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-imidazolidine rings, which are flanked by two o-xylene units. Basket-shaped hosts are constructed by attaching oxyethylene bridges to the xylene rings of 4. The new hosts are strong binders of aliphatic and aromatic diaminonium 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 clampshell-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 Ghidini,2h Sauvage,2i,j Schmidchen,2k Sutherland,2k Vögtle,2l,m Weber,2n and Whitlock,2o Many of these hosts are only accessible in low yield via long synthetic routes. In this paper we describe such a building block, viz. compound 4. It contains two fused 2-imidazolidine rings, which are flanked by two o-xylene 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

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(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 Alinger’s MM2 program predicted that the ss form of 4b is more stable than the ss form by $\Delta$ kcal mol$^{-1}$; see ref. 3a. More extended calculations are in progress and will be published in due time. (d) Petterson, l.; Liljefors, T. J. Comput. Chem. 1987, 8, 1139-1145. (4) Butler, A. R.; Leitch, E. J. Chem. Soc., Perkin Trans. 2 1980, 103-109.
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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. 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. 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-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 $C_2$ symmetry is lowered to $C_1$ by this distortion. Similar distortions have been observed in related systems. The distortion is illustrated by the torsion angle C(21)-C(9)-C(11)-C(27), which is 22°. 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.

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. For parameters not available (e.g., some of the torsion angles within the seven-membered ring), reasonable assumptions were made. 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 $\pm 1$ 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. 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. The twist in the diphenylglycoluril unit which is demonstrated by the X-ray structure is also found in the MMP2 local minimum 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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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$_2$)$_2$ bridges in 6e force the molecule to adapt the aa conformation. As the $^1$H NMR spectra of 6e and 4c show almost identical pairs of doublets for the CH$_2$N protons, we conclude that compound 4c also adopts the aa conformation in solution. Additional evidence for the aa conformation of 4 comes from the $^1$H 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$_2$CO$_3$ 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.$^8$ However, under these conditions, mainly carbon alkylation of the hydroquinone rings occurred instead of oxygen alkylation. The high yields with K$_2$CO$_3$ 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.

The basket-shaped hosts were characterized by FAB MS, elemental analyses, and infrared and $^1$H NMR spectroscopy. Evidence that ring closure had occurred between different hydroquinone units of 4b comes from the $^1$H 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 $^1$H NMR in CDCl$_3$ and DMSO-$d_6$ at room temperature. The changes in chemical shift of the hydroquinone aromatic protons and the NCH$_2$Ar 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 ($-\Delta G^o$) of the baskets 6f-h were determined by the pícrate extraction method in CHC$_3$ saturated with H$_2$O at 25 °C.$^7$ Table I lists the $-\Delta G^o$ values for Li$^+$, Na$^+$, K$^+$, Rb$^+$, Cs$^+$, NH$_4^+$, CH$_3$NH$_2^+$ and t- BuNH$_2^+$ 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 $-\Delta G^o$ values for Li$^+$, Na$^+$, K$^+$, Rb$^+$, Cs$^+$, NH$_4^+$, CH$_3$NH$_2^+$, and t-BuNH$_2^+$ picrates are shown. The data in this table are consistent with the trends observed in Figures 3 and 4.

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Table 1. Free Energies of Binding of Picrate Salt Guests to Hosts at 25 °C in CHCl₃ Saturated with H₂O

