

Inclusion Networks of a Calix[5]arene-Based Exoditopic Receptor and Long-Chain Alkyldiammonium Ions[†]

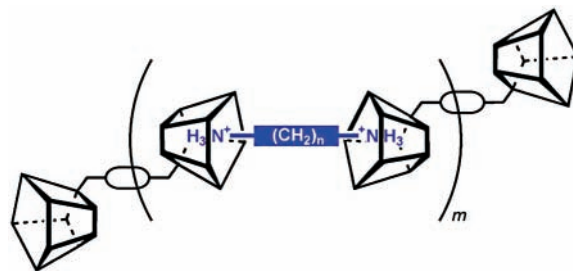
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ABSTRACT



Tail-to-tail connection of two cone calix[5]arene moieties by a rigid *p*-xylyl spacer affords the new exoditopic receptor **3** featuring two π -rich cavities (assembling cores) in a centrosymmetric divergent arrangement, as established by a single-crystal X-ray analysis. ¹H NMR complexation studies of **3** with alkyldiammonium ions support the formation of discrete bis-*endo*-cavity complexes and/or capsular assemblies along a polymer chain (polycaps), according to the length of the connector.

There is currently considerable interest in the design and synthesis of nanoscale molecular networks¹ based on iterative self-assembly of specific building blocks (molecular modules, e.g., tectons²) that display complementary molecular affinities. These higher-order architectures can be

designed by choosing topological features and/or chemical surfaces of the interconnecting modules, capable of establishing a number of noncovalent intermolecular interactions (H-bond,³ CH- π ,⁴ cation- π ⁵ interactions, and van der Waals attractive forces⁶), typical of host-guest and coordination chemistry.⁷

In the quest for new molecules optimized for the formation of molecular networks having a well-defined geometry, we have focused our attention on calix[5]arene-based exoditopic receptors as potential modules for the assembly of supramo-

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lecular structures based on iterative inclusion processes with appropriate connectors. We have already demonstrated that *p*-*tert*-butylcalix[5]arenes in a fixed C_{5v} cone-like arrangement form strong 1:1 inclusion complexes with linear alkylammonium ions⁸ and discrete dimeric capsules in the presence of long-chain alkyldiammonium ions.⁹ In the latter case, a single ditopic guest coordinates to a pair of calix[5]-arene units, oriented rim-to-rim to form a closed cavity entrapping the shape-complementary dication. Here we report that, when two such calix[5]arene molecules are covalently linked via their lower rims, as in **3** (vide infra), their cores diverge and inclusion of suitable alkyldiammonium ions results in the formation of polymeric capsular assemblies (polycaps).¹⁰

Bis-calixarene **3** in a fixed cone conformation was obtained by a two-step synthesis involving the tail-to-tail bridging of *p*-*tert*-butylcalix[5]arene **1**¹¹ with the α, α' -dibromo-*p*-xylene spacer and CsF in dry DMF at room temperature (to produce octol **2**), followed by the exhaustive alkylation of the residual hydroxyl groups with an excess of 4-methylpentyl tosylate and K_2CO_3 in refluxing acetonitrile (Figure 1). The structures

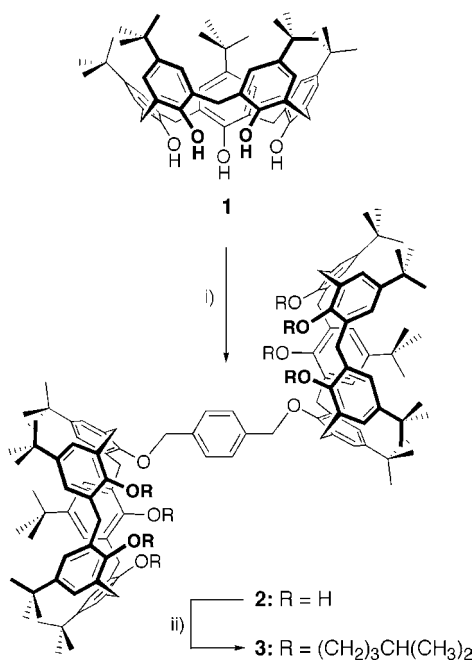


Figure 1. Reagents and conditions: (i) 1,4- $C_6H_4(CH_2Br)_2$ (0.5 equiv), CsF (5 equiv), DMF, rt, 44%; (ii) $(CH_3)_2CH(CH_2)_3OTs$ (24 equiv), K_2CO_3 (24 equiv), MeCN, reflux, 58%.

of **2** and **3** were assigned on the basis of NMR and ESI MS evidence and confirmed by a single-crystal X-ray analysis of **3**.¹²

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Crystals of **3** were shown to contain two independent molecules (**I** and **II**), each possessing an inversion center at the middle of the linking *p*-xylyl spacer (Figure 2). The

