Tetrakis(phenylamidinium)-Substituted Resorcin[4]arene Receptors for the Complexation of Dicarboxylates and Phosphates in Protic Solvents

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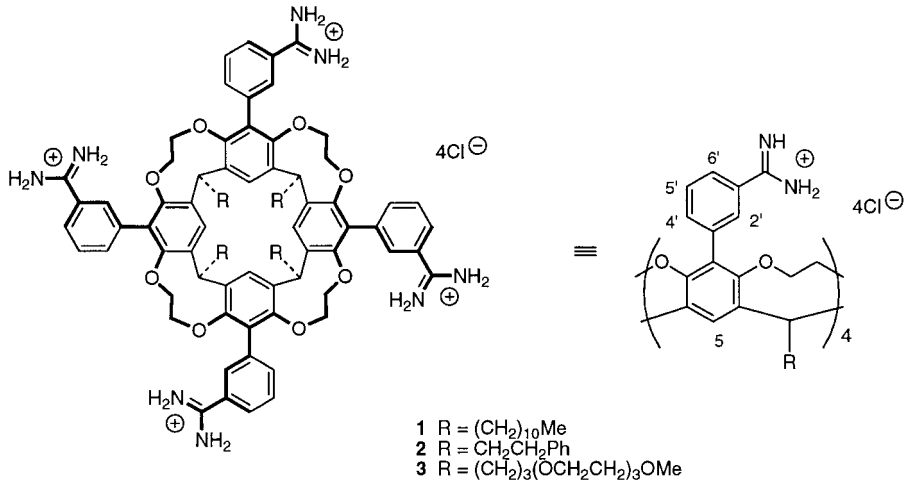
Three bowl-type cavitand receptors (**1**–**3**), consisting of a resorcin[4]arene core with four convergent phenylamidinium groups, were prepared in gram quantities by efficient synthetic routes (*Schemes 1* and *2*) for the recognition of organic anions in CD_3OD and D_2O. The key steps in the syntheses are the *Suzuki* cross-coupling reactions between the tetraiodo cavitands **12**, **13**, and **23**, respectively, with the *m*-cyanophenylboronic ester **14** and subsequent conversion of the nitrile to amidinium groups by the *Garigipati* reaction. Compounds **1** and **2** displayed limited solubility in protic solvents, and evidence for stoichiometric host-guest association between **2** and AMP (**28**) could only be obtained by FAB-MS analysis of a complex precipitated from MeOH (*Fig. 2*). In contrast, receptor **3** with four triethyleneglycol monomethyl ether side chains was readily soluble in the protic environments, and complexation of isophthalates and nucleotides **25**–**37** was extensively studied by ^{1}H-NMR titrations and *Job*'s method of continuous variation. In CD_3OD and pure D_2O, isophthalates **25** and **26** formed stable 1:2 host-guest complexes (*Table 1* and *Fig. 3*), whereas upon addition of borate (pH 9.2) or *Tris*/HCl buffer (pH 8.3) to the D_2O solution, the tendency for higher-order complexation vanishes. Stable 1:1 complexes formed in the buffered solutions (*Fig. 4*) with 5-methoxyisophthalate being selectively bound over the 5-NO_2 derivative. Complexation-induced upfield shifts of specific isophthalate ^{1}H-NMR resonances (*Fig. 5*) suggest a preferred inclusion of the methoxyphenyl ring into the receptor cavity. Cavitand **3** forms stable 1:1 host-guest complexes with nucleotides in *Tris*/HCl-buffered D_2O. Association constants increase strongly with increasing guest charge in the series cAMP < AMP < ADP < ATP (*Table 2*). Association strength is strongly reduced in the presence of high salt (NaCl) concentration (*Table 3*). Receptor **3** shows a slight preference for the complexation of AMP (*Fig. 7*) and analogs dAMP or ε-AMP (*Table 4*) over nucleotides containing G (guanine), C (cytosine), T (thymine), or U (uracil) as bases. According to the ^{1}H-NMR analysis, only the nucleobase adenine and derivatives thereof possess the necessary stereoelectronic complementarity for inclusion into the bowl-type cavity. The major forces stabilizing the complexes of **3** with isophthalates and nucleotides result from ion pairing and ionic H-bonding between the charged groups of host and guest, and from the desolvation of these groups upon complexation. Apolar interactions and hydrophobic desolvation do not seem to make a large contribution to the measured binding free enthalpies.

1. Introduction. – In the directly preceding paper [1], we described the complexation of dicarboxylate guests (glutarate, isophthalates) by a cleft-type bis(phenylamidinium) receptor in MeOH. Here, we report on the novel macrocyclic hosts **1**–**3** which feature a resorcin[4]arene core [2–6] with four convergent phenylamidinium groups and were designed for organic-anion recognition in H_2O [7]. Similar to the cleft-type receptors in the preceding study [1], compounds **1**–**3** were expected to complex with their amidinium residues organic anions by ion pairing and ionic H-bonding interactions. Additionally, they should display enhanced binding affinity and selectivity resulting from inclusion of complementary lipophilic segments of the anionic guests



into the bowl-type resorcinarene cavity, driven by hydrophobic desolvation and apolar host-guest interactions [8].

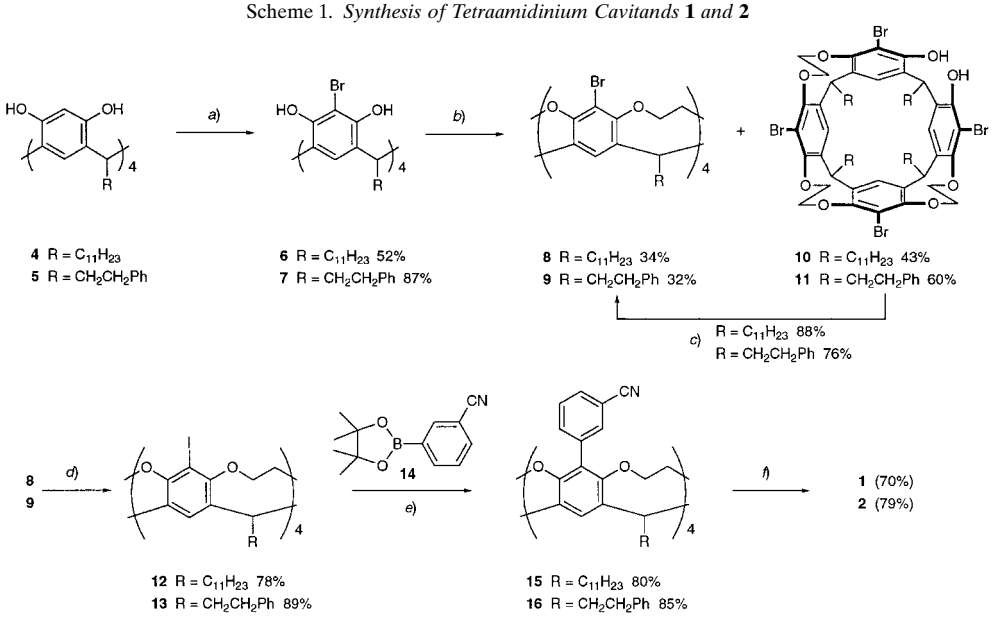
Since hydrophobic bonding is most effective in H_2O, good monodisperse H_2O-solubility of the resorcinarene-based anion receptors [9][10] was crucial for the success of this work. We show that this desirable property is best obtained by introducing triethyleneglycol monomethyl ether side chains as 'feet' into receptor **3**. The power of these side chains to enhance the H_2O-solubility of large organic molecules became previously apparent in our studies of dendrimers as biological mimics [11].

Anions considered in this investigation are dicarboxylates, such as isophthalates (for references to carboxylate-anion binding by synthetic receptors, see [1]) and phosphates, such as mononucleotides. In the past, macrocyclic and cleft-type receptors containing ammonium or guanidinium groups have often been investigated for both carboxylate and phosphate binding in aqueous solution. Efficient macrocyclic nucleotide receptors include protonated azacrown ethers [12] and azacryptands [13], tetrazonia[8.1.8.1]paracyclophanes [14], and sapphyrins [15]. Non-macrocyclic receptors containing one or two guanidinium ions for phosphate and nucleotide binding have been reported [16][17]. We found that cationic carriers, which contain two diquaternary 1,4-diaza[2.2.2]bicyclooctane units, undergo ion-pairing with nucleotide-5′-triphosphates and strongly accelerate their transport across liquid organic membranes [18]. Here, we show that resorcinarene **3** is a highly efficient nucleotide binder and analyze the contributions of polar and apolar interactions to the stability of the host-guest complexes formed in aqueous buffers.

2. Results and Discussion. – 2.1. *Synthesis.* We first prepared the target compounds **1** and **2** under the assumption that the four amidinium residues would be sufficient to provide good solubility in protic solvents. Octols **4** and **5** (*Scheme 1*) were prepared according to literature procedures starting from resorcinol and the corresponding aldehyde [19]. Subsequently, the Br substituents were introduced with *N*-bromosuccinimide (NBS) in butanone into the 2-positions of the resorcinol sub-units to yield

tetrabrominated **6** and **7**, respectively [20]. These octols were bridged with ethyleneglycol bis[*p*-toluenesulfonate] and Cs_2CO_3 in Me_2SO to provide the rigidified cavitands **8** and **9**. Triply-bridged compounds **10** and **11** were also isolated in this step; they were subsequently transformed into **8** and **9**, respectively, by a second cyclization step in MeCN. Drying of **8** and **9** was crucial for the success of the subsequent metallation step; therefore, residual solvent included in their cavity (H_2O, CH_2Cl_2 (^{1}H-NMR)) was removed by slow distillation of THF and benzene from solutions of the cavitands.

Scheme 1. *Synthesis of Tetraamidinium Cavitands* **1** *and* **2**



a) NBS, butanone, 20°, 1 d. *b*) $TsO(CH_2)_2OTs$, anh. Cs_2CO_3, Me_2SO, 65°, 40 h (**8**), 4 d (**9**). *c*) $TsO(CH_2)_2OTs$, anh. Cs_2CO_3, MeCN, 90°/1 d (**10**), 120°/3 d (**11**). *d*) 1. BuLi, THF, −100°, 35 min; 2. I_2, −100° → 20°, 12 h. *e*) [$PdCl_2(PPh_3)_2$], $AsPh_3$, Cs_2CO_3, dioxane, H_2O, 75°, 3 h. *f*) $MeAlNH_2Cl$, 1,2-dichlorobenzene, 70° – 80°, 6 d (**1**), 4 d (**2**).

Crystals of **9** were grown from CH_2Cl_2, and the X-ray crystal structure of the solvate with two CH_2Cl_2 molecules was solved. The solid-state structure (*Fig. 1*) showed interesting enclathration phenomena similar to those previously described by *Cram* and co-workers [2][19][20]. One CH_2Cl_2 molecule is located inside the cavitand bowl with one Cl-atom pointing deeply into the cavity. The second CH_2Cl_2 molecule is embedded in a second cavity shaped by the four 2-phenylethyl legs.

