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Synthesis and Binding Properties of Basket-Shaped Hosts

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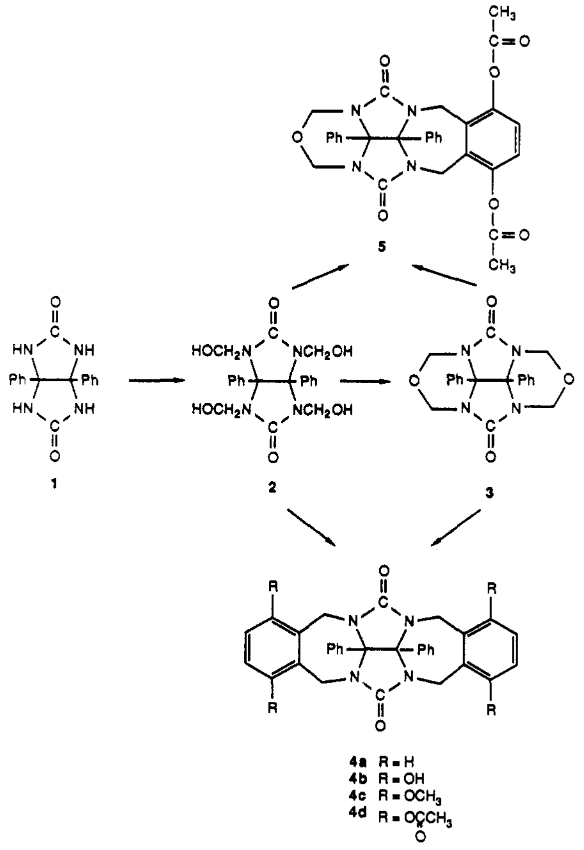
We describe a novel, concave building block (4) for the synthesis of organic hosts. Compound 4 contains two fused 2-imidazolidone rings, which are flanked by two *o*-xylylene units. Basket-shaped hosts are constructed by attaching oxyethylene bridges to the xylylene rings of 4. The new hosts are strong binders of aliphatic and aromatic diammonium guests. According to ^{1}H NMR, these guests are stretched out in the baskets. Alkali metal ions are bound in a 1:1 or 1:2 host:guest ratio. In the 1:1 complex, the metal ion is completely encapsulated by the host in a clamshell-like fashion. The 1:2 complex is assumed to have an open structure.

Introduction

In search of new and better catalysts, we try to learn from nature and mimic the best catalysts that exist: the enzymes. A simple model of an enzyme is an organic host containing a cavity or cleft with binding sites for a substrate and one or more catalytic centers (often a metal center) next to the cavity. Various host systems have been developed in the past years. A representative but incomplete list of recent examples includes systems created by Breslow,[2a] Collet,[2b,c] Cram,[2d,e] Diederich,[2f] Dougherty,[2g] Gokel,[2h,i] Gutsche,[2j] Koga,[2k] Lehn,[2l,m] Mock,[2n,o] Rebek,[2p,q] Reinhoudt,[2r] Sauvage,[2s,t] Schmidtchen,[2u] Sutherland,[2v] Vögtle,[2w,x] Weber,[2y] and Whitlock.[2z] Many of these hosts are only accessible in low yield via long synthetic routes. Our goal is to develop versatile host systems starting from cheap and readily available building blocks. In this paper we describe such a building block, viz. compound 4. It contains two fused 2-imidazolidone rings, which are flanked by two *o*-xylylene units. Its overall shape is concave, and its convex side is shielded by two phenyl substituents. The use of this building block in the synthesis of basket-shaped hosts is demonstrated.[3a]

Scheme I



Results and Discussion

Synthesis and Structure of Building Block. The synthetic route used to obtain intermediates **4a–c** is shown in Scheme I. Diphenylglycoluril (**1**) was prepared in nearly quantitative yield from the cheap starting materials benzil and urea.[4] Compound **1** contains two fused 2-

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(2) (a) O'Krongly, D.; Denmeade, S. R.; Chiang, M. Y.; Breslow, R. *J. Am. Chem. Soc.* **1985**, *107*, 5544–5545. (b) Canceill, J.; Lacombe, L.; Collet, A. *J. Am. Chem. Soc.* **1986**, *108*, 4230–4232. (c) Canceill, J.; Lacombe, L.; Collet, A. *J. Chem. Soc., Chem. Commun.* **1987**, 219–221. (d) Cram, D. J. *Angew. Chem.* **1986**, *98*, 1041–1060. (e) Cram, D. J. *J. Am. Chem. Soc.* **1987**, *109*, 3098–3107. (f) Diederich, F.; Dick, K.; Griebel, D. *J. Am. Chem. Soc.* **1986**, *108*, 2273–2286. (g) Shepodd, T. J.; Petti, H. A.; Dougherty, D. A. *J. Am. Chem. Soc.* **1986**, *108*, 6085–6087. (h) White, B. D.; Fronczek, F. R.; Gandour, R. D.; Gokel, G. W. *Tetrahedron Lett.* **1987**, *28*, 1753–1756. (i) Arnold, K. A.; Echegoyen, L.; Gokel, G. W. *J. Am. Chem. Soc.* **1987**, *109*, 3713–3715. (j) Gutsche, C. D.; Iqbal, H.; Stewart, D. *J. Org. Chem.* **1986**, *51*, 742–745. (k) Odashima, K.; Itai, A.; Iitaka, Y.; Koga, K. *J. Am. Chem. Soc.* **1980**, *102*, 2504–2505. (l) Lehn, J. M. *Science* **1985**, *227*, 849–856. (m) Hosseini, H. W.; Lehn, J. M. *Helv. Chim. Acta* **1986**, *69*, 587–597. (n) Freeman, W. A.; Mock, W. L.; Shih, N.-Y. *J. Am. Chem. Soc.* **1981**, *103*, 7376–7378. (o) Mock, W. L.; Shih, N.-Y. *J. Org. Chem.* **1986**, *51*, 4440–4446. (p) Rebek, J. *Science* **1987**, *235*, 1478–1484. (q) Rebek, J.; Ashew, B.; Killoran, M.; Nemeth, D.; Lin, F. T. *J. Am. Chem. Soc.* **1987**, *109*, 2426–2431. (r) Reinhoudt, D. N.; Dijkstra, D. J.; in't Veld, P. J. A.; Bugge, K. E.; Harkema, S.; Ungaro, R.; Ghidini, E. *J. Am. Chem. Soc.* **1987**, *109*, 4761–4762. (s) Chambron, J. C.; Sauvage, J. P. *Tetrahedron* **1987**, *43*, 895–904. (t) Dietrich-Buchecker, C. O.; Edel, A.; Kintzinger, J. P.; Sauvage, J. P. *Tetrahedron* **1987**, *43*, 333–344. (u) Schmidtchen, F. P.; *J. Inclusion Phenom.* **1987**, *5*, 161–164. (v) Sutherland, I. O. *Chem. Soc. Rev.* **1986**, 63–91. (w) Grammenudi, S.; Vögtle, F. *Angew. Chem.* **1986**, *98*, 1119–1121. (x) Stutle, P.; Kiggen, W.; Vögtle, F. *Tetrahedron* **1987**, *43*, 2065–2074. (y) Weber, E.; Josel, H. P.; Puff, H.; Franken, S. *J. Org. Chem.* **1985**, *50*, 3125–3132. (z) Skeridan, R. E.; Whitlock, H. W. *J. Am. Chem. Soc.* **1986**, *108*, 7120–7121.

