Practical Synthesis of Selectively Functionalized Cavitands

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Introduction

Cavitands are conformationally rigid derivatives of resorcinarenes with enforced cavities which bind complementary organic compounds or ions.[1] New monomeric cavitand derivatives continue to display fascinating and useful properties,[2] while noncovalently linked dimeric assemblies form the basis of reversible molecular capsules with intriguing possibilities.[3] On the other hand, the covalent linking of two bowl-shaped cavitand molecules rim-to-rim affords fully encapsulating, closed-shell container molecules (carcerands and hemicarcerands) which accommodate small guests from solvent molecules to exotic entities such as cyclobutadiene and benzyne.[4]

For thorough investigations into the effects of host structure upon guest binding, all potential functionality patterns about the rim of the cavitand must be accessible. Moreover, while elegant work into templation is allowing remarkably high-yielding routes to some carceplexes and hemicarceplexes,[5] the majority of these container molecules are still produced in low yields from precursor cavitands. In light of this frequently low-yielding shell closure step, optimal yields for the synthesis of unsymmetrical cavitands must be realized.[6] Also, in the push toward larger hosts made up of assemblies of four or more cavity molecules,[7] the efficient selective functionalization of symmetrical cavitand molecules is an important goal.

With two different groups at the rim of the bowl, four unsymmetrically-functionalized cavitands are possible (structures **4**−**7**, Figure 1). Compounds representing all four substitution patterns have been prepared previously, albeit in inefficient reactions. Much-utilized triols **4b** are formed in 5−20% yields as byproducts in the conversion

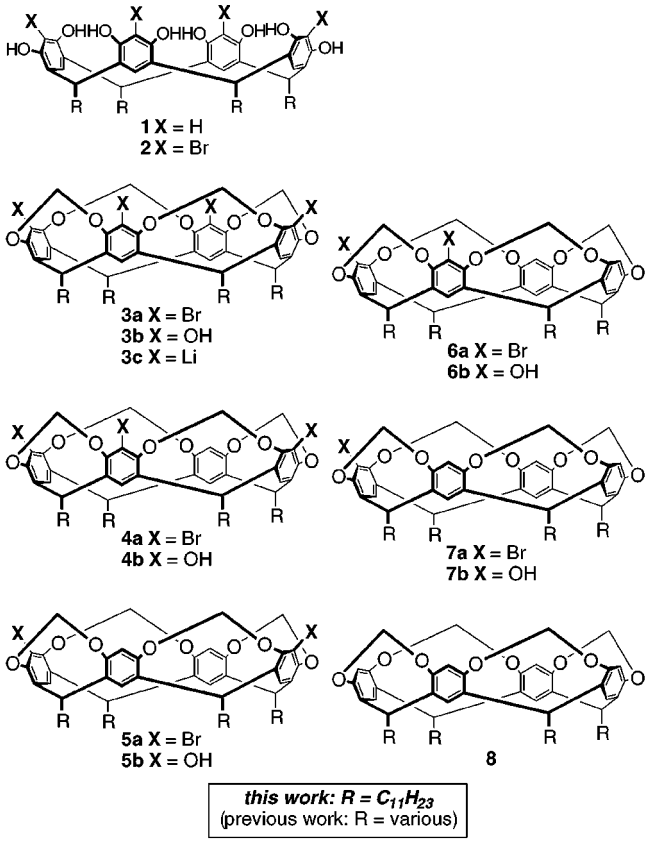

Figure 1.

of tetrabromides **3a** into tetrols **3b**.[8] Directed synthesis by bromination of the parent resorcinarene **1** with 3 mol equiv of NBS followed by installation of four methylene bridges, lithiation, arylboronate formation, and oxidation led to the formation of triol **4b** (5%) and a 2:1 mixture of A,C-diol **5b** and A,B-diol **6b** (8%).[9] The preparation of monol **7b** was recently reported in 11% yield,[5] once again as a byproduct en route to tetrol **3b**. Sorrell[10] and Reinhoudt[11] have reported high (75−80%) yielding procedures for the synthesis of A,B-difunctionalized cavitands such as **6a** by way of triply bridged resorcinarene derivatives.[11,12] Unfortunately, in addition to the extra synthetic step required to secure the cavitand, the requisite triply bridged resorcinarenes are themselves accessible in maximum yields of ca. 50%.[11] Herein we describe optimized procedures for the synthesis of all possible partially brominated cavitand molecules from

