Effects of Side Arm Length and Structure of *Para*-Substituted Phenyl Derivatives on Their Binding to the Host Cyclobis(paraquat-*p*-phenylene)

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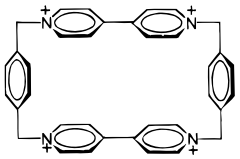
The binding constants with the host cyclobis(paraquat-*p*-phenylene), $\mathbf{1}^{4+}$, have been determined in CH_3CN by UV−vis spectrophotometry for a series of *p*-phenylene guests, symmetrically substituted with side arms of varying length and functionality. Semiempirical molecular orbital theory was employed to provide a detailed structural and energetic interpretation of the experimental binding data. In particular, the length of the side arms and the type and position of the heteroatoms on the side arms were systematically varied in order to understand the effects of external interactions on the association constants of the guests with host $\mathbf{1}^{4+}$. A large chelate effect involving the ethyleneoxy side arm oxygen atoms and a cooperative effect between the guest aromatic core and the side arms are significant factors which determine the binding with this host. Sequential ethyleneoxy linkages along the side arms markedly increase the binding constant with respect to a compound in which the same number of oxygens along the side arms are separated by longer aliphatic linkages. In addition, a multiplicative rather than additive effect on the binding constant is observed which demonstrates that the oxygen atoms exhibit a strong chelate effect. It was also discovered that while the side arms of these guests contribute most of the driving force for complexation, an aromatic core is necessary for the guest to reside in the cavity of the host. The binding of these guests then is dependent upon cooperation between the arms and the aromatic core. Furthermore, elongation of the central aromatic core with aliphatic side arms containing no heteroatoms leaves the association constant relatively unchanged and replacement of the oxygen atoms with sulfur markedly decreases the observed binding. These effects have been used to rationalize several observations regarding this system in the literature and may serve to improve the design of new supramolecular systems and to better understand the host/guest interaction process.

Introduction

Host−guest complexation comprises an important part of supramolecular chemistry.[1] One of the more commonly used hosts is cyclobis(paraquat-*p*-phenylene), $\mathbf{1}^{4+}$.[2] It has been employed as a receptor for various molecules including electron rich phenyl, phenylene, and biphenylene compounds,[3−12] TTF,[4] and neurotransmitters.[5] In addition, a wide number of rotaxanes,[6,7] catenanes[8,9] and molecular devices,[10] such as a switchable molecular shuttle,[11] involving host $\mathbf{1}^{4+}$ have also been synthesized. Although the body of literature involving host $\mathbf{1}^{4+}$ is large indeed, the design of these systems has been largely based upon trial and error. The true nature of binding in complexes involving host $\mathbf{1}^{4+}$ had never been addressed. We therefore undertook a systematic investigation of the forces involved in guest binding to host $\mathbf{1}^{4+}$.



$\mathbf{1}^{4+}$

In a previous paper, we reported on the nature of internal or cavity binding effects involving *para*-substituted phenyl and biphenyl guests with host $\mathbf{1}^{4+}$ using theoretical and experimental methods.[12] The guests in

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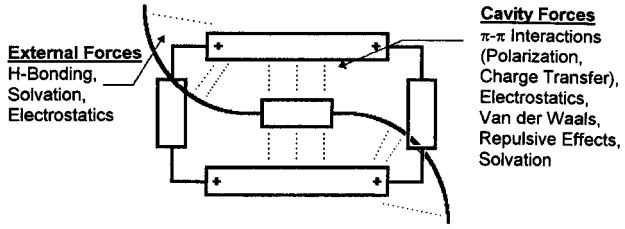
Scheme 1. Schematic Representation of Intermolecular Interactions between 1^{4+} and a Generic Guest



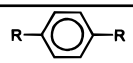
that study were aromatic molecules substituted with small functional groups. The binding occurred primarily in the cavity and the immediate vicinity of the host since the guests did not project out enough from the cavity to otherwise interact with the host. As shown in Scheme 1, the cavity binding between host $\mathbf{1}^{4+}$ and an aromatic core is dominated by polarization, electrostatics, and other forces.[12] While these data are useful in explaining molecular complexes of $\mathbf{1}^{4+}$ with small molecules, a separate investigation was necessary in order to understand the effect of the long chains that are commonly attached to these aromatic core molecules so as to make supramolecular assemblies.