(3) (a) Part of this work has been described in a preliminary paper: Smeets, J. W. H.; Sijbesma, R. P.; Niele, F. G. M.; Spek, A. L.; Smeets, W. J. J.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1987**, *109*, 928–929. (b) Allinger, N. L.; Yuh, Y. MM2/85, Chemistry Department, Indiana University, Bloomington, IN. (c) Our previous calculations using Allinger's MM2 program predicted that the *aa* form of **4b** is more stable than the *ss* form by ≈ 5 kcal mol^{-1}; see ref. 3a. More extended calculations are in progress and will be published in due time. (d) Pettersson, I.; Liljefors, T. *J. Comput. Chem.* **1987**, *8*, 1139–1145.

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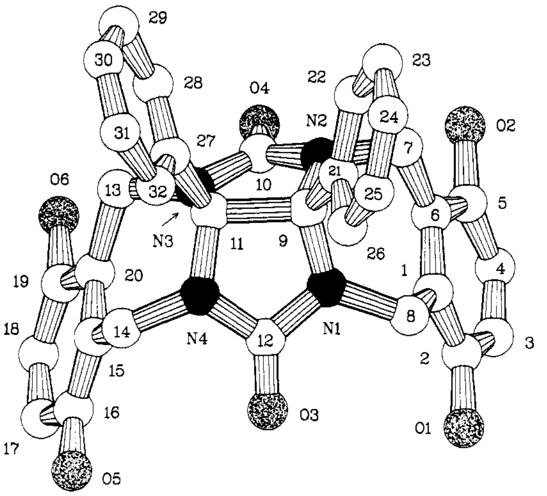


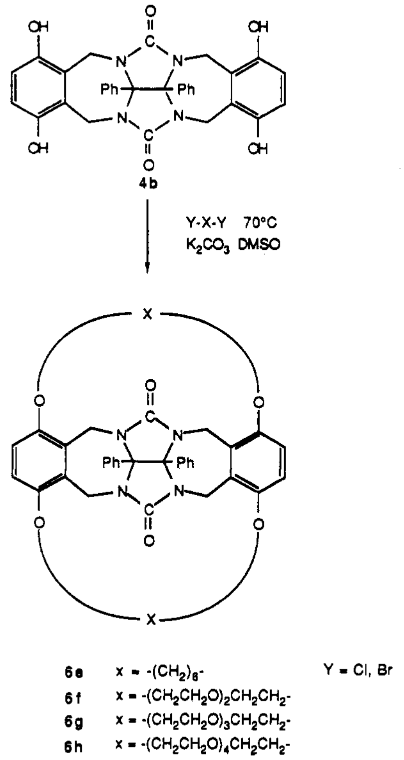
Figure 1. PLUTO drawing of **4b** with the adopted atom labeling. Hydrogen atoms have been omitted for clarity.

imidazolidone rings and has a rigid, bent configuration (vide infra). It was treated with paraformaldehyde and sodium hydroxide in DMSO to yield the tetrakis(hydroxymethyl) derivative **2** in 85% yield.[5] Compound **4a** was synthesized (35% yield) by refluxing **2** in benzene in the presence of an acidic catalyst. Compound **3** appeared to be an intermediate in this reaction. This compound was isolated and characterized.[5] It could also be used as starting material for the synthesis of **4** and **5**. Similarly, treatment of **2** with an excess of hydroquinone or 1,4-dimethoxybenzene in 1,2-dichloroethane gave **4b** and **4c** in 75% and 50% yield, respectively. When polar solvents were used like nitromethane or DMSO instead of 1,2-dichloroethane, no reaction took place. Another reason why we used 1,2-dichloroethane as a solvent is the fact that water, formed during the reaction, could be removed azeotropically by means of a Dean and Stark apparatus or a Soxhlet filled with molecular sieves. The removal of water appeared to be advantageous: without separation of water, it takes more than 3 h before **3** is converted, whereas with water separation, **3** is converted into **4b** within 1 h. The formation of **4** is an electrophilic aromatic substitution. Therefore, the reaction is facilitated when strong electron-donating substituents are present in the aromatic ring.

Molecular models indicate that the *o*-xylylene units of **4** can have anti (*a*) or syn (*s*) orientations with respect to the phenyl substituents, leading to three possible conformers: *aa*, *as*, or *ss*.

For compound **4b**, an X-ray structure determination was performed. The crystal structure consists of two discrete molecules of **4b** and 10 DMSO molecules in a triclinic unit cell. The four hydroxyl groups are involved in hydrogen bonding. Two of the hydrogen bonds are accepted by the carbonylic oxygen atoms of symmetry-related molecules; the other two hydrogen bonds are accepted by DMSO oxygen atoms. Two inversion-related molecules are linked by hydrogen bonds to each other and to translate molecule pairs, thus forming infinite chains running in the **a** direction. The central diphenylglycoluril moiety is significantly twisted. The potential C_{2v} symmetry is lowered to C_2 by this distortion. Similar distortions have been observed in related systems.[5] The distortion is illustrated by the torsion angle C(21)–C(9)–C(11)–C(27), which is 22 (2)°. Positional parameters, bond distances, bond angles, selected torsion angles, and hydrogen bonds are listed in the supplementary material. The molecular structure and the adopted numbering scheme of the complex are shown in Figure 1. This structure determination indicates that **4b** has the *aa* conformation in the solid state.

Scheme II



In order to get information about the relative stabilities of the *aa*, *as*, and *ss* conformations of **4b**, we performed molecular mechanics calculations by using Allinger's MMP2 program.[3b] For parameters not available (e.g., some of the torsion angles within the seven-membered ring), reasonable assumptions were made.[3c] Starting with the coordinates of the X-ray structure, a full optimization of all the atoms of **4b** was allowed. This afforded local minimum conformations for the *aa*, *as*, and *ss* forms with energy differences lying in the range of ≈1 kcal mol^{-1}. It is remarkable that the calculations reveal no preference for one of the conformations of **4b**, whereas the X-ray structure and the ^{1}H NMR experiments (vide infra) do. Recently, Pettersson et al. showed that MM2/MMP2 force-field calculations give an incorrect description of benzene–benzene interactions and overestimate the stability of benzene rings with a parallel "stacked" arrangement.[3d] This overestimation can raise the final energies to about 3 kcal mol^{-1} for MMP2 calculations as compared to ab initio calculations. In the *ss* conformation of **4b**, four benzene rings are more or less stacked. Therefore, our calculated energy values for this conformation can be expected to be too low.[3c,d] The twist in the diphenylglycoluril unit which is demonstrated by the X-ray structure is also found in the MMP2 local miminum conformations. For example, in the calculated *aa* conformation of **4b**, the torsion angles C(21)–C(9)–C(11)–C(27) and N(1)–C(9)–C(11)–N(4) are 18° and 14°, respectively. In the X-ray structure, these torsion angles are 22° and 17°, respectively.

The ^{1}H NMR spectrum of **4d** in CD$_2$Cl$_2$ and in DMSO-d_6 displays one pair of well-defined doublets for the CH$_2$ protons at δ 5.05 and 3.85 ppm (J = 16 Hz). The position and splitting pattern of the doublets did not change over

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[5] (a) Niele, F. G. M.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1988**, *110*, 172–177. (b) Niele, F. G. M. Ph.D. Thesis, 1987, Utrecht, The Netherlands.