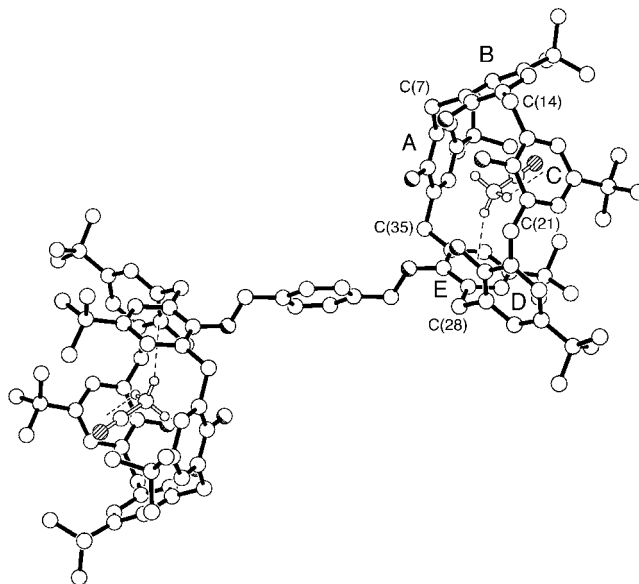


Figure 2. Molecular structure of one (**I**) of the two independent C_i symmetric bis-calix[5]arenes present in the crystals of **3** (the pendant isohexyl groups, which adopt an extended conformation, have been omitted for clarity).

conformations of **I** and **II** are very similar with both molecules having approximate local C_s symmetry about a plane passing through the methylene bridging carbon C(7) and bisecting ring D. The five linking methylene carbon atoms [C(7), C(14), C(21), C(28), and C(35)] are coplanar to within 0.43 and 0.38 Å in molecules **I** and **II**, respectively. The five phenol rings A–E in **I** (A'–E' in **II**) are inclined

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(12) **Crystal Data for 3:** $C_{166}H_{242}O_{10} \cdot 2MeCN$, $M = 2479.7$, triclinic, $P\bar{1}$ (no. 2), $a = 14.499(1)$ Å, $b = 22.921(2)$ Å, $c = 23.901(2)$ Å, $\alpha = 84.96(1)^\circ$, $\beta = 87.54(1)^\circ$, $\gamma = 86.32(1)^\circ$, $V = 7891(1)$ Å³, $Z = 2$ (two independent C_i symmetric molecules), $D_c = 1.044$ g/cm³, $\mu(Cu K\alpha) = 0.48$ mm⁻¹, $T = 183$ K, colorless platy prisms; 22 829 independent measured reflections, F^2 refinement, $R_1 = 0.080$, $wR_2 = 0.201$, 13 144 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 120^\circ$], 1789 parameters. CCDC 220755.

by 48 (57), 61 (52), 97 (95), 41 (38), and 92 (90°), respectively, to their respective methylene planes.

The cavity of each calix[5]arene moiety acts as a host for a guest acetonitrile solvent molecule, which is bound by a pair of C–H··· π hydrogen bonds with H··· π separations of 2.66 (C), 2.64 (E), 2.62 (C'), and 2.60 Å (E').

A preliminary screening of the binding affinity of **3** for the dipicrate salts of linear alkyldiammonium guest ions (G, [H₃N–(CH₂)_n–NH₃]²⁺; **4**, *n* = 9; **5**, *n* = 10) using the ESI MS technique¹³ ([**3**]/[G] = 2:1 to 1:2; 7.9 × 10^{−5} M, in CHCl₃/MeOH 2:1, v/v), provided evidence for the formation of three different types (A–C, Figure 3) of host–guest

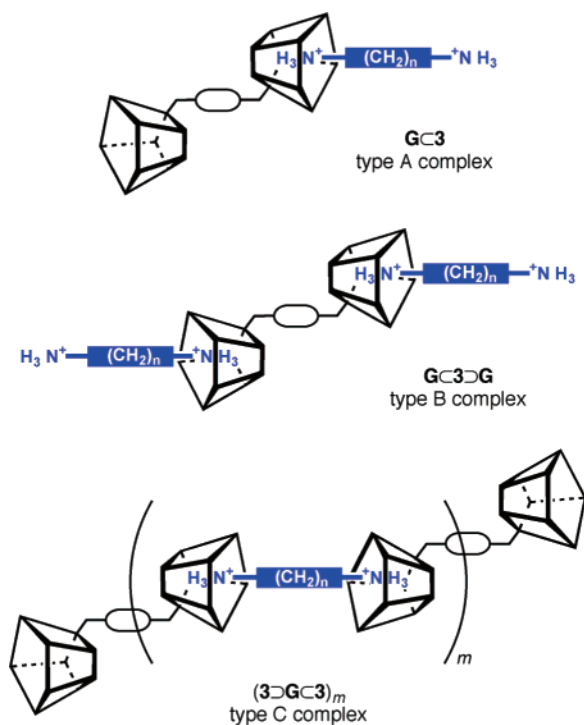


Figure 3. Schematic representation of the possible binding modes of **3** to alkyldiammonium ions.

complexes. Accordingly, the spectra display intense ion peaks of composition [G⊂3]²⁺ (type A complexes), moderately intense ion peaks corresponding to [3⊂G⊂3]²⁺ (type C complexes, *m* = 1),¹⁴ and low-intensity peaks due to [G⊂3⊂G – 2H]²⁺ (type B complexes).

