Facile Syntheses of New Cavitands with Mixed Substituents

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The $(CH_2Br)_4$ cavitand **1** and its reactions with NaOAc in varying stoichiometric ratios have been used to prepare a series of five different $(CH_2OAc)_{4-n}(CH_2Br)_n$ cavitands (n = 0–3) **2–6** with mixed substituents, which can be separated by column chromatography (combined yield >95%) and are thus available in multi-gram quantities. The substitution reaction is statistical and the yields of individual acetates are controlled by the amount of NaOAc relative to **1**. Careful hydrolysis of cavitands **2–6** with LiOH in THF-water results in the formation of the $(CH_2OH)_{4-n}(CH_2Br)_n$ cavitands (n = 0–3) **7–11** in yields of between 70–85%, Treatment of **2–6** with thiourea and NaOH affords the respective $(CH_2SH)_{4-n}(CH_2OH)_n$ cavitands (n = 0–3) **12–16** in yields of around 90%. Reactions of **2–6** with K-Phthalimide generate the respective $(CH_2Pht.)_{4-n}(CH_2OAc)_n$ cavitands (n = 0–3) **17–21**, which can be cleaved with hydrazine hydrate resulting in the $(CH_2NH_2)_{4-n}(CH_2OH)_n$ cavitands (n = 0–3) **22–26** in an overall yield of 60–70%.

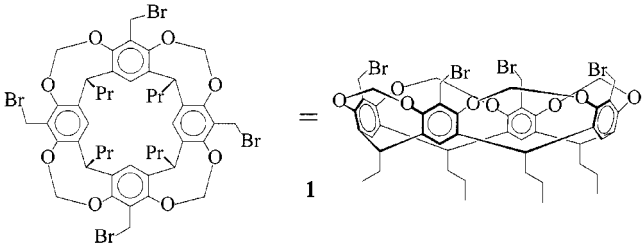
Introduction

Due mainly to the ground-breaking work of Cram and co-workers,[1] the concept of molecular encapsulation in cavitands and carcerands[2] or in so-called molecular capsules[3] is currently an area of active research within supramolecular chemistry.[4–7] One of the highlights in this field is the room temperature stabilisation of cyclobutadiene or benzyne locked up in a molecular prison.[8]

We are currently exploring whether cavitand frameworks can be used to coordinate metal ions next to or even within the cavity of such frameworks.[9–13] For this project cavitands are needed which contain several different substituents attached to the bowl.

Compared to the chemistry of calixarenes, the selective functionalization of cavitands is much less well explored[14] and not straightforward since the four identical subunits composing the cavitand are sterically as well as electronically virtually independent of each other.[15–23]

Consequently it will be difficult to functionalise a molecule such as **1** (Scheme 1) in a selective manner. Recently, however, preparative work by Reinhoudt et al. utilizing low priced starting materials provided facile synthetic access to the $(CH_2Br)_4$-substituted cavitand **1** in large amounts (>100 g), whose functional groups are very convenient for substitution reactions with nucleophiles. Consequently, depending on the availability of a good reagent, a statistical approach to partially functionalized cavitands may be a reasonable alternative to selective reactions. A reagent to effect the functionalisation should ideally meet a number of conditions: the reagent has to react in a very high yield with the benzyl bromide groups, the new substituents should be easily removed or transformed at a later stage of the synthesis, it should not interfere with other chemicals used for functionalization of the remaining benzyl bromides and it should invoke favorable properties for the separation of the partially substituted products. Some, but not all, of these requirements are fulfilled with K-phthalimide whose reactions with a pentyl-footed $(CH_2Br)_4$ cavitand were investigated by Reinhoudt and co-workers.[24]



Scheme 1

It is our opinion that all of the above-mentioned conditions are ideally met by NaOAc: a) almost quantitative yields and mild conditions for the reaction of NaOAc with benzyl bromides are observed, b) benzyl acetate can be easily cleaved (converted) under mildly basic conditions which do not affect the benzyl bromide groups to produce the synthetically highly useful $-CH_2OH$ group, c) acetate is quite polar, which contrasts with the unpolar cavitand and thereby facilitates chromatographic separation of the mixed acetate-bromides.

Consequently we wish to describe the synthesis of mixed $(CH_2OAc)_{4-n}(CH_2Br)_n$ cavitands (n = 0−3) and their transformation into the respective $(CH_2OH)_{4-n}(CH_2Br)_n$ cavitands (n = 0−3), $(CH_2SH)_{4-n}(CH_2OH)_n$ cavitands (n = 0−3) or $(CH_2NH_2)_{4-n}(CH_2OH)_n$ cavitands (n = 0−3).

Results and Discussion

The reaction of tetrabromocavitand **1** with NaOAc was tested in CH_3CN, diethyl ether, dimethylformamide and di-

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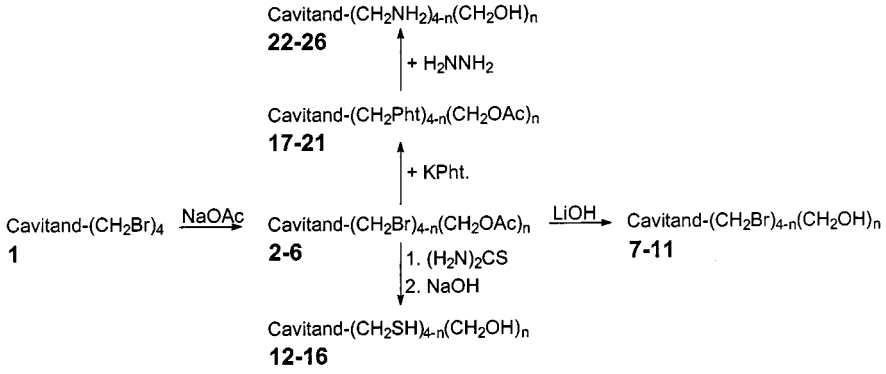
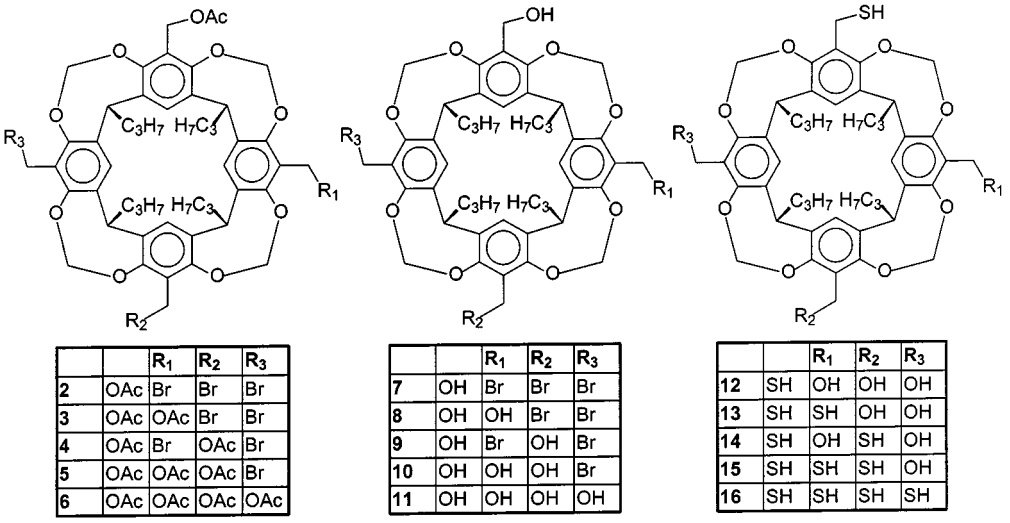
methylacetamide as solvents using different ratios of the two reactants. Due to the poor solubility of both starting materials the reaction is very slow in the first two solvents,[25] even when using phase-transfer catalysts and heating under reflux. In DMF the reaction at room temperature is usually complete within 24 h when using finely powdered NaOAc. Typical yields of the different acetates, however, are generally about 25% lower than in DMA, probably due to amine impurities in DMF.[26] Heating the reaction mixture to 50° C in DMA leads to completion of the nucleophilic substitution in less than 12 h. The solvent of choice therefore is DMA, which is best used for all reactions of cavitands with $-CH_2Br$ groups. A typical overall yield of the combined products for the acetate reaction after chromatographic purification is 90−95%. The acetate groups are introduced in a purely statistical manner and con-



