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Gas-Phase Complexation of Neutral Molecules by Upper Rim Bridged Calix[4]arenes

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Abstract: Diametrically bridged calix[4]arenes at the upper rim with molecular units bearing a xylyl or a 2,4-hexadiynyl mojety have been synthesized. The shape, rigidity and chemical structure of the bridge determine the host-guest complexation properties of these systems towards neutral molecules in the gas-phase.

INTRODUCTION

Calix[4]arenes are cavity-shaped cyclic molecules, whose structure is very attractive for studying host-guest interactions[1]. Although these compounds bear a lipophilic cavity, formation of stable endo-cavity complexes with neutral molecules has been observed only in the solid state[1,2]. The consideration that this behaviour can be due to both the conformational mobilty of calix[4]arenes in solution[1,2] and the small size of the cavity, led our group and others to adopt alternative synthetic strategies (1-3) producing calix[4]arene derivatives with improved affinity toward neutral guests *via*:

1- immobilization of the calix in the cone conformation, by functionalization at the lower rim[1-3].

2- extension of the lipophilic cavity by introducing rigid substituents[4] or bridges[3,5] at the upper rim containing aromatic or other π donor groups.

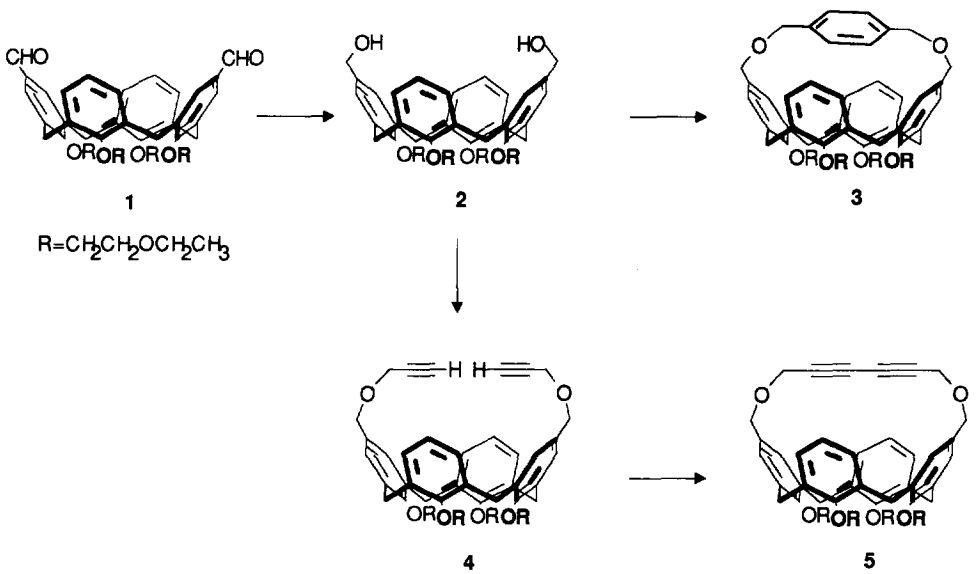
3- formation of molecular cages by connecting two calix[4]arenes units together at the upper rim[3,6].

In this paper the synthesis of new cavitands carrying a calix[4]arenes subunit is presented; preliminary data on gas-phase complexation are also reported. Desorption chemical ionization mass spectrometry had been used previously to study molecular complexes between cavitands and neutral guest molecules[7,8] held together by weak intermolecular interactions. In organic media these interactions are usually masked by the strong solvation of host and guest[9].

RESULTS AND DISCUSSION

Preliminary experiments using benzene-acetonitrile mixture as guests and some unbridged calix[4]arenes blocked in the cone conformation as hosts (tetrakis-2-ethoxyethoxy derivatives of calix[4]arene, p-tert-butylcalix[4]arene and 5,17-bisacetylaminocalix[4]arene **7**) showed no occurrence of host-guest complexation in the gas-phase. Therefore it was decided to extend the van der Waals surface by introducing bridges via