Since a fourfold *Suzuki* cross-coupling [21][22] of tetrabrominated **8** and **9** led to unsatisfactory conversions, the cavitands were metallated with BuLi in THF and iodinated with I_2 to give tetraiodides **12** and **13**, respectively. The second component for the *Suzuki* reaction, 'pinacol borate' **14**, was obtained by metallation of 3-bromobenzonitrile with BuLi, followed by reaction with $B(OMe)_3$ and transesterification with pinacol. Cross-coupling between **12** or **13** and **14** yielded the tetracyano-

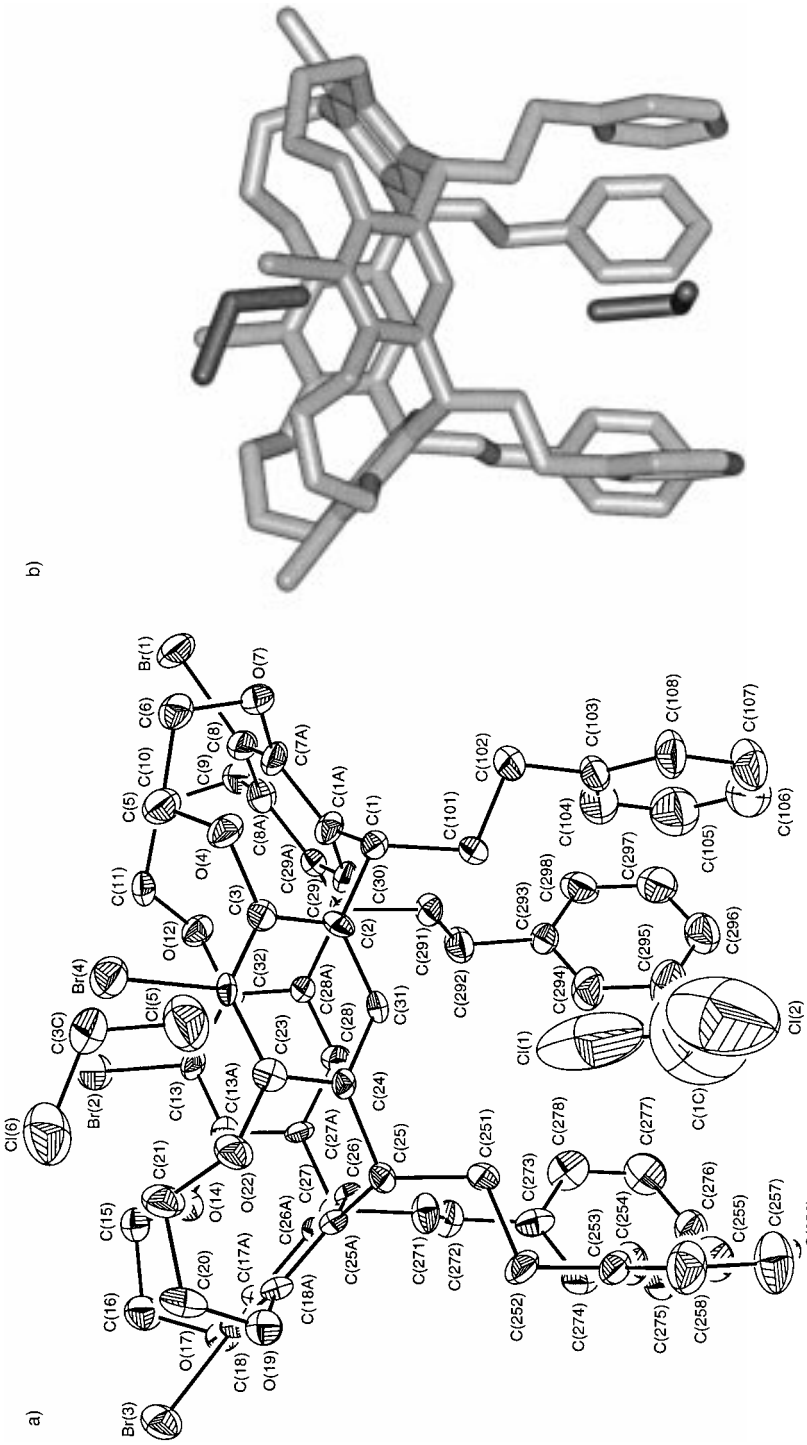
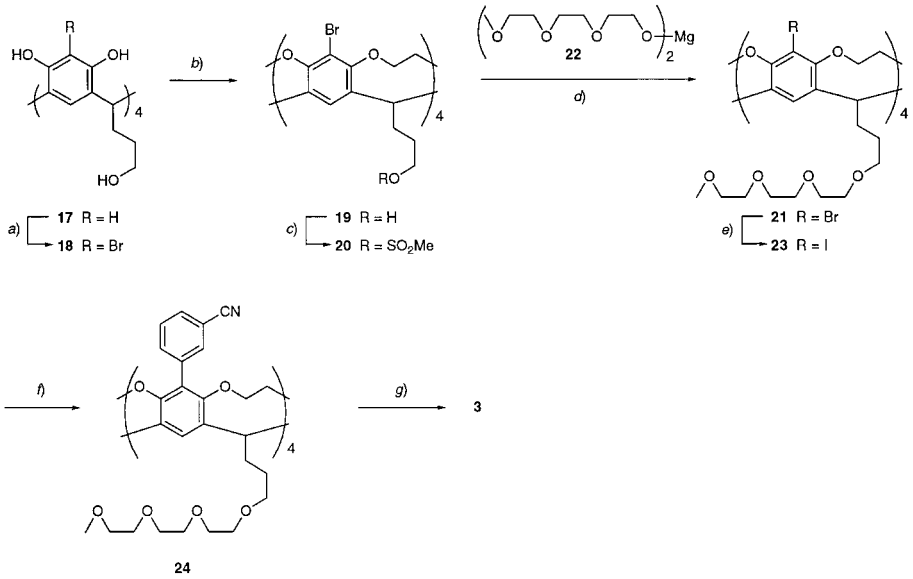


Fig. 1. *X-Ray crystal structure of* **9** *with two enclathrated* CH_2Cl_2 *molecules. a)* ORTEP Plot with atomic displacement parameters obtained at 293 K drawn at the 50% probability level. Arbitrary numbering. *b)* Visualization of the enclathration geometry showing only the bonding between non-H-atoms.

cavitands **15** and **16**, respectively. Finally, the tetraamidinium salts **1** and **2** were prepared from **15** and **16**, respectively, by the *Garigipati* method [23] with $MeAlNH_2Cl$.

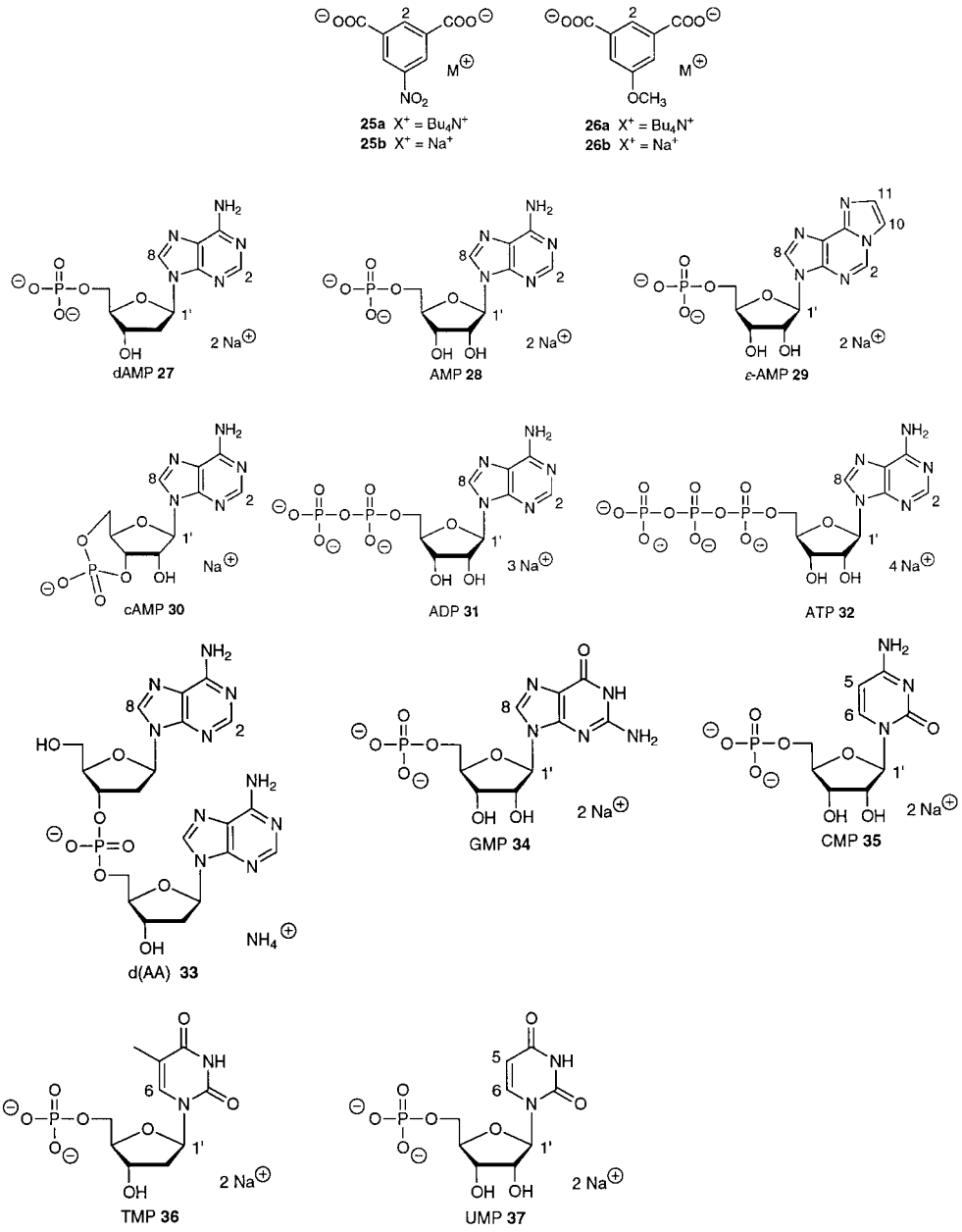
The synthesis of **3** (*Scheme 2*) with its polar triethyleneglycol monomethyl ether legs started from dodecaol **17**, which was obtained by acid-catalyzed condensation of resorcinol and 2,3-dihydrofuran according to the procedure published by *Sherman* and co-workers [24]. Bromination with NBS afforded **18**, which was transformed by *Williamson* cyclization to the rigid cavitand **19** and by subsequent mesylation into **20**. Nucleophilic substitution of tetrakis[methanesulfonate] **20** with the sodium salt of triethyleneglycol monomethyl ether (prepared with NaH) yielded **21**, which, however, was contaminated with a large amount of cavitand possessing the four triethyleneglycol monomethyl ether feet but lacking one of the four Br-atoms. This undesirable debromination could be avoided by using the dialkoxymagnesium derivative **22** in the S_N2 reaction. Substitution of **20** with **22**, formed from triethyleneglycol monomethyl ether with Mg and I_2, gave **21** in 78% yield. The residual conversions in the synthesis of **3** closely followed those applied in the route to **1** and **2**, leading *via* the sequence **21** → **23** → **24** → **3** to the desired receptor which was obtained in gram quantities.

Scheme 2. *Synthesis of the Tetraamidinium cavitand* **3**



a) NBS, butanone, MeOH, 20°, 15 h; 77%. *b*) $TsO(CH_2)_2OTs$,Cs_2CO_3, K_2CO_3, 2,6-bis(1,1-dimethylethyl)-4-methylphenol (BHT), *N*,*N*-dimethylacetamide (DMA), 20° (1 d), 45° (1 d), 65° (3 d); 42%. *c*) $MeSO_2Cl$, NEt_3, dioxane, 0° → 20°, 3 h; 92%. *d*) Dioxane, 60°, 16 h; 78%. *e*) 1. BuLi, THF, –100°, 30 min; 2. I_2, –100° → 20°, 2 h; 97%. *f*) **14**, Cs_2CO_3, $[PdCl_2(PhCN)_2]$, $AsPh_3$, dioxane, H_2O, 70°, 2 h; 84%. *g*) $MeAlNH_2Cl$, 1,2-dichlorobenzene, 70°–80°, 3 d; 91%.

2.2. *Complexation Studies.* Extensive ^{1}H-NMR binding studies were undertaken with substrates **25**–**37**. It soon became apparent that the low solubility of cavitands **1** and **2** in MeOH or H_2O was a major disadvantage, since no titration experiments could be successfully performed in these protic solvents. For example, upon mixing equimolar



solutions of **2** and AMP (**28**) in MeOH, a precipitate formed. The analysis of the solid by fast-atom-bombardment mass spectrometry (FAB-MS) confirmed the formation of a 1:1 host-guest complex (*Fig. 2*).

In contrast, receptor **3** was readily soluble in MeOH and H_2O, and all subsequent complexation studies were executed with this cavitand.