<table>
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<th>Host</th>
<th>Cation of guest</th>
<th>Kₚ M⁻¹</th>
<th>⁻ΔG°, kcal mol⁻¹</th>
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<tr>
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<td>Li⁺</td>
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<td></td>
<td>Na⁺</td>
<td>6.5 x 10⁴</td>
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<tr>
<td></td>
<td>K⁺</td>
<td>1.6 x 10⁴</td>
<td>7.3 (7.9)b</td>
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<td></td>
<td>Rb⁺</td>
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<tr>
<td></td>
<td>Cs⁺</td>
<td>6.8 x 10³</td>
<td>6.6 (6.2)b</td>
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<tr>
<td></td>
<td>NH₄⁺</td>
<td>2.7 x 10³</td>
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<td>CH₂NH₂⁺</td>
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<td>6.3</td>
</tr>
<tr>
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<td>Li⁺</td>
<td>7.7 x 10⁵</td>
<td>6.7 (6.4)c</td>
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<tr>
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<td></td>
<td>t-BuNH₂⁺</td>
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</tr>
<tr>
<td>6h</td>
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<td>K⁺</td>
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<td>t-BuNH₂⁺</td>
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Figure 4. Plots of ⁻ΔG° value vs the radius of the complexed cation: 6f (O) and benzo-15-crown-5 (●) (A); 6g (O) and benzo-18-crown-6 (●) (B); 6h (O) and benzo-21-crown-7 (●) (C).

values of the alkali metal picrate salt complexes of 6h 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 1).

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. Complexes in which the anion is well-separated from the cation display λmax values in CH₃Cl at ≈375 nm. Complexes in which the cation and anion form a contact ion pair absorb at ≈360 nm. We have measured the λmax values for the complexes between potassium picrate and 6g and 6h and found them to be at 375 and 374 nm, respectively. 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". 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-BuNH₂⁺ very weakly (⁻ΔG° ≈ 5 kcal/mol). Steric repulsion by the t-Bu group is probably the reason for this feature. CPK models indicate that it is very difficult to position this group at the inside of the host. The low value of ⁻ΔG° suggests that binding of t-BuNH₂⁺ 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, [H₂N(CH₃)₂]²⁺, n = 3–9, as guests. These experiments revealed that 6g and 6h form 1:1 complexes with aliphatic diamonium salts for which n ≥ 5, and 1:2 host–guest complexes when n = 3 (e.g., see Figure 3). With butane-diyld-1,4-bis(ammonium picrate), a ¹H NMR shift experi-

Table II. $^1$H NMR Chemical Shifts of Guests $^1$H$_2$N(CH$_2$)$_n$NH$_4^+$, $n = 3-9$, and $^1$H$_2$NCH$_2$C$_6$H$_4$CH$_2$NH$_4^+$ Bound in a 1:1 Ratio to 6g and 6h

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<th>guest chemical shifts, ppm</th>
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<tr>
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<td>$\alpha$</td>
</tr>
<tr>
<td>6g</td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
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* $^1$H NMR spectra were recorded in CDCl$_3$-DMSO-d$_6$ (6:1 (v/v)) at 25°C. $^b$ Tentative assignment.

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); $\alpha$, $\beta$, and $\gamma$ are protons of the complexed salt; $\alpha'$, $\beta'$, and $\gamma'$ are protons of the free salt.

At 25°C, the $^1$H NMR spectrum of a 1:2 mixture of 6g and $^1$H$_2$N(CH$_2$)$_n$NH$_4^+$ shows two sets of signals for the guest methyl 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 $\Delta G^\neq > 16.3$ kcal mol$^{-1}$. The $^1$H NMR spectra of a 1:2 mixture of 6g and $^1$H$_2$N(CH$_2$)$_n$NH$_4^+$ and a 1:2 mixture of 6g and $^1$H$_2$N(CH$_2$)$_n$NH$_4^+$ 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...
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Table III. Free Energies of Binding of Diammonium Dipicrate Salts to Hosts at 25 °C in CHCl₃ Saturated with H₂O

<table>
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<tr>
<th>host</th>
<th>cation of guest</th>
<th>K₄ x 10⁹, M⁻¹</th>
<th>ΔG° kcal mol⁻¹</th>
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<td>6g</td>
<td>+H₃N(CH₂)₉NH₃⁺</td>
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<td>0.15</td>
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<td>10.6</td>
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<tr>
<td>o-pHENylenediammonium</td>
<td>0.58</td>
<td>12.0</td>
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</table>

*See Experimental Section for methods. The values have been calculated assuming a distribution constant K₄ of 1 M⁻² for these lower limits (see Experimental Section).