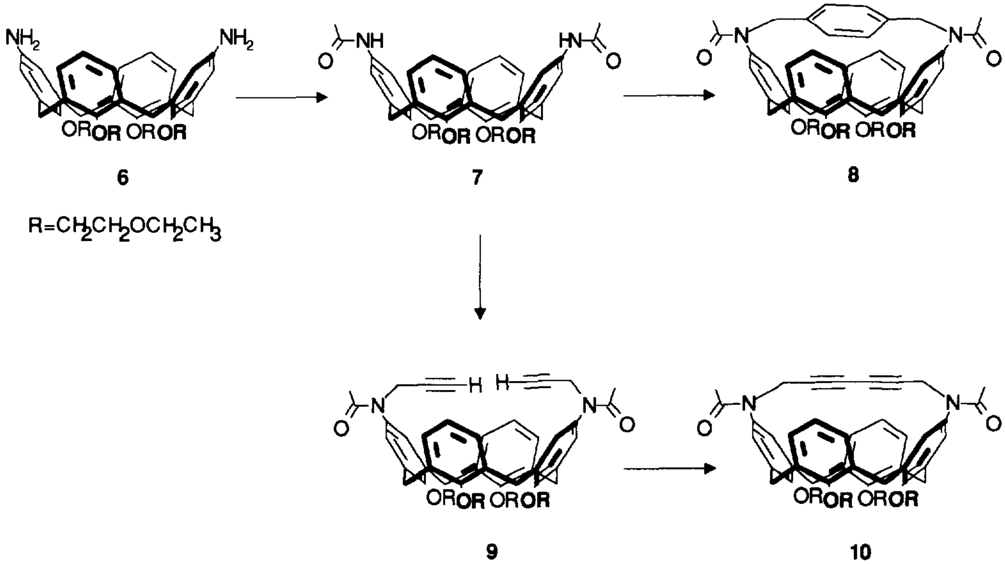
selective diametrical (1,3) functionalization of tetrakis(2-ethoxyethoxy)calix[4]arene blocked in the cone conformation[3]. The synthesis of cavitand **3** had been reported previously[5]. Following a similar scheme the 1,3-diformyl derivative **1**[3] was reduced to the dihydroxymethyl derivative **2**[5] which reacted with propargyl bromide to give the diether **4** subsequently transformed into the cavitand **5** by oxidative coupling (see Scheme 1).



Scheme 1

In order to gain information about the role played by the structure of the bridge on the binding properties of the host, a second series of cavitands (**8** and **10**, Scheme 2) was synthesized carrying the same binding sites but shorter bridging units. The 1,3-diamino derivative **6**[10] was first acetylated to give **7** and its di-sodium salt was reacted both with α,α'-dibromo-p-xylene to give cavitand **8** and with propargyl bromide to give cavitand **10**, after oxidative coupling (see Scheme 2).

The absolute and relative ability of these new cavitands to undergo host-guest complexation with neutral counterparts was investigated in the gas-phase using a mass spectrometric technique already described elsewhere[8]. In synthesis, a desorption chemical ionization probe was used to evaporate the cavitand within the ion source, while methane (≅ 99%) and small amounts of two candidate guests (≅ 0.5% each) constituted the stable gaseous atmosphere in it. Under such conditions the vaporized cavitand could interact with either one of the candidate guests and the complex could be ionized and detected. The two guests compete with each other for the binding cavity of the host, as they are in large excess with respect to the cavitand.



Scheme 2

Their relative complexation constants can be calculated as follows:

$$Ho + G_1 \overset{k_1}{\rightleftarrows} HoG_1 \qquad\qquad Ho + G_2 \overset{k_2}{\rightleftarrows} HoG_2$$

$$k_1 = [HoG_1]/[[Ho][G_1] \qquad\qquad k_2 = [HoG_2]/[[Ho][G_2]$$

$$Ka = k_1/k_2 = [HoG_1][G_2]/[HoG_2][G_1]$$

$$\text{since: } [G_1] \propto P_{G1} \text{ and } [G_2] \propto P_{G2} \qquad Ka \cong \frac{[HoG_1]}{[HoG_2]} \frac{P_{G2}}{P_{G1}}$$

where Ho, G_1, G_2, HoG_1, HoG_2 are the host, the two guests and the two complexes respectively, and P_{G1}, P_{G2}, are the partial pressures of the two guests into the ion source. The ratio $[HoG_1]$ / $[HoG_2]$ is measured by the relative abundance of the corresponding peaks in the mass spectra. The ratio P_{G1} / P_{G2} is determined by headspace gas chromatography. Bridged calix[4]arenes **3**, **5**, **8** and **10** were studied in sequence as hosts. In Table 1 the relative complexation costants for various G_1, G_2 couples are listed.

