 5.0•10^{-1} mbar): **1st Fraction (R_f = 0.60):** 66 mg (44%) of tetraethynylcalixarene **5** as colourless needles. M.p. > 300 °C. IR (KBr): ṽ = 3306 cm^{-1}, 2962, 2922, 2875, 2105, 1653, 1559, 1457, 1384, 1275, 1218, 1136, 1062, 1041, 1003, 959, 878, 650, 582, 500. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 209 (4.9, sh) nm, 222 (4.9), 250 (4.7, sh), 280 (3.7, sh), 287 (3.5, sh). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 0.96 ppm (t, J = 7.4 Hz, 12 H, OCH_2–CH_2–CH_3), 1.88 (m, 8 H, OCH_2-CH_2-CH_3), 2.88 (s, 4 H, C-C-H), 3.10 (d, J = 13.5 Hz, 4 H, Ar-CH_2-Ar), 3.84 (t, J = 7.5 Hz, 8 H, Ar-OCH_2-C_2H_5), 4.37 (d, J = 13.4 Hz, 4 H, Ar-CH_2-Ar), 6.83(s, 8 H, Ar-H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 10.3 ppm (q, O-CH_2-CH_2-$C$$H_3$), 23.2 (t, O-$CH_2$-$C$$H_2$-$CH_3$), 30.7 (t, Ar-$C$$H_2$-Ar), 75.9 (s, ArC-$C$CH), 77.0 (t, O-$C$$H_2$-$CH_2$-$CH_3$), 84.0 (d, H-$C$-C-Ar), 116.0 (s, HCC-Ar$C$), 132.3 (d, Ar$C$-H), 134.7 (s, Ar$C$-$CH_2$-Ar$C$), 157.2 (s, Ar$C$-O-). MS (70 eV, 270 °C): m/z (%): 690 (14) [M^+ + 2], 689 (52) [M^+ + 1], 688 (100) [M^+], 645 (7), 519 (7), 44 (9), 43 (6), 41 (8), 40 (6), 36 (6). Elemental analysis calcd. (%) for $C_{48}H_{48}O_4$ (688.89): C 83.69, H 7.02; found C 83.71, H 7.02. **Method B:** a solution of bromoalkene **7** (505 mg, 0.38 mmol) in THF (10 mL) was cooled to –78 °C and 1.7 mL of a 2 N *n*-butyllithium solution in pentane were added. The brownish solution was stirred at –78 °C for one hour and at room temperature for an additional hour. The reaction was quenched with water (5 mL) and the layers were separated. The organic layer was washed 3× with water (5 mL) and once with brine (5 mL) and dried with sodium sulfate. THF was removed in vacuo and methanol (3 mL) was added to the residue. After 5 min of ultra sonification a pale yellow solid precipitated. The solid was filtered and dried in vacuo (50 °C, 2.9·10^{-1} mbar) to give 200 mg (76%) of calixarene **5** with m.p. > 300 °C. ^{1}H NMR data are in agreement to those in method A.