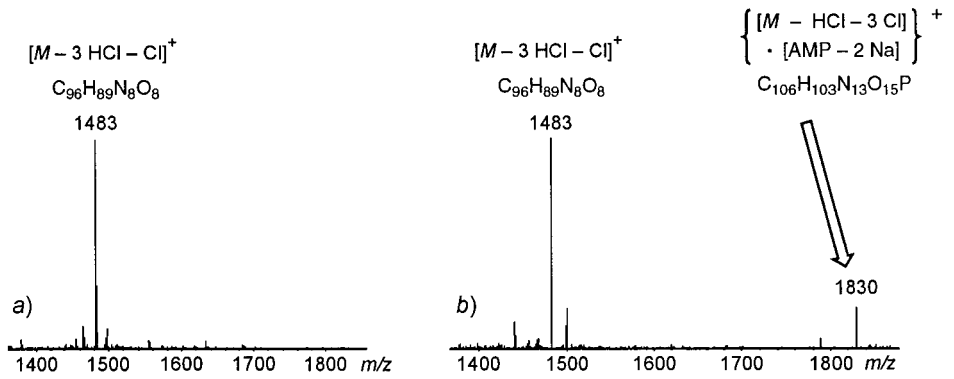


Fig. 2. *FAB Mass spectra* (3-nitrobenzyl alcohol as matrix) *of receptor* **2** (a) *and the 1:1 host-guest complex with AMP* (**28**), *which precipitated out of MeOH* (b)

2.2.1. *Complexation of Isophthalates.* In ^{1}H-NMR binding titrations (500 MHz, 300 K) with **3** in CD_3OD at fast host-guest exchange, the concentration of the ammonium salt **25a** was kept constant, and the data were fitted using the program *SPECFIT V. 2.11* [25]. Complexation of **25a** could not be described using a simple 1:1 host-guest binding model. Instead, a good fit of the data to the 1:2 host-guest

Table 1. *Association Constants and Complexation Free Enthalpies from ^{1}H-NMR Titrations for 1:1 and 1:2 Host-Guest Complexes of Isophthalates with Receptor* **3** ($T = 300$ K) *in CD_3OD and D_2O.* Also shown are the maximum observed complexation-induced shifts $\Delta\delta_{max\,obs}$ (–: upfield) of guest ^{1}H resonances monitored during the titrations.

Guest	K_a(**HG**)[a] [l mol^{-1}]	ΔG(**HG**) [kJ mol^{-1}]	K_a(**HG$_2$**)[b] [l mol^{-1}]	ΔG(**HG$_2$**) [kJ mol^{-1}]	$\Delta\delta_{max\,obs}$ [ppm]
In CD_3OD[c]					
25a	350000	-31.8 ± 2.7	60000	-27.3 ± 5.7	-0.145 (H–C(2))
					-0.091 (H–C(4))
In pure D_2O[d]					
25b	14800	-24.0 ± 0.3	3800	-20.6 ± 1.0	$+0.076$ (H–C(2))
					-0.278 (H–C(4))
26b	86000	-28.3 ± 0.4	7700	-22.3 ± 1.5	$+0.139$ (H–C(2))
					-0.548 (H–C(4))
In D_2O containing $Na_2B_4O_7$ (5 mM; pH = 9.2)[e]					
25b	4000	-20.7 ± 0.1			$+0.082$ (H–C(2))
					-0.268 (H–C(4))
26b	96500	-28.6 ± 0.3			$+0.148$ (H–C(2))
					-0.565 (H–C(4))
In D_2O containing *Tris*/HCl (2.5 mM, pH = 8.3)[f]					
25b	12200	-23.5 ± 0.2			$+0.094$ (H–C(2))
					-0.317 (H–C(4))
26b	118900	-29.2 ± 0.4			$+0.159$ (H–C(2))
					-0.599 (H–C(4))

[a]) Equilibrium constant for the 1:1 complexation step: $\mathbf{H} + \mathbf{G} \rightleftharpoons \mathbf{HG}$. [b]) Equilibrium constant for the 1:2 complexation step: $\mathbf{HG} + \mathbf{G} \rightleftharpoons \mathbf{HG_2}$. [c]) [**25a**] = 0.5 mM; [**3**] = 0.03–0.5 mM. [d]) Constant guest concentration: 0.5 mM. [e]) Constant guest concentration: 0.5 mM (**25b**), 0.2 mM (**26b**). [f]) Constant guest concentration: 0.5 mM (**25b**), 0.3 mM (**26b**).

association model was obtained, yielding high association constants for both 1:1 and 1:2 complexation steps (*Table 1*).

The 1:2 stoichiometry was confirmed using *Job*'s method of continuous variation (*Fig. 3*), where the complexation-induced shifts of host or guest ^{1}H-NMR resonances were followed as a function of the host or guest mole fraction, respectively, keeping their total concentration constant [26].

^{1}H-NMR Titrations in pure D_2O confirmed the results obtained in CD_3OD, and a 1:2 host-guest association was again observed (*Table 1*). Methoxyisophthalate **26b** was found to undergo a stronger association with **3** than the derivative **25b**. Although the 1:2 host-guest binding model is valid in both CD_3OD and D_2O, the association geometries in the two solvents are quite different, as indicated by the different $\Delta\delta$ values of the guest resonances. In CD_3OD, the resonance of proton H–C(2) displays a larger upfield shift than that of H–C(4). In contrast, only the resonance of H–C(4) is shifted upfield in D_2O (*Table 1*), with the shift being particularly large in the complexation of methoxy derivative **26b** (*Table 1*). The data suggest that complexation in CD_3OD occurs much more at the rim of the cavitand, whereas in D_2O, one of the two isophthalates is, in time average, included with the less polar segment of its phenyl ring into the receptor cavity. These findings are in agreement with previous work which showed that apolar cavity inclusion, driven largely by the release of solvent molecules into the bulk, is much more favorable in D_2O than in CD_3OD [8].

Interestingly, higher-order association between receptor **3** and isophthalates **25b** and **26b** is suppressed in deuterated aqueous borate buffer (pH 9.2), and complexation is readily described using the 1:1 host-guest binding model. The association behavior of the two guests in the presence of buffer is quite different. The association constant for the 1:1 complex between **3** and methoxyisophthalate **26b** in the borate buffer remains unchanged within experimental error, when compared to the first association constant of the 1:2 complex in unbuffered D_2O. In the case of nitro derivative **25b**, however, the association constant K_a in the borate buffer drops by a factor of four. Furthermore, the measured complexation-induced upfield shift of the resonance of H–C(4) in **26b** is twice as large as the shift measured for the corresponding resonance in **25b**. Apparently,

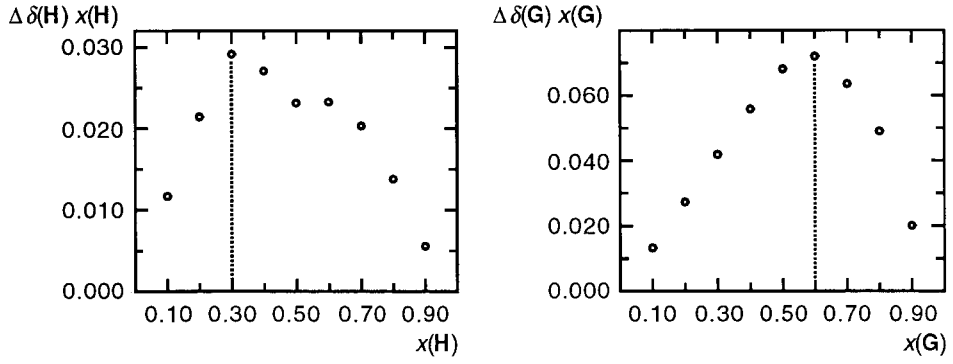


Fig. 3. Job *plots for the complex formed between* **3** *and* **25a** *in* CD_3OD *at 300 K*. The total concentration $c_0(\mathbf{H}) + c_0(\mathbf{G})$ was kept constant at 2 mM. The host (**H**) signal H–C(5′) (*left graph*) and the guest (**G**) signal H–C(2) (*right graph*) were followed. Host molar fraction $x(\mathbf{H})$ defined as $c_0(\mathbf{H})/c_0(\mathbf{H}) + c_0(\mathbf{G})$); guest molar fraction $x(\mathbf{G})$ defined as $c_0(\mathbf{G})/(c_0(\mathbf{H}) + c_0(\mathbf{G}))$.

methoxyisophthalate **26b** has a much higher stereoelectronic complementarity to the resorcinarene cavity than nitro derivative **25b**, leading to a deeper inclusion of its MeO-substituted phenyl ring. As a result, a more stable complex is formed [9], which is less affected by the competitive buffer anions. The 1:1 stoichiometry of the complexes in borate buffer was confirmed using *Job*'s method (*Fig. 4*).

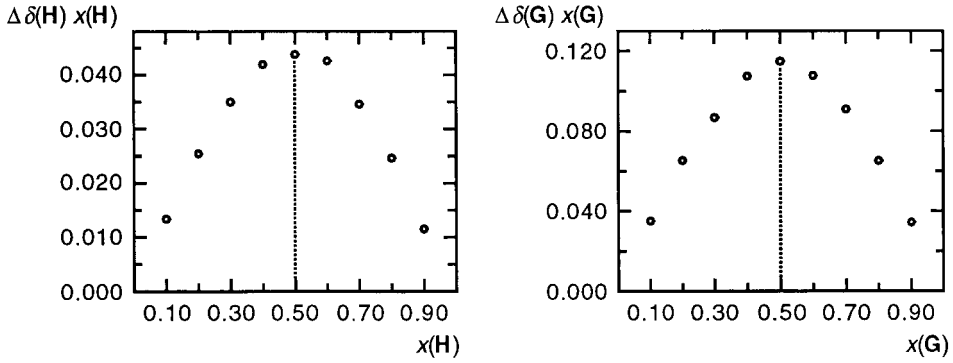


Fig. 4. Job *plots for the complex formed between* **3** *and* **25b** *in* D_2O *containing* $Na_2B_2O_7$ (5 mM) *at 300 K, pH 9.2.* The total concentration $c_0(\mathbf{H}) + c_0(\mathbf{G})$ was kept constant at 2 mM. The host signal H–C(2′) (*left graph*) and the guest signal H–C(4) (*right graph*) were followed. For further definitions, see *Caption* to *Fig. 3*.

The quality of the experimental titration data in borate buffer is documented in *Fig. 5*. It is readily apparent that, with increasing receptor concentration, the signal of H–C(2) of the guest moves downfield, whereas the signal of H–C(4) moves upfield. The fact that differential up- and downfield shifts are observed is generally an indicator for the formation of a geometrically highly structured complex rather than unspecific aggregation or association.

Isophthalate binding by cavitand **3** in aqueous solution was further studied in the presence of *Tris*/HCl buffer at pH 8.3 (*Tris* = 2-amino-2-(hydroxymethyl)propane-1,3-diol). The results are in good agreement with those from the study in the borate buffer. The cationic *Tris*/HCl buffer (pH 8.3) was found less competitive than the anionic borate buffer (pH 9.2), which was reflected in the increased value of the association constant, especially in the case of nitro derivative **25b**. Again, 1:1 host-guest stoichiometry was observed exclusively.

The complexation of the two isophthalates by **3** was also investigated by computer modeling. Results of energy minimizations (4000 steps) using the *Monte Carlo* multiple minimum simulation method implemented in *MacroModel V. 6.0* [27] with the *AMBER** force-field [28] and the *GB/SA* solvation model for H_2O [29] were in agreement with the experimentally observed formation of stable inclusion complexes. *Fig. 6* shows the energy-minimized structure of the complex formed by methoxyisophthalate. The aromatic ring of **26** is embedded into the host cavity while the carboxylate residues interact *via* ion pairing and ionic H-bonding with the surrounding benzamidinium residues. Such an inclusion geometry is supported experimentally by the substantial complexation-induced upfield shift observed for the ^{1}H-NMR resonance of H–C(4) in **26a/b**.