Considerable differences are evident in the gas-phase affinity of cavitands **3**, **5**, **8** and **10** towards neutral organic guests. The first macroscopic feature revealed by Table 1 is that cavitands **8** and **10** strongly interact with most candidate guests to give extensive complexation (yields up to 60%-90%), whereas the percentage of cavitand **3** undergoing host-guest complexation is low (10%-40%) and that of cavitand **5** is negligible, as for nonbridged calixarenes. This is the result of the different bridging unit, which is shorter and more rigid in **8** and

10 than in **3** and **5**. In particular, the existence of a rigid cavity seems to be a fundamental requisite for observing strong gas-phase supramolecular interactions.

Table 1- Gas-phase relative complexation costants of hosts **3**, **8**, **10** and neutral molecules.

	3		**10**		**8**	
G_1/ G_2	Ka	% compl.	Ka	% compl.	Ka	% compl.
CH_3COOn-Pr/ n-PrOH 1:1	>50	30	3.7	50	18	70
CH_3COOt-Bu/ CH_3COOn-Pr 1:1	4.2	30	3.8	80	2.7	80
CH_3COOt-Bu / t-BuOH 3:1	>50	10	1.4	50	4.5	75
t-BuOH / i-PrOH 1:1	/	< 5	1.9	75	4.6	70
CH_3COOi-Pr / i-PrOH 3:1	>50	20	5.7	70	33	90
CH_3COOi-Pr / CH_3COOEt 2:1	2.5	15	2.3	90	2.1	90
MeCOEt/ CH_3COOEt 1:1	0.81	40	1.7	85	1.8	90
CH_3CN/ CH_3COOEt 2:1	0.13	30	0.82	75	0.58	90
CH_3CN / C_6H_6 2:1	/	< 5	>50	45	>50	70

Table 2- Calculated gas-phase relative complexation costants.

Guest	**3**[a]		**10**[b]	**8**[b]
CH_3COOi-Pr	/	2.5	2.3	2.1
$CH_3COCH_2CH_3$	/	0.81	1.7	1.8
CH_3COOt-Bu	4.2	/	1.1	1.3
$CH_3COOC_2H_5$	/	**1**	**1**	**1**
CH_3COOn-Pr	**1**	/	0.29	0.48
CH_3CN	/	0.13	0.82	0.58
t-BuOH	< 0.08	/	0.76	0.28
i-PrOH	/	< 0.05	0.40	0.06
n-PrOH	< 0.02	/	0.08	0.03
C_6H_6	/	/	< 0.02	< 0.01

a: referred to CH_3COOn-Pr and CH_3COOEt; b: referred to CH_3COOEt.

The electronic properties of the bridging unit also play a role, not as crucial as geometrical properties. Nevertheless, from Table 1, it can be deduced that the presence of a p-xylyl unit in the bridge (cavitand **3** and **8**) favors host-guest complexation with respect to a 2,4-hexadiyne unit (cavitand **5** and **10**). This effect could be due to the better π donor ability of this molecular subunit, but can also be ascribed to its lower size (5.86 Å for p-xylene unit vs. 6.77 Å for 2,4-hexadiyne unit[11]). The cavitands exhibiting the highest complexation efficiency turn out to be also quite selective among the candidate guests (see Table 2). **8** and **10** undergo strong supramolecular interaction with esters, ketones and acetonitrile, but interact weakly with benzene and alcohols. Thus, the complex stability seems to be determined by multiple interactions between the acidic methyl hydrogen

of the guest (α to electron-withdrawing groups) and π electrons of the host cavity and bridge[12]. As for tri- and tetraquinoxaline bridged cavitands studied previously[7,8], σ–π interaction seems to play a key role in gas-phase host-guest complexation. Further interactions are possibly established between the highly branched alkyl groups (t-butyl, i-propyl) of the guests and the bulky lipophilic groups of calix[4]arenes.