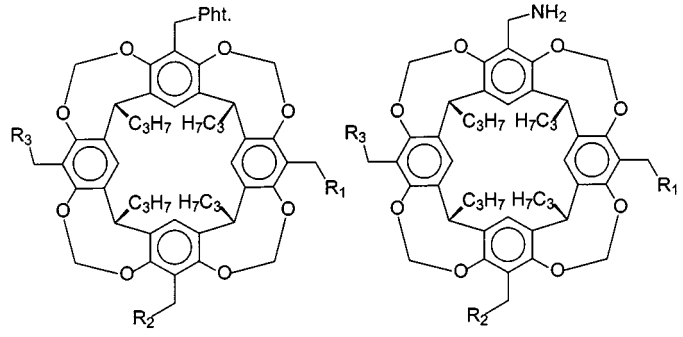
Scheme 2



		R_1	R_2	R_3
2	OAc	Br	Br	Br
3	OAc	OAc	Br	Br
4	OAc	Br	OAc	Br
5	OAc	OAc	OAc	Br
6	OAc	OAc	OAc	OAc

		R_1	R_2	R_3
7	OH	Br	Br	Br
8	OH	OH	Br	Br
9	OH	Br	OH	Br
10	OH	OH	OH	Br
11	OH	OH	OH	OH

		R_1	R_2	R_3
12	SH	OH	OH	OH
13	SH	SH	OH	OH
14	SH	OH	SH	OH
15	SH	SH	SH	OH
16	SH	SH	SH	SH



		R_1	R_2	R_3
17	Pht	OAc	OAc	OAc
18	Pht	Pht	OAc	OAc
19	Pht	OAc	Pht	OAc
20	Pht	Pht	Pht	OAc
21	Pht	Pht	Pht	Pht

		R_1	R_2	R_3
22	NH_2	OH	OH	OH
23	NH_2	NH_2	OH	OH
24	NH_2	OH	NH_2	OH
25	NH_2	NH_2	NH_2	OH
26	NH_2	NH_2	NH_2	NH_2

Scheme 3

sequently upon reaction of **1** and NaOAc mixtures of **1**, **2**, **3**, **4**, **5** and **6** are produced (Scheme 2 and 3). The ratio of mono-, di-, tri- and tetraacetate are variable and depend on the ratio of **1** and NaOAc; individual yields are given in Table 1.

Table 1. Product distribution in the reactions of **1** with variable amounts of NaOAc isolated after chromatography; Σ is the summed yield of all products (including **1**)

	1	**2**	**3** + **4**	**5**	**6**	Σ
+1.2 NaOAc	25%	32%	21%	9%	4%	91%
+2.2 NaOAc	7%	24%	31%	28%	6%	96%
+2.7 NaOAc	3%	10%	22%	29%	31%	95%

The two isomeric diacetate-dibromides are formed in the statistical ratio of 2:1 for the A,B- (**3**) and the A,C-isomer **4**. Due to the polar nature of the acetate group, the cavitands **1**−**6** can be separated by column chromatography. Since the R_f values of the isomeric A,B- and A,C cavitands **3** and **4** are quite close, the chromatographic purification of the two isomers is not always complete. Instead of using a large chromatographic column the rather different solubilities of **3** and **4** (the A,B-isomer **3** is always much more soluble) in a number of solvents (diethyl ether or THF) can be employed to extract the A,B-diacetate cavitand from the isomer mixture. The insoluble residue consists mainly of the A,C-diacetate.

The synthetic value of the acetate group can be demonstrated by a number of reactions. Under mild conditions (THF, LiOH) the acetates **2**, **3**, **5** and **6** can be hydrolyzed without affecting the $-CH_2Br$ groups to result in the respective mixed $(CH_2Br)_{4-n}(CH_2OH)_n$ cavitands **7**−**11** in 70−85% yield. Hydrolysis of the tetraacetate under the same conditions gives the respective tetra-alcohol **11** in 81% yield, which has been prepared recently with different feet, albeit in lower yields.[27,28]

The reaction of $(CH_2Br)_4$-substituted cavitands with thiourea and NaOH has been used previously to furnish the respective $(CH_2SH)_4$-substituted systems.[29−31] It can also be applied to the mixed $(CH_2Br)_{4-n}(CH_2OH)_n$ cavitands **7**−**10** to afford the $(CH_2SH)_{4-n}(CH_2OH)_n$ cavitands **12**−**15** in excellent yields. However, it is much more efficient to prepare the $(CH_2SH)_{4-n}(CH_2OH)_n$ cavitands directly from the respective $(CH_2Br)_{4-n}(CH_2OAc)_n$ cavitands **2**−**6**. Treatment with thiourea and NaOH affords the $(CH_2SH)_{4-n}(CH_2OH)_n$ cavitands **12**−**16** in excellent yields of around 90%, as the ester groups are cleaved during the NaOH treatment. The synthetic value of the mixed thiol-hydroxyl cavitands is greatly enhanced as the $-CH_2SH$ and $-CH_2OH$ groups can be reacted independent of each other.

The reaction of $(CH_2Br)_4$-substituted cavitands with K-phthalimide and hydrazine hydrate has been described by Reinhoudt et al. to give the respective $(CH_2NH_2)_4$ cavitands with pentyl feet.[32] This reaction can also be applied to the mixed acetate-bromide cavitands **2**−**6** in DMA to afford the respective $(CH_2Pht)_{4-n}(CH_2OAc)_n$ cavitands in good yields of between 60−70%. Cleavage of these compounds with hydrazine, followed by treatment with HCl affords the series of mixed $(CH_2NH_2)_{4-n}(CH_2OH)_n$ cavitands **22**−**26** in quantitative yields. Finally, it should be mentioned that while all of the substituted cavitands described here possess propyl feet, the same functionalisation reactions can be expected to work with cavitands substituted with feet other than propyl groups.[33]

Summary and Conclusions

Taking advantage of the ready availability of $(CH_2Br)_4$-substituted cavitands we were able to perform four types of useful functionalisation reactions leading to a series of previously unknown propyl-footed $(CH_2OAc)_{4-n}(CH_2Br)_n$ cavitands (n = 0−3), $(CH_2OH)_{4-n}(CH_2Br)_n$ cavitands (n = 0−3), $(CH_2SH)_{4-n}(CH_2OH)_n$ cavitands (n = 0−3) and $(CH_2NH_2)_{4-n}(CH_2OH)_n$ cavitands (n = 0−3). The reactions described here open a facile route to the synthesis of unsymmetrically substituted cavitands in multi-gram quantities with various functional groups that can be used as building blocks for a multitude of carcerands and hemicarcerands. We are currently exploring the metal-ion-coordinating properties of these compounds as well as those of carcerands and hemicarcerands derived from the mixed cavitands.

Experimental Section

General: Commercially available solvents and reagents were purified according to literature procedures.[34] 2-Methylresorcine and butyraldehyde were distilled prior to use. NBS was recrystallized and carefully dried. DMA was dried over molecular sieves. CH_2BrCl was used as received. NaOAc p.a. was dried (120° C, 0.1 Torr) prior to use. Column chromatography was done on silica MN60 (63−200 μm), TLC on Merck plates coated with silica gel 60, F254.

NMR Spectroscopy: Spectra were recorded at 300 K with a Bruker AC 300 (^{1}H NMR 200 MHz, ^{13}C NMR 75 MHz) or a Bruker AC 200 (^{1}H NMR, 200 MHz) spectrometer. ^{1}H NMR spectra were referenced to residual protonated impurities in the solvent and ^{13}C NMR to the solvent signals: $CDCl_3$ (δ_H = 7.26, δ_C = 77.0).