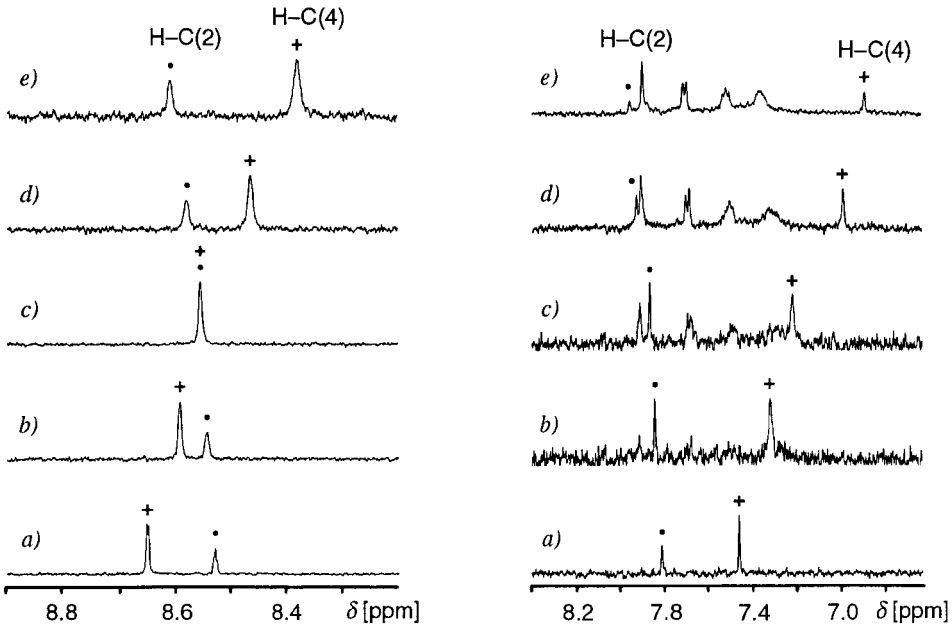


Fig. 5. *Two examples of ^{1}H-NMR titrations with isophthalates in D_2O containing $Na_2B_4O_7$* (5 mM) *at 300 K, pH 9.2. Left:* Part of the ^{1}H-NMR spectrum of **25b** (0.5 mM) alone (*a*) and in the presence of receptor at [**3**] = 0.12 (*b*), 0.21 (*c*), 0.50 (*d*), and 1.0 (*e*) mM. *Right:* Part of the ^{1}H-NMR spectrum of **26b** (0.2 mM) alone (*a*), and in the presence of receptor at [**3**] = 0.049 (*b*), 0.084 (*c*), 0.20 (*d*), and 0.41 (*e*) mM.

2.2.2. *Complexation of Phosphates.* Various nucleotides (*cf.* **25**–**37**) were chosen and their complexation with receptor **3** studied in aqueous solution. All phosphates were used as sodium salts except for dinucleotide d(AA) **33**, which was used as ammonium salt. ^{1}H-NMR Binding titrations were executed at 300 K in D_2O containing *Tris*/HCl (pH 8.3), a buffer commonly used in biological studies with nucleotides [30]. Stable complex formation was observed, and all data could be fitted to the 1:1 host-guest binding model since higher associations were not observed. The following results were obtained:

i) In D_2O containing *Tris*/HCl (2.5 mM), complexation strength increases with increasing guest charge: the association constant K_a increases in the series cAMP (**30**) < AMP (**28**) < ADP (**31**) < ATP (**32**) (*Table 2*). The thermodynamic data for ATP binding have a high uncertainty, since they exceed the limits of the used ^{1}H-NMR technique. Similar correlations between guest charge and binding affinity had been previously observed in the complexation of these nucleotides with protonated aza-crown ethers [12]. The 1:1 stoichiometry of AMP complexation with **3** was confirmed by *Job*-plot analysis (*Fig. 7*).

ii) The effects of varying buffer and salt (NaCl) concentrations on AMP (**28**) binding were the subject of further studies. It was found that a fourfold increase of the *Tris*/HCl buffer concentration did not significantly alter the association constant (*Table 3*). On the other hand, introduction of high salt concentrations decreased the binding constant dramatically. The buffer/salt system (10 mM *Tris*/HCl + 150 mM

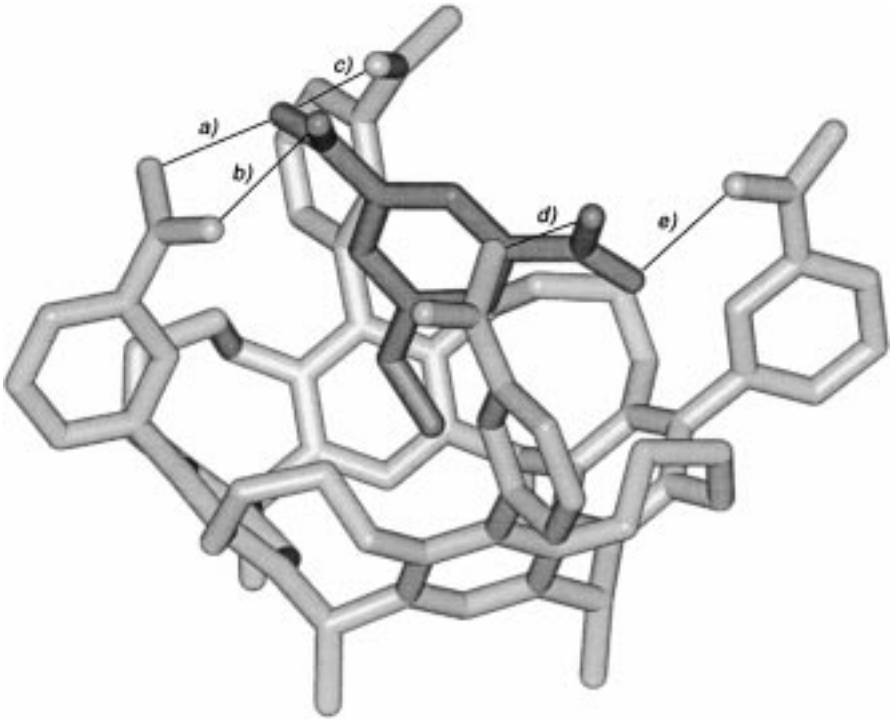


Fig. 6. *Energy-minimized structure of the complex formed between receptor* **3** *and 5-methoxyisophthalate* **26**. The calculations were performed with *MacroModel V. 6.0* (4000-step *Monte-Carlo* multiple minimum simulation, *AMBER** force-field, *GB/SA* solvation model for H_2O). Shown are the intermolecular H-bonding N···O distances in the complex: *a*) 2.65 Å, *b*) 2.74 Å, *c*)–*e*): 2.66 Å. For simplification, the $(CH_2)_3(OCH_2CH_2)_3OMe$ chains in **3** were replaced by Me groups.

Table 2. *Association Constants* (K_a) *and Complexation Free Enthalpies* (ΔG) *for the 1:1 Complexes of Adenosine Phosphates with Receptor* **3** *in* D_2O *Containing* Tris/*HCl* (2.5 mM, pH 8.3). $T = 300$ K. Also shown are the maximum observed complexation-induced upfield shifts $\Delta\delta_{max\,obs}$ of guest resonances monitored during the titrations.

Guest[a])	K_a [l mol^{-1}]	ΔG [kJ mol^{-1}]	$\Delta\delta_{max\,obs}$ [ppm]
cAMP (**30**)	1400	-18.1 ± 0.2	-0.020 (H–C(2))
			-0.091 (H–C(8))
			-0.066 (H–C(1′))
AMP (**28**)	10000	-23.0 ± 0.3	-0.412 (H–C(2))
			-0.091 (H–C(8))
			-0.106 (H–C(1′))
ADP (**31**)	48700	-26.9 ± 0.4	-0.067 (H–C(8))
			-0.186 (H–C(1′))
ATP (**32**)	660000	-33.4 ± 1.5	-0.100 (H–C(8))
			-0.202 (H–C(1′))

[a]) Constant guest concentrations: 1.0 mM (**30**), 0.4 mM (**28**), 0.3 mM (**31**), 0.2 mM (**32**).

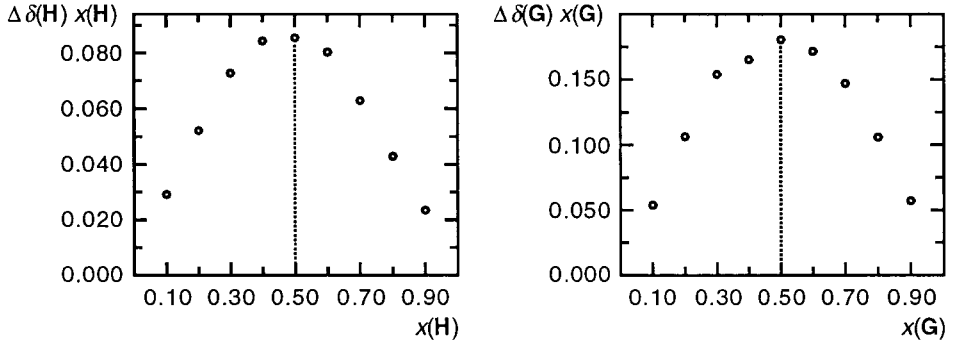


Fig. 7. Job *plots for the complex formed between AMP* (**28**) *and* **3** *in* D_2O *containing* Tris/*HCl* (5 mM) *at 300 K, pH 8.3*. The total concentration $c_0(\mathbf{H}) + c_0(\mathbf{G})$ was kept constant at 2 mM. The host signal H–C(2′) (*left graph*) and the guest signal H–C(2) (*right graph*) were followed. For further definitions, see *Caption* to *Fig. 3*.

Table 3. *Association Constants* (K_a) *and Complexation Free Enthalpies* (ΔG) *for the 1 : 1 Complex of AMP* (**28**) *with Receptor* **3** *in Different Buffer/Salt Systems.* $T = 300$ K. Also shown are the maximum observed complexation-induced upfield shifts $\Delta\delta_{max\ obs}$ of guest resonances[a]) monitored during the titrations.

c(*Tris*/HCl) [mM]	*c*(NaCl) [mM]	K_a [l mol^{-1}]	ΔG [kJ mol^{-1}]	$\Delta\delta_{max\ obs}$ [ppm]
2.5	0	10000	-23.0 ± 0.3	-0.412 (H–C(2))
				-0.091 (H–C(8))
				-0.106 (H–C(1′))
10.0	0	9600	-22.9 ± 0.2	-0.358 (H–C(2))
				-0.077 (H–C(8))
				-0.093 (H–C(1′))
10.0	150	720	-16.4 ± 0.3	-0.075 (H–C(2))
				-0.014 (H–C(8))
				-0.020 (H–C(1′))

[a]) Constant guest concentration: 0.4 mM.

NaCl), being the most competitive in the presented studies, is widely used as a standard medium in biochemistry for many DNA assays [30].

iii) Receptor **3** preferentially complexes AMP (**28**) over the other natural nucleotides GMP (**34**), CMP (**35**), TMP (**36**), or UMP (**37**), although differences in binding free enthalpy are not very large (*Table 4*). Substantial complexation-induced upfield shifts, indicative of cavity inclusion of the nucleobase, were only observed for the resonance of proton H–C(8) in bound AMP. This could suggest that the slight preference of the receptor for AMP could originate from additional apolar binding interactions and hydrophobic desolvation, associated with cavity inclusion. Interestingly, AMP (**28**) and its analogs dAMP (**27**), missing the C(2′)–OH group, and ε-AMP (**29**), with an extended tricyclic nucleobase, form complexes of similar stability with **3**. Particularly large complexation-induced upfield shifts of the resonances of H–C(10) ($\Delta\delta_{max\ obs} = -0.619$ ppm) and H–C(11) ($\Delta\delta_{max\ obs} = -0.805$ ppm) in ε-AMP (**29**) suggest that the additional fused imidazole ring of this guest is deeply embedded into the shielding cavity of the cavitand. The association strength, however, is not much affected by this cavity inclusion. Therefore, the present studies demonstrate that ion

Table 4. *Association Constants* (K_a) *and Complexation Free Enthalpies* (ΔG) *for the 1:1 Complexes of Nucleotides with Receptor* **3** *in* D_2O *Containing* Tris/*HCl* (2.5 mM, pH 8.3). $T = 300$ K. Also shown are the maximum observed complexation-induced upfield shifts $\Delta\delta_{max\,obs}$ of guest resonances monitored during the titrations[a]).

Guest	K_a [l mol^{-1}]	ΔG [kJ mol^{-1}]	$\Delta\delta_{max\,obs}$ [ppm]
AMP (**28**)[b])	10000	-23.0 ± 0.3	-0.412 (H–C(2))
			-0.091 (H–C(8))
			-0.106 (H–C(1′))
GMP (**34**)[b])	5200	-21.4 ± 0.2	-0.023 (H–C(8))
			-0.035 (H–C(1′))
CMP (**35**)[b])	3500	-30.4 ± 0.2	-0.031 (H–C(5))
			-0.021 (H–C(6))
			-0.025 (H–C(1′))
TMP (**36**)[b])	5900	-21.6 ± 0.3	-0.040 (Me)
			-0.021 (H–C(6))
			-0.026 (H–C(1′))
UMP (**37**)[b])	3800	-20.6 ± 0.3	-0.033 (H–C(5))
			-0.014 (H–C(6))
			-0.018 (H–C(1′))
dAMP (**27**)[b])	9500	-22.9 ± 0.2	-0.357 (H–C(2))
			-0.053 (H–C(8))
			-0.096 (H–C(1′))
ε-AMP (**29**)[b])	9200	-22.8 ± 0.3	-0.201 (H–C(2))
			-0.011 (H–C(8))
			-0.619 (H–C(10))
			-0.805 (H–C(11))
			-0.009 (H–C(1′))
d(AA) (**33**)[c])	330	-14.5 ± 0.2	-0.027 (H–C(2))
			-0.052 (H–C(8))

[a]) For numbering of the protons, see *Formulae* **25**–**37**. [b]) Constant guest concentration: 0.4 mM. [c]) Buffer concentration: 10 mM, constant guest concentration: 1.0 mM.

pairing and ionic H-bonding between the charged groups of host and guest, as well as desolvation of these groups upon complexation [1], rather than apolar interactions and hydrophobic desolvation, provide the major driving forces for nucleotide complexation by **3**.

iv) Dinucleotide d(AA) (**33**) forms a weak 1:1 complex with **3** (*Table 4*). Small complexation-induced changes in chemical shift were only observed for the ^{1}H resonances of one of the two nucleobases (adenosine with the free C(5′)–OH group), and cavity inclusion presumably is not very effective in the complex.