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Table 1. Reactions of Tetrabromocavitand 3a with Bu_3SnH[a]

3a + Bu_3SnH → **4a** + **5a** + **6a** + **7a** + **8**

run	Bu_3SnH (mol equiv)	initiator	temp (°C)	relative yields[b] (%) 3a	4a	5a	6a	7a	8
1	1.1	AIBN	80	40	43	6	9	2	
2	2.2	AIBN	80	6	26	19	20	22	7
3	3.3	AIBN	80			7	12	55	26
4	4.4	AIBN	80						100
5	1.1	BEt_3/O_2	25	31	45	7	13	4	

[a] Reactions were carried out with 100 μmol of **3a** in degassed toluene (1.0 mL) under Ar. See the Experimental Section for details. [b] Yields were measured by HPLC analysis of the product mixture.

Table 2. Reactions of Tetrabromocavitand 3a with *n*-BuLi; MeOH[a]

3a + *n*-BuLi →
[lithiocavitand intermediates] + (excess) MeOH →
4a + **5a** + **6a** + **7a** + **8**

run	*n*-BuLi (mol equiv)	temp (°C)	relative yields[b] (%) 3a	4a	5a	6a	7a	8
1	1.1	−78	10	81	5	4		
2	2.1	−78		18	61	8	8	4
3	3.1	−78			30	9	27	35
4	4.1	−78					9	91
5[c]	2.1	−110	40	4	4	3	8	41
6	2.1	25	1	26	53	11	8	1
7[d]	2 × 1.1	−78		16	34	36	13	1
8[d]	3 × 1.1	−78		2	13	11	57	18

[a] Reactions were carried out with 200 μmol of **3a** in dry, degassed THF (10 mL) under Ar. See the Experimental Section for details. [b] Yields were measured by HPLC analysis of the product mixture and are the average of two runs (variation between runs ±4%). [c] The solubility of **1** is poor at this temperature. [d] Performed by addition of 1.1 equiv of *n*-BuLi, stirring at −78 °C for 20 min, and then quenching with MeOH (1.1 equiv) before the next aliquot of *n*-BuLi is added.

tetrabromocavitand **3a** ($R = C_{11}H_{23}$) on a practical (1.0 mmol) scale in isolated yields of 30−69%. These compounds represent a platform to an unprecedented array of supramolecular building blocks.

Results and Discussion

In light of the poor selectivity encountered in resorcinarene bromination,[9] we have investigated protocols for reductive debromination of the readily accessible tetrabromide **3a** ($R = C_{11}H_{23}$)[11] based upon radical intermediates and organolithium intermediates. The results of radical reductions of tetrabromocavitand **3a** are depicted in Table 1. As might be expected, radical chain reduction with 1.1, 2.2, and 3.3 mol equiv of Bu_3SnH gave statistical yields of the five possible products and recovered starting material (Table 1, runs 1−3). Lowering the reaction temperature increased the time necessary for complete consumption of the stannane but did not improve the selectivity (compare runs 1 and 5). It appears, therefore, that the bromine atoms on the rim of the bowl are too far apart to exert any steric influences upon the direction of approach of the tributylstannyl radical in the bromine atom abstraction step.

The results of lithium−halogen exchange/protiolytic hydrolysis experiments are provided in Table 2. Rapid addition of freshly titrated *n*-butyllithium (1.1 equiv) to a cold (−78 °C), dilute solution of tetrabromocavitand **3a** in THF, followed by stirring at this temperature for 20 min and then quenching with excess methanol, resulted in the formation of tribromocavitand **4a** with excellent selectivity (Table 2, run 1). Repetition of this procedure on tetrabromocavitand **3a** with 2.1 mol equiv of *n*-BuLi gave A,C-dibromocavitand **5a** with high selectivity (Table 2, run 2). In contrast, 3.1 equiv of *n*-BuLi gave roughly equimolar quantities of A,C-dibromocavitand **5a**, monobromocavitand **7a**, and unbrominated cavitand **8**. Curiously, repetition of the reaction with 2.1 equiv of *n*-BuLi at −110 °C led to the formation of the product of exhaustive lithium−halogen exchange, **8**, along with unreacted starting material **3a** in equal quantities. We attribute this result to the poor solubility of the tetrabromocavitand **3a** at this temperature.[13] The selectivity of lithium−halogen exchange does not change considerably when the reaction is conducted at ambient temperature with rapid addition of *n*-BuLi (compare entries 2 and 6, Table 2).[14]

