Hemicarcerands That Encapsulate Hydrocarbons with Molecular Weights Greater than Two Hundred[1,2]

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Abstract: Syntheses are reported for the globe-shaped hemicarcerands **1** and **2** composed of two rigid bowl-like units (polar caps) attached to one another at their rims through four $OCH_2C{\equiv}CC{\equiv}CCH_2O$ units (equatorial spacers). Eight pendant $CH_3(CH_2)_4$ groups in **1** and $C_6H_5CH_2CH_2$ groups in **2** attached in assemblies of four to each polar cap render the hosts soluble in organic solvents. The important shell-closing reactions $2Ar(OCH_2C{\equiv}CH)_4 + [O] \rightarrow Ar(OCH_2C{\equiv}CC{\equiv}CCH_2O)_4Ar$ went in 5–8% yields in pyridine–O_2–$Cu(OAc)_2$ to give a hemicarcerand free of pyridine. The higher solubility of **1** (compared to that of **2**) in organic solvents led to an examination of its binding properties. By heating **1** dissolved either in potential guests or in 1,3,5-$[(CH_3)_3C]_3C_6H_3$ (too large to enter **1**) containing dissolved potential guests at 80–140 °C for 2–7 days, 1:1 hemicarceplexes mixed with the empty host were isolated in those cases when the potential guests were just *small* enough to enter the host's portals at high temperatures but *large* enough not to depart during isolation as stable solids. Thus, constrictive bonding played a large role in kinetic stabilization of the hemicarceplexes. The ^1H NMR spectra of both the host and the guest were markedly modified upon complexation. The half-lives in hours of representative complexes dissolved in $CDCl_3$ at 25 °C were as follows: **1**·1,3,5-$[(CH_3)_2CH]_3C_6H_3$, 1628; **1**·1,3,5-$Et_3C_6H_3$, 960; **1**·4-Et[2.2]paracyclophane, 24; **1**·1,3-dimethyladamantane, 13.5; **1**·[3.3]paracyclophane, 13; **1**·tetradehydro[2.2]paracyclophane, 11; **1**·[2.2]paracyclophane, 5; **1**·4,12-dihydroxy[2.2]paracyclophane, 4; and **1**·[2.3]paracyclphane, 0.5. Complexes of smaller guests such as $CHCl_3$, ferrocene, adamantane, and 1,3,5-trimethylbenzene were unstable to room-temperature isolation conditions. Larger guests such as [3.4]paracyclophane and 4,12-dinitro[2.2]paracyclophane did not enter the portals of **1** at temperatures under which host **1** was stable, whereas smaller guests such as CH_2Cl_2 and pyridine entered and departed the host at 25 °C rapidly on the NMR time scale. Catalytic reduction (H_2, PdC) of the eight acetylenic bonds of **1** produced an empty host of much more flexible structure, **3**, whose binding properties have not yet been examined.

This paper reports the syntheses of new potential hemicarcerands **1–3** and a survey of possible guests that are bound strongly enough in the interior of **1** to permit isolation of their complexes at ambient temperature. In earlier work, hosts of several types were found to be capable of exchanging their incarcerated guests in solution at high temperatures but were subject to isolation and characterization at 25–40 °C. In **4**, two hemispheric bowls are attached at their rims by only three out of a possible four OCH_2O spanning units, leaving a small portal for guest passage in and out of the hemicarcerand when in solution.[3] In **5**, four α,α'-binaphthyl units, each naphthalene substituted in its β-position with a CH_2 group, acted as spanners. When the binaphthyl dihedral angles are larger than about 60°, four portals of substantial size open to provide for entrance and egress of guests, but in CPK models, strain appeared to increase with increased dihedral angle.[4] In **6**, four rather wide portals are fixed in place, so the capture of guests at high temperature by **6** was limited to those which were relatively rigid and appropriately sized like ferrocene, camphor, or adamantane.[5] Host **7**, with four *o*-xylyl spanners in the conformation drawn, provides four sizable portals of moderate size, which close by twisting the northern hemisphere relative to the southern, thus increasing the bridge-to-bowl contacts and effectively closing the portals.[6] This host forms stable complexes with guests as small as CH_3CN and as large as *p*-xylene. Host **8**, drawn in its stable twisted form (120° around its C_3 axis), connects two [1.1.1]orthocyclophane saucer-shaped units with three $OCH_2C{\equiv}CC{\equiv}CCH_2O$ bridging units. This host complexes only small guests such as xenon, cubane, and $CHCl_3$, and the complexes are unstable in solution at ambient temperature.[7]