Nucleotide binding by **3** was also investigated by computer modeling with *MacroModel V. 6.0* (see above). In agreement with the experimental findings, AMP was calculated to preferentially form an inclusion complex with the nucleobase embedded into the cavity of the receptor (*Fig. 8*). In contrast, the smaller pyrimidine base in UMP (**37**) did not show a high propensity to bind into the bowl and preferred turning away form the cavity into the solution. The majority of the low-energy conformations generated for complexes of the nucleotides that were studied experimentally showed the involvement of three convergent amidinium residues in host-guest ion pairing, while the fourth aminidium residue was extending away from the cavity into the solution.

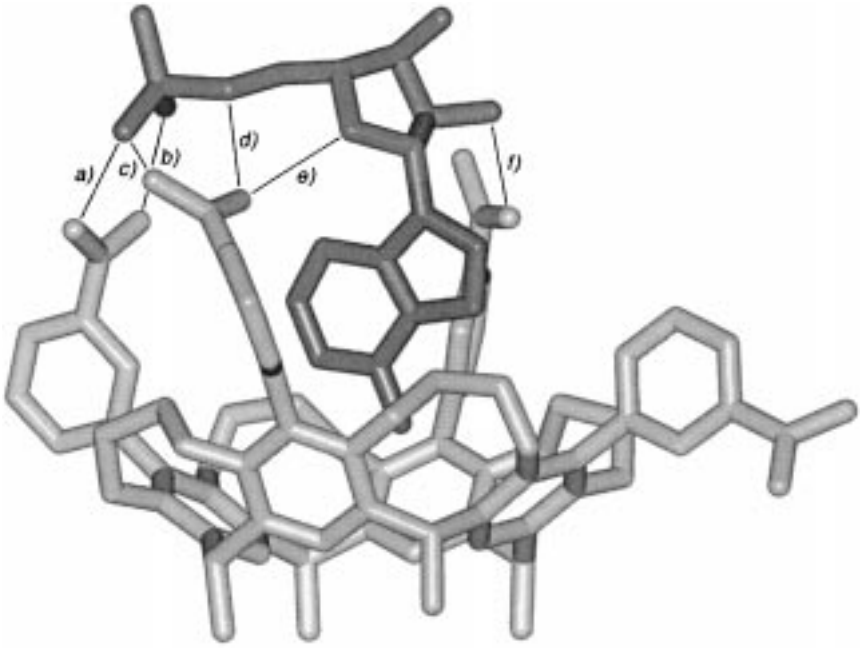


Fig. 8. *Energy-minimized structure of the complex formed between receptor* **3** *and AMP* (**28**). The calculations were performed with *MacroModel V. 6.0* (4000-step *Monte-Carlo* multiple-minimum simulation, *AMBER** force-field, *GB/SA* solvation model for H_2O). Shown are the intermolecular H-bonding N ··· O distances in the complex: *a*) 2.69 Å, *b*) 2.67 Å, *c*) 2.66 Å, *d*) 2.75 Å, *e*) 2.91 Å, *f*) 2.76 Å. For simplification, the $(CH_2)_3(OCH_2CH_2)_3OMe$ chains in **3** were replaced by Me groups.

3. Conclusion. – The tetrakis(phenylamidinium) cavitand **3** is readily prepared in gram quantities and represents an excellent anion receptor in CD_3OD and D_2O. In CD_3OD and pure D_2O, isophthalates **25** and **26** form stable complexes with 1:2 host-guest stoichiometry, as revealed by ^{1}H-NMR binding titrations and application of *Job*'s method of continuous variation. In aqueous buffers (borate, *Tris*/HCl), however, the tendency to form higher-order complexes vanishes, and the analysis of the titration data and *Job* plots confirmed the exclusive formation of 1:1 host-guest complexes. A substantial binding selectivity is observed between the two isophthalates in buffered D_2O solutions. The 5-MeO derivative **26b** forms a significantly more stable complex than the corresponding 5-NO_2 derivative **26b**. Specific complexation-induced changes in chemical shift of the aromatic guest resonances suggest that inclusion of the MeO-substituted phenyl ring of **26b** in the lipophilic receptor cavity is more favorable than inclusion of the NO_2-substituted phenyl ring of **25b**. This could explain the observed binding selectivity.

Stable host-guest complexes also form in *Tris*/HCl-buffered D_2O between cavitand **3** and a variety of nucleotides. The 1:1 stoichiometry of all complexes was clearly revealed by ^{1}H-NMR titration data and *Job*-plot analyses. Association constants increase strongly with increasing guest charge in the series cAMP (**30**) < AMP (**28**) < ADP (**31**) < ATP (**32**). A weaker complex with 1:1 host-guest stoichiometry also forms with the dinucleotide d(AA) (**33**). Association strength is strongly reduced in the

presence of high salt (NaCl) concentration. The receptor shows a slight selectivity for AMP and analogs over other nucleotides, such as GMP (**34**), CMP (**35**), TMP (**36**), or UMP (**37**). The analysis of the complexation-induced changes in chemical shift of the aromatic guest resonances suggests that the nucleobase in bound AMP, dAMP (**27**), and ε-AMP (**29**) is deeply embedded in the receptor cavity, which does not seem to be the case for the nucleobases in the other nucleotides. However, the additional gain in binding free enthalpy resulting from this cavity inclusion and, hence nucleotide selectivity, is only small. Therefore, it can be concluded that the major forces stabilizing the complexes of **3** with isophthalates and nucleotides result from ion-pairing and ionic H-bonding between the charged groups of host and guest and from the desolvation of these groups upon complexation [1]. Apolar interactions and hydrophobic desolvation do not seem to make a large contribution to the measured binding free enthalpies. The good synthetic availability and the excellent nucleotide-binding ability make the tetrakis(phenylamidinium) cavitand **3** a promising building block for the construction of oligomeric receptors that are capable of complexing oligonucleotides such as DNA and RNA fragments. Developments in this direction are now being pursued in our laboratory.

Experimental Part

General. See [1]. Resorcinarene cavitands were named according to [20]. An alternative name for the unsubstituted resorcinarene cavitand skeleton (*e.g.*, in **8** or **9**, but without Br-substituents and side chain R, *Scheme 1*) is: *2,5,9,12,16,19,23,26-octaoxanonacyclo[25.15.1.1^{28,42}.0^{6,40}.0^{8,38}.0^{13,36}.0^{15,34}.0^{20,32}.0^{22,30}]tetratetraconta-1(43),6,8(38),13,15(34),20,22(30),27,31,35,39,42-dodecaene.*

^{1}H-NMR Titrations. For the preparation of **25a** and **26a**, see [1]. The disodium isophthalates **25b** and **26b** were obtained by neutralization of MeOH solns. of the corresponding isophthalic acids with 2 equiv. of 1M aq. NaOH. The resulting soln. was concentrated *in vacuo*, and the residue was recrystallized from H_2O/MeOH to give, after drying (0.01 Torr, 80°, 12 h), the pure disodium salts **25b** and **26b**, resp. All nucleotides were purchased from *Sigma* or *Fluka* and used without further purification. Borate buffer (pH 9.2, 5 mM) was prepared by dissolving anh. $Na_2B_4O_7$ (*Aldrich*) in D_2O. *Tris*/HCl buffer (pH 8.2; 2.5 mM) was prepared from solid *Tris*/HCl (*Fluka*) and D_2O. All ^{1}H-NMR titrations were performed with a 500-MHz *Bruker AMX 500* instrument. The titrations were performed by adding a soln. of both components ($11 \times 20 - 300$ µl) to the soln. of one component in NMR tubes. The signals of the component which was kept at constant concentration were followed. The experimental data were fitted using the program *SPECFIT V. 2.11* [25].

Job *Plots*. A set of 11 samples was prepared with the total concentration of both components being kept constant at 2 mM in all samples. The host-guest ratio was varied in such a way that the host molar fraction ($c_0(\mathbf{H})/(c_0(\mathbf{H}) + c_0(\mathbf{G}))$ (c_0 = total initial concentration) increased (0, 0.10, 0.20, … 1.00; in intervals of 0.10) and the guest molar fraction ($c_0(\mathbf{G})/(c_0(\mathbf{H}) + c_0(\mathbf{G}))$ correspondingly decreased in the prepared samples. Resonances of both components were followed on a 500-MHz *Bruker AMX 500* instrument. The plots were generated using the program *proFit V. 5.0.1* [31].

Molecular Modeling. All calculations were carried out on *Silicon Graphics Indigo 2* or *Octane* workstations. Initial structures of host and guest were generated by a conjugate gradient minimization with the *AMBER** force-field and the *BatchMin* program implemented within *MacroModel V. 6.0*. For simplification, the $(CH_2)_3(OCH_2CH_2)_3OMe$ chains in **3** were replaced by Me groups. Counterions of host and guest were not included in the simulations. The guests were placed outside the resorcinarene cavity in the initial structures. These structures were further refined by a 4000-step *Monte-Carlo* multiple minimum simulation, using the *GB/SA* solvation model for H_2O. All conformations within 30 kJ mol^{-1} of the computed global minimum were stored, and the representative lowest-energy structure was analyzed for intermolecular close contacts and H-bonds.

5,11,17,23-Tetrabromo-2,8,14,20-tetraundecylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol (all-*cis*-stereoisomer; **6**). NBS (18.50 g, 104.00 mmol) was added portionwise at 35° to a stirred soln. of **4** (10.00 g, 9.00 mmol) in butanone (300 ml), and the mixture was stirred at 20° for 1 d under Ar in the dark. The formed solid was removed by filtration, washed with

cold butanone, and dried *in vacuo* to give **6** (6.69 g, 52%). M.p. 295–296° (dec.). IR (KBr): 3396*s*, 2923*s*, 2852*m*, 1616*w*, 1471*s*, 1434*m*, 1313*m*, 1156*m*, 1090*w*. ^{1}H-NMR ($(CD_3)_2CO$, 500 MHz): 8.28 (*s*, 8 H); 7.61 (*s*, 4 H); 4.44 (*t*, *J* = 6.5, 4 H); 2.29–2.30 (*m*, 8 H); 1.30–1.36 (*m*, 8 H); 1.25–1.30 (*m*, 64 H); 0.88 (*t*, *J* = 6.9, 12 H). ^{13}C-NMR ($(CD_3)_2CO$, 125 MHz): 149.69; 126.03; 124.47; 100.90; 34.53; 32.67; 30.52; 30.43; 30.36; 30.20; 30.05; 29.90; 29.74; 28.82; 23.33; 14.35. FAB-MS: 1421.4 (48, MH$^+$, $C_{72}H_{109}{}^{79}Br_2{}^{81}Br_2O_8^+$), 1342.5 (27, $[M + H - Br]^+$), 1265.2 (100, $[M + H - 2\,Br]^+$), 1185.3 (35). Anal. calc. for $C_{72}H_{108}Br_4O_8$ (1421.26): C 60.85, H 7.66, Br 22.49; found: C 60.96, H 7.57, Br 22.56.