***cone*-5,11,17-Tris(2,2-dibromoethenyl)-23-formyl-25,26,27,28-tetra-*n*-propoxycalix[4]arene (8) and *cone*-5,11,17,23-Tetrakis(2,2-dibromoethenyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (7):** Tetrabromomethane (688 mg, 2.08 mmol), zinc dust (136 mg, 2.08 mmol) and triphenylphosphane (545 mg, 2.08 mmol) were suspended in dry dichloromethane (7 mL) and stirred 22 hours at room temperature under an argon atmosphere. To the pink suspension a solution of tetraaldehyde **6** (180 mg, 0.26 mmol) in dry dichloromethane (2 mL) was added and the reaction mixture was stirred 2.5 hours at room temperature. Dichloromethane was evaporated under vacuum and the resulted solid was separated by column chromatography (PE/EA, 5:1) to give after drying in vacuo (50 °C, 2.8·10^{-1} mbar): **1st Fraction (R_f = 0.58):** 140 mg (41%) of bromoalkene **7** as colourless solid. M.p. 237–239 °C. IR (KBr): ṽ = 2965 cm^{-1}, 2928, 2874, 1595, 1465, 1387, 1277, 1226, 1146, 1068, 1037, 999, 960, 905, 895, 819, 633, 576, 547. UV/Vis ($C_2H_4Cl_2$): $\lambda_{\max.}$ (lg *ε*) = 271 nm (4.8), 231 (4.7). ^{1}H NMR (500.1 MHz, CDCl$_3$): *δ* = 1.00 ppm (t, *J* = 7.5 Hz, 12 H, -C*H*$_3$), 1.92 (hex, *J* = 7.5 Hz, 8 H, CH$_2$C*H*$_2$CH$_3$), 3.16 (d, *J* = 13.4 Hz, 4 H, Ar-CH$_2$-Ar), 3.86 (t, *J* = 7.5 Hz, 12 H, O-C*H*$_2$CH$_2$CH$_3$), 4.43 (d, *J* = 13.3 Hz, 4 H, Ar-CH$_2$-Ar), 6.89 (s, 8 H, Ar-H), 7.18 (s, 4 H, alkene-H). ^{13}C NMR (125.8 MHz, CDCl$_3$): *δ* = 10.32 ppm (q, -*C*H$_3$), 23.29 (t, CH$_2$*C*H$_2$CH$_3$), 30.97 (t, Ar-*C*H$_2$-Ar), 76.94 (t, *C*H$_2$CH$_2$CH$_3$), 87.47 (s, Ar-CH*C*Br$_2$), 128.72 (d, Ar*C*H), 129.21 (s, Ar*C*), 134.73 (s, Ar*C*), 136.46 (d, Ar-*C*HCBr$_2$), 156.69 (s, Ar*C*-O-). MS (70 eV, 290 °C): *m*/*z* (%): 1333 (1) [M$^+$ + 5], 1332 (1) [M$^+$ + 4], 1331 (2) [M$^+$ + 3], 1330 (3) [M$^+$ + 2], 1329 (2) [M$^+$ + 1], 1328 (4) [M$^+$], 1327 (2) [M$^+$ – 1], 1326 (4) [M$^+$ – 2], 1324 (1) [M$^+$ – 3], 156 (5), 124 (17), 122 (15), 99 (6), 82 (48), 81 (15), 80 (50), 79 (16), 70 (5), 58 (10), 57 (8), 55 (6), 44 (85), 43 (100), 42 (21), 41 (54), 40 (43), 39 (22). Elemental analysis calcd. (%) for $C_{48}H_{48}Br_8O_4$ (1328.11): 43.63, H 3.60; found C 43.41, H 3.64. **2nd Fraction (R_f = 0.29):** 85 mg (28%) of trisalkene **8** as colourless solid. M.p. 167–169 °C. IR (KBr): ṽ = 2962 cm^{-1}, 2931, 2874, 1696, 1595, 1465, 1386, 1275, 1225, 1144, 1067, 1002, 961, 893, 821, 647, 581, 546. UV/Vis ($C_2H_4Cl_2$): $\lambda_{\max.