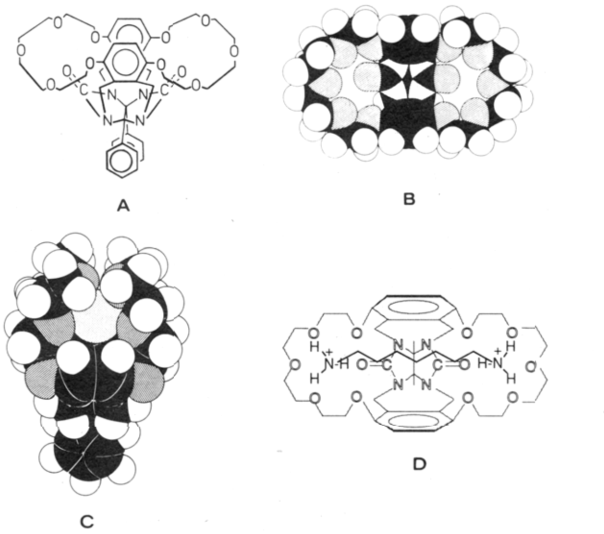

Figure 2. (A) Side-view drawing of basket **6g**. (B) CPK model of **6g**. The receptor sites are formed by the oxygen atoms of the urea units and the oxyethylene bridges. (C) CPK model of the complex between **6g** and an alkali metal ion. The flexible handles of the basket approach each other and encapsulate the guest. (D) Drawing of an aliphatic diammonium dipicrate salt complexed to **6g**. The diammonium guest is wedged in between the *o*-xylylene rings.

the temperature range from −95 to 150 °C. This suggests that either one conformer (*ss* or *aa*) is present or all three conformers interconvert rapidly. To solve this question, we synthesized compound **6e** (Scheme II, vide infra). The $(CH_2)_6$ bridges in **6e** force the molecule to adapt the *aa* conformation. As the ^1H NMR spectra of **6e** and **4c** show almost identical pairs of doublets for the CH_2N protons, we conclude that compound **4c** also adopts the *aa* conformation in solution. Additional evidence for the *aa* conformation of **4** comes from the ^1H NMR spectrum of **5**. The latter compound contains only one *o*-xylylene unit. The two aromatic protons of this unit are located at 7.06 ppm whereas those of **4d** are found at 6.92 ppm. The observed small but significant upfield shift in **4d** could well be due to a shielding effect caused by two xylylene rings being in parallel position as is the case in the *aa* conformer.

Synthesis and Structure of Baskets. Four basket-shaped hosts (**6e,f**) were prepared from building block **4** as shown in Scheme II. To this end, **4b** was treated with 2 equiv of a polyethylene glycol dichloride or aliphatic dibromide in DMSO with K_2CO_3 as base. The compounds were produced in very high yields, up to 75%. The ring-closure reactions were also tried with other base and solvent combinations, i.e., NaH in DMSO and aqueous NaOH in DMSO.[6] However, under these conditions, mainly carbon alkylation of the hydroquinone rings occurred instead of oxygen alkylation. The high yields with K_2CO_3 are obtained without applying high-dilution techniques. We explain this remarkable phenomenon by a template effect of the potassium ion, which assists the oxyethylene chains to adapt the appropriate conformation for ring closure. Remarkably, the two ring-closure reactions in **4b** proceed with different rates. For instance, when **4b** is treated with 1 equiv of pentaethylene glycol dichloride, the product with two closed rings is obtained exclusively. This feature probably also arises from the template effect of the potassium ion.

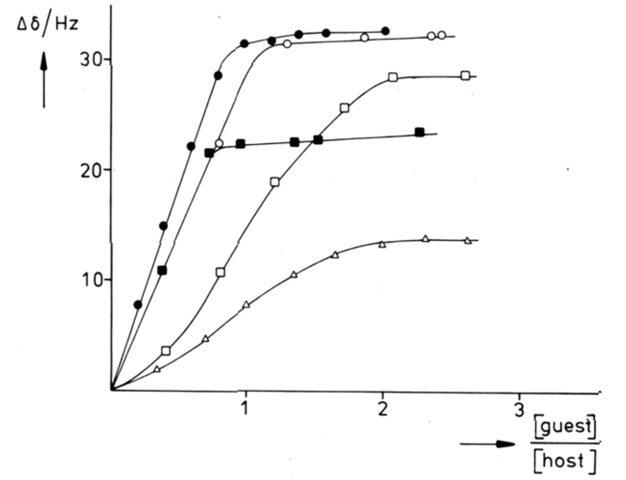

Figure 3. Stoichiometry of complexation: [guest]:[host] ratio vs induced chemical shift (Δδ) of the NC*H*HAr protons for **6g** when complexed to potassium picrate (○), KNCS (●), hexanediyl-1,6-bis(ammonium picrate) (■), and propanediyl-1,3-bis(ammonium picrate) (□) and for **6h** when complexed to potassium or cesium picrate (△).

The basket-shaped hosts were characterized by FAB MS, elemental analyses, and infrared and ^1H NMR spectroscopy. Evidence that ring closure had occurred between different hydroquinone units of **4b** comes from the ^1H NMR spectra of **6e–h**. These spectra show no upfield shifts of the CH_2 protons of the bridges. Such a shift would have been expected if ring closure had occurred within one hydroquinone unit. Compounds **6f–h** are baskets with a rigid framework and two flexible handles. In combination with the oxygen atoms of the urea units, these handles form two crown ether like receptor sites at the far ends of the molecule. A drawing of basket **6g** and a picture of its CPK model are presented in Figure 2, parts A and B.

Complexation of Alkali Metals and Ammonium Salts. Because of their resemblance to crown ethers, it was tempting to investigate the binding properties of baskets **6f–h** for alkali metals and ammonium salts. The stoichiometry of complexation of **6f–h** with potassium and cesium picrates and potassium thiocyanates were examined by ^1H NMR in $CDCl_3$ and DMSO-d_6 at room temperature. The changes in chemical shift of the hydroquinone aromatic protons and the NCH_2Ar protons were particularly useful in this study. The host was dissolved in $CDCl_3$–DMSO-d_6 (3:1 (v/v)), and the guest was added as a solid in small portions with the exception of KNCS, which was added as a solution in $CDCl_3$–DMSO-d_6 (3:1 (v/v)). The changes in chemical shifts after each addition were determined and plotted against the guest:host ratio. As an example, the complexation of **6g** with potassium picrate and KNCS is shown in Figure 3. It is evident that **6g** forms 1:1 complexes with K^+ ions. The same holds for **6f**. Not only potassium picrate but also the other alkali metal and ammonium picrate salts form 1:1 inclusion compounds with **6g**. Compound **6h** behaves differently. Depending on the concentration of the guest, it forms 1:1 as well as 1:2 complexes with K^+ and Cs^+ ions (Figure 3). The association constants (K_a) and free energies of complexation ($-\Delta G°$) of the baskets **6f–h** were determined by the picrate extraction method in $CHCl_3$ saturated with H_2O at 25 °C.[7] Table I lists the $-\Delta G°$ values for Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $CH_3NH_3^+$ and t-$BuNH_3^+$ picrates based on an assumed 1:1 complex formation. For comparison, values for benzo-15-crown-5, benzo-18-crown-6, and benzo-21-crown-7 are also included in this table.[8] In Figure 4, the $-\Delta G°$