5,11,17,23-Tetrabromo-2,8,14,20-tetrakis(2-phenylethyl)pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,31-dodecaene-4,6,10,12,16,18,22,24-octol (all-*cis*-stereoisomer; **7**). NBS (185.73 g, 88.0 mmol) was added portionwise to a stirred soln. of **5** (10.00 g, 9.00 mmol) in butanone (300 ml), and the mixture was stirred at 20° for 1 d under Ar in the dark. The formed solid was removed by filtration, washed with cold butanone, and dried *in vacuo* to give **7** (11.80 g, 87%). M.p. 280° (dec.) ([32]: 260° (dec.)). IR (KBr): 3404*s*, 3024*m*, 2937*m*, 2861*w*, 1613*m*, 1473*s*, 1305*s*, 1201*s*, 1157*s*, 1098*s*, 749*m*, 699*s*. ^{1}H-NMR ($(CD_3)_2SO$, 300 MHz): 9.24 (*s*, 8 H); 7.49 (*s*, 4 H); 7.10–7.20 (*m*, 20 H); 4.39 (*t*, *J* = 6.5, 4 H); 2.45–2.50 (*m*, 16 H). ^{13}C-NMR ($(CD_3)_2CO/CD_3OD$ 1:1, 125 MHz): 150.10; 143.14; 129.41; 129.30; 126.67; 126.32; 124.40; 100.48; 37.35; 36.84; 35.49. FAB-MS: 1221.0 (67, MH$^+$, $C_{60}H_{53}{}^{79}Br_2{}^{81}Br_2O_8^+$), 1115.5 (100, $[M + H - C_8H_8]^+$), 1037.4 (19, $[M + H - C_8H_8 - Br]^+$). Anal. calc. for $C_{60}H_{52}Br_4O_8$ (1220.68): C 59.04, H 4.29; Br 26.18; found: C 59.01, H 4.22, Br 25.97.

*8,13,18,32-Tetrabromo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetraundecyl-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin* (all-*cis*-stereoisomer; **8**). A mixture of dry **6** (3.30 g, 2.32 mmol), $TsO(CH_2)_2OTs$ (7.11 g, 19.20 mmol), anh. Cs_2CO_3 (12.12 g, 37.20 mmol), and dry Me_2SO (100 ml) was degassed and stirred under Ar at 65° for 40 h. Filtration through a pad of *Celite* and concentration *in vacuo* left a residue which was mixed with H_2O (100 ml) and extracted with CH_2Cl_2 (3 × 100 ml). The combined org. layers were washed with H_2O (2 × 100 ml), dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) afforded **8** (1.20 g, 34%) as a colorless oil besides **10** (1.53 g, 43%) as a white solid. A mixture of **10** (1.45 g, 965 mmol), $TsO(CH_2)_2OTs$ (715 mg, 1.93 mmol), anh. Cs_2CO_3 (1.80 g, 5.52 mmol), and dry MeCN (30 ml) was degassed and stirred under Ar at 90° for 1 d. Evaporation and workup as described before yielded **8** (1.29 g, 88%). Colorless oil. IR (KBr): 2918*s*, 2852*s*, 1464*s*, 1439*s*, 1302*m*, 1095*s*, 1061*s*, 1040*m*, 881*m*, 862*m*, 622*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.24 (*s*, 4 H); 5.26 (*t*, *J* = 8.2, 4 H); 4.44–4.47 (*m*, 8 H); 3.74–3.78 (*m*, 8 H); 2.03–2.06 (*m*, 8 H); 1.20–1.34 (*m*, 72 H); 0.88 (*t*, *J* = 7.0, 12 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 151.65; 137.10; 123.16; 113.29; 70.48; 34.89; 34.21; 31.85; 29.58; 29.55; 29.29; 27.63; 22.58; 13.99. FAB-MS: 1525.8 (100, MH$^+$, $C_{80}H_{117}{}^{79}Br_2{}^{81}Br_2O_8^+$). Anal. calc. for $C_{80}H_{116}Br_4O_8$ (1525.41): C 62.99, H 7.66, Br 20.95; found: C 63.15, H 7.54, Br 20.74.

*8,13,18,32-Tetrabromo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(2-phenylethyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin* (all-*cis*-stereoisomer; **9**). A mixture of dry **7** (18.95 g, 15.52 mmol), $TsO(CH_2)_2OTs$ (46.0 g, 124.2 mmol), anh. Cs_2CO_3 (80.9 g, 248.4 mmol), and dry Me_2SO (800 ml) was degassed and stirred under Ar at 65° for 4 d. Filtration through a pad of *Celite* and concentration *in vacuo* left a residue, which was mixed with H_2O (400 ml) and extracted with CH_2Cl_2 (3 × 350 ml). The combined org. layers were washed with H_2O (2 × 350 ml), dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) gave **9** (6.65 g, 32%) and **11** (12.16 g, 60%) as white solids. A mixture of **11** (12.16 g, 9.36 mmol), $TsO(CH_2)_2OTs$ (7.32 mg, 19.75 mmol), anh. Cs_2CO_3 (14.86 g, 45.6 mmol), and dry MeCN (300 ml) was degassed and stirred under Ar at 120° for 3 d. Evaporation *in vacuo* and workup as described before yielded **9** (9.38 g, 76%). White solid. M.p. 184–186°. IR (KBr): 2927*m*, 1774*w*, 1602*w*, 1496*w*, 1446*s*, 1301*m*, 1097*s*, 1060*s*, 881*w*, 751*m*, 700*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.31 (*s*, 4 H); 7.17–7.19 (*m*, 12 H); 7.07–7.09 (*m*, 8 H); 5.42 (*t*, *J* = 7.9, 4 H); 4.49–4.52 (*m*, 8 H); 3.81–3.85 (*m*, 8 H); 2.51–2.55 (*m*, 8 H); 2.37–2.40 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 151.75; 141.46; 136.85; 128.49; 128.35; 125.96; 122.87; 113.53; 70.52; 36.79; 35.33; 34.39. FAB-MS: 1325.1 (100, MH$^+$, $C_{68}H_{61}{}^{79}Br_2{}^{81}Br_2O_8^+$). Anal. calc. for $C_{68}H_{60}Br_4O_8$ (1324.83): C 61.65, H 4.56, Br 24.13; found: C 61.76, H 4.57, Br 24.38. X-ray: see *Figure 1*.

*8,13,18,32-Tetraiodo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetraundecyl-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin* (*all-cis*-stereoisomer; **12**). Dry **8** (4.78 g, 3.13 mmol) was dissolved in dry THF (150 ml) under Ar, and the soln. was cooled to −100°. BuLi (1.6M in hexane, 19.6 ml, 31.4 mmol) was slowly added, and the mixture was stirred for 35 min. I_2 (9.54 g, 37.6 mmol) was added, and the mixture was warmed to 20° and stirred for 12 h, concentrated *in vacuo*, washed with sat. aq. $NaHSO_3$ soln. (250 ml), and extracted with CH_2Cl_2 (3 × 100 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) yielded **12** (4.19 g, 78%). Colorless oil, which solidified upon standing. M.p. 140°. IR (KBr): 2923*s*, 2852*s*, 1456*m*, 1439*s*, 1094*s*, 1061*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.29 (*s*, 4 H); 5.26 (*t*, *J* = 8.1, 4 H); 4.44–4.47 (*m*, 8 H); 3.74–3.77 (*m*, 8 H); 2.01–2.06 (*m*, 8 H);

1.17–1.35 (*m*, 72 H); 0.88 (*t*, *J* = 7.0, 12 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 154.37; 136.44; 124.76; 89.86; 70.38; 35.49; 34.78; 31.92; 29.67; 29.66; 29.65; 29.62; 29.38; 27.70; 22.68; 14.10. FAB-MS: 1714.1 (100, MH^+). Anal. calc. for $C_{80}H_{116}I_4O_8$ (1713.41): C 56.08, H 6.82, I 29.63; found: C 56.00, H 6.70, I 29.71.

*8,13,18,32-Tetraiodo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(2-phenylethyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo-[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin* (all-*cis*-stereoisomer; **13**). Dry **9** (11.68 g, 8.82 mmol) was dissolved in dry THF (350 ml) under Ar, and the soln. was cooled to −100°. BuLi (1.6M in hexane, 55.1 ml, 88.2 mmol) was slowly added, and the mixture was stirred for 30 min. I_2 (26.85 g, 105.8 mmol) was added, and the mixture was warmed to 20° and stirred for 12 h. The mixture was concentrated *in vacuo*, washed with sat. aq. $NaHSO_3$ soln. (300 ml), and extracted with CH_2Cl_2 (3 × 200 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) yielded **13** (11.92 g, 89%). White solid. M.p. 304–305°. IR (KBr): 3023*m*, 2923*s*, 1603*m*, 1496*m*, 1440*s*, 1297*m*, 1095*s*, 1060*s*, 862*m*, 749*m*, 699*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.34 (*s*, 4 H); 7.17–7.19 (*m*, 12 H); 7.05–7.08 (*m*, 8 H); 5.42 (*t*, *J* = 7.9, 4 H); 4.49–4.52 (*m*, 8 H); 3.79–3.83 (*m*, 8 H); 2.50–2.53 (*m*, 8 H); 2.34–2.39 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 154.65; 141.42; 136.30; 128.49; 128.35; 125.95; 124.51; 90.20; 70.42; 37.30; 35.84; 34.41. FAB-MS: 1512.5 (100, M^+). Anal. calc. for $C_{68}H_{60}I_4O_8$ (1512.84): C 53.99, H 4.00, I 33.55; found: C 54.14, H 4.06, I 33.54.

3-(4,4,5,5-Tetramethyl[1,3,2]dioxaborolan-2-yl)benzonitrile (**14**). BuLi (1.6M in hexane, 30.1 ml, 48.16 mmol) was added at −100° under Ar to 3-bromobenzonitrile (3.50 g, 19.23 mmol) in dry THF (150 ml), and the soln. was stirred for 15 min. $B(OMe)_3$ (22 ml, 193.7 mmol) was added at −100°, and the mixture was slowly warmed up and stirred for 14 h at 20°. After evaporation *in vacuo*, pinacol (2.80 g, 23.69 mmol), NH_4Cl (1 g), and PhMe (150 ml) were added. The mixture was heated to reflux for 3 h, then concentrated *in vacuo*. The residue was suspended in H_2O (300 ml), acidified with 2M HCl (30 ml), and extracted with CH_2Cl_2 (3 × 100 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. Bulb-to-bulb distillation (100°, 0.1 Torr) yielded **14** (4.17 g, 95%). White crystals. M.p. 80–81° (hexane). IR (KBr): 2976*s*, 2227*s*, 1604*s*, 1487*m*, 1421*s*, 1353*s*, 1272*m*, 1147*s*, 1091*m*, 966*m*, 879*m*, 847*m*, 804*m*, 700*s*, 672*m*, 560*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.08 (br. *s*, 1 H); 8.00 (*d*, *J* = 7.6, 1 H); 7.69–7.74 (*m*, 1 H); 7.46 (*t*, *J* = 7.6, 1 H); 1.34 (*s*, 12 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 138.71; 138.36; 134.36; 128.36; 118.78; 112.05; 84.46; 24.81. EI-MS: 229.2 (21, M^+); 214.2 (66), 143.1 (100), 130.1 (65). Anal. calc. for $C_{13}H_{16}BNO_2$ (229.09): C 68.16, H 7.04, N 6.11; found: C 68.29, H 7.04, N 6.06.

*3,3′,3″,3‴-(5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetraundecyl-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin-8,13,18,32-tetrayl)tetrakis[benzonitrile]* (all-*cis*-stereoisomer; **15**). A degassed mixture of **12** (7.00 g, 4.09 mmol), **14** (9.36 g, 40.9 mmol), Cs_2CO_3 (19.97 g, 61.3 mmol), $[PdCl_2(PPh_3)_2]$ (720 mg, 1.00 mmol), $AsPh_3$ (2.40 g, 7.80 mmol), dioxane (180 ml), and H_2O (7.2 ml) was stirred under Ar at 75° for 3 h. After cooling to 20°, H_2O (200 ml) was added and the precipitated solid was collected by filtration, washed with H_2O, and dried *in vacuo*. CC (SiO_2; $CH_2Cl_2 \rightarrow CH_2Cl_2$/AcOEt 98:2) yielded **15** (5.29 g, 80%). White solid. M.p. 237–238°. IR (KBr): 2922*s*, 2852*s*, 2230*m*, 1603*w*, 1579*w*, 1458*s*, 1265*m*, 1095*s*, 1063*s*, 1043*m*, 796*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.65 (*td*, *J* = 7.7, 1.3, 4 H); 7.62 (*s*, 4 H); 7.50 (*t*, *J* = 7.7, 4 H); 7.47 (br. *s*, 4 H); 7.41 (*d*, *J* = 7.7, 4 H); 5.23 (*t*, *J* = 8.1, 4 H); 3.82–3.86 (*m*, 8 H); 3.34–3.38 (*m*, 8 H); 2.19–2.23 (*m*, 8 H); 1.39–1.40 (*m*, 8 H); 1.25–1.30 (*m*, 64 H); 0.88 (*t*, *J* = 7.0, 12 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 151.53; 136.50; 136.37; 134.23; 133.24; 131.26; 129.00; 128.90; 124.85; 118.45; 112.38; 72.25; 34.74; 33.88; 31.94; 29.74; 29.72; 29.69; 29.41; 27.93; 22.69; 14.10. FAB-MS: 1615.2 (100, MH^+, $C_{107}{}^{13}CH_{133}N_4O_8^+$). Anal. calc. for $C_{108}H_{132}N_4O_8$ (1614.25): C 80.36, H 8.24, N 3.47; found: C 80.25, H 8.14, N 3.41.