The host–guest behavior of bis-calix[5]arene **3** toward alkyldiammonium ions **4** and **5** was then investigated by ¹H NMR titration experiments in CDCl₃–CD₃OD (2:1, v/v). The various complexation modes of ditopic receptor **3** to alkyldiammonium ions could be differentiated and monitored by following the host–guest spectral changes as a function of the [**3**]/[G] ratio. Upon addition of increasing amounts of the guest salt (up to 6 equiv) to a 2.0 × 10^{−3} M solution of

the host, the ¹H NMR spectra showed distinct signals for the free and complexed host and guest species, in a slow exchange regime on the ¹H NMR time scale.^{8,9} In agreement with the *endo*-cavity nature of the assemblies, the high-field region of the spectra (−1.9 to 0.7 ppm) displayed one or more sets of signals for the alkylene protons of the included guest, according to the number/type of complexed species present in solution.

The ¹H NMR titration experiments with **4** firmly establish that the formation of capsular assemblies (type C complexes) in solution is prevented by the short length of the guest alkyl chain, whereas the filling of the two calix[5]arene cavities of **3** to produce the type B complex proceeds in a stepwise manner via the type A complex. The formation of a type A complex (1:1 host/guest) is detected at low guest concentrations (≤ 0.5 equiv), as substantiated by the desymmetrization of the two components (doubling of both host and guest resonance patterns). As expected, an increase in the concentration of **4** (up to 6 equiv) shifts the complexation equilibrium toward the formation of the type B complex (1:2 host/guest).

The evolution of the ¹H NMR spectra in the titration experiment of **3** with the longer dication **5** is shown in Figure 4. In this case, the host/guest spectral changes observed for

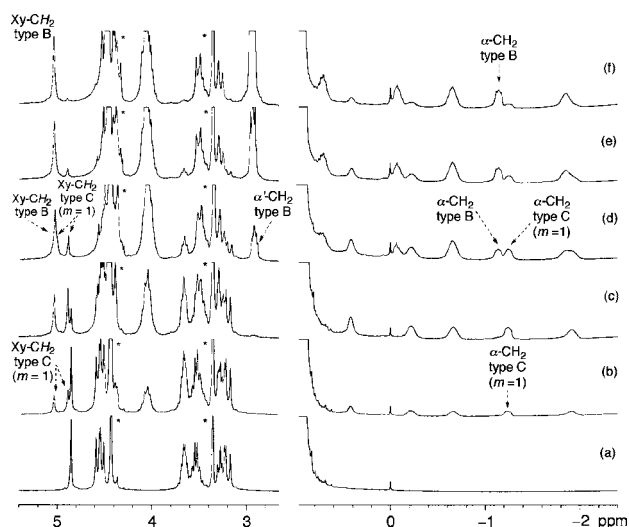


Figure 4. Selected regions of the ¹H NMR (300 MHz; 22 ± 1 °C; CDCl₃/CD₃OD 2:1) titration experiment of **3** (2.0 × 10^{−3} M) with **5**: (a) **3**; (b) **3/5** 1:0.25; (c) **3/5** 1:0.5; (d) **3/5** 1:1.5; (e) **3/5** 1:3; (f) **3/5** 1:6. Asterisks indicate residual solvent peaks.

[**3**]/[**5**] ≥ 2 (Figure 4, traces b and c) are commensurate with the nearly exclusive presence of the type C complex (*m* = 1), as previously evidenced by ESI MS. Contrary to type A complexes, the 3⊂5⊂3 capsular assembly causes desymmetrization of the host only, while the included guest remains symmetric and shows the expected resonance pattern in the high-field region of the spectrum. At lower [**3**]/[**5**] ratios (Figure 4, trace d), one can observe the appearance of a second less shielded set of signals for the included guest

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arising from the type B complex.¹⁵ The presence of such species, featuring, besides the symmetric host, two units of desymmetrized guest, is supported by a diagnostic triplet at δ 2.91 ppm (α' -CH₂ protons of **5**).¹⁶ When the [3]/[5] ratio is lowered further, the relative intensity of the set of signals associated with type B complex increases considerably with a concomitant decrease of the intensity of the set of signals due to the capsular (type C) complex (Figure 4, traces e and f).