formation with hosts 6g and 6h. The K₄ and −ΔG° values in Table III are lower limits, because the distribution constant of the uncomplexed guest between CHCl₃ and H₂O could not be measured accurately.13 Compound 6f forms host–guest complexes with diamonium salts that have −ΔG° 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 (CH₂)n chain. CPK models suggest that different types of binding occur between the various combinations of host 6g and guests +H₃N(CH₂)₉NH₃⁺. 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 +H₃N(CH₂)₉NH₃⁺ n increases from 3 to 9; the bridges are likely to move apart. The angle between them changes from ≈180° 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 CH₂ protons are only slightly upfield shifted as compared to those of guests with n ≤ 6. The complex with n = 9 has its most upfield shifted methylene protons only at δ 0.76 ppm, whereas the complex n = 5 has these protons at δ −0.15 ppm.

For complexes of 6h with +H₃N(CH₂)₆NH₃⁺, 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 ≤ 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.

It can be expected that guests with odd and even numbers of CH₂ functions bind differently. In the former case, the NH₃⁺ 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 −ΔG° value of the complex between 6g and +H₃N(CH₂)₉NH₃⁺ is lower than the −ΔG° value of the complex between 6g and +H₃N(CH₂)₆NH₃⁺.

Besides the aliphatic diamonium salts, aromatic diamonium 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-xylelenediammonium picrate (ammonium picrate) suggests that the guest is sandwiched between the o-xylene 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-xylene 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-xylene 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 −ΔG° for the diamonium guests (Table III) are minimum values and are very high. As far as we know, −ΔG° values of ≥13.5 kcal mol⁻¹ for protonated amines have not been measured before.611 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 diamonium 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 CaCl₂ 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 (CH₃)₂Si. Coupling constants are reported in hertz. Elemental analyses were...
Smeets et al.

For Applied Chemistry TNO, Zeist, The Netherlands. Melting point apparatus. It appeared that all new compounds were synthesized according to literature procedure.

1,3,4,6-Tetraakis(hydroxymethyl)tetrahydro-3,6a-diphenylimidazo[4,5-d]imidazole-2,5-(1'H,3'H)-dione (4). This compound was synthesized according to a procedure developed in our laboratory. A mixture of 0.56 g (0.00242 mol) of 2 and 2.3 g (0.0121 mol) of p-toluenesulfonic acid dichloride (1.72 g, 7.5 mmol) as described for 4b. FAB MS (glycerol, thioglycerol, acetic acid) m/z 563 (M + H)+. Anal. Calcd for C32H26N2O4C: 65.75; H, 5.84; O, 20.19. Found: C, 66.90; H, 5.84; O, 20.12.

1,3,4-Bis(2-oxapropylene)tetrahydro-3,6a-diphenylimidazo[4,5-d]imidazole-2,5-(1'H,3'H)-dione (5). A mixture of 19 g (0.15 mol) of 1,1,3,4,6-tetrakis(hydroxy methyl)tetrahydro-3,6a-diphenylimidazo[4,5-d]imidazole-2,5-(1'H,3'H)-dione (6e). A mixture of 19 g (0.15 mol) of 2,3 g (0.0121 mol) of p-toluenesulfonic acid dichloride (1.72 g, 7.5 mmol) as described for 4b. FAB MS (triethyl citrate) m/z 555 (M + H)+. Anal. Calcd for C52H26N2O14C: 65.75; H, 5.84; O, 20.12.