The outcomes of these reactions can be explained by electrostatic repulsion between the reacting organolithium moieties. To distinguish between kinetic and thermodynamic control, a preformed solution of tetralithiocavitand **3c** was allowed to mix with a solution of tetrabromocavitand **3a** at −78 °C for the standard reaction time. After the reaction was quenched with alcohol, a mixture rich in the tetrabrominated and unbrominated cavitands **3a** and **8** was produced, demonstrating that lithium−bromine exchange between the lithioarene and bromoarene moieties is slow under the standard reaction conditions. When this experiment was repeated, this time allowing **3c** and **3a** to react at 0 °C for 20 min, a much greater degree of equilibration occurred, with tribromocavitand **4a** and A,C-dibromocavitand **5a** being the major products obtained after quenching. From these experiments we conclude that the selectivity observed in runs 1 and 2 (Table 2) is due *primarily* to kinetically controlled reactions in which the approaching *n*-butyllithium aggregate reacts preferentially with unlithiated cavitand molecules. Once all unlithiated cavitand molecules are consumed, lithium−bromine exchange proceeds with a high degree of selectivity at the aromatic ring on the resorcinarene framework *opposite* that carrying the lithium atom.

With high-yielding routes to **4a** and **5a** in hand, we turned our attention to the development of procedures for the synthesis of A,B-dibromocavitand **6a** and monobromocavitand **7a**. We reasoned that selective monolithiation/alcohol quenching of tribromocavitand **4a** should furnish an excess of A,B-dibromocavitand **6a** since exchange at the B-ring would be favored over reaction at the C-ring on both steric and statistical grounds. In the event, roughly equimolar amounts of the A,B- and A,C-dibromocavitands were produced, indicating that subtle electronic effects dominate the proceedings. Gratifyingly, addition of a third equivalent of *n*-BuLi to this mixture followed by an alcohol quench produces a mixture rich in the monobromocavitand **7a** (Table 2, run 8; cf. run 3). These procedures are most conveniently carried out in a

(13) The solubility of lithiated cavitands is presumably much higher than the parent tetrabromocavitand **1**, thereby facilitating the conversion to the tetralithiocavitand.

(14) Under these conditions, a white suspension is formed immediately after addition of the *n*-BuLi. This suspension dissolves within a few seconds.

"one-pot" sequence involving the successive addition of aliquots of *n*-BuLi and methanol to tetrabromide **3a**.

In summary, optimized procedures have been developed for the preparation of tribromocavitand **4a**, A,C-dibromocavitand **5a**, A,B-dibromocavitand **6a**, and monobromocavitand **7a**. While mixtures of products are generated in these reactions, separation of all six compounds can be carried out easily by column chromatography, and gram quantities of these unsymmetrically substituted derivatives are readily accessible. These procedures have been developed with the undecyl-footed cavitand. Solubility problems notwithstanding, the same levels of product selectivity will prevail with other cavitands. Finally, the suite of transformations already developed for the tetrabromide **3a**[1] can now be carried out upon the unsymmetrical bromides reported here, procedures which will allow much greater flexibility in the design of new cavitand-based hosts.

Experimental Section[15]

***C*-Undecyltetrabromooctahydroxycalix[4]resorcinarene 2 (R = $C_{11}H_{23}$).** **2** was prepared by slight modification of Reinhoudt's procedure.[11] To a slurry of *C*-undecylcalix[4]-resorcinarene **1**[16] (110 g, 100 mmol) in 2-butanone (625 mL) was added *N*-bromosuccinimide (85.4 g, 480 mmol) slowly, maintaining the temperature below 25 °C by cooling on an ice bath. The resulting solution was stirred for 18 h at 25 °C in the dark under N_2, then poured directly into boiling MeOH (2.0 L), reheated to boiling, and filtered while hot. The precipitate was washed with hot MeOH and dried in vacuo to give the tetrabromoresorcinarene **2** as an off-white powder (123 g, 87%): $R_f = 0.66$ (1:1 hexane/ethyl acetate); mp 290−291 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79 (br s, 8H), 7.20 (s, 4H), 4.40 (t, $J = 7.7$ Hz, 4H), 2.10 (m, 8H), 1.30−1.23 (m, 72H), 0.83 (t, $J = 6.8$ Hz, 12H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.5, 124.9, 123.1, 101.1, 35.2, 33.7, 31.0, 28.9, 28.9, 28.8, 28.7 (two coincident resonances), 28.4, 27.3, 21.7, 13.4 ppm; IR (KBr) 3395, 2924, 2852 cm^{-1}; FAB-MS *m*/*z* 1419.5 ($M^+ + 3H$, 19), 1265.3 ($M^+ - 2Br$, 100). Anal. Calcd for $C_{72}H_{108}Br_4O_8$: C, 60.85; H, 7.66; Br, 22.49. Found: C, 60.49; H, 7.86; Br, 22.33.