It is expected that long chains (side arms) connected to the aromatic core will influence the binding in ways radically different from that of the smaller substituents which do not extend out from the binding cavity (Scheme 1) since these chains are long enough to wrap around and interact with different parts of the host. Data pointing to some important effects of these chains on the binding have already been reported,[3a] but no direct investigation of these effects has been done. In our report, we use an aromatic core symmetrically substituted with chains of varying length and functionality to examine the effects of guest side arm structure upon binding with host $\mathbf{1}^{4+}$.

Results and Discussion

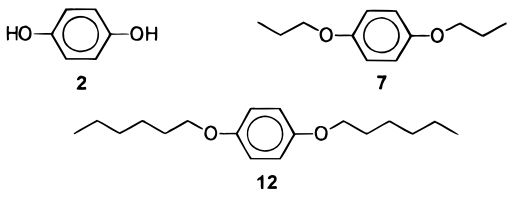
Table 1 shows the structures of the compounds used in this study along with the association constants and

Table 1. Guest Structure and UV−Vis Binding Data in CH_3CN at 298 K



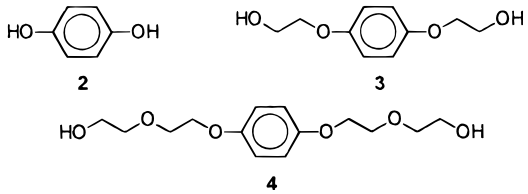
Guest	R	K (M^{-1})	ε ($M^{-1}cm^{-1}$)	λ_{max} (nm)
2	—OH	18	670	473
3	—O⌒⌒OH	340	479	472
4	—O⌒⌒O⌒⌒OH	3400	434	465
5	—O⌒⌒OCH_3	290	470	469
6	—O⌒⌒O⌒⌒OCH_3	3200	210	468
7	—O⌒⌒⌒	28	389	478
8	—O⌒⌒O⌒⌒	320	212	465
9	—O⌒⌒O⌒⌒SH	180	492	468
10	—O⌒⌒⌒⌒⌒OH	54	555	477
11	—O⌒⌒O⌒⌒O⌒⌒OH	3200	3817	330
12	—O⌒⌒⌒⌒⌒	22	371	479
13	—O⌒⌒O⌒⌒O⌒⌒SH	1200	314	460

other data obtained from the UV−vis titrations of the guests with host $\mathbf{1}^{4+}$. The first hypothesis tested was whether simple aliphatic elongation of the hydroquinone core had any effect on the binding energy. This was investigated by the addition of aliphatic chains of different lengths to hydroquinone, **2**, to produce **7** and **12**.



Comparison of the binding constants for guests **2**, **7**, and **12** shows that the binding constants remain the same, within experimental error, when the hydroxyl groups are alkylated with propyl groups and then with hexyl groups. Elongation of the hydroquinone core with hydrocarbon chains does not affect the binding constant.

Elongation of the central core with ethyleneoxy functionality, however, has a dramatic effect on the binding constant. The series **2**, **3**, and **4** demonstrates the large



effect that side arm oxygen atoms have on the binding. The binding constant increases from 18, to 340, to 3400 M^{-1}, respectively. Thus, some sort of heteroatom functionality along the chain, not just aliphatic elongation of the side arms, is necessary to increase the binding energy of the complex. This is in agreement with the data reported by Stoddart and co-workers.[3a] Interestingly, the binding constants increase only slightly for each ethyleneoxy unit added after the second ethyleneoxy unit on the chain.[3a] The main effect of chain extension with ethyleneoxy groups takes place within the first two units out from the core. Crystal structures of these complexes[3a] and our computed structures suggest that the ethyl-