}$ (lg *ε*) = 270 nm (4.6), 228 (4.6). ^{1}H NMR (500.1 MHz, CDCl$_3$): *δ* = 0.99 ppm (t, *J* = 7.5 Hz, 6 H, -C*H*$_3$), 1.00 (t, *J* = 7.4 Hz, 6 H, -C*H*$_3$), 1.91 (hex, *J* = 7.5 Hz, 4 H, CH$_2$C*H*$_2$CH$_3$), 1.92 (hex, *J* = 7.5 Hz, 4 H, CH$_2$C*H*$_2$CH$_3$), 3.17 (d, *J* = 13.6 Hz, 2 H, Ar-C*H*$_2$-Ar), 3.25 (d, *J* = 13.5 Hz, 2 H, Ar-C*H*$_2$-Ar), 3.86 (t, *J* = 7.4 Hz, 6 H, O-C*H*$_2$CH$_2$CH$_3$), 3.93 (t, *J* = 7.4 Hz, 2 H, O-C*H*$_2$CH$_2$CH$_3$), 4.43 (d, *J* = 13.5 Hz, 2 H, Ar-C*H*$_2$-Ar), 4.47 (d, *J* = 13.4 Hz, 2 H, Ar-C*H*$_2$-Ar), 6.83 (s, 2 H, Ar-H), 6.88 (s, 2 H, Ar-H), 6.93 (d, *J* = 2.0 Hz, 2 H, Ar-H), 7.05 (s, 1 H, alkene-H), 7.19 (2 superimposed signals, both s, 2 H, alkene-H and 2 H, Ar-H), 9.67 (s, 1 H, Ar-C*H*O). ^{13}C NMR (125.8 MHz, CDCl$_3$): *δ* = 10.27 ppm, 10.30, 10.33 (all q, -OCH$_2$CH$_2$*C*H$_3$), 23.28, 23.30, 23.32 (all t, -OCH$_2$*C*H$_2$CH$_3$), 30.93, 30.99 (both t, Ar-*C*H$_2$-Ar), 76.88, 76.96, 77.12 (all t, O*C*H$_2$CH$_2$CH$_3$), 86.98 87.75 (both s, Ar-CH*C*Br$_2$), 128.61, 128.78, 128.95 (all d, Ar-H), 129.09, 129.38 (both s, Ar*C*-CHCBr$_2$), 130.15 (d, Ar*C*-H), 131.23 (s, Ar*C*-CHO), 134.29, 134.79, 134.95, 135.80 (all s, Ar*C*-CH$_2$-*C*Ar), 136.28, 136.38 (both d, Ar-*C*HCBr$_2$), 156.68, 156.73, 161.99 (all s, Ar*C*-O-), 191.30 (d, Ar-*C*HO). MS (70 eV, 250 °C): *m*/*z* (%): 1176 (<1) [M$^+$ + 4], 1175 (<1) [M$^+$ + 3], 1174 (<1) [M$^+$ + 2], 1173 (<1) [M$^+$ + 1], 1172 (<1) [M$^+$], 1171 (<1) [M$^+$ – 1], 1170 (<1) [M$^+$ – 2], 1169 (<1) [M$^+$ – 3], 1168 (<1) [M$^+$ – 4],124 (18), 122 (18), 82 (25), 81 (8), 80 (26), 79 (8), 44 (9), 43 (100), 42 (13), 41 (50), 40 (6), 39 (14) Elemental analysis calcd. (%) for $C_{47}H_{48}Br_6O_5$·½CH$_2$Cl$_2$ (1214.79): C 46.96, H 4.07; found C 47.06, H 3.86.

***cone*-5,11,17,23-Tetrakis(2,2-dibromoethenyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (7):** Tetrabromomethane (2.394 g, 7.2 mmol), zinc dust (460 mg, 7.03 mmol) and triphenylphosphane (1.84 g, 7.04 mmol) were suspended in dry dichloromethane (25 mL) and stirred 22 hours at room temperature under an argon atmosphere. To the pink suspension a solution of tetraaldehyde **6** (470 mg, 0.58 mmol) in dry dichloromethane (5 mL) was added and the reaction mixture was stirred 3 hours at room temperature. The suspension was filtered through a pad of 5 g silica gel, washed three times with dichloromethane (30 mL) and the filtrate was evaporated to dryness to obtain ≈ 1.80 g of a colourless solid. The solid was dissolved in dichloromethane and slowly diluted with the same volume of methanol. The resulted colourless needles were filtered and dried in vacuo (50 °C, 2.7·10^{-1} mbar) to give 570 mg (74%) of calixarene **7** with m.p. 237–239 °C (^{1}H NMR spectroscopic data are in agreement to those described above).