An examination of the CPK molecular models of **1**, **2**, and potential guests suggests that the hosts possess large enough portals in the conformations drawn to allow entry from the solvent to the interior cavity and that in the presumed stable twisted conformation, the polar caps are distant enough from one another to accommodate organic molecules of dimensions in excess of 200 molecular weight. Another attractive feature of the two hosts is that they might be catalytically reduced with hydrogen to hosts such as **3**, containing four $O(CH_2)_6O$ bridges, which cannot be made directly from **9** or **10** because of competing intramolecular bridging of two hydroxyls in the same hemisphere.[8] Host **1** containing eight $(CH_2)_4CH_3$ appendages was chosen because these "feet" impart greater solubility to their globe-shaped container moieties than shorter or $CH_2CH_2C_6H_5$ feet. Host **2** was also selected since crystal structures containing these pendant groups tended in the past to produce less disordered crystal structures than those of **1**.

Results

Synthesis. Tetrol **9** has been reported[9] as has the tetrabromide precursor **11** of tetrol **10**,[10] which was converted to **10** (75%) by

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(1) Host–Guest Complexation. 65.

(2) We warmly thank the U.S. Public Health Services for supporting grant GM-12640.

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(7) Cram, D. J.; Tanner, M. E.; Keipert, S. J.; Knobler, C. B. *J. Am. Chem. Soc.* **1991**, *113*, 8909–8916.

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(10) Bryant, J. A.; Blanda, M. T.; Vicenti, M.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2167–2172.

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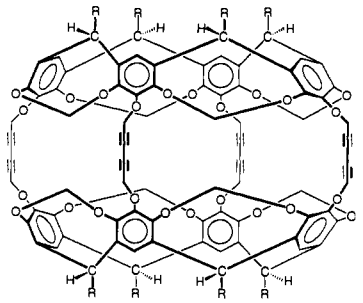
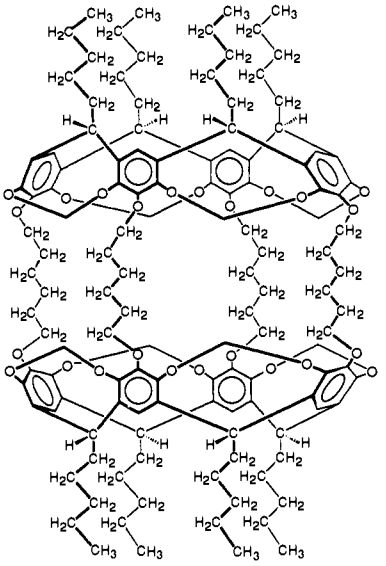


1, R = $(CH_2)_4CH_3$
2, R = $CH_2CH_2C_6H_5$



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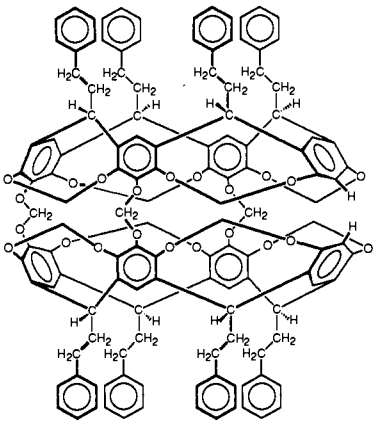