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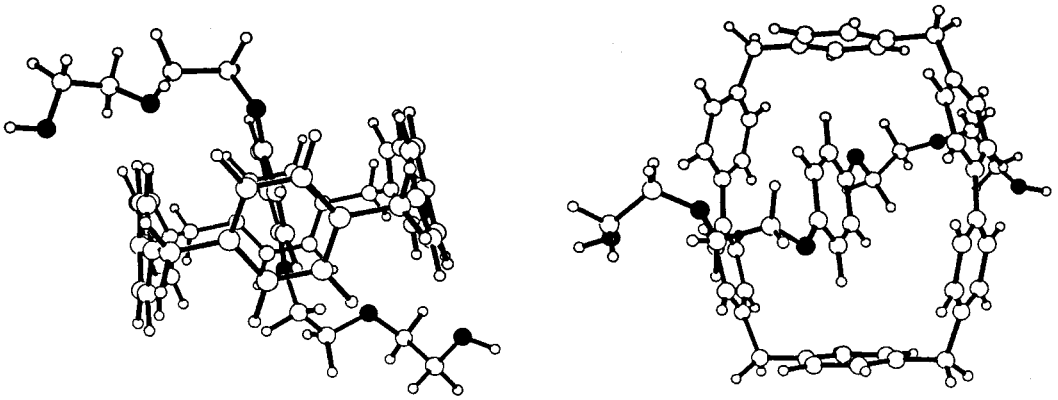


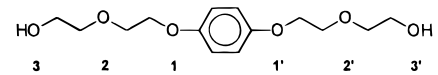
Figure 1. PM3 geometry minimized complex of host $\mathbf{1}^{4+}$ with guest **4**.

eneoxy chains are wrapping back around the bipyridinium units of the host so that the oxygen atoms can interact with this area of the macrocycle, as shown in Figure 1. The effect is definitely due to the oxygen atoms and not simply to the increasing chain length as explained above. The wrapping effect can obviously operate only in the region where the chains are geometrically positioned close to the bipyridinium units. Once this requirement has been satisfied, further elongation with ethyleneoxy functionality has little effect. This explains the tapering of the binding constants after addition of the second ethyleneoxy unit. Exactly what the oxygens on the chains are interacting with is not clear from the crystallographic data especially since crystal packing forces have to be taken into account. It could be an interaction with the positively charged nitrogen atom or, since the positive charge is delocalized over the whole bipyridinium ring, the interaction could be with the ring itself. An alternative explanation is that the oxygen is participating in a hydrogen bond with the relatively acidic protons on the bipyridinium ring.[12]

Semiempirical molecular orbital calculations were used to understand the nature of the specific interactions of the side arm oxygens with the host. One to one complexes of various guests with host $\mathbf{1}^{4+}$ were subjected to PM3 geometry minimization. As shown in our previous work on cavity bound complexes of host $\mathbf{1}^{4+}$, the number of conformations of the complexes are few since the fit of aromatic guests into the cavity of $\mathbf{1}^{4+}$ is ideal.[12] In our current study, the chain extension further complicates the potential energy surface by adding many more degrees of freedom and, as a consequence, a full exploration of the conformations would be required. This is a very time and computer intensive process and the topic of ongoing research in our groups. Instead, the minimized hydroquinone/$\mathbf{1}^{4+}$ complex was used as a starting configuration for any chain extension or modification. Chain orientations were arranged to maximize favorable electrostatic interactions with the host by orienting the ethyleneoxy oxygens toward the host. Several different starting guest orientations were used to initiate the energy minimizations and the final computed binding energies were always within 2 kcal/mol or within 10% of each other. The final structures used for interpretation are the lowest energy structures found for each complex to have a qualitative view of the binding process and of the effects of chain extension.

Table 2 shows the computed distances between the side arm oxygens and various atoms of the host for several guests in these minimizations. The favored interaction of the oxygen atoms seems to be a hydrogen bond with

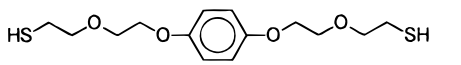
Table 2. Interatomic Distances (Å) in PM3-Minimized $\mathbf{1}^{4+}$ Complexes