***cone*-23-Ethenyl-25,26,27,28-tetra-*n*-propoxy-5,11,17-tris(2-pyridylethynyl)calix[4]arene (11a) and *cone*-25,26,27,28-Tetra-*n*-propoxy-5,11,17,23-tetrakis(2-pyridylethynyl)calix[4]arene (10a):** To a degassed solution of tetraethynylcalixarene 5 (310 mg, 0.45 mmol) and 2-bromopyridine (886 mg, 5.61 mmol) in triethylamine (10 mL) bis(triphenylphosphane)-palladium(II) chloride (73 mg, 0.10 mmol) and copper(I) iodide (32 mg, 0.17 mmol) were added and heated 14 h at 60 °C. The reaction mixture was cooled to room temperature, dichloromethane (35 mL) was added and filtered through Celite 535. The organic filtrate was washed four times with water (25 mL) and solvents were removed by rotary evaporation to get ≈ 1.08 g of a brown suspension. 2-Bromopyridine was removed by bulb-to-bulb distillation (5.0·10^{-1} mbar, 110 °C) and 540 mg of a brown solid remained. TLC (PE/EA, 1:6): R_f = 0.64, 0.45 (11a), 0.12 (10a). The brown residue was separated and purified by column chromatography (PE/EA, 1:6) to give after drying in vacuo: **1. Fraction (R_f = 0.45):** 112 mg (25%) of calixarene **11a** as pale yellow solid. M.p. 158–162 °C. IR (KBr): ṽ = 2960 (cm^{-1}), 2928, 2873, 2329, 2209, 1580, 1467, 1427, 1384, 1337, 1243, 1217, 1127, 1036, 1001, 962, 875, 777, 738. UV/Vis (CH$_3$CN): $\lambda_{\max.}$ (lg *ε*) = 313 nm (4.8, sh), 295 (4.9), 277 (4.8, sh), 232 (4.9, sh), 196 (5.0). ^{1}H NMR (400.1 MHz, CDCl$_3$): *δ* = 0.99 ppm (t, *J* = 7.5 Hz, 6 H, -C*H*$_3$), 1.04 (t, *J* = 7.5 Hz, 3 H, -C*H*$_3$), 1.05 (t, *J* = 7.5 Hz, 3 H, -C*H*$_3$), 1.93 (m, 8 H, CH$_2$C*H*$_2$CH$_3$), 3.18 (d, *J* = 13.6 Hz, 4 H, Ar-CH$_2$-Ar), 3.82 (t, *J* = 7.5 Hz, 2 H, O-C*H*$_2$CH$_2$CH$_3$), 3.85 (t, *J* = 7.5 Hz, 2 H, O-C*H*$_2$CH$_2$CH$_3$), 3.96 (m, *J* = 7.5 Hz, 4 H, O-C*H*$_2$CH$_2$CH$_3$), 4.45 (d, *J* = 13.5 Hz, 4 H, Ar-CH$_2$-Ar), 4.76 (d, *J* = 11.0 Hz, 1 H, Ar-CH=C*H*$_2$), 5.31 (d, *J* = 7.6 Hz, 1 H, Ar-CH=C*H*$_2$), 6.40 (dd, *J* = 17.3 Hz, 9.8 Hz, 1 H, Ar-C*H*=CH$_2$), 6.56 (s, 2 H, Ar-H), 6.83 (s, 2 H, Ar′′-H), 7.12–7.17 (m, 6 H, two superimposed signals, Py′-5-H, Ar′-3/5-H), 7.45 (d, *J* = 7.6 Hz, 2 H, Py′-3-H), 7.53 (“t”, two superimposed signals; 3 H, Py-3-H, Py′-4-H), 7.64 (t, ^3J = 8.0, ^4J = 1.5 Hz, 1 H, Py-4-H), 8.50 (d, *J* = 4.0 Hz, 2 H, Py′-6-H), 8.57 (d, *J* = 4.0 Hz, 1 H, Py-6-H). ^{13}C NMR (100.6 