***C*-Undecyltetrabromocavitand 3a (R = $C_{11}H_{23}$).** **3a** was prepared by slight modification of Reinhoudt's procedure.[11] To a slurry of *C*-undecyltetrabromocalix[4]resorcinarene **2** (106 g, 75.0 mmol) and potassium carbonate (135 g, 973 mmol) in dry DMF (2.2 L) was added bromochloromethane (73.1 mL, 1.13 mol), and the mixture was stirred at 65 °C for 2 days under N_2. After 24 h, more bromochloromethane (10 mL, 154 mmol) was added. The DMF was removed in vacuo to give a dark brown gum. Ethyl ether (600 mL) was added to the residue, and then 2 M HCl (1 L) was slowly added, with stirring. After the mixture was stirred for 20 min, the ether phase was collected and the aqueous phase was extracted with more ether. The combined ether phases were washed with saturated brine, then dried over $MgSO_4$, and filtered. Evaporation of the solvent gave a clear brown gum which was subjected to column chromatography (1 kg of SiO_2, 1:1 hexane/CH_2Cl_2; $R_f = 0.83$ in 1:3 hexane/CH_2Cl_2) and then recrystallized (THF/MeOH) to afford the pure tetrabromocavitand product as colorless rhombs (78.5 g, 72%): mp 69−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (s, 4H), 5.96 (d, $J = 7.4$ Hz, 4H), 4.86 (t, $J = 8.1$ Hz, 4H), 4.39 (d, $J = 7.4$ Hz, 4H), 2.23−2.17 (m, 8H), 1.42−1.27 (m, 72H), 0.89 (t, $J = 6.8$ Hz, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 140.0, 119.8, 114.2, 99.2, 37.0, 31.6, 29.6, 29.4 (four coincident resonances), 29.3, 29.1, 27.4, 22.4, 13.8 ppm; IR (KBr) 3001, 2924, 2852 cm^{-1}; UV−vis (hexane) λ_{max} 280 nm ($\epsilon = 4900$); FAB-MS *m*/*z* 1468.4 ($M^+ + 4H$, 100). Anal. Calcd for $C_{76}H_{108}Br_4O_8$: C, 62.13; H, 7.41; Br, 21.75. Found: C, 61.72; H, 7.34; Br, 21.73.

General Procedure for Radical Reductions (Table 1). To a stirred, degassed solution of tetrabromocavitand **3a** (147 mg, 100 μmol) in toluene (1.0 mL) under an argon atmosphere were added tributyltin hydride (quantity as listed in Table 1) and AIBN (2.0 mg, 10 μmol). The mixture was heated to 80 °C for 4 h, then cooled to room temperature, and diluted with ether. The resulting solution was washed with 30% aqueous ammonium hydroxide solution and saturated brine and dried over $MgSO_4$ before the solvent was evaporated in vacuo. Removal of the majority of the tin byproducts was accomplished by filtration through a short plug of SiO_2 (5 g) eluting with diethyl ether. The product mixture was obtained as a colorless oil. HPLC analysis was performed on a 50 μL aliquot of a ca. 0.01 M solution of the crude cavitand mixture dissolved in hexane. For entry 5, BEt_3 (100 μL of 1.0 M solution in hexanes, 100 μmol) and O_2 (50 μL of air, bubbled into solution) were added instead of AIBN, and the resulting mixture was stirred at 25 °C. This reaction required 27 h for complete consumption of the stannane.