Guest	Sidearm Oxygen Atom	Atoms on Bipyridinium Unit of Host[a] N	H_α	H_β	$H_{\beta 2}$	$H_{\alpha 2}$	N_2
3	1	4.05	4.02	4.02	4.56	5.91	6.02
	2	4.59	3.15	2.63	3.29	5.06	6.12
	1'	4.94	3.62	3.60	4.62	6.08	6.84
	2'	4.93	3.36	1.83	2.48	4.42	5.70
3	1	5.92	5.30	4.52	4.39	4.98	5.66
	2	4.37	2.62	3.01	4.14	6.11	7.11
	1'	6.02	5.18	4.39	4.34	4.98	5.82
	2'	4.39	2.64	3.34	4.56	6.50	7.44
4	1	5.82	5.32	4.48	4.24	4.80	5.38
	2	4.34	2.77	3.46	4.56	6.46	7.37
	3	4.87	2.92	2.47	3.54	5.70	6.94
	1'	5.89	5.13	4.21	4.08	4.69	5.49
	2'	4.61	3.04	3.91	5.09	6.93	7.80
	3'	3.73	1.77	3.79	5.53	7.94	8.68
4	1	4.48	4.45	4.56	4.94	6.15	6.31
	2	4.06	2.67	2.94	3.86	5.75	6.62
	3	5.43	3.73	2.40	2.69	4.51	5.99
	1'	4.99	3.68	3.66	4.94	6.26	6.84
	2'	4.95	3.40	1.83	2.59	4.40	5.59
	3'	4.96	3.79	2.63	3.08	5.33	6.39

[a] Refers to atoms on the side of the bipyridinium unit around which the guest sidearm curves from nearest to farthest nitrogen atom.

the α and/or β protons of the bipyridinium rings of the host since these distances are shorter on average than the oxygen−nitrogen distances. This is supported by the lower binding constants for the thiolated guest analogs, **9** and **13** (the binding constant for the oxy analog of **13** has previously been measured to be 2241 M^{-1}),[3a] since a hydrogen bond with sulfur is much weaker than that with oxygen. This seems to imply that the hardness of the oxygen is again important as was found in the cavity interactions.[12] The binding constant for **9** is even smaller



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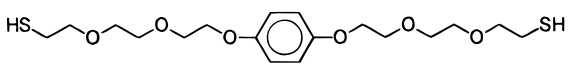

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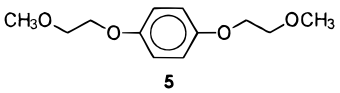
than the constant for **8**, where the sulfur atoms are replaced by methylene groups, and the constants for **9** and **13** are smaller than those for **3** and **4** where the last mercaptoethylene unit has been omitted. This might suggest that a steric effect involving the sulfur could be in operation. Interaction of the side arm oxygens directly with the bipyridinium rings or with the nitrogen atoms can be disregarded since the chains are too far away for any large effect as shown in Table 2. The heteroatom effect was to be probed further with nitrogen analogs of

these compounds, but not surprisingly, it was discovered that these compounds were strong enough bases to deprotonate the host so binding studies were not experimentally feasible.

To examine any effects of the terminal hydroxyl proton on the binding, we prepared **5** and **6**, the methylated analogs of **3** and **4**. Compounds **5** and **6** gave virtually



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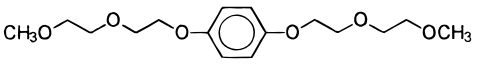

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the same binding constants as the unmethylated analogs. The slight drop in binding can be explained by steric congestion about the terminal oxygen, thereby impeding its interaction with the bipyridinium rings. It can then be assumed that the terminal hydroxyl hydrogen is not involved in a major way in the binding of these compounds to host $\mathbf{1}^{4+}$.

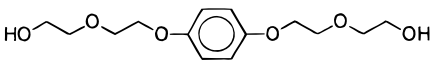
The necessity of having oxygen functionality all along the chain was explored using compounds **7** and **8**. These are analogs of **3** and **4** in which propyl groups have replaced the terminal hydroxyl groups. The association

7

8

constants show that this drammatically decreases the binding to where they revert essentially to the values for **2** and **3**. So even with some oxygen functionality along the chain, extra elongation without heteroatoms has no effect.

One of the most interesting properties of this system was discovered using guest **10**. We compared its binding to that of guests **4** and **8**. Each of these guests has the



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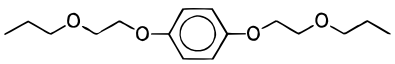

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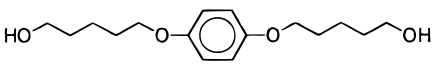
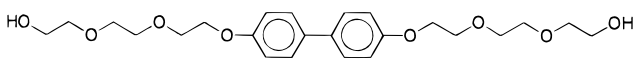