1,3,4,6-Tetrahydro-3a,6a-diphenylimidazo[4,5-d]imidazole-2,5-(1'H,3'H)-dione (4a). A mixture of 1g (0.00217 mol) of 2 and 2.3 g (0.02171 mol) of p-toluenesulfonic acid monohydrate in 70 mL of benzene was refluxed while being stirred under N2 for 4 days. Water was removed either by a Dean–Stark apparatus or by a Soxhlet apparatus filled with LH-20 (eluent CH2Cl2) to yield 0.42 g (35%) of 4a as a white solid: X H NMR (CDCl3) δ 7.13 and 7.10 ppm (5 H, Ar), 7.09 (s, 10 H, Ar H), 6.92 (s, 4 H, Ar H), 5.06 and 3.83 (2 d, 8 H, NCH2Ar, J = 16 Hz), 3.52-2.26 (m, 8 H, CH2, J = 16 Hz); FAB MS (triethyl citrate) m/z 349 (M + H)+. Anal. Calcd for C26H22N2O2C: 61.62; H, 5.12; O, 15.11. Found: C, 61.59; H, 5.15; O, 15.25.

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

1,3,4,6-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 h. The solvent was evaporated under reduced pressure. Traces of acetic acid and acetic acid anhydride were removed by condensation with a few milliliters of toluene. Finally, the white solid was dried under high vacuum to yield 0.72 g (100%) of 4d. FAB MS (glycerol, thioglycerol, acetic acid) m/z 731 (M + H)+. Anal. Calcd for C26H20N2O2C: 57.82; H, 5.02; O, 14.58. Found: C, 57.76; H, 4.98; O, 14.55.

1,3,4,6-Tetrahydro-3a,6a-diphenylimidazo[4,5-d]imidazole-2,5-(1'H,3'H)-dione (4e). A mixture of 1.82 g (7.47 mmol) of 1,8-dimethoxynaphthalene, 1.24 g (7.47 mmol) of phenyl acetonitrile, and 1.72 g (7.47 mmol) of p-toluenesulfonic acid dichloride (1.72 g, 7.5 mmol) as described for 4b. FAB MS (triethyl citrate) m/z 569 (M + H)+. Anal. Calcd for C24H22N2O2C: 60.62; H, 5.14; O, 15.05. Found: C, 60.56; H, 5.20; O, 15.05.

1,3,4-Bis(3,6-diacetoxy-1,2-xylene)tetrahydro-3,6a-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 h. The solvent was evaporated under reduced pressure. Traces of acetic acid and acetic acid anhydride were removed by condensation with a few milliliters of toluene. Finally, the white solid was dried under high vacuum to yield 0.72 g (100%) of 4d. FAB MS (glycerol, thioglycerol, acetic acid) m/z 731 (M + H)+. Anal. Calcd for C26H20N2O2C: 57.82; H, 5.02; O, 14.58. Found: C, 57.76; H, 4.98; O, 14.55.

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Synthesis and Binding Properties of Basket-Shaped Hosts

6.37; O, 21.84. Found: C, 65.37; H, 6.08; N, 6.35; O, 22.20.

Synthesis and Binding Properties of Basket-Shaped Hosts

[4,5-]<1,2-xylylene|tetrahydro-3a,6a-diphenylimidazo-

1,6,3,4-Bis[3,3'-6,6'-bis(1,4,7,10,13,16-hexaoxahexadecamethylen)]-1,2-xyylene|tetrahydro-3a,6a-diphenylimidazo-

967 (M + H)+. Anal. Calcd for C52H62N4O14: 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 $K_c$ and $\Delta G^\circ$ Values. The picrate salt extraction technique from H2O into CHCl3 described by Cram et al.12 was applied to determine $K_c$ and $\Delta G^\circ$ 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 10 ¿iL, 75 ¿iL were used in the setting angles of 17 reflections in the range 9.7° to 158°. Then, the four hydroxyl 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/A³ 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 package22 was used for geometrical calculations and illustrations.

**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 Ka), therefore only data of a rather limited quality could be obtained. All reflections were measured at $\psi$ values with the A-vector method14 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 with two settings within the range of observed and calculated structure factor amplitudes (22 pages). 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.

Acknowledgment. We thank Prof. W. Drenth and Dr. F. G. M. Niele for helpful discussions and P. van der Sluis for preparing the crystals for the X-ray structure determination. X-ray data were kindly collected by Dr. B. P. van Eijck. This work was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Foundation for Scientific Research (NWO).

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.