Mass Spectra: ESI-MS were recorded on a Bruker Esquire-LC. Starting materials were commercially available or synthesized according to literature procedures: The $(CH_2Br)_4$ cavitand[32,35] was prepared analogously to the procedure given by Reinhoudt and coworkers for the pentyl-footed analogue. However, after performing this reaction many times we often noticed that the bromination was not complete within the given time. In such cases more AIBN was added (sometimes several times) and reflux continued (for up to 48 h) until the reaction was complete (TLC control).

Synthesis of $(CH_2Br)_3(CH_2OAc)_1$ Cavitand, A,B-$(CH_2Br)_2$-$(CH_2OAc)_2$ Cavitand, A,C-$(CH_2Br)_2(CH_2OAc)_2$ Cavitand and $(CH_2Br)_1(CH_2OAc)_3$ Cavitand: The $(CH_2Br)_4$ cavitand (**1**) (12.0 g, 11.2 mmol) and NaOAc (2.02 g, 24.6 mmol, 2.2 equivalents) were added to dimethylacetamide (300 mL) and the reaction mixture stirred at 50° C. After 12 h the solvent was removed in vacuo and water (100 mL) added to the residue to completely extract the re-

maining solvent. After stirring the suspension for 30 min. the liquid was decanted and the remaining solid dissolved in CH_2Cl_2. The organic layer was separated, dried over $MgSO_4$ and filtered. Silica (ca. 50 g) was added to the solution to adsorb the products, and the volatiles were carefully evaporated. The product mixture and the silica were applied to a column with silica (1000 g) and cyclohexane/ethyl acetate (6:1). The different products were chromatographed with cyclohexane/ethyl acetate mixtures and the polarity of the eluents was changed when elution of each product was finished. For the $(CH_2Br)_4$ cavitand and $(CH_2Br)_3(CH_2OAc)_1$ cavitand a 6:1 mixture was used; for the $(CH_2Br)_2(CH_2OAc)_2$ cavitand a 4:1 mixture was used; for the $(CH_2Br)_1(CH_2OAc)_3$ cavitand a 2:1 mixture was used; for the $(CH_2OAc)_4$ cavitand a 1:1 mixture was used. The overall yield of isolated products corresponds to a total yield of 95%. A typical product distribution is $(CH_2Br)_4$ cavitand = 7%, $(CH_2Br)_3(CH_2OAc)_1$ cavitand = 24% $(CH_2Br)_2(CH_2OAc)_2$ cavitand = 31% (as the combined yield of A,B and A,C isomers, which are produced in a statistical 2:1 ratio), $(CH_2Br)_1(CH_2OAc)_3$ cavitand = 28% and $(CH_2OAc)_4$ cavitand = 6%. The R_f values of the cavitands in cyclohexane/ethyl acetate (3:1) are as follows: $(CH_2Br)_4$: R_f = 0.90; $(CH_2Br)_3(CH_2OAc)_1$: R_f = 0.68; A,C-$(CH_2Br)_2(CH_2OAc)_2$: R_f = 0.52; A,B-$(CH_2Br)_2(CH_2OAc)_2$: R_f = 0.48; $(CH_2Br)_1(CH_2OAc)_3$: R_f = 0.21; $(CH_2OAc)_4$: R_f = 0.08. Alternatively, $CH_2Cl_2 \rightarrow CH_2Cl_2$/EtOAc (95:5) can be used for the chromatography, which gives a better separation of the isomeric diacetates.

$(CH_2Br)_3(CH_2OAc)_1$ Cavitand (2): ^{1}H NMR ($CDCl_3$): δ = 7.15, 7.20 (s, 1+3 H, ArH), 6.03 (d, J = 7.0 Hz, 2 H, OC*H*HO), 5.94 (d, J = 7.4 Hz, 2 H, OC*H*HO outer), 4.94 (s, 2 H, $ArCH_2OAc$), 4.82 (t, J = 8.1 Hz, 2 H, ArCHAr), 4.81 (t, J = 8.1 Hz, 2 H, ArCHAr), 4.57 (d, J = 7.0 Hz, 2 H, OCH*H*O inner), 4.50 (d, J = 7.4 Hz, 2 H, OCH*H*O), 4.47 (s, 4 H, CH_2Br), 4.39 (s, 2 H, CH_2Br), 2.14−2.29 (m, 8 H, $CHCH_2$), 1.95 (s, 3 H, $OOCCH_3$), 1.30−1.47 (m, 8 H, $CH_2CH_2CH_3$), 1.03 (t, J = 7.4 Hz, 6 H, CH_3), 1.03 (t, J = 7.7 Hz, 6 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.8, 154.4, 153.7, 153.6, 138.2, 138.2, 138.1, 138.1, 124.6, 121.8, 121.5, 121.4, 121.0, 99.5, 99.2, 57.0, 56.2, 36.5, 32.2, 32.1, 23.2, 20.9, 14.2. − $C_{50}H_{55}Br_3O_{10}\cdot H_2O$ (1074): calcd. C 55.93, H 5.35; found C 56.17, H 5.23.

A,B-$(CH_2Br)_2(CH_2OAc)_2$ Cavitand (3): ^{1}H NMR ($CDCl_3$): δ = 7.21 (s, 2 H, ArH), 7.14 (s, 2 H, ArH), 6.03 (d, J = 7.4 Hz, 1 H, OC*H*HO), 5.92 (d, J = 7.4 Hz, 2 H, OC*H*HO outer), 5.87 (d, J = 7.0 Hz, 1 H, OC*H*HO), 4.98 (s, 4 H, $ArCH_2OAc$), 4.76−4.87 (m, 4 H, ArCHAr), 4.58 (d, J = 7.4 Hz, 1 H, OCH*H*O), 4.50 (d, J = 7.4 Hz, 2 H, OCH*H*O), 4.42 (d, J = 7.0 Hz, 1 H, OCH*H*O inner), 4.45 (s, 4 H, CH_2Br), 2.15−2.28 (m, 8 H, $CHCH_2$), 2.01 (s, 6 H, $OOCCH_3$), 1.32−1.45 (m, 8 H, $CH_2CH_2CH_3$), 0.99−1.08 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.7, 154.4, 153.7, 153.6, 138.3, 138.2, 138.1, 124.7, 121.8, 121.4, 121.1, 99.8, 99.4, 99.2, 57.1, 36.5, 32.2, 32.1, 23.2, 21.1, 20.9, 14.2. − $C_{48}H_{52}O_8\cdot H_2O$ (1053): calcd. C 59.32, H 5.74; found C 58.79, H 5.54.

A,C-$(CH_2Br)_2(CH_2OAc)_2$ Cavitand (4): ^{1}H NMR ($CDCl_3$): δ = 7.19 (s, 2 H, ArH), 7.15 (s, 2 H, ArH), 5.94 (d, J = 7.0 Hz, 4 H, OC*H*HO outer), 4.92 (s, 4 H, $ArCH_2OAc$), 4.81 (t, J = 8.1 Hz, 4 H, ArCHAr), 4.53 (OCH*H*O inner, d, 4 H, J = 7.0 Hz), 4.53 (s, 4 H, CH_2Br), 2.14−2.28 (m, 8 H, $CHCH_2$), 2.03 (s, 6 H, $OOCCH_3$), 1.40 (m, 8 H, J = 7.7 Hz, $CH_2CH_2CH_3$), 1.03 (t, J = 7.4 Hz, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.9, 154.4, 153.9, 138.1, 138.1, 124.7, 121.9, 121.4, 121.2, 99.5, 57.0, 36.5, 32.2, 23.2, 21.1, 20.9, 14.2. − $C_{48}H_{52}O_8\cdot H_2O$ (1053): calcd. C 59.32, H 5.74; found C 59.23, H 5.88.