For the first time calix[4]arene derivatives have been involved in host-guest complexation with neutral counterparts in the gas-phase. By this mass spectrometric method host-guest complex formation was evidenced whenever the calix[4]arene structure is forced into a rigid cone conformation by a diametrical bridge at the upper rim of the calix and this bridge bears π-electron donor groups. The complexation efficiency strongly depends on the length and structure of the bridge. High selectivity towards neutral molecules carrying acidic methyl groups was evidenced. In order to achieve a better knowledge on the complexation mechanism and the specific supramolecular interactions occuring between hosts and guests systematic gas-phase complexation studies on bridged calix[4]arenes and diffractometric analysis of crystalline complexes are in progress.

EXPERIMENTAL

All reactions were carried out under nitrogen. THF was freshly distilled from sodium benzophenone kethyl prior to use, DMF was freshly distilled under nitrogen and stored over molecular sieves 4 Å, CH_3CN was dried over molecular sieves 4 Å for at least 3 h and triethylamine was stored over KOH. All other reagents and solvents were of reagent grade quality, obtained from commercial supplies, and used without further purification. ^{13}C and ^1H NMR spectra were recorded in $CDCl_3$ (unless otherwise indicated) on Brucker AC 100 and AMX 400 instruments operating at 25, 400 MHz respectively. Chemical shifts (δ) are expressed in ppm relative to the internal tetramethylsilane (TMS). Infrared spectra were recorded on a Perkin Elmer mod. 298. Mass spectra were determined in the CI mode (CH_4) using a Finnigan MAT SSQ 710. Melting points were measured with an Electrothermal Melting point apparatus and are uncorrected. Gas phase complexation studies were performed at Dipartimento di Chimica Analitica of the University of Torino, using a Finnigan MAT 95 Q mass spectrometer[7,8]. Analytical thin layer chromatography were performed on precoated silica gel plates (Merck, 60 F_{254}). Calix[4]arenes **1**[3], **2**[5], **3**[5] and **6**[10] were prepared according to literature procedures.

5,17-Bis(2-oxa-4-pentinyl)-25,26,27,28-tetrakis(2-ethoxyethoxy)calix[4]arene ***4****.*

Calix[4]arene **2** (200 mg, 0.26 mmol) was dissolved in DMF (5 ml), and NaH (14 mg, 0.58 mmol) was added, then propargyl bromide (124 mg, 1.04 mmol) was added to the heterogeneous mixture. The reaction was stirred at room temperature for additional 6 h and quenched with methanol (caution!). The solvent was evaporated under reduced pressure, the residue taken up with water (50 ml) and extracted with ethyl acetate (50 ml). The organic layer was separated, washed with water (2x50 ml) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, purification by preparative chromatography (hexane:ethyl acetate = 70:30) afforded 150 mg (70% yield) of **4** as viscous oil.

^1H NMR ($CDCl_3$, 400 MHz) δ 1.21 and 1.22 (2t, 12H, J= 6.8 Hz, $-OCH_2\underline{CH_3}$); 2.44 (t, 2H, J= 2.2 Hz, $-CH_2C{\equiv}\underline{CH}$); 3.15 (d, 4H, J= 13.4 Hz, $ArC\underline{H_2}Ar$, Heq); 3.52-3.60 (m, 8H, $-OC\underline{H_2}CH_3$); 3.83-3.89 (m, 8H, $ArOCH_2C\underline{H_2}O$-; $ArOC\underline{H_2}CH_2O$-); 4.07 (d, 4H, $-C\underline{H_2}C{\equiv}CH$); 4.09 (t, 4H, J= 5.9 Hz, $ArOCH_2C\underline{H_2}O$-); 4.15 (t, 4H, $ArOC\underline{H_2}CH_2O$-); 4.33 (s, 4H, $ArC\underline{H_2}O$-); 4.52 (d, 4H, $ArC\underline{H_2}Ar$, Hax); 6.49-6.58 (m, 6H, Ar