General Procedure for Ionic Reductions (Table 2). To a one-necked 25 mL round-bottomed flask fitted with a septum and stirrer bar containing tetrabromcavitand **1** (294 mg, 200 μmol) was added dry, freshly distilled THF (2.0 mL), and the resulting solution was evaporated to dryness at 80 °C and 0.1 mmHg. The vacuum was replaced with Ar, and the procedure was repeated two more times. To this dried sample of **1** was added THF (10 mL), and once dissolution was complete, the solution was cooled to −78 °C under argon, whereupon *n*-butyllithium (ca. 1.30 M, quantity as listed in Table 2) was added dropwise. After being stirred for 20 min, the reaction mixture was quenched at −78 °C by the addition of dry methanol (1.0 mL), and the mixture was allowed to warm to room temperature. The solvents were removed in vacuo, and the residue was passed through a short plug of SiO_2 (5 g) eluting with diethyl ether. The product mixture was obtained as a colorless oil. HPLC analysis was performed on a 50 μL aliquot of a ca. 0.01 M solution of the crude cavitand mixture dissolved in hexane. For entries 7 and 8, quenching was performed at −78 °C by addition of a 2% v/v solution of methanol in THF (405 μL, 200 μmol) followed by stirring for 10 min before addition of the next aliquot of *n*-BuLi.

***C*-Undecyltribromocavitand 4a (R = $C_{11}H_{23}$).** To *C*-undecyltetrabromocavitand **3a** (1.47 g, 1.00 mmol) was added dry, freshly distilled THF (10 mL), and the solution was evaporated to dryness and then heated to 80 °C at 0.1 mmHg for 1 h. Repeating this process twice gave material sufficiently dry for the selective reductive debromination reaction. After dissolution in anhydrous THF (50 mL), the reaction mixture was cooled to −78 °C, and *n*-butyllithium (495 μL of a 2.22 M in hexanes, 1.10 mmol) was added rapidly. After 0.25 h, methanol (1.0 mL) was added rapidly, then the cooling bath was removed, and the mixture was allowed to warm to room temperature. Solvent evaporation gave a residue which was taken up in ether and washed with water and saturated brine and dried over anhydrous $MgSO_4$ to give the crude product mixture as a colorless solid (1.33 g). Pure *C*-undecyltribromocavitand **4a** was obtained by flash column chromatography (60 g of SiO_2, 2:1 → 1:1 → 1:2 hexane/CH_2Cl_2) as a colorless powder (963 mg, 69%): mp 72−74 °C (*t*-BuOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 1H), 7.04 (s, 3H), 6.53 (s, 1H), 5.95 (d, $J = 7.4$ Hz, 2H), 5.85 (d, $J = 7.4$ Hz, 2H), 4.85 (t, $J = 8.0$ Hz, 2H), 4.78 (t, $J = 8.0$ Hz, 2H), 4.41 (d, $J = 7.4$ Hz, 2H), 4.38 (d, $J = 7.4$ Hz, 2H), 2.22−2.17 (m, 8H), 1.41−1.24 (m, 72H), 0.88 (t, $J = 6.8$ Hz, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 152.4−152.0, 139.8, 139.5, 139.4, 139.3, 138.5, 121.0, 119.3, 119.2, 117.0, 113.5, 99.1, 98.7, 37.8, 37.2, 32.1, 29.9, 29.7, 29.7, 29.6, 29.4, 29.3, 27.9, 22.8, 14.1 ppm; IR (KBr) 2996, 2924, 2851 cm^{-1}; UV−vis (hexane) λ_{max} 280 nm ($\epsilon = 3800$); FAB-MS *m*/*z* 1390.5 ($M^+ + 4H$, 100). Anal. Calcd for $C_{76}H_{109}Br_3O_8$: C, 65.65; H, 7.90; Br, 17.24. Found: C, 65.39; H, 7.93; Br, 16.88.

***C*-Undecyl-A,C-dibromocavitand 6a (R = $C_{11}H_{23}$).** A sample of *C*-undecyltetrabromocavitand **3a** (1.47 g, 1.00 mmol) was dried as described above. After the dried sample was dissolved in anhydrous THF (50 mL), the solution was cooled to −78 °C, and *n*-butyllithium (945 μL of a 2.22 M solution in hexanes, 2.10 mmol) was added rapidly. After 0.25 h, methanol (1.0 mL) was added rapidly, then the cooling bath was removed, and the mixture was allowed to warm to room temperature. Workup as above gave the crude product as a colorless solid (1.28 g). Pure *C*-undecyl-A,C-dibromocavitand **6a** was obtained by

(15) For general details, see the Supporting Information.