$(CH_2Br)_1(CH_2OAc)_3$ Cavitand (5): ^{1}H NMR ($CDCl_3$): δ = 7.22 (s, 1 H, ArH), 7.20 (s, 2 H, ArH), 7.14 (s, 1 H, ArH), 5.93 (d, J = 7.4 Hz, 2 H, OC*H*HO outer), 5.86 (d, J = 7.0 Hz, 2 H, OC*H*HO inner), 5.05 (s, 2 H, $ArCH_2OAc$), 4.94 (s, 4 H, $ArCH_2OAc$), 4.84 (t, J = 8.1 Hz, 2 H, ArCHAr), 4.81 (t, J = 8.5 Hz, 2 H, ArCHAr), 4.53 (d, J = 7.4 Hz, 2 H, OCH*H*O), 4.38 (d, J = 7.0 Hz, 2 H, OCH*H*O), 4.51 (s, 2 H, CH_2Br), 2.14−2.29 (m, 8 H, $CHCH_2$), 2.00 (s, 9 H, $OOCCH_3$), 1.31−1.47 (m, 8 H, $CH_2CH_2CH_3$), 0.99−1.08 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.8, 170.5, 154.4, 154.2, 153.8, 138.4, 138.3, 138.1, 124.8, 121.8, 121.6, 121.3, 121.2, 99.8, 99.4, 57.3, 57.0, 36.5, 32.1, 23.3, 21.1, 20.9, 14.2. − $C_{54}H_{61}O_{14}Br\cdot 2H_2O$ (1050): calcd. C 61.77, H 6.24; found C 61.74, H 5.86.

Separation of the Isomeric Diacetate Cavitands (3) and (4): The separation of the two isomeric diacetates **3** and **4** by column chromatography is difficult and often incomplete. Alternatively, the diacetate mixture from column chromatography may also be enriched in the respective isomer by extraction with diethyl ether. It is, however, very important for the reproducibility of this separation to completely remove any residual solvent from the cavitands by drying the mixture at 60° C in vacuo (0.1 Torr) for at least 12 h. Adding 20 mL of diethyl ether per 1.0 g of isomer mixture (initially containing a 2:1 ratio of the A,B and A,C isomers) and stirring for 6 h gives an ether solution which contains almost pure A,B-diacetate (ca. 500 mg). The residue consists mostly of the A,C isomer. The ratios of the products were determined by ^{1}H NMR spectroscopy.

Reaction of the $(CH_2Br)_4$ Cavitand (1) with NaOAc (1.2 equiv. and 2.7 equiv.). − 1.2 Equiv. of NaOAc: $(CH_2Br)_4$ cavitand (1.08 g, 1.00 mmol); NaOAc (0.099 g, 1.20 mmol); DMA (25 mL).
Products: $(CH_2Br)_4$ cavitand = 270 mg (25%); $(CH_2Br)_3(CH_2OAc)_1$ cavitand = 330 mg (32%); $(CH_2Br)_2(CH_2OAc)_2$ cavitand = 205 mg (21%) (combined yield of A,B- and A,C-isomers); $(CH_2Br)_1(CH_2OAc)_3$ cavitand = 90 mg (9%); $(CH_2OAc)_4$ cavitand = 40 mg (4%).
2.7 equiv. NaOAc: $(CH_2Br)_4$ cavitand (1.08 g, 1.00 mmol); NaOAc (0.223 g, 2.70 mmol); DMA (25 mL).
Products: $(CH_2Br)_4$ cavitand = 35 mg (3%); $(CH_2Br)_3(CH_2OAc)_1$ cavitand = 95 mg (10%); $(CH_2Br)_2(CH_2OAc)_2$ cavitand = 210 mg (22%) (combined yield of A,B- and A,C-isomers); $(CH_2Br)_1(CH_2OAc)_3$ cavitand = 275 mg (29%); $(CH_2OAc)_4$ cavitand = 300 mg (31%).

Synthesis of the $(CH_2OAc)_4$ cavitand (6): The procedure is analogous to that of the partially substituted cavitands except that 10 equivalents of NaOAc per $(CH_2Br)_4$ cavitand are used. Following chromatography on silica with cyclohexane/ethyl acetate (1:1) the $(CH_2OAc)_4$ cavitand was isolated in a yield of 81%. − ^{1}H NMR ($CDCl_3$): δ = 7.20 (s, 4 H, ArH), 5.85 (d, J = 7.4 Hz, 4 H, OC*H*HO outer), 4.99 (s, 8 H, $ArCH_2OAc$), 4.83 (t, J = 8.1 Hz, 4 H, ArCHAr), 4.35 (d, J = 7.4 Hz, 4 H, OCH*H*O inner), 2.23 (q, J = 7.7 Hz, 8 H, $CHCH_2$), 2.01 (s, 12 H, $OOCCH_3$), 1.40 (m, J = 7.4 Hz, 8 H, $CH_2CH_2CH_3$), 1.04 (t, J = 7.4 Hz, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.6, 154.4, 138.3, 121.9, 121.4, 99.8, 57.1, 36.5, 32.1, 21.2, 20.9, 14.2.

General Procedure for the Hydrolysis of the Bromide−Acetate cavitands. Synthesis of the $(CH_2Br)_3(CH_2OH)_1$ Cavitand, A,B-$(CH_2Br)_2(CH_2OH)_2$ Cavitand $(CH_2Br)_1(CH_2OH)_3$ Cavitand and $(CH_2OH)_4$ Cavitand: A solution of the respective $(CH_2Br)_n(CH_2OAc)_{4-n}$ cavitand (n = 0−3; 1.00 g) in THF (100 mL) was added dropwise to a solution of LiOH (5 equiv. per acetate group) in water (5 mL) to produce a very fine precipitate of LiOH. The reaction mixture was stirred for 18 h, followed by

removal of the solvent in vacuo at room temperature. The residue was extracted with CH_2Cl_2, and silica added. The volatiles were evaporated, the residue applied to a column filled with silica and cyclohexane/ethyl acetate and purified by chromatography.

$(CH_2Br)_3(CH_2OH)_1$ Cavitand (7): $(CH_2Br)_3(CH_2OAc)_1$ cavitand (580 mg, 0.54 mmol), cyclohexane/ethyl acetate (1:1), yield: 402 mg (70%). – ^{1}H NMR ($CDCl_3$): δ = 7.15 (s, 3 H, ArH), 7.14 (s, 1 H, ArH), 6.02 (d, *J* = 7.4 Hz, 2 H, OC*H*HO outer), 5.97 (d, *J* = 7.4 Hz, 2 H, OC*H*HO outer), 4.82 (t, *J* = 8.1 Hz, 2 H, ArCHAr), 4.80 (t, *J* = 8.1 Hz, 2 H, ArCHAr), 4.57 (d, *J* = 7.4 Hz, 2 H, OCH*H*O inner), 4.50 (d, *J* = 7.4 Hz, 2 H, OCH*H*O inner), 4.52 (s, 2 H, $ArCH_2OH$), 4.45 (s, 4 H, CH_2Br), 4.40 (s, 2 H, CH_2Br), 2.10–2.32 (m, 8 H, $CHCH_2$), 1.60 (s, 1 H, CH_2OH), 1.29– 1.47 (m, 8 H, $CH_2CH_2CH_3$), 1.03 (t, *J* = 7.4 Hz, 6 H, CH_3), 1.02 (t, *J* = 7.4 Hz, 6 H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 138.4, 138.1, 138.0, 126.5, 124.7, 124.5, 121.3, 121.0, 120.2, 99.5, 99.2, 55.9, 36.5, 32.2, 32.1, 23.3, 23.1, 20.9, 14.2. – $C_{48}H_{53}Br_3O_9$ (1013.7): calcd. C 56.88, H 5.27; found C 56.11, H 5.45.