10,11,12,22,23,24-H); 6.75 (s, 4H, Ar 4,6,16,18-H). ^{13}C ($CDCl_3$, 25 MHz) δ 15.3 (q, $-OCH_2\underline{C}H_3$); 30.8 (t, $Ar\underline{C}H_2Ar$); 56.8, 66.4, 69.7, 71.7, 73.2, 73.5 (t, $-\underline{C}H_2C{\equiv}CH$, $Ar\underline{C}H_2O$-, $-O\underline{C}H_2CH_3$, $ArOCH_2\underline{C}H_2O$-, $ArO\underline{C}H_2CH_2O$-); 74.9 (d, $-CH_2C{\equiv}\underline{C}H$); 80.3 (s, $-CH_2\underline{C}{\equiv}CH$); 122.7, 128.1, 128.5 (d, Ar 4,6,10,11,12,16,18,22,23,24-C); 134.5, 135.4 (s, Ar 1,3,5,7,9,13,15,17,19,21-C); 157.0 (s, Ar 25,26,27,28-C); mass spectrum: m/e 849 $(M+H)^+$; IR (NaCl) cm^{-1}: 3230 (C≡C-H), 2100 (-C≡C-).

Cavitand **5**.

$Cu(CH_3COO)_2{\cdot}H_2O$ (230 mg, 1.15 mmol) was dissolved in CH_3CN (5 ml). The solution was heated at 60 °C and then calix[4]arene **4** (160 mg, 0.19 mmol) dissolved in CH_3CN (5 ml) was added dropwise. The reaction mixture was stirred at 60 °C for additional 4 h then quenched with HCl (50 ml, 0.01 N) and extracted with ethyl acetate (100 ml). The organic layer was separated, washed with water (2x50 ml) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, purification by preparative chromatography (hexane:ethyl acetate = 70:30) afforded 95 mg (60% yield) of **5** as viscous oil.

^1H NMR ($CDCl_3$, 400 MHz) δ 1.16 and 1.22 (2t, 12H, J= 7.0 Hz, $-OCH_2C\underline{H}_3$); 3.16 (d, 4H, J= 13.0 Hz, $ArC\underline{H}_2Ar$, Heq); 3.52 and 3.56 (2q, 8H, $-OC\underline{H}_2CH_3$); 3.73 (t, 4H, J= 5.4 Hz, $ArOCH_2C\underline{H}_2O$-); 3.87 (t, 4H, $ArOC\underline{H}_2CH_2O$-); 3.97 (t, 4H, J= 6.8 Hz, $ArOCH_2C\underline{H}_2O$-); 4.07 (s, 4H, $-C\underline{H}_2C{\equiv}C$-); 4.17 (s, 4H, $ArC\underline{H}_2O$-); 4.35 (t, 4H, $ArOC\underline{H}_2CH_2O$-); 4.50 (d, 4H, $ArC\underline{H}_2Ar$, Hax); 6.32 (s, 4H, Ar 4,6,16,18-H); 6.91 (t, 2H, J= 7.4 Hz, Ar 11,23-H); 7.11 (d, 4H, Ar 10,12,22,24-H). ^{13}C ($CDCl_3$, 25 MHz) δ 15.3, 15.4 (q, $-OCH_2\underline{C}H_3$); 30.9 (t, $Ar\underline{C}H_2Ar$); 58.6, 66.2, 66.5, 69.5, 69.7, 72.3, 74.2 (t, $-\underline{C}H_2C{\equiv}C$-, $Ar\underline{C}H_2O$-, $-O\underline{C}H_2CH_3$, $ArOCH_2\underline{C}H_2O$-, $ArO\underline{C}H_2CH_2O$-); 73.0, 79.7 (s, $-CH_2\underline{C}{\equiv}C$-, $-CH_2C{\equiv}\underline{C}$-); 122.6, 125.1, 128.9, (d, Ar 4,6,10,11,12,16,18,22,23,24-C); 131.8, 133.1, 136.3 (s, Ar 1,3,5,7,9,13,15,17,19,21-C); 153.6, 157.5 (s, Ar 25,26,27,28-C); mass spectrum: m/e 847 $(M+H)^+$.

5,17-Bis(acetylamino)-25,26,27,28-tetrakis(2-ethoxyethoxy)calix[4]arene **7**.