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flash chromatography (60 g of SiO_2, 2:1 → 1:1 → 1:2 hexane/CH_2Cl_2) followed by radial chromatography (75 × 4 mm plate, hexane → hexane/15% ether) as a colorless powder (600 mg, 46%): mp 70−71 °C (*t*-BuOMe/EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 2H), 7.06 (s, 2H), 6.52 (s, 2H), 5.85 (d, J = 7.3 Hz, 2H), 4.78 (t, J = 8.1 Hz, 2H), 4.40 (d, J = 7.3 Hz, 2H), 2.22−2.16 (m, 8H), 1.41−1.27 (m, 72H), 0.88 (t, J = 6.8 Hz, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 152.0, 139.4, 138.3, 120.9, 118.9, 116.3, 113.1, 99.0, 37.0, 31.9, 29.9, 29.8, 29.7, 29.4, 27.8, 22.7, 14.1 ppm; IR (KBr) 2991, 2923, 2851 cm^{-1}; UV−vis (hexane) λ_{max} 279 nm (ϵ = 4800); FAB-MS m/z 1310.6 (M^+ + 2H, 100). Anal. Calcd for $C_{76}H_{110}Br_2O_8$: C, 69.60; H, 8.45; Br, 12.19. Found: C, 69.87; H, 8.58; Br, 11.93.

***C*-Undecyl-A,B-dibromocavitand 5a (R = $C_{11}H_{23}$).** A sample of *C*-undecyltetrabromocavitand **3a** (1.47 g, 1.00 mmol) was dried as described above. After the dried sample was dissolved in anhydrous THF (50 mL), the solution was cooled to −78 °C, and *n*-butyllithium (495 μL of a 2.22 M solution in hexanes, 1.10 mmol) was added rapidly. After 0.25 h, 2-methyl-2-propanol (103 μL, 1.10 mmol) was added rapidly, and stirring was continued at −78 °C for 5 min. A second aliquot of *n*-butyllithium (495 μL of a 2.22 M solution in hexanes, 1.10 mmol) was added rapidly, and the reaction mixture was stirred at −78 °C for 0.25 h. Methanol (1.0 mL) was added rapidly, the cooling bath was removed, and the mixture was allowed to warm to room temperature. Workup as above gave the crude product as a colorless solid (1.37 g). Pure *C*-undecyl-A,B-dibromocavitand **5a** was obtained by flash chromatography (60 g of SiO_2, 2:1 → 1:1 → 1:2 hexane/CH_2Cl_2) followed by radial chromatography (75 × 4 mm plate, hexane → hexane/15% ether) as a colorless powder (387 mg, 30%): mp 73−75 °C (*t*-BuOMe/EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 2H), 7.06 (s, 2H), 6.51 (s, 2H), 5.95 (d, J = 7.3 Hz, 1H), 5.85 (d, J = 7.2 Hz, 2H), 5.75 (d, J = 7.2 Hz, 1H), 4.84 (t, J = 8.1 Hz, 1H), 4.78 (t, J = 8.0 Hz, 2H), 4.72 (t, J = 8.1 Hz, 1H), 4.45 (d, J = 7.2 Hz, 1H), 4.40 (d, J = 7.2 Hz, 2H), 4.37 (d, J = 7.3 Hz, 1H), 2.23−2.10 (m, 8H), 1.41−1.22 (m, 72H), 0.88 (t, J = 6.8 Hz, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 154.7, 154.6, 152.1, 151.9, 151.7, 139.6, 139.3, 139.1, 138.5, 138.3, 137.9, 120.8, 120.6, 119.0, 188.8, 116.7, 113.1, 99.4, 98.9, 98.5, 65.8, 37.6, 36.9, 36.2, 31.9, 29.8, 29.8, 29.7, 29.4, 27.8, 22.7, 15.2, 14.1 ppm; IR (KBr) 2999, 2919, 2850 cm^{-1}; UV−vis (hexane) λ_{max} 278 nm (ϵ = 5200); FAB-MS m/z 1310.7 (M^+ + 2H, 100). Anal. Calcd for $C_{76}H_{110}Br_2O_8$: C, 69.60; H, 8.45; Br, 12.19. Found: C, 69.43; H, 8.60; Br, 11.87.