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Table I. Free Energies of Binding of Picrate Salt Guests to Hosts at 25 °C in $CHCl_3$ Saturated with H_2O[a]

host	cation of guest	K_a, M^{-1}	$-\Delta G°$, kcal mol^{-1}
6f	Li^+	3.8×10^5	7.6 (7.3)[b]
	Na^+	6.5×10^5	7.9 (8.4)[b]
	K^+	1.6×10^5	7.1 (7.9)[b]
	Rb^+	6.8×10^4	6.6 (7.0)[b]
	Cs^+	6.8×10^4	6.6 (6.2)[b]
	NH_4^+	2.7×10^4	5.8 (6.1)[b]
	$CH_3NH_3^+$	4.2×10^4	6.3
	t-$BuNH_3^+$	$\ll 0.42 \times 10^4$	$\ll 5$
6g	Li^+	7.7×10^4	6.7 (6.4)[c]
	Na^+	3.8×10^6	9.0 (7.9)[c]
	K^+	4.2×10^8	11.5 (10.0)[c]
	Rb^+	2.4×10^7	10.1 (9.2)[c]
	Cs^+	6.3×10^6	9.3 (8.4)[c]
	NH_4^+	9.5×10^6	9.5 (9.0)[c]
	$CH_3NH_3^+$	9.1×10^5	8.1
	t-$BuNH_3^+$	1.3×10^4	5.5
6h	Li^+	7.4×10^4	6.6 (6.0)[d]
	Na^+	5.3×10^5	7.8 (7.7)[d]
	K^+	9.3×10^6	9.5 (8.5)[d]
	Rb^+	3.4×10^6	8.9 (8.9)[d]
	Cs^+	3.6×10^6	8.9 (9.0)[d]
	NH_4^+	2.9×10^6	8.8 (8.4)[d]
	$CH_3NH_3^+$	2.3×10^5	7.3
	t-$BuNH_3^+$	1.1×10^4	5.5

[a] See Experimental Section for methods. [b] Free energies of binding for benzo-15-crown-5. [c] Free energies of binding for benzo-18-crown-6. [d] Free energies of binding for benzo-21-crown-7.

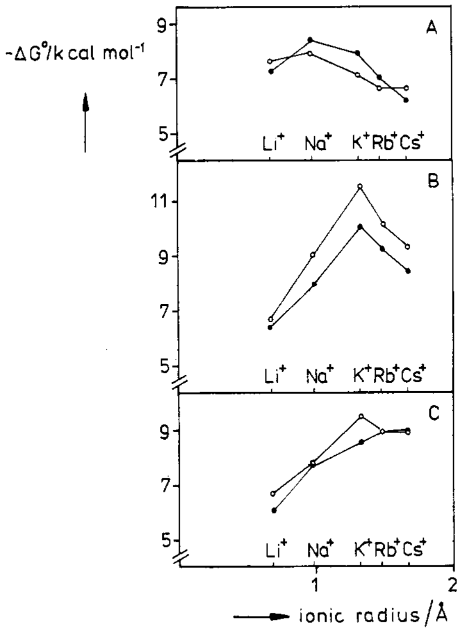

Figure 4. Plots of $-\Delta G°$ value vs the radius of the complexed cation: 6f (○) and benzo-15-crown-5 (●) (A); 6g (○) and benzo-18-crown-6 (●) (B); 6h (○) and benzo-21-crown-7 (●) (C).

values of the alkali metal picrate salt complexes of **6f–h** and the corresponding crown ethers are plotted against the size of the cation.

It is remarkable that host **6g** forms 1:1 complexes with alkali metals, exclusively. One could argue that 1:2 host–guest complexation is disfavored because of electrostatic repulsion. However, the distance between the centers of the two receptor sites at the far ends of basket **6g** (≈9 Å) is too large for an appreciable electrostatic repulsion to occur.[10a,b] The effect is not caused by the anion as substituting NCS^- for picrate did not change the stoichiometry of complexation. What probably happens is the following (see Figure 2, part C). The flexible handles of the basket can be folded to encapsulate the metal ion in a kind of clamshell complex. Apparently, this type of binding is so favorable that **6g** does not form 2:1 complexes with alkali metal ions. According to CPK models, the rings of **6h** are too large to accommodate an alkali metal ion in the way **6g** does. In line with this, **6h** forms weaker complexes with guest molecules (Table I).

Inoue et al. have recently shown that for a series of metal picrate crown ether and cryptand complexes the position of the major absorption band of the picrate ion depends on the geometry of the host–guest complex.[9a] Complexes in which the anion is well-separated from the cation display λ_{max} values in CH_2Cl_2 at ≈375 nm. Complexes in which the cation and anion form a contact ion pair absorb at ≈360 nm. We have measured the λ_{max} values for the complexes between potassium picrate and **6g** and **6h** and found them to be at 375 and 374 nm, respectively.[9b] These values suggest that our complexed salts exist as separated ion pairs. For **6g** this result is not surprising because this host completely encapsulates the K^+ ion. For **6h** we would have expected a contact ion pair since CPK models suggest that the 1:2 host to guest complex has an open structure. Apparently for some steric reason the picrate ion in the **6h** complex is not able to approach the K^+ ion. We hope to clarify this point with the help of an X-ray analysis.

Figure 4 shows that host **6f** and its corresponding crown ether benzo-15-crown-5 have similar binding patterns. The same holds for **6g** and benzo-18-crown-6, and for **6h** and benzo-21-crown-7. In most cases, except for **6f**, the baskets are better binders than the benzo crown ethers. The difference in free energy of complexation of K^+ with **6g** and of K^+ with benzo-18-crown-6 is 1.5 kcal/mol. One of the reasons for the better binding of **6g** could be what Cram calls the "principle of preorganization".[7] The basket contains a higher degree of conformational immobility than the benzo crown ether. Another reason could be the presence of the C=O groups in the rings of the basket. Carbonyl oxygen atoms are better binders than ether oxygens. All three baskets bind t-$BuNH_3^+$ very weakly ($-\Delta G° \approx 5$ kcal/mol). Steric repulsion by the t-Bu group is probably the reason of this feature. CPK models indicate that it is very difficult to position this group at the inside of the host. The low value of $-\Delta G°$ suggests that binding of t-$BuNH_3^+$ does not take place at the outside of the host.

Complexation of Aliphatic and Aromatic Diammonium Salts. Because of the presence of two receptor sites in **6f–h**, it was of interest to investigate the complexation behavior of these hosts with protonated diamines. ^1H chemical shift experiments were carried out as described above for **6g** and **6h** using aliphatic diammonium salts of various chain lengths, $^+H_3N(CH_2)_nNH_3^+$, $n = 3$–9, as guests. These experiments revealed that **6g** and **6h** form 1:1 complexes with aliphatic diammonium salts for which $n \geq 5$, and 1:2 host–guest complexes when $n = 3$ (e.g., see Figure 3). With butanediyl-1,4-bis(ammonium picrate), a ^1H NMR shift experi-

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(9) (a) Inoue, Y.; Fujiwara, C.; Wada, K.; Tai, A.; Hakushi, T. *J. Chem. Soc., Chem. Commun.* **1987**, 393–394. (b) Absorption maxima were measured of potassium picrate extracted into dichloromethane with hosts **6g** and **6h**. The extractions were conducted at 25 °C with a dichloromethane solution (10 mL) of the host (0.3 mM) and an aqueous solution (10 mL) of potassium picrate (3.0 mM).