Calix[4]arene **6** (500 mg, 0.67 mmol) was dissolved in CH_2Cl_2 (5 ml), and triethylamine (220 mg, 2.18 mmol) was added, then acetic anhydride (200 mg, 2.01 mmol) was added. The reaction mixture was stirred at room temperature for additional 12 h and then quenched with water (100 ml) and extracted with ethyl acetate (100 ml). The organic layer was separated, washed with water (2x50 ml) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, purification by preparative chromatography (ethyl acetate) afforded 275 mg (50% yield) of **7** as pure compound. mp: 110 °C.

^1H NMR ($CDCl_3$, 400 MHz) δ 1.17 and 1.22 (2t, 12H, J= 6.8 Hz, $-OCH_2C\underline{H}_3$); 1.83 (bs, 6H, $-COC\underline{H}_3$); 3.13 (d, 4H, J= 13.2 Hz, $ArC\underline{H}_2Ar$, Heq); 3.56 and 3.61 (2q, 8H, J= 6.8 Hz, $-OC\underline{H}_2CH_3$); 3.78 (t, 4H, J= 4.8 Hz, $ArOCH_2C\underline{H}_2O$-); 3.87 (t, 4H, J= 6.4 Hz, $ArOCH_2C\underline{H}_2O$-); 3.96 (t, 4H, $ArOC\underline{H}_2CH_2O$-); 4.23 (t, 4H, $ArC\underline{H}_2CH_2O$-); 4.50 (d, 4H, $ArC\underline{H}_2Ar$, Hax); 6.35 (s, 4H, Ar 4,6,16,18-H); 6.77 (t, 2H, J= 7.6 Hz, Ar 11,23-H); 6.91 (d, 4H, Ar 10,12,22,24-H); 7.16-7.22 (bs, 2H, $ArN\underline{H}$-). ^{13}C ($CDCl_3$, 25 MHz) δ 15.6 (q, $-OCH_2\underline{C}H_3$); 24.1 (q, $-CO\underline{C}H_3$); 31.1 (t, $Ar\underline{C}H_2Ar$); 66.5, 66.7, 69.8, 69.9, 72.9, 74.0 (t, $-O\underline{C}H_2CH_3$, $ArOCH_2\underline{C}H_2O$-, $ArO\underline{C}H_2CH_2O$-); 122.1, 122.7, 128.3 (d, Ar 4,6,10,11,12,16,18,22,23,24-C); 131.8, 134.7, 136.0 (s, Ar 1,3,5,7,9,13,15,17,19,21-C); 153.0, 157.5 (s, Ar 25,26,27,28-C); 168.8 (s, $-\underline{C}OCH_3$); mass spectrum: m/e 827 $(M+H)^+$; IR (NaCl) cm^{-1}: 3300 (NH); 1660 (C=O); 1600 (NH).