10

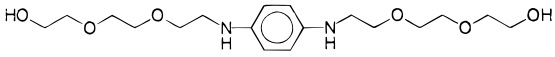
same chain length but differs in the number and position of the oxygen atoms along the chain. The binding constant for compound **10** would be expected to be close to the value for compound **8** since they both have two oxygen atoms along the chain. Actually, the binding constant for **10** is about an order of magnitude lower than that for **8**. The first oxygen along the chain then seems, upon interacting with the host, to guide the next which then guides the next oxygen atom as in compound **4**. This is not possible in compound **10** since the second oxygen is six atoms away with no intervening heteroatom. This is an impressive chelate effect which becomes more remarkable when it is noted that the positioning of the oxygen at the terminal end of compound **10** would actually allow it to better wrap around and interact with the bipyridinium rings than when the oxygen is positioned closer in on the chain as in compound **8**. *Therefore, the binding of these oxygens is cooperative in nature and not just the number of the heteroatoms but their placement along the chain is extremely important.*

This information can be used to explain some of the mysteries in the literature concerning this supramolecular system. The binding constant for **14**, a guest similar to **4** but where the hydroquinone moiety has been replaced with biphenol, has been reported.[6b] The value,

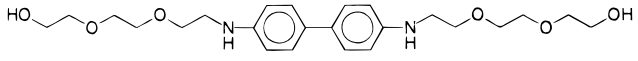


14

$K = 104\ M^{-1}$, is extremely low compared to that of **4**, $K = 3429\ M^{-1}$, even though there is an additional ethyleneoxy unit on the side arms. The value is equal, within experimental error, to the binding constant for biphenol itself, $K = 140\ M^{-1}$.[6b] Therefore elongation of biphenol with ethyleneoxy chains has no effect on the binding. If it is assumed that the increase in binding upon elongation of the core molecules in this system operates as demonstrated above, then it becomes obvious why elongation of biphenol has no effect on the association constant. Because of its size, the biphenol core positions the first few oxygen atoms along the ethyleneoxy chains much farther out from the cavity of the host than in the hydroquinone system. Figure 2 shows the PM3 semiempirical molecular orbital method geometry optimized structure of one of the complexes of these guests with host $\mathbf{1}^{4+}$. The interaction of the side arm oxygens with the host is substantially reduced. Since the effect of these chains on the binding dies away after the first few ethoxy units, and there is a chelate effect necessitating the first few oxygen atoms, even making the chains longer to compensate for the lack of interaction of the first few oxygens would have little effect. The same trend is seen in the phenylenediamine and benzidine analogs, **15** and **16**, whose binding constants with host $\mathbf{1}^{4+}$ have also been reported. The elongated phenylenediamine guest binds



15



16

more strongly to host $\mathbf{1}^{4+}$, $K = 1150\ M^{-1}$, than phenylenediamine itself, $K = 112\ M^{-1}$, but the elongated benzidine guest, $K = 1100\ M^{-1}$, is about equal to benzidine itself, $K = 1044\ M^{-1}$, in its association constant with $\mathbf{1}^{4+}$.[6a] *The chelating effect of these first few heteroatoms then is essential for strong binding and explains the weak interaction with host* $\mathbf{1}^{4+}$ *observed for the elongated biphenyl compounds as compared to the phenyl core molecules.*

The high and apparently anomalous association constant for guest **17** can be understood using the same arguments. Binding constants on the order of $10^4\ M^{-1}$ have been reported for guests similar to **4** but where the hydroquinone has been replaced by a 1,5-naphthalenedioxo group.[13] Although there are many reports in the literature of supramolecular systems involving 1,5-bis(oligoethyleneoxy)naphthalene units and host $\mathbf{1}^{4+}$, including various catenanes and rotaxanes,[2c] the binding

(13) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1994**, 181 and references cited therein.