MHz, CDCl$_3$): *δ* = 10.11 ppm (q, -*C*H$_3$), 10.37 (q, -*C*H$_3$), 23.14 (t, CH$_2$*C*H$_2$CH$_3$), 23.27 (t, CH$_2$*C*H$_2$CH$_3$), 30.72 (t, Ar-*C*H$_2$-Ar), 30.94 (t, Ar-*C*H$_2$-Ar), 76.84 (t, *C*H$_2$CH$_2$CH$_3$), 76.88 (t, *C*H$_2$CH$_2$CH$_3$), 87.33 (s, Ar-*C*C-Py), 90.64 (s, Ar-C*C*-Py), 112.00 (t, Ar-CH=*C*H$_2$), 115.76 (s, Ar*C*-CC-Py), 116.11 (s, Ar*C*-CC-Py′), 122.01 (d, Py-C-3, Py′-C-3), 126.14, 127.01, 127.09 (all d, all ArC-H), 132.12 (d, Py′-C-5), 132.39 (s, Ar*C*-CH=CH$_2$), 132.50 (d, Py-C-5), 132.66, 133.78, 134.31, 135.28 (all s, all Ar*C*-CH$_2$-Ar), 135.86 (d, Py′-C-4), 135.99 (d, Py-C-4), 136.59 (d, Ar-*C*H=CH$_2$), 143.70 (s, Py′-C-2), 143.96 (s, Py-C-2), 149.44 (d, Py′-C-6), 149.55 (d, Py-C-6), 155.87, 157.09, 158.02 (all s, all Ar*C*-O-). MS (FAB): *m*/*z* (%): 984 (9) [M$^+$

+ 63], 938 (6), 923 [M + H$^+$] (68), 896 (23) [M$^+$ – C_2H_3], 880 (7). Elemental analysis calcd. (%) for $C_{63}H_{59}N_3O_4 \cdot ½CH_2Cl_2$ (964.64): C 79.06, H 6.27, N 4.36; found C 78.80, H 6.43, N 4.13. **2. Fraction (R_f = 0.12):** 275 mg (61%) of calixarene **10a** as pale yellow solid. M.p. > 300 °C. IR (KBr): $\tilde{\nu}$ = 3044 cm^{-1}, 2962, 2919, 2875, 2210, 1581, 1561, 1469, 1427, 1385, 1243, 1215, 1128, 1041, 1000, 960, 875, 776, 738, 559. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 308 nm (4.7, sh), 295 (4.8), 279 (4.6,sh), 233 (4.7). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.01 ppm (t, J = 7.5 Hz, 12 H, -CH_3), 1.94 (sext, J = 7.5 Hz, 8 H, $CH_2CH_2CH_3$), 3.17 (d, J = 13.4 Hz, 4 H, Ar-CH_2-Ar), 3.89 (t, J = 7.5 Hz, 12 H, O-$CH_2CH_2CH_3$), 4.43 (d, J = 13.4 Hz, 4 H, Ar-CH_2-Ar), 7.00 (s, 8 H, Ar-H), 7.02 (dt, ^3J = 4.0, J = 1.9 Hz, 4 H, Py-5-H), 7.40 (m, 8 H, Py-3-H, Py-4-H), 8.43(d, J = 4.6 Hz, 4 H, Py-6-H). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 10.25 ppm (q, -CH_3), 23.21 (t, $CH_2CH_2CH_3$), 30.74 (t, Ar-CH_2-Ar), 76.79 (t, $CH_2CH_2CH_3$), 87.59 (s, Ar-C*C*-Py), 90.03 (s, Ar-*C*C-Py), 116.29 (s, Ar*C*-CC-Py), 121.83 (d, Py-C-3), 127.02 (d, Ar*C*-H), 132.40 (d, Py-C-5), 134.75 (s, Ar*C*-CH_2-Ar), 135.63 (d, Py-C-4), 143.90 (s, Py-C-2), 149.56 (d, Py-C-6), 157.33 (s, Ar*C*-O-). MS (FAB): *m*/*z* (%): 997 [M + H$^+$] (100). Elemental analysis calcd. (%) for $C_{68}H_{60}N_4O_4 \cdot H_2O$ (1015.26): C 80.45, H 6.16, N 5.52; found C 80.14, H 6.36, N 5.26.