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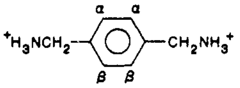
Table II. ^{1}H NMR Chemical Shifts of Guests $^+H_3N(CH_2)_nNH_3^+$, n = 3–9, and $^+H_3NCH_2C_6H_4CH_2NH_3^+$ Bound in a 1:1 Ratio to 6g and 6h[a]

		guest chemical shifts, ppm				
host	guest	α	β	γ	δ	ϵ
6g	$^+H_3N(CH_2)_nNH_3^+$					
	$n = 3$	2.55	1.77			
	$n = 4$	2.13	0.14			
	$n = 5$	2.27	0.19	−0.18		
	$n = 6$	2.47	0.45	0.20		
	$n = 7$	2.59	0.93	0.37	0.61	
	$n = 8$	2.23[b]	1.08[b]	1.08[b]	0.75[b]	
	$n = 9$	2.30[b]	0.76[b]	1.07[b]	1.07[b]	1.07[b]
		7.05	6.25			
6h	$^+H_3N(CH_2)_nNH_3^+$					
	$n = 3$	2.80	1.95			
	$n = 4$	2.43	1.10			
	$n = 5$	2.33	0.69	0.34		
	$n = 6$	2.59	0.52	0.21		
	$n = 7$	2.80	1.03	−0.13	0.14	
	$n = 8$	2.79[b]	1.15[b]	0.64[b]	0.02[b]	
	$n = 9$	2.79[b]	1.10[b]	0.68[b]	0.09[b]	0.68[b]

[a] ^{1}H NMR spectra were recorded in $CDCl_3$–DMSO-d_6 (6:1 (v/v)) at 25°C. [b] Tentative assignment.

ment could not be done because this guest was only sparingly soluble in the solvent mixture ($CDCl_3$–DMSO-d_6 (6:1 (v/v)). However, from the shift values of the methylene protons of the complexed guest (vide infra, Table II) we may conclude that butanediyl-1,4-bis(ammonium picrate) forms a 1:1 complex with **6g** and a 1:2 complex with **6h**. The stoichiometry of complexation could also be derived from a plot of the peak width at half-height ($\Delta\nu_{1/2}$) of the guest protons against the guest:host ratio. This procedure gave the same results as the chemical shift procedure described above.

In the complexes, the diammonium guests are wedged in between the *o*-xylylene rings (Figure 2, part D). This can be concluded from the observed upfield shifts (up to 1.5 ppm) of the guest CH_2 or ArH protons in the ^{1}H NMR spectra. In Figure 5, the ^{1}H NMR spectrum of the free hexanediyl-1,6-bis(ammonium picrate) salt and the spectrum of the salt complexed to **6g** are shown. All guest methylene protons have shifted to higher field, the largest shift values being observed for the γ-methylene protons which lay in the middle of the shielding zone of the *o*-xylylene rings. For a series of 1:1 complexes between diammonium salts $^+H_3N(CH_2)_nNH_3^+$, n = 3–9, or $^+H_3NCH_2C_6H_4CH_2NH_3^+$ and hosts **6g** and **6h**, the observed shift values are compiled in Table II.

At 25 °C, the ^{1}H NMR spectrum of a 1:2 mixture of **6g** and $^+H_3N(CH_2)_6NH_3^+$ shows two sets of signals for the guest methylene protons (Figure 5). One set can be assigned to the methylene groups of the free guest whereas the other set of signals, located near the TMS signal, can be assigned to the methylene groups of the complexed guest. This observation indicates that at 25 °C the rate of exchange between free and complexed guest is slow on the NMR time scale. The coalescence point was found to be above the boiling point of the solvent mixture (≈60 °C). The activation free energy of decomplexation was estimated to be $\Delta G^\ddagger > 16.3$ kcal mol^{-1}. The ^{1}H NMR spectra of a 1:2 mixture of **6g** and $^+H_3N(CH_2)_7NH_3^+$ and a 1:2 mixture of **6g** and $^+H_3N(CH_2)_5NH_3^+$ show at 25 °C broad signals for the protons of the free and complexed guest, indicating that for these host–guest complexes the coalescence point is not far from room temperature. At 60 °C, the former complex shows one set of sharp signals, which splits into two sets at −45 °C. The ^{1}H NMR spectra of a 1:2 mixture of **6g** and the other measured aliphatic diammonium salts ($^+H_3N(CH_2)_nNH_3^+$, n = 3, 4, 8, 9) show only one set of average signals for the guest protons, indicating that for these complexes exchange is rapid on the NMR time scale. The same holds for the 1:2 mixtures of **6h** and $^+H_3N(CH_2)_nNH_3^+$, n = 5–9.

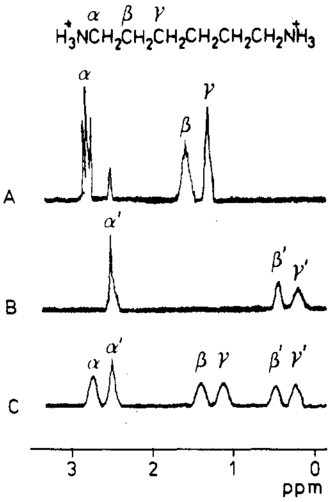


Figure 5. ^{1}H NMR spectrum ($CDCl_3$–DMSO-d_6, 450:75 v/v) of free hexanediyl-1,6-bis(ammonium picrate) salt (A), hexanediyl-1,6-bis(ammonium picrate) salt complexed to **6g** in a 1:1 ratio (B), and hexanediyl-1,6-bis(ammonium picrate) salt complexed to **6g** in a 2:1 ratio (C); α', β', and γ' are protons of the complexed salt; α, β, and γ are protons of the free salt.

The association constants and the free energies of complexation (−$\Delta G°$) of diammonium guests to **6g** and **6h** were determined by the picrate extraction method in $CHCl_3$ saturated with H_2O at 25 °C.[13] Table III lists K_a and −$\Delta G°$ values for $^+H_3N(CH_2)_nNH_3^+$ dipicrate salts, *m*- and *p*-xylylenediammonium picrate salts, and *o*- and *p*-phenylenediammonium picrate salts, assuming 1:1 complex

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(11) Behr, J. P.; Lehn, J. M.; Vierling, P. *J. Chem. Soc., Chem. Commun.* **1976**, 621.

(12) (a) Koenig, K. E.; Lein, G. M.; Stuckler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3553–3566. (b) Moore, S. S.; Tarnowski, T. L.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6398–6405.

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Table III. Free Energies of Binding of Diammonium Dipicrate Salts to Hosts at 25 °C in $CHCl_3$ Saturated with H_2O^a

host	cation of guest	$K_a \times 10^{-9}$, M^{-1}	$-\Delta G°$,[b] kcal mol^{-1}
6g	$^+H_3N(CH_2)_nNH_3^+$		
	$n = 3$	1.0×10^{-2}	≈9.5
	$n = 4$	0.19	11.3
	$n = 5$	1.8	12.6
	$n = 6$	6.1	13.3
	$n = 7$	6.0	13.3
	$n = 8$	6.1	13.3
	$n = 9$	7.7	13.5
	p-xylylenediammonium	2.4	12.8
	m-xylylenediammonium	2.1	12.7
	p-phenylenediammonium	0.23	11.4
	o-phenylenediammonium	1.0	12.3
6h	$^+H_3N(CH_2)_nNH_3^+$		
	$n = 3$	0.2×10^{-2}	<9
	$n = 4$	1.5×10^{-2}	≈9.8
	$n = 5$	3.0×10^{-2}	10.2
	$n = 6$	0.27	11.5
	$n = 7$	1.5	12.5
	$n = 8$	11.2	13.7
	$n = 9$	11.2	13.7
	p-xylylenediammonium	0.15	11.2
	m-xylylenediammonium	0.11	11.0
	p-phenylenediammonium	0.06	10.6
	o-phenylenediammonium	0.58	12.0

[a] See Experimental Section for methods. [b] The values have been calculated assuming a distribution constant K_d of 1 M^{-2}; they are lower limits (see Experimental Section).

formation with hosts **6g** and **6h**. The K_a and $-\Delta G°$ values in Table III are lower limits, because the distribution constant of the uncomplexed guest between $CHCl_3$ and H_2O could not be measured accurately.[13] Compound **6f** forms host–guest complexes with diammonium salts that have $-\Delta G°$ values smaller than 9 kcal/mol. Under our experimental conditions, we could not measure these values accurately.