*3,3′,3″,3‴-[5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetrakis(2-phenylethyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzonitrile]* (all-*cis*-stereoisomer; **16**). A degassed mixture of **13** (6.54 g, 4.32 mmol), **14** (9.90 g, 43.2 mmol), Cs_2CO_3 (21.11 g, 64.8 mmol), $[PdCl_2(PPh_3)_2]$ (250 mg, 0.35 mmol), $AsPh_3$ (1.00 g, 3.25 mmol), dioxane (170 ml), and H_2O (6.8 ml) was stirred under Ar at 75° for 3 h. After cooling to 20°, ice (180 g) was added, and the solid was collected by filtration, washed with H_2O, and dissolved in CH_2Cl_2 (250 ml). The soln. was filtered, dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2/AcOEt 98:2) afforded **16** (5.17 g, 85%). White solid. M.p. 355–357°. IR (KBr): 2926*m*, 2228*m*, 1602*w*, 1581*w*, 1496*w*, 1455*s*, 1442*s*, 1268*m*, 1235*w*, 1096*s*, 1063*s*, 864*w*, 800*m*, 751*m*, 699*s*. ^{1}H-NMR ($CDCl_2CDCl_2$, 500 MHz): 7.66 (*s*, 4 H); 7.57 (*d*, *J* = 7.7, 4 H); 7.43 (*t*, *J* = 7.7, 4 H); 7.37–7.38 (*m*, 8 H); 7.04–7.08 (*m*, 20 H); 5.28 (*t*, *J* = 7.9, 4 H); 3.75–3.76 (*m*, 8 H); 3.26–3.28 (*m*, 8 H); 2.48–2.52 (*m*, 16 H). ^{13}C-NMR ($CDCl_2CDCl_2$, 125 MHz): 151.95; 142.02; 136.52; 136.48; 134.70; 133.54; 131.64; 129.42; 129.23; 128.83; 126.82; 126.32; 124.88; 119.15; 112.29; 72.59; 37.33; 34.86; 34.50. FAB-MS: 1413.2 (100, M^+). Anal. calc. for $C_{96}H_{76}N_4O_8 \cdot H_2O$ (1413.70 + 18.02): C 80.54, H 5.49, N 3.91; found: C 80.64, H 5.64, N 3.89.

*3,3′,3″,3‴-(5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetraundecyl-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′-j′]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin-8,13,18,32-tetrayl)tetrakis[benzamidinium] Tetrachloride* (all-*cis*-stereoisomer; **1**). A suspension of NH_4Cl (5.79 g, 108.2 mmol) in 1,2-dichlorobenzene (45 ml) was slowly added at −10° under Ar to Me_3Al (2M in PhMe, 50 ml, 100.0 mmol), and the mixture was stirred at 20° for 2 h, then evaporated at 20°/0.1 Torr to give $MeAlNH_2Cl$. A suspension of **15** (5.29 g, 3.28 mmol) in a soln. of $MeAlNH_2Cl$ (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was stirred under Ar at 70° for 1 d, additional $MeAlNH_2Cl$ (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was added, and the mixture was stirred at 80° for 5 d. The mixture was cooled to 0°, ice (100 g) and MeOH (50 ml) were slowly added, and the suspension was filtered through a pad of *Celite*. The solid was washed with MeOH (500 ml), and the combined filtrates were concentrated *in vacuo*. The residue was dried *in vacuo* (0.01 Torr), stirred in a mixture of acetone (200 ml) and i-PrOH (0.2 ml) at 20° for 8 h, and filtered. The solid was washed with acetone (500 ml), dried, and washed with H_2O (500 ml). Recrystallization ($MeOH/Et_2O$ 2:3) afforded **1** (4.22 g, 70%). White solid. M.p. >300° (dec.). IR (KBr): 3406*s*, 2923*s*, 2853*m*, 1674*s*, 1458*m*, 1439*m*, 1093*m*. ^{1}H-NMR (CD_3OD, 500 MHz): 7.84 (*td*, *J* = 7.9, 1.5, 4 H); 7.78 (br. *s*, 8 H); 7.74 (*s*, 4 H); 7.66 (*t*, *J* = 7.9, 4 H); 5.32 (*t*, *J* = 8.1, 4 H); 3.72–3.76 (*m*, 8 H); 3.56–3.60 (*m*, 8 H); 2.29–2.33 (*m*, 8 H); 1.47–1.49 (*m*, 8 H); 1.38 (br. *s*, 64 H); 0.95 (*t*, *J* = 7.0, 12 H). ^{13}C-NMR (CD_3OD, 125 MHz): 167.98; 153.07; 138.47; 137.41; 131.85; 130.57; 129.94; 129.07; 127.98; 125.94; 73.49; 35.52; 35.34; 33.16; 30.90; 30.87; 30.77; 30.59; 29.25; 23.80; 14.52. FAB-MS: 1682.0/1683.0 (91/100, $[M-3\,H-4\,Cl]^+$). HR-FAB-MS: 1682.1199 $[M-3\,H-4\,Cl]^+$, $C_{108}H_{145}N_8O_8^+$; calc. 1682.1185). Anal. calc. for $C_{108}H_{148}N_8O_8Cl_4 \cdot 1.5\ CH_3OH$ (1828.22 + 24.03): C 70.10, H 8.27, N 5.97; found: C 70.11, H 8.19, N 5.99.

*3,3′,3″,3‴-[5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetrakis(2-phenylethyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzamidininium] Tetrachloride* (all-*cis*-stereoisomer; **2**). Me_3Al (2M in PhMe, 50 ml, 100.0 mmol) was slowly added to a suspension of NH_4Cl (5.79 g, 108.2 mmol) in 1,2-dichlorobenzene (45 ml) at −10° under Ar, and the mixture was stirred at 20° for 2 h, then evaporated at 20°/0.1 Torr. A suspension of **16** (5.29 g, 3.74 mmol) in a soln. of $MeAlNH_2Cl$ (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was stirred under Ar at 80° for 1 d, then additional $MeAlNH_2Cl$ (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was added, and the mixture was stirred at 80° for 3 d. After cooling to 0°, ice (100 g) and MeOH (50 ml) were slowly added, and the suspension was filtered through a pad of *Celite*. The solid was washed with MeOH (500 ml), and the combined filtrates were concentrated *in vacuo*. The residue was dried *in vacuo* (0.01 Torr), stirred at 20° for 8 h with a mixture of acetone (200 ml) and i-PrOH (0.2 ml), and filtered. The solid was washed with acetone (500 ml), dried, and washed with H_2O (500 ml). The obtained solid was recrystallized ($MeOH/Et_2O$ 1:2) to provide **2** (4.81 g, 79%). White solid. M.p. 327–329° (dec.). IR (KBr): 3382 (br.), 3111*s* (br.), 1675*s*, 1455*m*, 1094*m*, 700*m*. ^{1}H-NMR (CD_3OD, 500 MHz): 7.82–7.87 (*m*, 16 H); 7.68 (*t*, *J* = 8.0, 4 H); 7.17–7.22 (*m*, 20 H); 5.43 (*t*, *J* = 7.2, 4 H); 3.73–3.77 (*m*, 8 H); 3.59–3.64 (*m*, 8 H); 2.60–2.64 (*m*, 16 H). ^{13}C-NMR (CD_3OD, 125 MHz): 167.96; 153.29; 143.35; 138.43; 137.44; 137.34; 132.01; 130.58; 129.99; 129.54; 129.51; 129.05; 128.03; 126.91; 126.04; 73.53; 38.18; 35.68; 35.49. FAB-MS: 1482.6 (100, $[M-3\,H-4\,Cl]^+$). Anal. calc. for $C_{96}H_{92}Cl_4N_8O_8 \cdot 2\ CH_3OH$ (1627.64 + 32.04): C 69.66, H 5.85, N 6.63; found: C 69.48, H 5.98, N 6.55.

5,11,17,23-Tetrabromo-2,8,14,20-tetrakis(3-hydroxypropyl)pentacyclo[19.3.1.1^{3,7}*.1*^{9,13}*.1*^{15,19}*]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol* (all-*cis*-stereoisomer; **18**). NBS (11.1 g, 62.4 mmol) was added at 20° to a suspension of **17** (10.00 g, 13.9 mmol) in butanone (133 ml) and MeOH (57 ml), and the soln. was stirred in the dark for 3 h. Additional NBS (4.93 g, 27.7 mmol) was added, and the mixture was stirred in the dark for additional 12 h. The formed solid was isolated by filtration, washed with cold butanone, and dried *in vacuo* to yield **18** (11.10 g,77%). White powder. M.p. 282–283° (dec.) ([24]: 220° (dec.)). ^{1}H-NMR (CD_3OD, 200 MHz): 7.15 (*s*, 4 H); 4.50 (*t*, *J* = 7.7, 4 H); 3.61 (*t*, *J* = 6.4, 8 H); 2.13–2.24 (*m*, 8 H); 1.47–1.54 (*m*, 8 H).

*3,3′,3″,3‴-(8,13,18,32-Tetrabromo-5,6,10,11,15,16,20,21-octahydro-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin-1,25,27,29-tetrayl)tetrakis[propanol]* (all-*cis*-stereoisomer; **19**). A soln. of **18** (11.19 g, 10.8 mmol) in DMA (50 ml) was added at 20° under Ar *via* syringe pump over 2 d to a mixture of $TsO(CH_2)_2OTs$ (18.00 g, 48.6 mmol), anh. Cs_2CO_3 (45.74 g, 140.4 mmol), and BHT (1 mg) in dry DMA (400 ml). The suspension was stirred at 20° for 1 d, additional $TsO(CH_2)_2OTs$ (12.00 g, 32.4 mmol) and anh. Cs_2CO_3 (40.00 g, 122.8 mmol) were added, and stirring was continued at 45° for 1 d. Additional $TsO(CH_2)_2OTs$ (12.00 g, 32.4 mmol) and anh. K_2CO_3 (43.70 g, 316.2 mmol) were added, and the mixture was stirred at 65° for 3 d. After evaporation *in vacuo*, the solid residue was stirred with H_2O (1 l) at 20° for 2 d, filtered, and dried. The solid was heated to reflux in dioxane (400 ml), the insoluble part was filtered off, and the filtrate was concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2/MeOH 95:5 → 90:10) and recrystallization (dioxane/PhMe/CH_2Cl_2 1:10:10) afforded **19** (5.14 g, 42%). White solid. M.p. 380–390°. IR (Br): 3421*s*, 2932*m*,

2869*m*, 1447*s*, 1302*m*, 1100*m*, 1058*s*. ^{1}H-NMR ($(CD_3)_2SO$, 500 MHz): 7.82 (*s*, 4 H); 5.11 (*t*, *J* = 8.3, 4 H); 4.38 (*t*, *J* = 5.0, 4 H); 4.29–4.33 (*m*, 8 H); 3.69–3.73 (*m*, 8 H); 3.40–3.43 (*m*, 8 H); 2.48–2.50 (*m*, 8 H); 1.24–1.30 (*m*, 8 H). ^{13}C-NMR ($(CD_3)_2SO$, 125 MHz): 150.99; 136.60; 124.97; 112.57; 70.36; 60.27; 34.63; 30.83; 29.45. FAB-MS: 1140.0 (53, M^+), 955.5 (100). HR-FAB-MS: 1140.0150 (M^+, $C_{48}H_{52}{}^{79}Br_2{}^{81}Br_2O_{12}^+$; calc. 1140.0151).