***cone*-25,26,27,28-Tetra-*n*-propoxy-5,11,17,23-tetrakis(3-pyridylethynyl)calix[4]arene (10b):** To a degassed solution of tetraethynylcalixarene **5** (200 mg, 0.29 mmol) and 3-bromopyridine (1.0 mL, 10.38 mmol) in triethylamine (10 mL) bis(triphenylphosphane)palladium(II) chloride (60 mg, 0.09 mmol) and copper(I) iodide (32 mg, 0.17 mmol) were added and heated three days at 70 °C. After cooling to room temperature dichloromethane (35 mL) was added and the mixture was washed four times with water (25 mL) and once with brine (25 mL). Solvents were removed by rotary evaporation to remain a brown residue. TLC (EA/MeOH, 6:1): R_f = 0.72, 0.59, 0.44 (**11b**), 0.12 (**10b**). The residue was separated by column chromatography to give after drying in vacuo: **1. Fraction** (R_f = 0.12): 124 mg (43%) of calixarene **10b** as pale yellow solid. M.p. 268–271 °C. IR (KBr): $\tilde{\nu}$ = 2960 cm^{-1}, 2927, 2873, 2210, 1633, 1480, 1459, 1406, 1384, 1288, 1235, 1214, 1125, 1023, 1002, 961, 874, 802, 704. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 309 nm (5.0, sh), 289 (5.1), 233 (5.1). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.03 ppm (t, J = 7.5 Hz, 12 H, -CH_3), 1.96 (sext, J = 7.5 Hz, 8 H, $CH_2CH_2CH_3$), 3.23 (d, J = 13.5 Hz, 4 H, Ar-CH_2-Ar), 3.93 (t, J = 7.5 Hz, 12 H, O-$CH_2CH_2CH_3$), 4.48 (d, J = 13.6 Hz, 4 H, Ar-CH_2-Ar), 6.99 (s, 8 H, Ar-H), 7.11 (br. s, 4 H, Py-5-H), 7.67 (d, J = 8.0 Hz, 4 H, Py-4-H), 8.44 (br. s, 4 H, Py-6-H), 8.67 (br. s, 4 H, Py-2-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.3 ppm (q, -CH_3), 23.2 (t, $CH_2CH_2CH_3$), 30.9 (t, Ar-CH_2-Ar), 77.1 (t, $CH_2CH_2CH_3$), 84.8 (s, Ar-C*C*-Py), 93.3 (s, Ar-*C*C-Py), 116.3 (s, Ar*C*-CC-Py), 132.0 (d, Ar-H), 135.0 (s, Ar*C*-CH_2-Ar), 138.2 (d, Py-C-4), 147.7 (s, Py-C-3), 151.7 (d, Py-C-6), 157.4 (s, Ar*C*-O-). MS (FAB): *m*/*z* (%): 997 [M + H$^+$] (100). Elemental analysis calcd. (%) for $C_{68}H_{60}N_4O_4 \cdot CH_2Cl_2$ (1082.18): C 76.58, H 5.77, N 5.17; found C 76.59, H 6.07, N 4.78.

***cone*-25,26,27,28-Tetra-*n*-propoxy-5,11,17,23-tetrakis(4-pyridylethynyl)calix[4]arene (10c):** Tetraethynyl **5** (150 mg, 0.22 mmol) and 4-bromopyridine hydrochloride (350 mg, 1.79 mmol) were suspended in dry diisopropylamine (20 mL) and bis(triphenylphosphane)palladium(II) chloride (40 mg, 0.06 mmol) and copper(I) iodide (20 mg, 0.12 mmol) were added. The reaction mixture was stirred for 3d at 50–60 °C under an argon atmosphere. After cooling to room temperature, the mixture was filtered through a pad of celite 535 and washed twice with dichloromethane (25 mL). The filtrate was washed 3 times with water (50 mL), once with brine (50 mL) and the solvents of the organic layer were removed by rotary evaporation to remain 240 mg of a brown residue. Purification by column chromatography (EA/MeOH, 6:1, R_f = 0.10) and drying in vacuo gave 60 mg (27%) of calixarene **10c** as yellow solid. M.p. 184–188 °C (decomposing is observed at higher temperature). IR (KBr): $\tilde{\nu}$ = 3035 cm^{-1}, 2962, 2932, 2873, 2358, 2209, 1732, 1589, 1535, 1489, 1460, 1406, 1384, 1337, 1288, 1238, 1217, 1126, 1065, 1036, 999, 961, 875, 819, 546, 490, 419. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 311 nm (4.4), 291 (4.5), 236 (4.5), 213 (4.5), 202 (4.6). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.01 ppm (t, J = 7.4 Hz, 12 H, -CH_3), 1.93 (sext, J = 7.4 Hz, 8 H, $CH_2CH_2CH_3$), 3.20 (d, J = 13.6 Hz, 4 H, Ar-CH_2-Ar), 3.91 (t, J = 7.4 Hz, 12 H, O-$CH_2CH_2CH_3$), 4.46 (d, J = 13.4 Hz, 4 H, Ar-CH_2-Ar), 6.97 (s, 8 H, Ar-H), 7.23 (br. d, J = 4.8 Hz, 4 H, Py-3/5-H), 8.43 (br. s, 4 H, Py-2/6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.2 ppm (q, -CH_3), 23.2 (t, $CH_2CH_2CH_3$), 30.8 (t, Ar-CH_2-Ar), 77.2 (t, $CH_2CH_2CH_3$), 85.8 (s, Ar-C*C*-Py), 94.8 (s, Ar-*C*C-Py), 115.9 (s, Ar*C*-CC-Py), 125.4 (s, Py*C*-CC-Ar), 131.9 (s, Ar*C*-CH_2-Ar), 132.3 (d, Py-C-3/5), 135.0 (d, Ar-H), 149.2 (s, Py-C-2/6), 157.8 (s, Ar*C*-O-). MS (FAB): *m*/*z* (%): 997 [M + H$^+$] (100). Elemental analysis calcd. (%) for $C_{68}H_{60}N_4O_4$ (997.25): C 81.90, H 6.06, N 5.76; found[33] C 79.26, H 7.48, N 4.05.

4-(3-Hydroxy-3-methylbut-1-ynyl)-2,6-dimethyl-1-*n*-propoxybenzene (13): To a degassed solution of 4-bromo-2,6-dimethyl-1-*n*-propoxylbenzene[34] (646 mg, 2.66 mmol) and butynol **12** (391 mg, 4.65 mmol) in triethylamine (10 mL) bis(triphenylphosphane)palladium(II) chloride (90 mg, 0.13 mmol) and copper(I) iodide (45 mg, 0.07 mmol) were added. The reaction mixture was stirred 20 h at 90 °C. After cooling to room temperature the mixture was filtered through a small silica pad and washed twice with ethyl acetate (15 mL). Solvents were removed by rotary evaporation to remain a brown oil. Purification by column chromatography (PE/EA, 5:1; R_f = 0.24) gave 580 mg (89%) of an orange coloured oil. Bulb-to-bulb distillation (225 °C/0.35 mbar) gave 411 mg (63%) of model compound **13** as pale yellow oil. IR (film): $\tilde{\nu}$ = 3395 cm^{-1}, 2977, 2932, 2876, 2329, 2224, 1747, 1584, 1480, 1376, 1317, 1231, 1167, 1143, 1065, 1041, 1002, 963, 949, 907, 876, 807, 757, 693. UV/Vis (CH_3CN): $\lambda_{max.}$ (lg ε) = 254 nm (4.5, sh), 246 (4.3), 211 (4.5). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.09 ppm (t, J = 7.3 Hz, 3 H, -$OCH_2CH_2CH_3$), 1.62 [s, 6 H, -C(CH_3)$_2$OH], 1.84 (sext, J = 7.0 Hz, 2 H, -$OCH_2CH_2CH_3$), 2.26 (s, 6 H, Ar-CH_3), 3.73 (t, J = 7.0 Hz, 2 H, O-$CH_2CH_2CH_3$), 7.11 (s, 2 H, Ar-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 10.6 ppm (q, -$OCH_2CH_2CH_3$), 16.1 (t, $OCH_2CH_2CH_3$), 23.6 (q, Ar-CH_3-), 31.6 [q, C(CH_3)$_2$OH], 65.6 [s, *C*(CH_3)$_2$OH], 74.0 (t, $OCH_2CH_2CH_3$), 82.2 [s, Ar-*C*C-C(CH_3)$_2$OH], 92.7 [s, Ar-C-*C*-C(CH_3)$_2$OH], 117.7 (s, Ar*C*-CC-), 131.1 (s, Ar*C*-CH_3), 132.2 (d, Ar*C*-H), 156.4 (s, Ar*C*-O). MS (EI, 70 eV): *m*/*z* (%): 247 (8) [M$^+$ + 1], 246 (47) [M$^+$], 231 (27), 190 (13), 189 (100), 188 (7), 187 (6), 161 (5), 147 (5), 146 (6), 145 (12), 128 (6), 115 (9), 91 (7), 77 (5), 59 (16), 58 (5), 43 (83), 41 (15), 39 (7), 29 (5), 27 (12). Elemental analysis calcd. (%) for $C_{16}H_{22}O_2$ (246.35): C 78.01, H 9.00; found C 77.80, H 8.78.