*Cavitand **8**.*

Calix[4]arene **7** (170 mg, 0.21 mmol) was dissolved in DMF (70 ml), and NaH (15 mg, 0.63 mmol) was added, then α,α'-dibromo-p-xylene (60 mg, 0.63 mmol) was added to the heterogeneous mixture. The reaction mixture was stirred at room temperature for additional 36 h and quenched with methanol (caution!). The solvent was evaporated under reduced pressure, the residue taken up with water (50 ml) and extracted with ethyl acetate (50 ml). The organic layer was separated, washed with water (2x50 ml) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, purification by preparative chromatography (hexane:ethyl acetate = 30:70) afforded 40 mg (20% yield) of **8** as pure compound. mp: 92-94 °C.
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 and 1.22 (2t, 12H, J= 6.5 Hz, -OCH$_2$C<u>H</u>$_3$); 1.90 (s, 6H, -COC<u>H</u>$_3$); 3.12 (d, 4H, J= 12.5 Hz, ArC<u>H</u>$_2$Ar, Heq); 3.56-3.61 (m, 8H, -OC<u>H</u>$_2$CH$_3$); 3.69 (t, 4H, J= 4.6 Hz, ArOCH$_2$C<u>H</u>$_2$O); 3.95 (t, 4H, ArOC<u>H</u>$_2$CH$_2$O-); 4.02 (t, 4H, J= 6.5 Hz, ArOCH$_2$C<u>H</u>$_2$O-); 4.28 (t, 4H, ArOC<u>H</u>$_2$CH$_2$O-); 4.46 (d, 4H, ArC<u>H</u>$_2$Ar, Hax); 4.77 (s, 4H, -C<u>H</u>$_2$xylyl); 6.28 (s, 4H, Ar 4,6,16,18-<u>H</u>); 6.48 (s, 4H, Ar-<u>H</u> xylyl); 6.92 (t, 2H, J= 7.5 Hz, Ar 11,23-<u>H</u>); 7.07 (d, 4H, Ar 10,12,22,24-<u>H</u>); ^{13}C ($CDCl_3$, 25 MHz) δ 15.2, 15.4 (q, -OCH$_2$<u>C</u>H$_3$); 23.1 (q, -CO<u>C</u>H$_3$); 29.6, 30.7 (t, Ar<u>C</u>H$_2$Ar); 49.1 (t, Ar-<u>C</u>H$_2$ xylyl); 66.3, 66.4, 69.3, 69.6, 72.0, 75.0 (t, -O<u>C</u>H$_2$CH$_3$, ArOCH$_2$<u>C</u>H$_2$O-, ArO<u>C</u>H$_2$CH$_2$O-); 123.1; 126.6; 127.2; 128.4 (d, Ar 4,6,10,11,12,16,18,22,23,24-<u>C</u>, Ar-<u>C</u> xylyl); 133.9, 135.7, 135.9 (s, Ar 1,3,5,7,9,13,15,17,19,21-<u>C</u>); 153.0, 156.5 (s, Ar 25,26,27,28-<u>C</u>); 171.1 (s, -<u>C</u>OCH$_3$); mass spectrum: m/e 929 $(M+H)^+$; IR(NaCl) cm^{-1}: 1660 (C=O).

*5,17-Bis[acetyl(2-propinyl)amino]-25,26,27,28-tetrakis(2-ethoxyethoxy)calix[4]arene **9**.*

Calix[4]arene **7** (220 mg, 0.27 mmol) was dissolved in THF (5 ml), and NaH (14 mg, 0.58 mmol) was added, then propargyl bromide (140 mg, 1.18 mmol) was added to the heterogeneous solution. The reaction mixture was stirred at room temperature for additional 12 h and quenched with methanol (caution!). The solvent was evaporated under reduced pressure, the residue taken up with water (50 ml) and extracted with ethyl acetate (50 ml). The organic layer was separated, washed with water (2x50 ml) and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave compound **9** as viscous oil in quantitative yield.
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 and 1.21 (2t, 12H, J= 6.8 Hz, -OCH$_2$C<u>H</u>$_3$); 1.83 (s, 6H, -COC<u>H</u>$_3$); 2.16 (t, 2H, J= 2.4 Hz, -CH$_2$C≡C<u>H</u>); 3.13 (d, 4H, J= 13.4 Hz, ArC<u>H</u>$_2$Ar, Heq); 3.48 and 3.55 (2q, 8H, J= 6.8 Hz, -OC<u>H</u>$_2$CH$_3$); 3.76 (t, 4H, J= 5.3 Hz, ArOCH$_2$C<u>H</u>$_2$O); 3.87 (t, 4H, J= 5.8 Hz, ArOCH$_2$C<u>H</u>$_2$O-); 3.95 (t, 4H, ArOC<u>H</u>$_2$CH$_2$O-); 4.28 (t, 4H, ArOC<u>H</u>$_2$CH$_2$O-); 4.45 (d, 4H, -C<u>H</u>$_2$C≡CH); 4.51 (d, 4H, ArC<u>H</u>$_2$Ar, Hax); 6.22 (d, 4H, J= 6.5 Hz, Ar 10,12,22,24-<u>H</u>); 6.31 (t, 2H, Ar 11,23-<u>H</u>); 6.92 (s, 4H, Ar 4,6,16,18-<u>H</u>); ^{13}C ($CDCl_3$, 25 MHz) δ 15.3 (q, -OCH$_2$<u>C</u>H$_3$); 22.3 (q, -CO<u>C</u>H$_3$); 30.7 (t, Ar<u>C</u>H$_2$Ar); 38.2 (t, -<u>C</u>H$_2$C≡CH); 66.0, 66.5, 69.5, 69.9, 72.0, 73.8 (t, -O<u>C</u>H$_2$CH$_3$, ArOCH$_2$<u>C</u>H$_2$O-, ArO<u>C</u>H$_2$CH$_2$O-); 72.8 (d, -CH$_2$C≡<u>C</u>H); 79.2 (s, -CH$_2$<u>C</u>≡CH); 122.7, 127.8, 127.9 (d, Ar 4,6,10,11,12,16,18,22,23,24-<u>C</u>); 133.1, 136.0, 137.6 (s, Ar 1,3,5,7,9,13,15,17,19,21-<u>C</u>); 155.0, 157.5 (s, Ar 25,26,27,28-<u>C</u>); 170.3 (s, -<u>C</u>OCH$_3$); mass spectrum: m/e 904 $(M+H)^+$; IR (NaCl) cm^{-1}: 3310 (C≡C-H); 2250 (-C≡C-);1650 (C=O).