*8,13,18,32-Tetrabromo-5,6,10,11,15,16,20,21-octahydro-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4-dioxonino][6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4-benzodioxonin]-1,25,27,29-tetrayltetrakis[propane-1,3-diyl]tetrakis[methanesulfonate]* (all-*cis*-stereoisomer; **20**). MsCl (2.5 ml, 32.2 mmol) was added *via* syringe pump over 40 min at 0° under Ar to **19** (500 mg, 438 mmol) in dry dioxane (40 ml) and Et_3N (20 ml), and the suspension was stirred for 3 h at 20°. After addition of ice (100 g), the mixture was extracted with CH_2Cl_2 (3 × 100 ml). The combined org. layers were washed with sat. aq. NH_4Cl soln. (100 ml), sat. aq. $NaHCO_3$ soln. (100 ml), dried (Na_2SO_4), and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2/AcOEt 85:15 → 75:25) yielded **20** (589 mg, 92%). White solid. M.p. 160–165°. IR (KBr): 2936*m*, 1461*s*, 1446*s*, 1351*s*, 1173*s*, 1102*m*, 1058*s*, 937*s*, 528*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.40 (*s*, 4 H); 5.29 (*t*, *J* = 8.4, 4 H); 4.45–4.48 (*m*, 8 H); 4.31 (*t*, *J* = 6.1, 8 H); 3.76–3.80 (*m*, 8 H); 3.06 (*s*, 12 H); 2.26–2.31 (*m*, 8 H); 1.63–1.67 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 151.73; 136.42; 123.32; 113.45; 70.55; 70.33; 37.42; 34.57; 29.80; 27.44. FAB-MS: 1451.7 (100, M^+). HR-FAB-MS: 1449.9273 (M^+, $C_{52}H_{60}{}^{79}Br_3{}^{81}BrO_{20}S_4^+$; calc. 1449.9274); 1451.9249 (M^+, $C_{52}H_{60}{}^{79}Br_2{}^{81}Br_2O_{20}S_4^+$; calc. 1451.9253).

*8,13,18,32-Tetrabromo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(3-[2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin* (all-*cis*-stereoisomer; **21**). Mg (1.00 g, 41.1 mmol) was activated with a crystal of I_2 at 200°, triethyleneglycol monomethyl ether (15 ml, 95.7 mmol) was added, and the suspension was stirred at 140° for 1.5 h. After cooling to 20°, dioxane (10 ml) was added to yield a soln. of **22**. This soln. (41.1 mmol) was added to **20** (1.20 g, 826 mmol) in dioxane (20 ml), and the mixture was stirred at 60° for 16 h. The residue obtained by evaporation *in vacuo* was dissolved in AcOEt (60 ml), the resulting soln. was washed with sat. aq. NH_4Cl soln. (100 ml), and the aq. layer was extracted with AcOEt (4 × 100 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. (150 ml) and H_2O (150 ml). The combined aq. layers were extracted with AcOEt (3 × 80 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*, and the residue was dried at 160° (bulb-to-bulb, 0.1 Torr). CC (SiO_2; CH_2Cl_2/MeOH 98:2 → 94:6) yielded **21** (1.11 g, 78%). Colorless, viscous oil. IR (KBr): 2922*s*, 2868*s*, 1448*s*, 1349*m*, 1302*m*, 1246*m*, 1102*s*, 1056*s*, 934*m*, 862*m*, 623*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.19 (*s*, 4 H); 5.25 (*t*, *J* = 8.2, 4 H); 4.38–4.42 (*m*, 8 H); 3.70–3.74 (*m*, 8 H); 3.48–3.61 (*m*, 48 H); 3.44 (*t*, *J* = 6.5, 8 H); 3.31 (*s*, 12 H); 2.08–2.10 (*m*, 8 H); 1.43–1.46 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 151.46; 136.57; 122.78; 113.17; 71.73; 70.41; 70.38; 70.35; 70.31; 70.28; 69.88; 58.82; 34.23; 30.29; 27.29. FAB-MS: 1725.4 (100, MH^+).

*8,13,18,32-Tetraiodo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(3-[2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin* (all-*cis*-stereoisomer; **23**). BuLi (1.6M in hexane, 13.5 ml, 21.6 mmol) was added at −100° under Ar to dry **21** (3.24 g, 1.88 mmol) in dry THF (100 ml), and the soln. was stirred for 30 min at −100°. I_2 (6.67 g, 26.3 mmol) was added at −100°, then the mixture was slowly warmed to 20° and stirred for 2 h. Evaporation *in vacuo* provided a residue which was dissolved in CH_2Cl_2 (100 ml). The soln. was washed with sat. aq. $NaHSO_3$ soln. (100 ml), and the aq. layer was extracted with CH_2Cl_2 (4 × 100 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2/MeOH 98:2 → 95:5) yielded **23** (3.50 g, 97%). Colorless, viscous oil. IR (KBr): 2922*s*, 2868*s*, 1441*s*, 1349*m*, 1297*m*, 1104*s*, 1033*s*, 932*m*, 860*m*, 619*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.23 (*s*, 4 H); 5.24 (*t*, *J* = 8.2, 4 H); 4.37–4.41 (*m*, 8 H); 3.69–3.71 (*m*, 8 H); 3.47–3.61 (*m*, 48 H); 3.43 (*t*, *J* = 6.5, 8 H); 3.31 (*s*, 12 H); 2.04–2.09 (*m*, 8 H); 1.41–1.44 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 154.30; 135.98; 124.40; 89.79; 71.68; 70.36; 70.33; 70.29; 70.26; 70.14; 69.82; 58.79; 34.71; 30.74; 27.25. FAB-MS: 1914.1 (100, MH^+). HR-FAB-MS: 1913.3501 (MH^+, $C_{76}H_{109}I_4O_{24}^+$; calc. 1913.3488).

*3,3′,3″,3‴-{5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetrakis(3-[2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propyl)-2,24:3,23-dimetheno-1*H,*25*H,*27*H,*29*H-*bis[1,4]dioxonino[6,5*-j:*6′,5′*-j′*]benzo[1,2*-e:*5,4*-e′*]bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzonitrile]* (all-*cis*-stereoisomer; **24**). A degassed mixture of **23** (760 mg, 397 mmol), **14** (910 mg, 3.97 mmol), Cs_2CO_3 (1.94 g, 5.96 mmol), $[PdCl_2(PhCN)_2]$ (30 mg, 78 mmol), $AsPh_3$ (150 mg, 490 mmol), dioxane (9.6 ml), and H_2O (0.4 ml) was stirred under Ar at 70° for 2 h. The mixture was cooled to 20° and filtered through a pad of *Celite* and $MgSO_4$ (1:1) using CH_2Cl_2 (200 ml) and AcOEt (100 ml). After evaporation *in vacuo*, CC (SiO_2; CH_2Cl_2/MeOH 98:2 → 95:5) provided **24** (607 mg, 84%). Colorless viscous oil which solidified upon standing. M.p. 78–80°. IR (KBr): 2922*s*, 2868*s*, 2228*m*, 1457*s*, 1443*s*, 1266*m*, 1100*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.62 (*d*, *J* = 7.8, 4 H); 7.60 (*s*, 4 H); 7.49 (*t*, *J* = 7.8, 4 H); 7.45 (*s*, 4 H); 7.42 (*d*, *J* = 7.8, 4 H); 5.25 (*t*, *J* = 8.1, 4 H); 3.80–3.83 (*m*, 8 H); 3.51–3.65 (*m*, 64 H); 3.35 (*s*, 12 H); 2.24–2.28 (*m*, 8 H); 1.54–1.59 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 151.61; 136.34; 136.00; 134.28; 133.13; 131.16;

129.05; 128.88; 124.57; 118.37; 112.16; 72.16; 71.84; 70.68; 70.51; 70.49; 70.42; 69.99; 58.92; 33.32; 30.78; 27.67. FAB-MS: 1815.0 (100, MH$^+$). HR-FAB-MS: 1813.8656 (MH$^+$, $C_{104}H_{125}N_4O_{24}^+$; calc. 1813.8684; M^+, $C_{103}{}^{13}CH_{124}N_4O_{24}^+$; calc. 1813.8639).

*3,3′,3″,3‴-{5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetrakis(3-{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propyl)-2,24:3,23-dimetheno-1*H,25H,27H,29H-*bis[1,4]dioxonino[6,5-*j*:6′,5′-*j′*]benzo[1,2-*e*:5,4-*e′*]bis[1,4]benzodioxonin-8,13,18,32-tetrayl}tetrakis[benzamidininium] Tetrachloride* (all-*cis*-stereoisomer; **3**). MeAlNH$_2$Cl (2M in 1,2-dichlorobenzene, 30 ml, 60.0 mmol) was added to **24** (2.78 g, 1.53 mmol) in dry 1,2-dichlorobenzene (20 ml), and the mixture was stirred under Ar at 70° for 1 d. Additional MeAlNH$_2$Cl (2M in 1,2-dichlorobenzene, 30 ml, 60.0 mmol) was added, and stirring was continued at 80° for 2 d. After cooling to 0°, ice (50 g) and MeOH (20 ml) were slowly added, and the suspension was filtered through a pad of *Celite*. The solid was washed with MeOH (500 ml), and the combined filtrates were concentrated *in vacuo*. The residue was dried *in vacuo* (0.01 Torr), stirred with PhMe (300 ml) at 20° for 4 h, and filtered. The solid was washed with PhMe (200 ml), dried, washed with cold 20% aq. NaOH soln. (100 ml) and H_2O (800 ml). The residue was dissolved in MeOH (50 ml), 6M ethanolic HCl soln. (3 ml) was added, and the solvents were removed *in vacuo*. The product was dried *in vacuo* (0.05 Torr) and recrystallized (MeOH/Et$_2$O 1:4) to afford **3** (2.83 g, 91%). White solid. M.p. 306–310° (dec.). IR (KBr): 3104 (br.), 2932*s*, 2867*s*, 1677*s*, 1521*m*, 1457*m*, 1097*s*. ^{1}H-NMR (D$_2$O, 500 MHz): 8.01 (*s*, 4 H); 7.87 (*d*, J = 7.7, 4 H); 7.70 (*t*, J = 7.7, 4 H); 7.63 (*d*, J = 7.7, 4 H); 7.62 (*s*, 4 H); 5.25 (*t*, J = 8.2, 4 H); 3.84–3.86 (*m*, 8 H); 3.53–3.72 (*m*, 64 H); 3.34 (*s*, 12 H); 2.45–2.48 (*m*, 8 H); 1.61–1.75 (*m*, 8 H). ^{13}C-NMR (CD$_3$OD, 125 MHz): 167.93; 153.21; 138.45; 137.41; 137.30; 131.90; 130.62; 129.95; 129.05; 127.99; 126.08; 73.51; 72.96; 71.83; 71.63; 71.59; 71.56; 71.38; 71.30; 59.11; 34.90; 31.54; 29.16. FAB-MS: 1882.9 (100, [M – 3 H – 4 Cl]$^+$). HR-FAB-MS: 1881.9748 ([M – 3 H – 4 Cl]$^+$, $C_{104}H_{137}N_8O_{24}^+$; calc. 1881.9746). Anal. calc. for $C_{104}H_{140}Cl_4N_8O_{24}\cdot 0.5\ H_2O$ (2028.10 + 9.01): found: C 61.29, H 7.42, N 5.50; found: C 61.10, H 7.16, N 5.02.

X-Ray Crystal Structure of **9**$\cdot$*2 CH$_2$Cl$_2$*. X-Ray crystal data for $C_{71}H_{66}Br_4Cl_6O_8$ (M_r = 1579.58): monoclinic space group $P2_1/c$, D_c = 1.568 g cm^{-3}, Z = 4, a = 16.853(9), b = 16.312(10), c = 24.37(2) Å, β = 92.97(5)°, V = 6691(7) Å^3, MoK_α radiation, λ = 0.71073 Å, $1.67 \le \theta \le 20.04°$, 2913 unique reflections, T = 293 K. The structure was solved by direct methods (SHELXS 86) and refined by full-matrix least-squares analysis (SHELXL-93). All heavy atoms were refined anisotropically; H-atoms fixed isotropically, H-positions are based on stereochemical considerations. Final $R(F)$ = 0.0361, $wR(F^2)$ = 0.0764 for 746 parameters and 2913 reflections with $I > 2\sigma(I)$. C–Cl Distances of the solvent molecules are restrained to be equal. Crystallographic data (excluding structure factors) for compound **9**$\cdot$2 CH$_2$Cl$_2$ have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-137143. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336033; e-mail: deposit@ccdc.cam.ac.uk).

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