A,B-$(CH_2Br)_2(CH_2OH)_2$ Cavitand (8): $(CH_2Br)_2(CH_2OAc)_2$ cavitand (88 mg, 0.085 mmol), cyclohexane/ethyl acetate = 1:2, yield: 56 mg (69%). – ^{1}H NMR ($CDCl_3$): δ = 7.15 (s, 2 H, ArH), 7.14 (s, 2 H), 6.01 (d, *J* = 7.4 Hz, 1 H, OC*H*HO outer), 5.94 (d, *J* = 7.4 Hz, 3 H, OC*H*HO outer), 4.75–4.88 (m, 4 H, ArC*H*Ar), 4.63 (d, *J* = 7.4 Hz, 1 H, OCH*H*O inner), 4.52 (d, *J* = 7.4 Hz, 3 H, OCH*H*O inner), 4.55 (s, 4 H, $ArCH_2OH$), 4.44 (s, 4 H, CH_2Br), 2.10–2.29 (m, 8 H, $CHCH_2$), 1.65 (s, 2 H, CH_2OH), 1.30–1.48 (m, 8 H, $CH_2CH_2CH_3$), 0.98–1.10 (m, 12 H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 153.7, 153.6, 138.3, 138.0, 126.3, 124.6, 121.1, 120.4, 99.9, 99.4, 99.1, 55.8, 36.5, 32.2, 23.1, 20.9, 14.2. – $C_{48}H_{54}Br_2O_{10}$ (950.8): calcd. C 60.64, H 5.72; found C 60.17, H 6.15.

A,C-$(CH_2Br)_2(CH_2OH)_2$ Cavitand (9): Due to the initially poor solubility of cavitand **4**, its THF suspension must be heated to reflux to obtain a clear solution. The aq. LiOH is added after cooling the solution to room temperature. A,C-$(CH_2Br)_2(CH_2OAc)_2$ cavitand (160 mg, 0.15 mmol); cyclohexane/ethyl acetate (1:2); yield: 117 mg (0.12 mmol, 80%). – ^{1}H NMR ($CDCl_3$): δ = 7.08, 7.06 (s, 2+2 H, ArH), 5.91 (d, *J* = 7.2 Hz, 4 H, OC*H*HO outer), 4.73 (t, *J* = 8.1 Hz, 4 H, ArCHAr), 4.47 (s, 4 H, CH_2Br), 4.46 (d, *J* = 7.2 Hz, 4 H, OCH*H*O inner), 4.39 (d, *J* = 5.9 Hz, 4 H, $ArCH_2OH$), 2.13 (m, 8 H, $CHCH_2$), 1.30 (m, 8 H, $CH_2CH_2CH_3$), 0.96 (t, 12 H, *J* = 7.2 Hz, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 153.8, 153.6, 138.2, 138.0, 126.7, 124.5, 121.5, 120.0, 99.4, 56.0, 36.5, 32.2, 23.3, 20.9, 14.2. – $C_{48}H_{54}Br_2O_{10}$ (950.8): calcd. C 60.64, H 5.72; found C 60.28, H 6.00.

Separation of the Cavitands 8 and 9: The chromatographic separation (cyclohexane/ethyl acetate, 1:2) of the cavitands **8** and **9** is much easier than that of the related diacetates **3** and **4**. Consequently, for the synthesis of **8** and **9** it is preferable to hydrolyse the mixture of the diacetates **3** and **4** first and to separate **8** and **9** afterwards by chromatography.

$(CH_2Br)_1(CH_2OH)_3$ Cavitand (10): $(CH_2Br)_1(CH_2OAc)_3$ cavitand (150 mg, 0.15 mmol), cyclohexane/ethyl acetate = 1:2, yield: 103 mg (83%). – ^{1}H NMR ($CDCl_3$): δ = 7.17 (s, 1 H, ArH), 7.13 (s, 2 H, ArH), 7.12 (s, 1 H, ArH), 5.94 (d, *J* = 7.0 Hz, 2 H, OC*H*HO outer), 5.92 (d, *J* = 7.4 Hz, 2 H, OC*H*HO outer), 4.84 (t, *J* = 8.1 Hz, 2 H, ArCHAr), 4.79 (t, *J* = 8.1 Hz, 2 H, ArCHAr), 4.59 (d, *J* = 7.0 Hz, 2 H, OCH*H*O inner), 4.39 (d, *J* = 7.4 Hz, 2 H, OCH*H*O inner), 4.62 (s, 2 H, CH_2OH), 4.51 (s, 4 H, CH_2OH), 4.48 (s, 2 H, CH_2Br), 2.12–2.35 (m, 8 H, $CHCH_2$), 1.30–1.48 (m, 8 H, $CH_2CH_2CH_3$), 1.04 (t, 6 H, *J* = 7.4 Hz, CH_3), 1.03 (t, 6 H, *J* = 7.4 Hz, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 153.8, 153.7, 153.6, 153.6, 138.3, 138.1, 137.9, 126.6, 126.1, 124.9, 121.1, 120.7, 120.2, 100.0, 99.3, 55.9, 55.1, 36.5, 32.2, 32.1, 22.9, 20.9, 14.2. – $C_{48}H_{55}BrO_{11}\cdot H_2O$ (905.9): calcd. C 63.64, H 6.34; found C 63.66, H 6.52.

$(CH_2OH)_4$ Cavitand (11): A solution of the tetraacetate (1.98 g, 2 mmol) in THF (25 mL) was added to a solution of KOH (0.56 g, 10 mmol) in C_2H_5OH (15 mL). Stirring was continued for 30 min. at 40° C and the reaction mixture then evaporated to dryness. The residue was first extracted with water to remove the KOH and KOAc. The residue was dissolved in CH_2Cl_2, filtered and evaporated to give the pure product. $(CH_2OH)_4$ cavitand (1.00 g, 1.01 mmol); ethyl acetate; yield: 1.68 g (97%). – ^{1}H NMR ($CDCl_3$): δ = 7.19 (s, 1 H, ArH), 5.91 (d, *J* = 7.0 Hz, 2 H, OC*H*HO outer), 4.82 (t, *J* = 8.1 Hz, 2 H, ArCHAr), 4.54 (s, 2 H, CH_2OH), 4.42 (d, *J* = 7.4 Hz, 2 H, OCH*H*O inner), 2.18 (m, 8 H, $CHCH_2$), 2.0 (s, OH), 1.39 (m, 8 H, $CH_2CH_2CH_3$), 1.03 (t, *J* = 7.4 Hz, 6 H, CH_3). – ^{13}C NMR ($CDCl_3$): δ = 153.6, 138.3, 126.4, 120.4, 99.8, 56.7, 36.5, 32.1, 21.0, 14.2. – $C_{48}H_{56}O_{12}\cdot H_2O$ (842.98): calcd. C 68.39, H 6.93; found C 68.66, H 6.20.

General Procedure for the Synthesis of the mixed Thiol–Hydroxyl Cavitands: $(CH_2SH)_1(CH_2OH)_3$ Cavitand, A,B-$(CH_2SH)_2$-$(CH_2OH)_2$ Cavitand, A,C-$(CH_2SH)_2(CH_2OH)_2$ Cavitand, $(CH_2SH)_3(CH_2OH)_1$ Cavitand and $(CH_2SH)_4$ Cavitand: To a solution of the $(CH_2OAc)_{4-n}(CH_2Br)_n$ cavitand (*n* = 0–3) in dimethylacetamide (30 mL) under nitrogen-atmosphere was added thiourea and the reaction mixture stirred for 2 h. An ice-cold degassed aqueous solution of NaOH was then added dropwise. The reaction mixture was stirred for another hour. After evaporation of the solvent, acetic acid (5%) was added until the mixture became acidic. The product formed as a white precipitate and was collected by filtration. This solid was dissolved in $CHCl_3$, dried with $MgSO_4$ and filtered. After evaporation of the volatiles the respective pure $(CH_2OH)_{4-n}(CH_2SH)_n$ cavitands were obtained.