*Cavitand **10**.*

$Cu(CH_3COO)_2{\cdot}H_2O$ (320 mg, 1.6 mmol) was dissolved in CH_3CN (5 ml). The solution was heated at 60 °C and then calix[4]arene **9** (240 mg, 0.27 mmol) dissolved in CH_3CN (5 ml) was added dropwise. The reaction mixture was stirred at 60 °C for 1 h and quenched with HCl (50 ml, 0.01 N) and extracted with ethyl

acetate (100 ml). The organic layer was separated, washed with water (2x50 ml) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, purification by preparative chromatography (hexane:ethyl acetate = 15:85) afforded 50 mg (20% yield) of **10** as pure compound; mp: 158 °C.

^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 and 1.24 (2t, 12H, J= 7.0 Hz, -$OCH_2\underline{CH_3}$); 1.76 (s, 6H, -$COCH_3$); 3.20 (d, 4H, J= 12.4 Hz, Ar$\underline{CH_2}$Ar, Heq); 3.54 and 3.60 (2q, 8H, -OCH_2CH_3); 3.71 (t, 4H, J= 5.0 Hz, $ArOCH_2\underline{CH_2}O$-); 4.04 (t, 4H, $ArOCH_2CH_2O$-); 4.11 (t, 4H, J= 6.9 Hz, $ArOCH_2\underline{CH_2}O$-); 4.35 (t, 4H, $ArOCH_2CH_2O$-); 4.51 (s, 4H, -$CH_2C{\equiv}C$-); 4.60 (d, 4H, Ar$\underline{CH_2}$Ar, Hax); 6.61 (s, 4H, Ar 4,6,16,18-H); 6.82 (t, 2H, J= 7.8 Hz, Ar 11,23-H); 7.20 (d, 4H, Ar 10,12,22,24-H); ^{13}C ($CDCl_3$, 25 MHz) δ 15.0, 15.3 (q, -$OCH_2\underline{C}H_3$); 22.6 (q, -$CO\underline{C}H_3$); 30.9 (t, Ar$\underline{C}H_2$Ar); 36.3 (t, -$\underline{C}H_2C{\equiv}C$-); 66.4, 66.5, 69.2, 69.7, 72.0, 74.9 (t, -$O\underline{C}H_2CH_3$, $ArOCH_2\underline{C}H_2O$-, $ArO\underline{C}H_2CH_2O$-); 68.2, 71.2 (s, -$CH_2C{\equiv}\underline{C}$-, -$CH_2\underline{C}{\equiv}C$-); 123.6, 126.3, 128.6 (d, Ar 4,6,10,11,12,16,18,22,23,24-C); 134.7, 135.0, 135.3 (s, Ar 1,3,5,7,9,13,15,17,19,21-C); 154.2, 156.0 (s, Ar 25,26,27,28-C); 170.0 (s, -$\underline{C}OCH_3$); mass spectrum: m/e 901 $(M+H)^+$; IR (NaCl) cm^{-1}: 2280 (-C≡C-); 1640 (C=O).

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