Because of the flexibility of the handles, the host can adapt itself to the guest. The same holds vice versa for the guest molecules which have a flexible $(CH_2)_n$ chain. CPK models suggest that different types of binding occur between the various combinations of host **6g** and guests $^+H_3N(CH_2)_nNH_3^+$. These types are shown in Figure 6. This view is supported by the following ^1H NMR observations.

The AA′BB′ patterns of the protons of the oxyethylene bridges in **6g** change when in the guest $^+H_3N(CH_2)_nNH_3^+$ n increases from 3 to 9; the bridges are likely to move apart. The angle between them changes from ≈0° for $n = 4$ to ≈180° for $n = 9$. For $n > 6$, the carbon chain of the guest must be bent because the ^1H NMR spectra (Table II) indicate that the guest CH_2 protons are only slightly upfield shifted as compared to those of guests with $n \leq 6$. The complex with $n = 9$ has its most upfield shifted methylene protons only at δ 0.76 ppm, whereas the complex with $n = 5$ has these protons at δ −0.15 ppm.

For complexes of **6h** with $^+H_3N(CH_2)_nNH_3^+$, n = 3–9, the situation is similar to that of **6g**, the difference being that in **6h** the distance between the centers of the receptor sites is larger (12 Å for **6h**, 9 Å for **6g**). Therefore, the carbon chain of the guest is still stretched for $n \leq 8$, as is obvious from CPK models. This is the reason why we find a high upfield shift for the methylene protons of guests with $n = 8$ or 9 bound to **6h** (Table II). It is striking that for **6g** and **6h** the binding free energies reach an upper value for guests with $n = 6$ and $n = 8$, respectively, and stay at that value for longer chains. These upper values are reached at maximum chain lengths of the guest for which it is possible to be completely stretched out in the host.

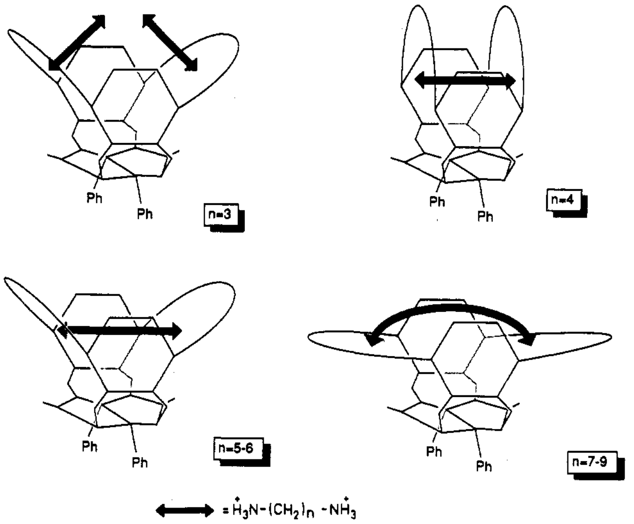

Figure 6. Schematic representation of complex formation between picrate salts of $^+H_3N(CH_2)_nNH_3^+$, n = 3–9, and **6g**; the guest molecule is represented by an arrow.

It can be expected that guests with odd and even numbers of CH_2 functions bind differently. In the former case, the NH_3^+ groups converge toward the binding sites of the host, whereas in the latter case, they diverge. This effect will be most pronounced for short-chain guests. This feature could be the reason why the $-\Delta G°$ value of the complex between **6g** and $^+H_3N(CH_2)_4NH_3^+$, is lower than the $-\Delta G°$ value of the complex between **6g** and $^+H_3N(CH_2)_5NH_3^+$.

Besides the aliphatic diammonium salts, aromatic diammonium salts also form complexes with hosts **6g** and **6h** (Tables II and III). The ^1H NMR spectrum of the 1:1 complex between **6g** and *p*-xylylenebis(ammonium picrate) suggests that the guest is sandwiched between the *o*-xylylene side walls of the host. Two aromatic protons of the guest show an upfield shift of 1.14 ppm as compared to the free guest. These are the protons that lie in the shielding zone of the *o*-xylylene rings of the host. The two other aromatic protons of the guest display an upfield shift of 0.34 ppm only. They apparently are situated above the cage. The *o*-xylylene protons of the host lay in the shielding zone of the aromatic ring of the guest and are shifted 0.42 ppm upfield.

The values of $-\Delta G°$ for the diammonium guests (Table III) are minimum values and are very high. As far as we know, $-\Delta G°$ values of ≥13.5 kcal mol^{-1} for protonated amines have not been measured before.[2o,11] The combination of two receptor sites and the presence of a cavity make the basket-shaped hosts described in this paper ideal binders for various aliphatic and aromatic diammonium salts.

Experimental Section

General. Unless otherwise indicated, commercial materials were used as received. DMSO, methanol, benzene, and 1,2-dichloroethane were dried over 3-Å sieves prior to use. Chloroform was distilled from $CaCl_2$ prior to use. FAB mass spectra were recorded on a VG ZAB 2f spectrometer. IR spectra were taken on a Perkin-Elmer 283 spectrometer. UV/vis measurements were performed on Perkin-Elmer 555 and 552 spectrophotometers. ^1H NMR spectra were recorded on Varian EM 390, Varian EM 360, Bruker AW-80, and Bruker WP 200 instruments. Chemical shifts are reported in parts per million downfield from internal $(CH_3)_4Si$. Coupling constants are reported in hertz. Elemental analyses were carried out by the Elemental Analytical Section of the Institute for Applied Chemistry TNO, Zeist, The Netherlands. Melting points were determined on a Mettler FP5/FP51 photoelectric melting point apparatus. It appeared that all new compounds decomposed above 250 °C. Silica gel 60 (Merck, particle size 0.040–0.063 mm, 230–400 mesh, ASTM), neutral alumina (Janssen, active, 50–200 μm, 70–290 mesh, ASTM), and Sephadex LH-20 (Pharmacia) were used in column chromatography. Thin-layer chromatography was performed with plates of silica gel 60F254 (Merck) and alumina 60F254 (Merck, neutral, type E).

Tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5-(1*H*,3*H*)-dione (1). This compound was synthesized according to a literature procedure.[4]

1,3,4,6-Tetrakis(hydroxymethyl)tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (2). This compound was synthesized according to a procedure developed in our laboratory.[5]

1,6:3,4-Bis(2-oxapropylene)tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (3). This compound was synthesized according to a procedure developed in our laboratory.[5]

1,6:3,4-Bis(1,2-xylylene)tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (4a). A mixture of 1 g (0.00242 mol) of **2** and 2.3 g (0.0121 mol) of *p*-toluenesulfonic acid monohydrate in 70 mL of benzene was refluxed while being stirred under N_2 for 4 days. Water was removed either by a Dean–Stark apparatus or by a Soxhlet apparatus filled with molecular sieves (4 Å). The reaction mixture was added to 70 mL of basic water (pH = 12). The organic layer was separated and dried ($MgSO_4$), and the solvent was evaporated. The remaining light brown solid was chromatographed over Sephadex LH-20 (eluent $CHCl_3$) to yield 0.42 g (35%) of **4a** as a white solid: IR (KBr) 3420, 3040, 3010, 2960, 2905, 1700, 1465, 1425 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.16 (m, 18 H, Ar H), 4.77 and 4.15 (2 d, 8 H, CH_2, *J* = 16 Hz); FAB MS (triethyl citrate) *m/e* 499 (M + H)$^+$. Anal. Calcd for $C_{32}H_{26}N_4O_2$: C, 77.04; H, 5.26; N, 11.24. Found: C, 77.20; H, 5.27; N, 11.21.