$(CH_2SH)_1(CH_2OH)_3$ Cavitand (12): $(CH_2OAc)_3(CH_2Br)_1$ cavitand (1.00 g, 0.98 mmol); thiourea (75 mg, 0.98 mmol). $(CH_2SH)(CH_2OH)_3$ cavitand (740 mg, 0.87 mmol). Yield = 89%. – ^{1}H NMR ($CDCl_3$): δ = 7.09, 7.06, 6.98 (s, 1+2+1 H, ArH), 5.86, 5.84 (d, *J* = 7 Hz, 2+2 H, OC*H*HO outer), 4.74 (m, 4 H, ArCHAr), 4.51, 4.45 (s, 2+4 H, CH_2OH), 4.43, 4.31 (d, *J* = 7 Hz, 2+2 H, OCH*H*O inner), 3.52 (d, *J* = 7 Hz, 2 H, CH_2SH), 2.15 (m, 8 H, $CH_2CH_2CH_3$), 1.70 (t, *J* = 7 Hz, 1 H, SH), 1.31 (m, 8 H, $CH_2CH_2CH_3$), 0.96 (m, 12 H, $CH_2CH_2CH_3$). – ^{13}C NMR ($CDCl_3$): δ = 153.6, 153.5, 153.4, 153.0, 138.2, 138.1, 137.9, 127.4, 126.3, 125.9, 120.5, 120.2, 119.1, 99.8, 99.7, 55.6, 55.3, 36.4, 32.0, 31.9, 20.9, 17.9, 14.1. – ESI-MS: *m*/*z* (%) = 863.4 (100) [M + Na]. – $C_{48}H_{56}O_{11}S\cdot 2H_2O$ (877.1): calcd. C 65.73, H 6.90; found C 65.48, H 6.71.

A,B-$(CH_2SH)_2(CH_2OH)_2$ Cavitand (13): A,B-$(CH_2OAc)_2(CH_2Br)_2$ cavitand (1.02 g, 0.98 mmol), thiourea (152 mg, 1.99 mmol). A,B-$(CH_2SH)_2(CH_2OH)_2$ cavitand (750 mg, 0.87 mmol). Yield = 89%. – ^{1}H NMR ($CDCl_3$): δ = 7.08, 6.98 (s, 2+2 H, ArH), 5.87, 5.86 (d, *J* = 7 Hz, 2+2 H, OC*H*HO outer), 4.73 (m, 4 H, ArCHAr), 4.49 (s, 4 H, CH_2OH), 4.38, 4.30 (d, *J* = 7 Hz, 2+2 H, OCH*H*O inner), 3.48 (d, *J* = 7 Hz, 4 H, CH_2SH), 2.14 (m, 8 H, $CH_2CH_2CH_3$), 1.74 (t, *J* = 7 Hz, 2 H, SH), 1.33 (m, 8 H, $CH_2CH_2CH_3$), 0.96 (m, 12 H, $CH_2CH_2CH_3$). – ^{13}C NMR ($CDCl_3$): δ = 153.6, 153.5, 152.9, 152.7, 138.2, 138.1, 127.4, 126.1, 120.4, 119.1, 99.8, 55.4, 36.5, 32.1, 20.8, 18.1, 14.1. – ESI-MS: *m*/*z* (%) = 879.5 (30) [M + Na^+], 899.4 (100) [M + H^+ + CH_3CN].

− $C_{48}H_{56}O_{10}S_2 \cdot 2H_2O$ (893.1): calcd. C 64.55, H 6.77; found C 64.12, H 6.40.

A,C-$(CH_2SH)_2(CH_2OH)_2$ Cavitand (14): A,C-$(CH_2OAc)_2(CH_2Br)_2$ cavitand (209 mg, 0.20 mmol); thiourea (31 mg, 0.40 mmol); A,C-$(CH_2SH)_2(CH_2OH)_2$ cavitand (167 mg, 0.19 mmol). Yield: 95%. − ^{1}H NMR ($CDCl_3$) δ = 7.06, 7.00 (s, 2+2 H, ArH), 5.87 (d, *J* = 7 Hz, 4 H, OC*H*HO outer), 4.73 (m, 4 H, ArCHAr), 4.49 (s, 4 H, CH_2OH), 4.37 (d, *J* = 7 Hz, 4 H, OCH*H*O inner), 3.49 (d, *J* = 7 Hz, 4 H, CH_2SH), 2.14 (m, 8 H, $CH_2CH_2CH_3$), 1.82 (t, *J* = 7 Hz, 2 H, SH), 1.31 (m, 8 H, $CH_2CH_2CH_3$), 0.96 (m, 12 H, $CH_2CH_2CH_3$). − ^{13}C NMR ($CDCl_3$): δ = 153.6, 152.8, 138.3, 138.1, 127.3, 126.3, 120.3, 119.5, 99.8, 55.6, 36.5, 32.1, 20.9, 18.2, 14.2. − ESI-MS: *m*/*z* (%) = 879.3 (100) [M + Na^+]. − $C_{48}H_{56}O_{10}S_2 \cdot 2H_2O$ (893.1): calcd. C 64.55, H 6.77; found C 64.31, H 6.39.

$(CH_2SH)_3(CH_2OH)_1$ Cavitand (15): $(CH_2OAc)_1(CH_2Br)_3$ cavitand (705 mg, 0.66 mmol), thiourea (152 mg, 1.99 mmol). $(CH_2SH)_3(CH_2OH)_1$ cavitand (450 mg, 0.51 mmol). Yield = 77%. − ^{1}H NMR ($CDCl_3$): δ = 7.08, 7.00, 6.98 (ArH, s, 1+2+1 H), 5.88, 5.87 (OC*H*HO outer, d, *J* = 7 Hz, 2+2 H), 4.72 (ArCHAr, m, 4 H), 4.53 (s, 2 H, CH_2OH), 4.45, 4.34 (OCH*H*O inner, d, *J* = 7 Hz, 2+2 H), 3.55, 3.46 (CH_2SH, d, *J* = 7 Hz, 2+4 H), 2.14 (m, 8 H, $CH_2CH_2CH_3$), 1.85, 1.71 (SH, t, *J* = 7 Hz, 2+1 H), 1.32 (m, 8 H, $CH_2CH_2CH_3$), 0.96 ($CH_2CH_2CH_3$, m, 12 H). − ^{13}C NMR ($CDCl_3$): δ = 153.6, 152.9, 152.7, 152.6, 138.2, 138.0, 137.9, 127.2, 120.4, 119.3, 119.1, 99.8, 55.4, 36.5, 32.1, 20.8, 18.2, 17.9, 14.1. − ESI-MS: 895.4 (40%, M + Na^+), 915.4 (100%, M + H^+ + CH_3CN). − $C_{48}H_{56}O_9S_3 \cdot H_2O$ (891.2): calcd. C 64.69, H 6.56; found C 64.37, H 6.53.

$(CH_2SH)_4$ Cavitand (16): Preparation as described by Sherman for the CH_3-footed cavitand.[30] ^{1}H NMR ($CDCl_3$): δ = 7.08 (s, 4 H, ArH), 5.96 (d, *J* = 7 Hz, 4 H, OCH*H*O), 4.78 (m, 4 H, ArCHAr), 4.47 (d, *J* = 7 Hz, 4 H, OCH*H*O), 3.62 (s, 8 H, CH_2SH), 2.19 (m, 8 H, $CH_2CH_2CH_3$), 1.96 (m, 4 H, SH), 1.38 (m, 8 H, $CH_2CH_2CH_3$), 1.02 (m, 12 H, $CH_2CH_2CH_3$). − $C_{48}H_{56}O_8S_4 \cdot H_2O$ (907.24): calcd. C 63.55, H 6.44; found C 62.22, H 6.50.

General Procedure for the Synthesis of the Mixed Phthalimido−Acetate Cavitands: $(CH_2Pht)_1(CH_2OAc)_3$ Cavitand, A,B-$(CH_2Pht)_2(CH_2OAc)_2$ Cavitand, A,C-$(CH_2Pht)_2(CH_2OAc)_2$ Cavitand and $(CH_2Pht)_3(CH_2OAc)_1$ Cavitand: A mixture of the respective $(CH_2OAc)_{4-n}(CH_2Br)_n$ cavitand and K-phthalimide in dimethylacetamide (60 mL) was stirred for 4 h. For the workup the volume of the reaction mixture was reduced to ca. 5 mL, water (50 mL) added and the resulting precipitate filtered off. The solid was dissolved in CH_2Cl_2 and extracted with aq. NaOH. The organic layers were separated, dried over $MgSO_4$ and filtered. The solvents were removed in vacuo and the residue purified by chromatography (cyclohexane/ethyl acetate, 1:1).