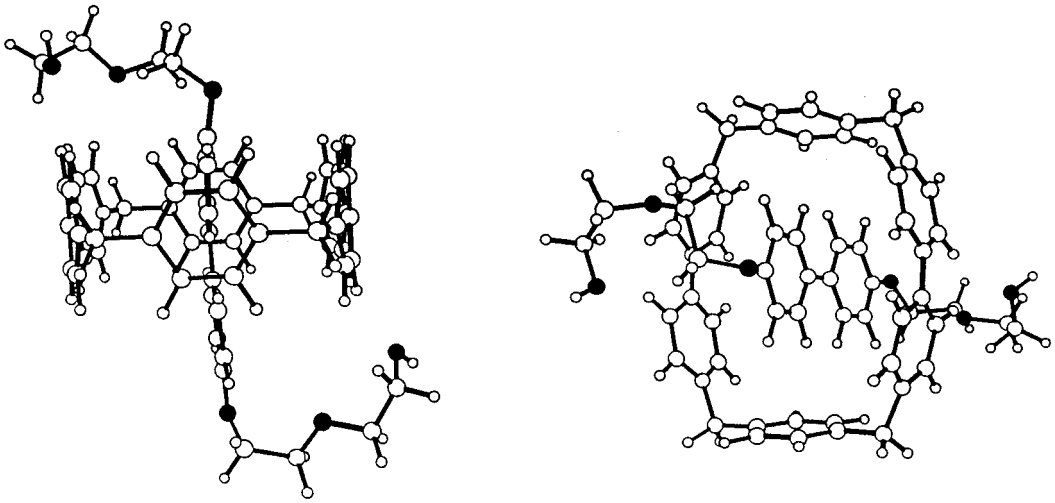


Figure 2. PM3 geometry minimized complex of host $\mathbf{1}^{4+}$ with guest **14**.

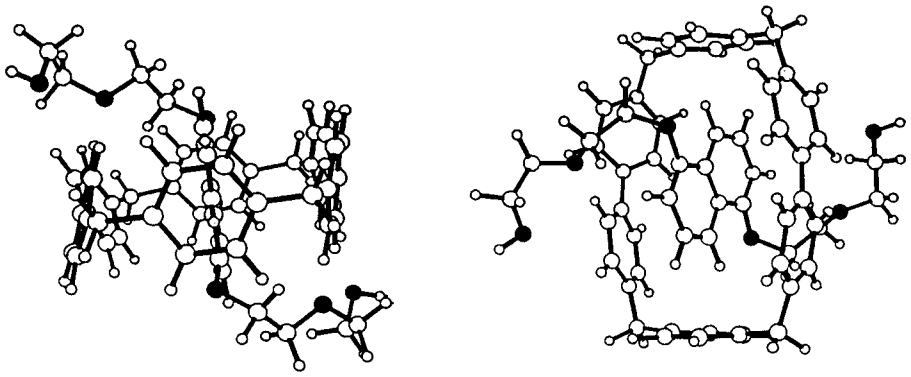
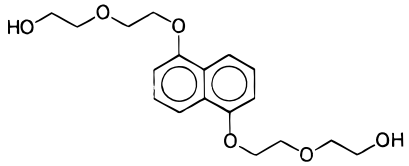


Figure 3. PM3 geometry minimized complex of host $\mathbf{1}^{4+}$ with guest **17**.

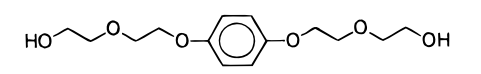
constant for **17** with host $\mathbf{1}^{4+}$, an important constituent of many of these systems, has not, to our knowledge, been reported. We therefore synthesized guest **17**[14] and determined the association constants of **17** and its core, 1,5-naphthalenediol, with host $\mathbf{1}^{4+}$. Guest **17** has the



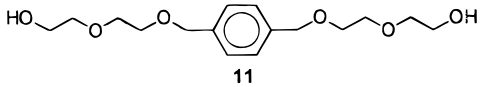
17

same functionality as the biphenol analog and virtually the same total π surface yet it has a much higher binding constant, $K = 25\ 397\ M^{-1}$. The 1,5-naphthalenediol core has a binding constant of $768\ M^{-1}$, more than an order of magnitude less than that of **17** but much more than that of biphenol. Because of its structure, the naphthalene core should be more polarizable and can place more of its π surface inside the host at one time than the biphenyl analogs, but the binding data show that the large binding constant of the elongated core is not due to the core itself since, even though the core itself is a stronger binder than biphenol, the elongated molecule is better by more than an order of magnitude. More importantly, the core of guest **17** also has the same length, from the 1 position to the 4 position, as a hydroquinone core. This allows the chains to achieve their maximum interaction with the host because when the core has achieved its binding conformation, the chains are not pushed away from the host as in the biphenyl compounds, Figure 3. This effect explains the much larger association constants involving these types of guests.