***C*-Undecylmonobromocavitand 7a (R = $C_{11}H_{23}$).** A sample of *C*-undecyltetrabromocavitand **3a** (1.47 g, 1.00 mmol) was dried as described above. After the dried sample was dissolved in anhydrous THF (50 mL), the solution was cooled to −78 °C, and *n*-butyllithium (495 μL of a 2.22 M solution in hexanes, 1.10 mmol) was added rapidly. After 0.25 h, 2-methyl-2-propanol (103 μL, 1.10 mmol) was added rapidly, and stirring was continued at −78 °C for 5 min. While the reaction mixture was maintained at −78 °C, there followed successive rapid additions of *n*-BuLi (495 μL of a 2.22 M solution in hexanes, 1.10 mmol), 2-methyl-2-propanol (103 μL, 1.10 mmol), and *n*-butyllithium (495 μL of a 2.22 M solution in hexanes, 1.10 mmol). Finally, methanol (1.0 mL) was added rapidly, the cooling bath was removed, and the mixture was allowed to warm to room temperature. Workup as above gave the crude product as a colorless solid (1.25 g). Pure *C*-undecylmonobromocavitand **7a** was obtained by flash chromatography (60 g of SiO_2, 2:1 → 1:1 → 1:2 hexane/CH_2Cl_2) as a colorless powder (668 mg, 54%): mp 65−66 °C (*t*-BuOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 3H), 7.06 (s, 1H), 6.50 (s, 2H), 6.49 (s, 1H), 5.85 (d, J = 7.2 Hz, 2H), 5.74 (d, J = 7.2 Hz, 2H), 4.78 (t, J = 8.1 Hz, 2H), 4.72 (t, J = 8.1 Hz, 2H), 4.44 (d, J = 7.2 Hz, 2H), 4.39 (d, J = 7.2 Hz, 2H), 2.24−2.17 (m, 8H), 1.42−1.23 (m, 72H), 0.88 (t, J = 6.8 Hz, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 154.9, 154.7, 152.0, 139.5, 139.4, 138.7, 138.4, 138.1, 120.8, 120.5, 119.0, 116.6, 113.0, 99.5, 99.0, 37.0, 36.3, 31.9, 31.9, 31.2, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.4, 27.9, 27.8, 22.7, 22.6, 14.1 ppm; IR (KBr) 2996, 2922, 2851 cm^{-1}; UV−vis (hexane) λ_{max} 278 nm (ϵ = 6400); FAB-MS m/z 1231.7 (M^+ + H, 100). Anal. Calcd for $C_{76}H_{111}BrO_8$: C, 74.06; H, 9.08; Br, 6.48. Found: C, 73.87; H, 8.97; Br, 6.35.

***C*-Undecylcavitand 8 (R = $C_{11}H_{23}$).** A sample of *C*-undecyltetrabromocavitand **3a** (735 mg, 500 μmol) was dried as described above. After the dried sample was dissolved in anhydrous THF (25 mL), the solution was cooled to −78 °C, and *n*-butyllithium (1.39 mL of a 1.61 M solution in hexanes, 2.24 mmol) was added rapidly. After 0.25 h, methanol (2.0 mL) was added rapidly, then the cooling bath was removed, and the mixture was allowed to warm to room temperature. Workup as above gave the crude product as a colorless solid (605 mg). Pure *C*-undecylcavitand **8** was obtained as a colorless powder after recrystallization from *t*-BuOMe/EtOH (574 mg, 99%): mp 115−116 °C (*t*-BuOMe/EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (s, 4H), 6.48 (s, 4H), 5.74 (d, J = 7.2 Hz, 4H), 4.72 (t, J = 8.1 Hz, 4H), 4.43 (d, J = 7.2 Hz, 4H), 2.24−2.19 (m, 8H), 1.42−1.27 (m, 72H), 0.89 (t, J = 6.8 Hz, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 138.4, 120.6, 116.4, 99.5, 36.3, 31.9, 29.9, 29.8, 29.8, 29.7 (three coincident resonances), 29.4, 27.9, 22.7, 14.1 ppm; IR (KBr) 2920, 2850 cm^{-1}; UV−vis (hexane) λ_{max} 277 nm (ϵ = 6700); FAB-MS m/z 1152.9 (M^+, 100). Anal. Calcd for $C_{76}H_{112}O_8$: C, 79.12; H, 9.78. Found: C, 79.08; H, 9.57.

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Supporting Information Available: General experimental procedures, representative HPLC traces, and ^{1}H and ^{13}C NMR spectra of **3a**, **4a**, **5a**, **6a**, **7a**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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