$(CH_2OAc)_3(CH_2Pht)_1$ Cavitand (17): $(CH_2OAc)_3(CH_2Br)_1$ cavitand (1.00 g, 0.98 mmol); K-phthalimide (250 mg, 1.35 mmol). Yield: 72% (770 mg, 0.71 mmol). − ^{1}H NMR ($CDCl_3$): δ = 7.81−7.68 (m, 4 H, Pht), 7.17 (s, 3 H, ArH), 7.08 (s, 1 H, ArH), 5.86 (d, *J* = 7.3 Hz, 2 H, OC*H*HO outer), 5.82 (d, *J* = 7.2 Hz, 2 H, OC*H*HO outer), 5.04 (s, 4 H, CH_2OAc), 4.90 (s, 2 H, CH_2OAc), 4.84−4.72 (m, 4 H, ArCHAr), 4.62 (s, 2 H, CH_2Pht), 4.37 (d, *J* = 7.4 Hz, 2 H, OCH*H*O inner), 4.34 (d, *J* = 7.3 Hz, 2 H, OCH*H*O inner), 2.19−2.06 (m, 8 H, $CHCH_2$), 2.00 (s, 9 H, $OOCCH_3$), 1.39−1.23 (m, 8 H, $CH_2CH_2CH_3$), 1.01−0.95 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.9, 170.5, 168.0, 154.6, 154.3, 154.2, 153.8, 138.3, 138.1, 134.1, 132.1, 123.4, 121.9, 121.8, 121.7, 121.5, 120.4, 99.8, 57.4, 57.0, 36.6, 32.8, 32.1, 21.3, 21.1, 14.3.

A,B-$(CH_2OAc)_2(CH_2Pht)_2$ Cavitand (18): A,B-$(CH_2OAc)_2$-$(CH_2Br)_2$ cavitand (1.00 g, 0.97 mmol); K-phthalimide (580 mg, 3.13 mmol). Yield: 64% (723 mg, 0.62 mmol). − ^{1}H NMR ($CDCl_3$): δ = 7.80−7.68 (m, 8 H, Pht), 7.17 (s, 2 H, ArH), 7.08 (s, 2 H, ArH), 5.81 (d, *J* = 7.2 Hz, 2 H, OC*H*HO outer), 5.77 (d, *J* = 7.2 Hz, 2 H, OC*H*HO outer), 4.96 (s, 4 H, CH_2OAc), 4.74−4.64 (m, 4 H, ArCHAr), 4.65 (s, 4 H, CH_2Pht), 4.37 (d, *J* = 7.3 Hz, 2 H, OCH*H*O inner), 4.36 (d, *J* = 7.2 Hz, 1 H, OCH*H*O inner), 4.34 (d, *J* = 7.2 Hz, 1 H, OCH*H*O inner), 2.21−2.09 (m, 8 H, $CHCH_2$), 2.00 (s, 6 H, $OOCCH_3$), 1.35−1.24 (m, 8 H, $CH_2CH_2CH_3$), 1.03−0.94 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.7, 168.0, 154.6, 154.2, 154.1, 153.9, 138.2, 138.1, 134.1, 132.1, 123.4, 121.6, 121.5, 121.4, 120.3, 99.9, 57.4, 36.6, 32.8, 32.2, 21.2, 21.0, 14.3.

A,C-$(CH_2OAc)_2(CH_2Pht)_2$ Cavitand (19): A,C-$(CH_2OAc)_2$-$(CH_2Br)_2$ cavitand (1.00 g, 0.97 mmol); K-phthalimide (580 mg, 3.13 mmol). Yield: 65% (734 mg, 0.63 mmol). − ^{1}H NMR ($CDCl_3$): δ = 7.79−7.69 (m, 8 H, Pht), 7.16 (s, 2 H, ArH), 7.09 (s, 2 H, ArH), 5.87 (d, *J* = 6.1 Hz, 4 H, OC*H*HO outer), 5.06 (s, 4 H, CH_2OAc), 4.76−4.67 (m, 4 H, ArCHAr), 4.61 (s, 4 H, CH_2Pht), 4.39 (d, *J* = 6.4 Hz, 4 H, OCH*H*O inner), 2.22−2.14 (m, 8 H, $CHCH_2$), 2.05 (s, 6 H, $OOCCH_3$), 1.32−1.24 (m, 8 H, $CH_2CH_2CH_3$), 0.99−0.93 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.4, 168.0, 154.5, 153.6, 138.3, 137.9, 134.0, 132.1, 123.3, 121.8, 121.6, 121.4, 120.3, 99.7, 57.5, 36.5, 32.7, 32.0, 21.3, 20.8, 14.2.

$(CH_2OAc)_1(CH_2Pht)_3$ Cavitand (20): $(CH_2OAc)_1(CH_2Br)_3$ cavitand (1.00 g, 0.95 mmol); K-phthalimide (700 mg, 3.8 mmol). Yield: 58% (695 mg, 0.55 mmol). − ^{1}H NMR ($CDCl_3$): δ = 7.81−7.68 (m, 12 H, Pht), 7.16, (s, 2 H, ArH), 7.08 (s, 2 H, ArH), 5.83 (d, *J* = 7.3 Hz, 2 H, OC*H*HO outer), 5.78 (d, *J* = 7.2 Hz, 2 H, OC*H*HO outer), 5.02 (s, 2 H, CH_2OAc), 4.76−4.72 (m, 4 H, ArCHAr), 4.67 (s, 2 H, CH_2Pht), 4.61 (s, 4 H, CH_2Pht), 4.41 (d, *J* = 7.4 Hz, 2 H, OCH*H*O inner), 4.37 (d, *J* = 7.3 Hz, 2 H, OCH*H*O inner), 2.22−2.13 (m, 8 H, $CHCH_2$), 2.07 (s, 3 H, $OOCCH_3$), 1.32−1.24 (m, 8 H, $CH_2CH_2CH_3$), 0.99−0.93 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.6, 168.1, 168.0, 154.5, 154.1, 154.0, 153.7, 138.2, 138.1, 137.9, 134.1, 132.2, 123.4, 121.6, 121.5, 120.3, 99.9, 99.7, 57.7, 36.6, 32.8, 32.4, 32.2, 21.2, 21.0, 14.3.

$(CH_2Pht)_4$ Cavitand (21): $(CH_2Br)_4$ cavitand (1.00 g, 0.93 mmol); K-phthalimide (850 mg, 4.6 mmol). Yield: 59% (734 mg, 0.55 mmol). − ^{1}H NMR ($CDCl_3$): δ = 7.83−7.67 (m, 16 H, Pht), 7.02 (s, 4 H, ArH), 5.76 (d, *J* = 7.0 Hz, 2 H, OC*H*HO outer), 4.73−4.68 (m, 4 H, ArCHAr), 4.63 (s, 8 H, CH_2Pht), 4.40 (d, *J* = 6.9 Hz, 2 H, OCH*H*O inner), 2.16−2.14 (m, 8 H, $CHCH_2$), 1.32−1.23 (m, 8 H, $CH_2CH_2CH_3$), 0.99−0.94 (m, 12 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 168.1, 154.0, 138.0, 134.1, 132.2, 123.4, 121.2, 120.2, 99.8, 36.6, 32.9, 32.4, 21.0, 14.3.

General Procedure for the Synthesis of the Mixed Amino−Hydroxy Cavitands: $(CH_2NH_2)_1(CH_2OH)_3$ Cavitand, A,B-$(CH_2NH_2)_2$-$(CH_2OH)_2$ Cavitand, A,C-$(CH_2NH_2)_2(CH_2OH)_2$ Cavitand and $(CH_2NH_2)_3(CH_2OH)_1$ Cavitand: A solution of $(CH_2Pht)_{4-n}$-$(CH_2OAc)_n$ cavitand (1.21 mmol) and hydrazine hydrate (1.1 mL, 35.4 mmol) in a mixture of ethanol (175 mL) and THF (20 mL) was heated under reflux overnight. After addition of conc. HCl (4.2 mL, 37% aq.) the reaction mixture was heated under reflux for another hour. Next, NaOH (17 mL, 2 M aq.) was added and the solution was reduced to a volume of ca. 10 mL in a rotary evaporator. The resulting precipitate was filtered, washed with $CHCl_3$ (ca. 10 mL) and the residue dissolved in $CHCl_3$/methanol (5:1). The organic extract was dried over $MgSO_4$, filtered and the solvent evaporated.