Another interesting facet of this study is the inherent effect of the hydroquinone core of these guests upon the binding of the guest. Since in our previous study involving *para*-substituted aromatic molecules we reported on how the cavity binding operates in host $\mathbf{1}^{4+}$, we synthesized compound **11** to gauge the relative effects of the two parts of the now elongated guest, the core and the side arms. This compound has the same chain characteristics as **4**, but the ring's oxygen substituents have been moved one methylene away from the ring. The



4



11

aromatic nucleus in guest **11** is substantially depleted of π-donor character as compared to the hydroquinone-derived guests. We can then measure the chain effects upon binding without the influence of the electron rich ring. The binding constant for compound **11** turns out to be as high, within experimental error, as compound **4**. This shows that the increase in binding constant

(14) Brown, C. L.; Philp, D.; Spencer, N.; Stoddart, J. F. *Isr. J. Chem.* **1992**, *32*, 61.

caused by elongating the chain is due to the chain itself and not to some effect that the chain might have on the central aromatic core. Also, it becomes evident that to achieve strong binding using these elongated guests, an electron rich ring is not required; the chains do most of the work as long as they are allowed within a certain distance of the host. The next obvious question is whether an aromatic core is needed at all since the chains bind so much more strongly than the core.

Hexa(ethylene glycol) was used as a model for this since it has the ethyleneoxy functionality without an aromatic system at is core. UV−vis titration was not possible in this case since there is no charge transfer band to measure. A ^{1}H NMR experiment was then performed in which $\mathbf{1}^{4+}$ was mixed with 5 equiv of hexa(ethylene glycol) in CD_3CN to see if there were any shifts in the proton resonances of either compound. The same experiment was done using a 5:1 ratio of $\mathbf{1}^{4+}$ to glycol. No shifts in the proton resonances were seen in either case. It was therefore assumed that there is minimal interaction between the glycol and the cyclophane and that some sort of central aromatic core is necessary to anchor the guest molecule in the cavity of the host so that the glycol chains can then wrap around the bipyridinium units. *The binding of these guests in this system then is cooperative in nature where the aromatic core places the guest in the host cavity so that the chains can interact effectively with the host.*

Conclusions

We have used a series of elongated guest molecules with an aromatic core to probe the effects of chain length and structure on binding to host $\mathbf{1}^{4+}$ by measuring the binding constants using a UV−vis titration method. It was discovered that oxygen functionality along these chains is responsible for a majority of the observed binding. It was also noted that replacing the oxygens with sulfur reduces the association constant to a value similar to that of a compound not containing a heteroatom at all in that position. Two very significant observations are that the guests exhibit a pronounced chelate effect where adjacent oxygens help each other in the binding process and that while an aromatic core is not responsible for an appreciable amount of the binding, the aromatic core is essential in placing the guest in the host cavity. Neither component of the guest, the core or the side arms, binds well by itself, but together they exert a substantial cooperative effect which directs the binding. This information has been used to understand some of the literature results involving these types of systems and can be used in the rational and directed design of more efficient host/guest complexes.

Experimental Section

All calculations were performed using the Spartan 4.1.1[15] software package on an IBM RS/6000 Model 590 workstation equipped with 512 Mb of physical memory. Geometry optimizations were carried out using PM3 semiempirical methods.[16] No assumptions were made concerning the symmetry of the complexes. The details of each calculation are provided in the supporting information.

Binding studies were performed as previously described[6a] and typically have an error margin of about 10%. ^{1}H NMR spectra were recorded at 400 MHz. Host $\mathbf{1}^{4+}$ was used as the hexafluorophosphate salt. Host $\mathbf{1}^{4+}$ and guest **4** were synthesized according to literature procedures.[3a] The other guests, unless otherwise noted, were synthesized by alkylation of the hydroquinone dianion, prepared in absolute ethanol using NaOH or KOH, with an excess of the appropriate alkyl halide and a catalytic amount of KI under N_2 at reflux for 3−5 days. The mixtures were concentrated and partitioned between CH_2Cl_2 and 1 N NaOH(aq), and the organic layer washed with H_2O, dried over Na_2SO_4, and concentrated. The residues, when solid, were recrystallized from MeOH/H_2O or CH_2Cl_2/hexanes. Oils were clarified using activated charcoal. Compound **3** was obtained commercially (Aldrich), and compounds **9** and **13** were available from previous studies.[8] All new compounds gave satisfactory combustion analyses. Melting points are uncorrected.