1,6:3,4-Bis(3,6-dihydroxy-1,2-xylylene)tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (4b). A mixture of 15.2 g (0.037 mol) of **2** and 28.0 g (0.15 mol) of *p*-toluenesulfonic acid monohydrate was suspended in 250 mL of 1,2-dichloroethane. A Soxhlet apparatus filled with molecular sieves (4 Å) was used for removal of water. The reaction mixture was refluxed while being stirred under N_2 for 10 min. To the resulting clear solution was added 16.0 g (0.15 mol) of hydroquinone and refluxing was continued. After 1 min, a white precipitate was formed. According to TLC, the reaction was completed with 1 h. After cooling, 60 mL of methanol was added. The precipitate was removed by filtration, and the residue was dissolved in 200 mL of DMSO at 90 °C and stirred at this temperature for 0.5 h under N_2. The still hot solution was added dropwise to 500 mL of methanol with stirring. The resulting solid was collected by filtration, washed with methanol and ether, and dried under high vacuum: yield 15.5 g (75%) of pure **4b** as a white solid; IR (KBr) 3350, 2900, 1720, 1690, 1475, 1450 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 8.67 (s, 4 H, OH), 7.10 (s, 10 H, Ar H), 6.47 (s, 4 H, Ar H), 5.37 and 3.57 (2 d, 8 H, CH_2, *J* = 16 Hz); FAB MS (glycerol, thioglycerol, acetic acid) *m/e* 563 (M + H)$^+$. Anal. Calcd for $C_{32}H_{26}N_4O_6$: C, 68.32; H, 4.66; N, 9.96; O, 17.06. Found: C, 68.03; H, 5.07; N, 9.92; O, 16.99.

1,6:3,4-Bis(3,6-dimethoxy-1,2-xylylene)tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (4c). This compound was prepared from **2** and 1,4-dimethoxybenzene as described for **4b**. The reaction mixture was refluxed for 3 days. On cooling, the crude product precipitated. This precipitate was collected by filtration, washed with methanol, and crystallized from $CHCl_3$ to give 50% of pure **4c**: IR (KBr) 3420, 2995, 2930, 2835, 1710, 1485, 1460, 1070, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.06 (s, 10 H, Ar H), 6.45 (s, 4 H, Ar H), 5.57 and 3.72 (2 d, 8 H, CH_2, *J* = 16 Hz), 3.68 (s, 12 H, OCH_3); FAB MS (glycerol) *m/e* 619 (M + H)$^+$. Anal. Calcd for $C_{36}H_{34}N_4O_6$: C, 69.89; H, 5.54; N, 9.06; O, 15.52. Found: C, 69.95; H, 5.52; N, 9.05; O, 15.48.

1,6:3,4-Bis(3,6-diacetoxy-1,2-xylylene)tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (4d). A mixture of 0.56 g (1 mmol) of **4b**, 5 mL of acetic acid anhydride, and 0.5 mL of pyridine was stirred at 90 °C for 1.5 h. The solvent was evaporated under reduced pressure. Traces of acetic acid and acetic acid anhydride were removed by codistillation with a few milliliters of toluene. Finally, the white solid was dried under high vacuum to yield 0.72 g (100%) of **4d**: IR (KBr) 3430, 3030, 2930, 1760, 1715, 1460, 1210, 1180, 1020 cm^{-1}; ^{1}H NMR ($CD_{C}l_2$) δ 7.09 (s, 10 H, Ar H), 6.92 (s, 4 H, Ar H), 5.06 and 3.83 (2 d, 8 H, NCH_2Ar, *J* = 16 Hz), 2.34 (s, 12 H, $C(O)CH_3$); FAB MS (triethyl citrate) *m/e* 731 (M + H)$^+$, 689 (M – H_2C_2O) + H)$^+$, 647 (M – $(H_2C_2O)_2$ + H)$^+$, 605 (M – $(H_2C_2O)_3$ + H)$^+$, 563 (M – $(H_2C_2O)_4$ + H)$^+$. Anal. Calcd for $C_{40}H_{34}N_4O_{10}$: C, 65.75; H, 4.69; N, 7.67; O, 21.90. Found: C, 65.80; H, 4.72; N, 7.65; O, 21.84.

1,6-(2-Oxapropylene)-3,4-(3,6-diacetoxy-1,2-xylylene)-tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5-(1*H*,3*H*)-dione (5). A mixture of 4.14 g (10 mmol) of **2**, 0.22 g (2 mmol) of hydroquinone, and 7.6 g (40 mmol) of *p*-toluenesulfonic acid monohydrate was refluxed for 1 h in 100 mL of 1,2-dichloroethane. The solvent was evaporated under reduced pressure, and the residue was washed two times with 100 mL of an aqueous sodium hydrogen carbonate solution. The remaining solid was acetylated (see **4d**) and purified by chromatography over Sephadex LH-20 (eluent $CHCl_3$–CH_3OH, 5:1 v/v): yield 65 mg (6%) of pure **5** as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.13 and 7.10 (2 s, 10 H, Ar H), 7.06 (s, 2 H, Ar H), 5.16 and 3.95 (2 d, 4 H, NCH_2Ar, *J* = 16 Hz), 5.48 and 4.37 (2 d, 4 H, NCH_2O, *J* = 11 Hz), 2.41 (s, 6 H, CH_3CO); FAB MS (triethyl citrate) *m/e* 555 (M + H)$^+$. Anal. Calcd for $C_{30}H_{26}N_4O_7$: C, 64.98; H, 4.73; N, 10.10; O, 20.19. Found: C, 65.05; H, 4.70; N, 10.13; O, 20.12.

1,6:3,4-Bis{[3,3':6,6'-bis(1,8-dioxaoctamethylene)]-1,2-xylylene}tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (6e). A mixture of 2.0 g (3.55 mmol) of **4b** and 1.82 g (7.47 mmol) of 1,6-dibromohexane in 100 mL of DMSO was heated at 60 °C under N_2 while being stirred until a clear solution was obtained. Potassium carbonate (6.9 g, 49.93 mmol) was suspended in this solution. The color of the reaction mixture changed immediately from colorless to yellow and after 1 min to dark green. The reaction mixture was kept for 2 days at 70 °C. After this period, the mixture was poured into an equal volume of water, upon which a fine solid precipitated. This precipitate was collected by filtration over infusorial earth, dissolved in $CHCl_3$, washed six times with water, and evaporated under reduced pressure until a brown solid remained. This solid was purified by column chromatography (silica, eluent $CHCl_3$–acetone, 10:1 v/v): yield 0.88 g (34%) of pure **6e** as a white solid; IR (KBr) 3440, 2940, 2860, 1740, 1720, 1465, 1430, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.06 (s, 10 H, Ar H), 6.70 (s, 4 H, Ar H), 5.61 and 3.68 (2 d, 8 H, NCH_2Ar, *J* = 16 Hz), 3.98 (br, 8 H, OCH_3), 2.35–0.90 (m, 17 H, $(CH_2)_4$); FAB MS (triethyl citrate) *m/e* 727 (M + H)$^+$. Anal. Calcd for $C_{44}H_{46}N_4O_6$: C, 72.71; H, 6.38; N, 7.71; O, 13.20. Found: C, 73.06; H, 6.24; N, 7.63; O, 13.07.