NMR Titrations: Titrations were carried out on a Bruker DRX 400 at 303 K in $CDCl_3$/CD_3CN (9:1) by dilution experiments: 0.5 mL of a stock solution (5–9 mM) of the guest compound was added to 10–20 mg calixarene and gradual diluted with the same stock solution. The concentration of the calixarene was determined by a factor of diagnostic integrals of signals of the host and guest compound multiplied with the concentration of the used stock solution. The association constants were estimated by nonlinear curve fitting of the determined data to the following Equation (1).[28] Maximum errors of K_{ass} and $\Delta\delta_{max}$ were estimated as ±15%.

$$\delta_{obs} - \delta_G = \frac{\delta_{WG} - \delta_G}{[G_0]} \cdot \left(\frac{[W_0]+[G_0]}{2K_{ass}} - \sqrt{\frac{([W_0]+[G_0])^2}{4K_{ass}^2} - [W_0][G_0]} \right) \quad (1)$$

Supporting Information: See also the footnote on the first page of this article. Fitted NMR titrations curves of the compounds **3**, **4**, **10a**, and **10c** with NMP$^+$iodide; Job-Plot of Calixarene **4** with NMP$^+$ iodide. FAB mass spectra of ground mixtures of the compounds **3** and **4** with NMP$^+$ iodide, FAB mass spectra of ground mixtures of the compounds **3**, **4**, **10a**, and **10b** with TMA$^+$ cloride, FAB mass spectrum of **4** with choline chloride and AM1-optimized structures of the complexes **10a**·NMP$^+$ and **10b**·NMP$^+$.

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$> 2\sigma(I)] = 0.0440$, $wR2 = 0.0782$ (all reflections), max./min. residual electron density 0.178/–0.197 e·Å^{-3}. The intensity data were collected on a Xcalibur2 (Oxford Diffraction) diffractometer (Mo-K_{α} radiation), $T = 103(2)$ K. Crystal data for **7**: $C_{48}H_{48}Br_8O_4$, $M_r = 1328.14$ g·mol^{-1}, $0.46 \times 0.14 \times 0.12$ mm, monoclinic, space group *Cc*, $a = 27.182(2)$ Å, $b = 13.5077(9)$ Å, $c = 18.259(2)$ Å, $\beta = 131.34(1)$, $V = 5033.4(12)$ Å^3, $Z = 4$, $\rho_{calcd.} = 1.753$ g·cm^{-3}, $2\Theta_{max} = 50.4°$, $\mu = 6.414$ mm^{-1}, numerical absorption correction, $T_{min.} = 0.439$, $T_{max.} = 0.550$, 30464 measured, 9035 unique ($R_{int} = 0.0826$), 4094 observed [$I > 2\sigma(I)$] reflections, 491 parameters (TWIN-refinement), $R1$ [$I > 2\sigma(I)$] = 0.0600, $wR2 = 0.1548$ (all reflections), max./min. residual electron density 0.830/–0.520 e·Å^{-3}. The intensity data were collected on a Xcalibur2 (Oxford Diffraction) diffractometer (Mo-K_{α} radiation), $T = 293(2)$ K. Both structures were solved by direct methods and refined by full-matrix least-squares using SHELXTL-97.[35] All non-hydrogen atoms were refined using anisotropic thermal parameters; hydrogen atoms were included by use of a riding model and fixed isotropic thermal parameters. CCDC-268338 (for **5**) and CCDC-268339 (for **7**) contain 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.

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