$(CH_2NH_2)_1(CH_2OH)_3$ Cavitand (22): $(CH_2Pht)_3(CH_2OAc)_1$ cavitand (1.00 g, 0.93 mmol). Yield: 95% (948 mg, 0.88 mmol). − ^{1}H NMR ([D$_6$]DMSO): δ = 7.55 (s, 3 H, ArH), 7.51 (s, 1 H, ArH), 5.82 (d, *J* = 7.5 Hz, 2 H, OC*H*HO outer), 5.81 (d, *J* = 7.6 Hz, 2 H, OC*H*HO outer), 4.65−4.61 (m, 4 H, ArCHAr), 4.48 (d, *J* = 7.6 Hz, 2 H, OCH*H*O inner), 4.39 (d, *J* = 7.8 Hz, 2 H, OCH*H*O inner), 4.32 (s, 6 H, CH_2OH), 3.45 (s, 2 H, CH_2NH_2), 2.35−2.32 (m, 8 H, $CHCH_2$), 1.32−1.25 (m, 8 H, $CH_2CH_2CH_3$), 1.04−0.94 (m, 12 H, CH_3). − ^{13}C NMR ([D$_6$]DMSO): δ = 153.0, 152.8, 152.4, 137.7, 137.6, 129.2, 127.3 121.3, 99.8, 99.3, 52.9, 36.3, 31.2, 26.3, 20.5, 13.9. − MS (ESI): *m*/*z* (%) = 824.4 (100) [M + H$^+$]. − $C_{48}H_{57}NO_{11}$ (823.98): calcd. C 68.97, H 6.97, N 1.78; found C 67.39, H 6.85, N 1.79.

A,B-$(CH_2NH_2)_2(CH_2OH)_2$ Cavitand (23): A,B-$(CH_2Pht)_2(CH_2OAc)_2$ cavitand (1.00 g, 0.86 mmol). Yield: 93% (657 mg, 0.79 mmol). − ^{1}H NMR ([D$_6$]DMSO): δ = 7.55 (s, 2 H, ArH), 7.51 (s, 2 H, ArH), 5.84 (d, *J* = 7.5 Hz, 2 H, OC*H*HO outer), 5.83 (d, *J* = 7.6 Hz, 2 H, OC*H*HO outer), 4.67−4.61 (m, 4 H, ArCHAr), 4.50 (d, *J* = 7.6 Hz, 2 H, OCH*H*O inner), 5.40 (d, *J* = 7.8 Hz, 2 H, OCH*H*O inner), 4.32 (s, 4 H, CH_2OH), 3.51 (s, 4 H, CH_2NH_2), 2.42−2.31 (m, 8 H, $CHCH_2$), 1.35−1.28 (m, 8 H, $CH_2CH_2CH_3$), 1.03−0.95 (m, 12 H, CH_3). − ^{13}C NMR ([D$_6$]DMSO): δ = 152.5, 152.4, 152.0, 137.2, 137.1, 126.7, 120.7, 119.9, 99.0, 52.3, 35.8, 34.6, 30.7, 19.9, 13.2. − MS (ESI): *m*/*z* (%) = 863.5 (40) [M + K$^+$]. − $C_{48}H_{58}N_2O_{10}$ (822.9): calcd. C 70.05, H 7.10, N 3.40; found C 69.10, H 7.23, N 3.21.

A,C-$(CH_2NH_2)_2(CH_2OH)_2$ Cavitand (24): A,C-$(CH_2Pht)_2(CH_2OAc)_2$ cavitand (1.00 g, 0.86 mmol). Yield: 98% (93 mg, 0.84 mmol). − ^{1}H NMR ([D$_6$]DMSO): δ = 7.55 (s, 2 H, ArH), 7.52 (s, 2 H, ArH), 5.86 (d, *J* = 7.6 Hz, 4 H, OC*H*HO outer), 4.65−4.61 (m, 4 H, ArCHAr), 4.41 (d, *J* = 7.7 Hz, 4 H, OCH*H*O inner), 4.28 (s, 4 H, CH_2OH), 3.48 (s, 4 H, CH_2NH_2), 2.34−2.33 (m, 8 H, $CHCH_2$), 1.32−1.26 (m, 8 H, $CH_2CH_2CH_3$), 1.01−0.94 (m, 12 H, CH_3). − ^{13}C NMR ([D$_6$]DMSO): δ = 152.9, 152.5, 137.8, 137.1, 128.9, 127.3, 121.3, 120.4, 99.5, 79.1, 52.9, 36.3, 35.1, 31.1, 20.5, 13.9. − MS (ESI): *m*/*z* (%) = 823.5 (100) [M + H$^+$]. − $C_{48}H_{58}N_2O_{10}$ (822.9): calcd. C 70.05, H 7.10, N 3.40; found C 68.88, H 7.50, N 3.69.

$(CH_2NH_2)_3(CH_2OH)_1$ Cavitand (25): $(CH_2OPht)_3(CH_2OAc)_1$ cavitand (1.00 g, 0.80 mmol). Yield: 95% (624 mg, 0.76 mmol). − ^{1}H NMR ([D$_6$]DMSO): δ = 7.54 (s, 1 H, ArH), 7.51 (s, 3 H, ArH), 5.87 (d, *J* = 7.6 Hz, 2 H, OC*H*HO outer), 5.86 (d, *J* = 7.5 Hz, 2 H, OC*H*HO outer), 4.68−4.60 (m, 4 H, ArCHAr), 4.47 (d, *J* = 7.6 Hz, 2 H, OCH*H*O inner), 4.35 (d, *J* = 7.7 Hz, 2 H, OCH*H*O inner), 4.30 (s, 2 H, CH_2OH), 3.48 (s, 6 H, CH_2NH_2), 2.35−2.32 (m, 8 H, $CHCH_2$), 1.32−1.25 (m, 8 H, $CH_2CH_2CH_3$), 1.01−0.94 (m, 12 H, CH_3). − ^{13}C NMR ([D$_6$]DMSO): δ = 153.0, 152.5, 152.4, 137.7, 137.6, 128.9, 120.4, 99.6, 52.8, 36.3, 35.14, 31.2, 26.3, 20.5, 13.9. − MS (ESI): *m*/*z* (%) = 805.4 (100) [M + H$^+$ − H_2O], 822.4 (42) [M + H$^+$]. − $C_{48}H_{59}N_3O_9$ (822.0): calcd. C 70.14, H 7.23, N 5.11; found C 69.19, H 7.15, N 5.78.

$(CH_2NH_2)_4$ Cavitand (26): Preparation as described for the C_5H_{11}-footed cavitand,[32] but with *n*-propanol/THF (1:1) as solvent mixture. $(CH_2Pht)_4$ cavitand (1.00 g, 0.75 mmol). Yield: 96% (591 mg, 0.72 mmol). − ^{1}H NMR ([D$_6$]DMSO): δ = 7.50 (s, 4 H, ArH), 5.88 (d, *J* = 7.4 Hz, 2 H, OC*H*HO outer), 4.66−4.61 (m, 4 H, ArCHAr), 4.41 (d, *J* = 7.5 Hz, 2 H, OCH*H*O inner), 3.47 (s, 8 H, CH_2NH_2), 2.34−2.32 (m, 8 H, $CHCH_2$), 1.31−1.27 (m, 8 H, $CH_2CH_2CH_3$), 1.00−0.96 (m, 12 H, CH_3). − ^{13}C NMR ([D$_6$]DMSO): δ = 152.5, 137.7, 129.2, 120.3, 99.5, 36.3, 35.2, 31.2, 20.5, 13.9. − MS (ESI, positive): *m*/*z* (%) = 804.5 (100) [M + H$^+$ − NH_2], 822.4 (33) [M + H$^+$]. − $C_{48}H_{60}N_4O_{10}$ (853.0): calcd. C 67.59, H 7.09, N 6.57. Found 66.61, H 7.37, N 6.63.

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