1,6:3,4-Bis{[3,3':6,6'-bis(1,4,7,10-tetraoxadecamethylene)]-1,2-xylylene}tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (6f). This compound was synthesized from **4b** (2.0 g, 3.55 mmol) and triethylene glycol dichloride (1.40 g, 7.5 mmol) as described for **6e**. The brown solid was purified by chromatography, first over a shirt alumina column (eluent $CHCl_3$–CH_3OH, 10:1 v/v) and afterward over Sephadex LH-20 (eluent $CHCl_3$–CH_3OH, 5:1 v/v): yield 0.45 g (16%) of pure **6f** as a white solid; IR (KBr) 3420, 2910, 2860, 1710, 1455, 1135, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.10 (s, 10 H, Ar H), 6.60 (s, 4 H, Ar H), 5.55 (d, 4 H, NC*H*HAr, *J* = 16 Hz), 4.30–3.40 (m, 28 H, NCH*H*Ar and OCH_2CH_2); FAB MS (triethyl citrate, acetic acid) *m/e* 791 (M + H)$^+$. Anal. Calcd for $C_{44}H_{46}N_4O_{10}$: C, 66.82; H, 5.86; N, 7.08; O, 20.23. Found: C, 66.90; H, 5.84; N, 7.06; O, 20.20.

1,6:3,4-Bis{[3,3':6,6'-bis(1,4,7,10,13-pentaoxatridecamethylene)]-1,2-xylylene}tetrahydro-3a,6a-diphenylimidazo-[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (6g). This compound was synthesized from **4b** (2.0 g, 3.55 mmol) and tetraethylene glycol dichloride (1.72 g, 7.5 mmol) as described for **6e**. The product was purified by chromatography over an alumina column (eluent, $CHCl_3$–CH_3OH, 10:1 v/v): yield 2.34 g (75%) of pure **6g** as a light yellow solid; IR (KBr) 3420, 2910, 2860, 1715, 1475, 1450, 1130, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.05 (s, 10 H, Ar H), 6.65 (s, 4 H, Ar H), 5.65 (d, 4 H, NC*H*HAr, *J* = 16 Hz), 3.50–4.35 (m, 36 H, NCH*H*Ar, and OCH_2CH_2); FAB MS (triethyl citrate) *m/e* 879 (M + H)$^+$. Anal. Calcd for $C_{48}H_{54}N_4O_{12}$: C, 65.59; H, 6.19; N, 6.37; O, 21.84. Found: C, 65.37; H, 6.08; N, 6.35; O, 22.20.

1,6:3,4-Bis{[3,3′:6,6′-bis(1,4,7,10,13,16-hexaoxahexadecamethylene)]-1,2-xylylene}tetrahydro-3a,6a-diphenylimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (6h). This compound was synthesized from **4b** (2.0 g, 3.55 mmol) and pentaethylene glycol dichloride (2.06 g, 7.47 mmol) as described for **6e**: yield 1.89 g (55%) of pure **6h** as a light yellow solid; IR (KBr) 3420, 2865, 1710, 1455, 1135, 1070 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.05 (s, 10 H, Ar H), 6.70 (s, 4 H, Ar H), 5.55 (d, 4 H, NCH*H*Ar, J = 16 Hz), 4.20–3.50 (m, 44 H, NC*H*HAr, CH$_2$CH$_2$O); FAB MS (triethyl citrate) *m/e* 967 (M + H)$^+$. Anal. Calcd for $C_{52}H_{62}N_4O_{14}$: C, 64.58; H, 6.46; N, 5.79; O, 23.16. Found: C, 64.68; H, 6.48; N, 5.80; O, 23.04.

Determination of K_a and $-\Delta G°$ Values. The picrate salt extraction technique from H$_2$O into CHCl$_3$ described by Cram et al.[12] was applied to determine K_a and $-\Delta G°$ values. All these values were calculated and recorded as 1:1 complexes (Tables I and III). The extraction experiments involving diammonium dipicrate salts differed slightly from Cram's technique. Instead of 0.015 M host and guest solutions, 0.001 M solutions were used, and instead of 10 μL, 75 μL of the organic and aqueous phase were diluted to 5 mL with CH$_3$CN. The equations used to calculate the K_a values in Table III were reported previously by us.[13]

Structure Determination and Refinement of 4b. Crystals were obtained by slow recrystallization from dimethyl sulfoxide (DMSO). A colorless plate-shaped crystal suitable for an X-ray study was introduced in a Lindemann glass capillary to avoid loss of DMSO and transferred to an Enraf-Nonius CAD-4F diffractometer for data collection. Crystals were found to be poorly reflecting at diffraction angles higher than 40° (Cu Kα); therefore only data of a rather limited quality could be obtained. All reflections were measured at Ψ values calculated with the A-vector method[14] in order to minimize the observed splitting of the reflection profiles. Crystal data and details of the structure determination are given in the supplementary material. Unit cell parameters were determined from a least-squares treatment of the setting angles of 17 reflections in the range $9.7° < \theta < 12.4°$. The triclinic unit cell was checked for the presence of higher lattice symmetry.[15] Data were collected for one hemisphere $[0 \leq h \leq 9; -15 \leq k \leq 15; -16 \leq l \leq 15)$ and corrected for Lp and for a linear decay of 6.1% during the 91 h of X-ray exposure time. Standard deviations based on counting statistics were increased according to an analysis of the excess variance of the three reference reflections: $\sigma^2(l) = \sigma_{cs}^2 (l) + (0.027l)^2$.[16] Space group $P\bar{1}$ was discriminated from $P1$ during the structure determination process.

The structure was solved by direct methods (SHELXS86[17]) and subsequent difference Fourier maps. Refinement on F was carried out by full-matrix least-squares techniques using SHELX76[18] on a MicroVAX-II. Sulfur and oxygen atoms were refined with anisotropic thermal parameters. In view of the limited number of observed reflections, carbon and nitrogen atoms were refined with isotropic thermal parameters. Carbon-bonded hydrogen atoms were introduced on calculated positions [d(C–H) = 0.98 Å] and included in the refinement riding on their carrier atom with separate common isotropic thermal parameters for the main molecule and DMSO. The four hydroxylic H atoms were refined with Waser-type constraints and a separate overall isotropic thermal parameter. Weights were introduced in the final refinement cycles, and convergence was reached at R = 0.138. A final difference Fourier synthesis revealed residual densities between 1.03 and −0.92 e/Å^3 near S atoms. Neutral atom scattering factors were taken from ref 19 and corrected for anomalous dispersion.[20] Data collection was done with a modified CAD-4F software package.[21] The EUCLID package[22] was used for geometrical calculations and illustrations.

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Supplementary Material Available: Numerical details of the structure determination, anisotropic thermal parameters, all positional parameters, and tables of bond distances, bond angles, selected torsion angles, and hydrogen bonds (9 pages); a listing of observed and calculated structure factor amplitudes (22 pages). Ordering information is given on any current masthead page.

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