1,4-Bis(2-methoxyethoxy)benzene (5): white solid, mp 44 °C; ^{1}H NMR ($CDCl_3$) δ 3.42 (6 H, s), 3.75 (4 H, t), 4.05 (4 H, t), 6.85 (4 H, s). Anal. Calcd: C, 63.70; H, 8.02. Found: C, 63.76; H, 8.10.

1,4-Bis[2-(2-methoxyethoxy)ethoxy]benzene (6): yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.35 (6 H, s), 3.55 (4 H, t), 3.70 (4 H, t), 3.80 (4 H, t), 4.05 (4 H, t), 6.80 (4 H, s). Anal. Calcd: C, 61.13; H, 8.34. Found: C, 60.92; H, 8.23.

1,4-Dipropoxybenzene (7): off white solid, mp 47 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 (6 H, t), 1.78 (4 H, m), 3.85 (4 H, t), 6.80 (4 H, s). Anal. Calcd: C, 74.19; H, 9.34. Found: C, 73.92; H, 9.27.

1,4-Bis(2-propoxyethoxy)benzene (8): yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.90 (6 H, t), 1.60 (4 H, m), 3.45 (4 H, t), 3.70 (4H, t), 4.02 (4 H, t), 6.80 (4 H, s). Anal. Calcd: C, 68.06; H 9.28. Found: C, 67.95; H, 9.21.

1,4-Bis(5-hydroxypentyl)benzene (10): white solid, mp 79 °C; ^{1}H NMR ($CDCl_3$) δ 1.25 (2 H, b), 1.50 (4 H, m), 1.60 (4 H, m), 1.75 (4 H, m), 3.65 (4 H, t), 3.90 (4 H, t), 6.80 (4 H, s). Anal. Calcd: C, 68.06; H, 9.28. Found; C, 67.87; H, 9.24.

α,α′-Bis[2-(2-hydroxyethoxy)ethoxy)]-*p*-xylene (11). Na (1.03 g, 45 mmol) was added to a solution of diethylene glycol (60 g, 565 mmol) in dry THF (100 mL) under N_2 at 80 °C. After the Na dissolved, α,α′-dibromo-*p*-xylene (5 g, 19 mmol) was added along with a catalytic amount of KI, and the solution was stirred at 80 °C for 2 days. The solution was concentrated under vacuum and the residue partitioned between H_2O (100 mL) and CH_2Cl_2 (150 mL). The organic phase was washed with H_2O (2 × 50 mL) and dried over Na_2SO_4. It was concentrated to give the impure product as a light yellow oil, 2.04 g. A second fraction, 820 mg, this time a colorless oil, was obtained by again extracting the combined aqueous layers using CH_2Cl_2 (150 mL), drying over Na_2SO_4, and concentrating. Column chromatography (silica, 1:1 CH_2Cl_2/acetone) gave the pure product as a light yellow oil. The combined yield was 48%. ^{1}H NMR ($CDCl_3$): δ 2.75 (2 H, t), 3.50−3.70 (16 H, m), 4.50 (4 H, s), 7.25 (4 H, s). Anal. Calcd: C, 61.13; H, 8.34. Found: C, 61.17; H, 8.38.

1,4-Bis(hexyloxy)benzene (12): off white solid, mp 44 °C; ^{1}H NMR ($CDCl_3$) δ 0.90 (4 H, t), 1.30−1.50 (12 H, m), 1.75 (4 H, m), 3.90 (4 H, t), 6.80 (4 H, s). Anal. Calcd: C, 77.65; H, 10.86. Found: C, 77.70; H, 10.89.

Acknowledgment. This research was supported by the NSF (Grants CHE-9304262 and CHE-9633434 to A.E.K.). J.D.E. thanks the donors of the Petroleum Research Fund, administered by the American Chemical Society, the University of Miami General Research Council for a Summer Award in Natural Science and Engineering, and the Department of Defense (Grant DAAH04-96-1-0311).

Supporting Information Available: Details of the PM3 semiempirical molecular orbital calculations (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9610321

(15) Spartan 4.1.1, Wavefunction, Inc., Irvine, CA.
(16) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *209*, 221.