Evidence of polycapsular assemblies was provided by a series of ¹H NMR dilution experiments on a more concentrated 1:0.9 host/guest mixture ([3] = 5.0×10^{-2} M and [5] = 4.5×10^{-2} M) in CDCl₃/CD₃OD (9:1, v/v)¹⁷ shown in Figure 5. Scrutiny of the ¹H NMR spectrum of the 3/5

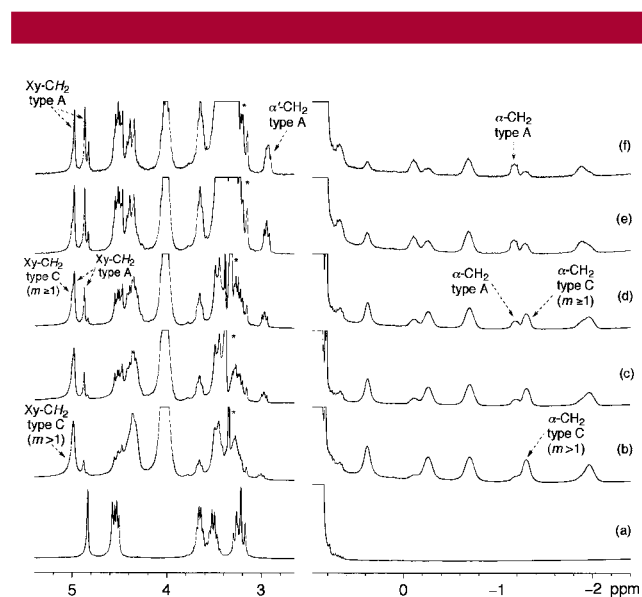


Figure 5. Selected regions of the ¹H NMR (300 MHz; 22 ± 1 °C; CDCl₃/CD₃OD 9:1) spectra of: (a) **3** (5.0×10^{-2} M); (b) a host–guest stock solution ([3] = 5.0×10^{-2} M and [5] = 4.5×10^{-2} M) and after dilution to (c) 1/5; (d) 1/10; (e) 1/50; and (f) 1/100. Asterisks indicate residual solvent peaks.

solution at the highest concentration under study (Figure 5, trace b) revealed that (i) free host and guest species are almost absent and (ii) the probe benzylic (Xy–CH₂) and

(14) In agreement with our earlier observations on single-cavity calix[5]arene hosts,⁹ the [3⊃G⊃3]²⁺ ion peak (capsule formation) could be barely seen with the short 1,9-nonanediammonium ion (**4**).

α -CH₂ protons display essentially single broad resonances at δ 4.98 and -1.30 ppm, respectively. On the basis of symmetry considerations, this pattern is consistent with the formation of polycapsular assemblies of **3** and **5** (type C complexes, $m > 1$). At the same time it rules out both the presence of the type C complex ($m = 1$) and that of the 5⊃3⊃5⊃3⊃5 assembly (formally a type C ($m = 1$) complex with both external cavities filled by two additional guest molecules). The former would show two anisochronous benzyl singlets, whereas the latter would display two equally intense resonances (at slightly different chemical shifts,¹⁵ see trace d of Figure 4) for the four included α -CH₂ groups. All these observations point to the formation, at high host–guest concentrations, of self-organized capsular assemblies of **3** and **5** modules along a polymer chain via iterative inclusion processes.

Disruption of the polycapsular assembly takes place by progressive dilution of the original NMR stock solution (Figure 5, traces c–f). At the lowest concentration investigated (Figure 5, trace f), the ¹H NMR spectrum is in agreement with the ultimate formation of the type A complex. The asymmetric nature of this complex gives rise to a pair of singlets for the Xy–CH₂ groups of the host and distinct resonances for the α - and α' -CH₂ groups of the included guest.

In conclusion, we have shown by NMR spectroscopy that exoditopic bis-calix[5]arene **3** reversibly forms polycapsular assemblies with 1,10-decanediammonium ions via iterative inclusion processes. Fine-tuning of the assembly process by subtle structural variations of the modules employed is currently under active investigation.

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Supporting Information Available: Experimental procedures and characterization data for compounds **2** and **3**, ESI MS spectra, selected ¹H NMR data of the host–guest assemblies formed, and a crystallographic CIF file for **3**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(15) CIS values indicate that the N-terminal group of the guest is more deeply included in type B than in type C complexes, in agreement with our earlier observations on capsules derived from single-cavity calix[5]arenes.⁹

(16) Concerning type A and B inclusion complexes, we arbitrarily designate the guest end-groups located inside and outside the calixarene cavity as α -CH₂ and α' -CH₂, respectively.

(17) Change of solvent was dictated by the limited solubility of **3** in the original CDCl₃–CD₃OD mixture at higher concentrations.