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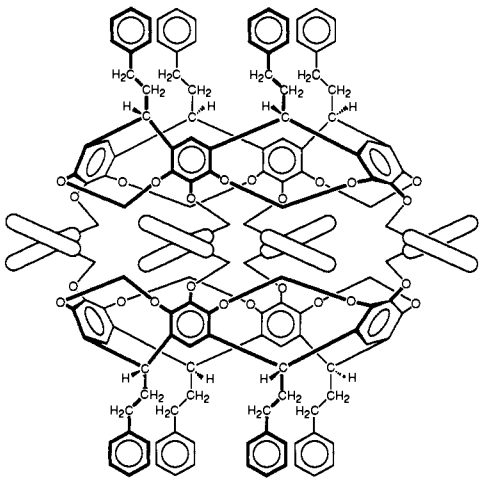

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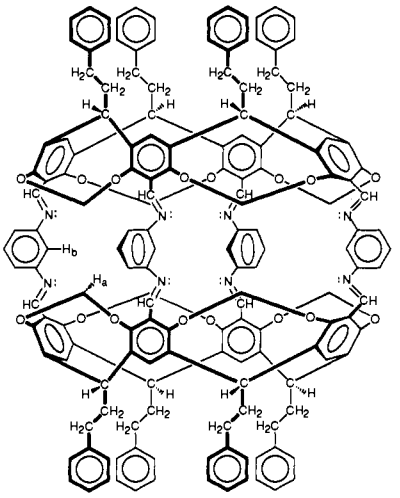

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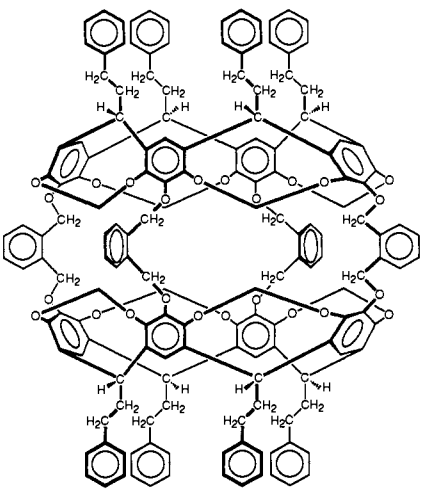

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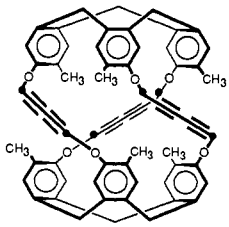

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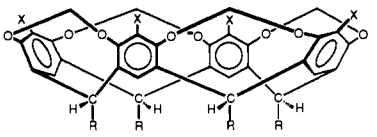
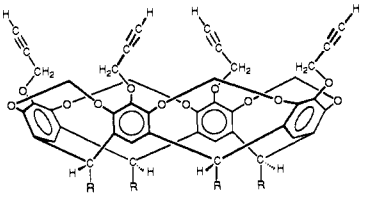


9, R = $CH_2CH_2C_6H_5$, X = OH
10, R = $(CH_2)_4CH_3$, X = OH
11, R = $(CH_2)_4CH_3$, X = Br

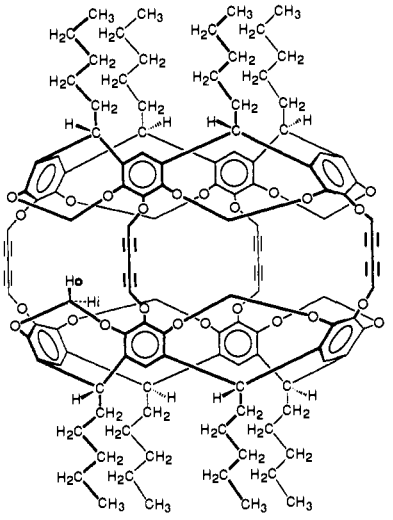


12, R = $CH_2CH_2C_6H_5$
13, R = $(CH_2)_4CH_3$

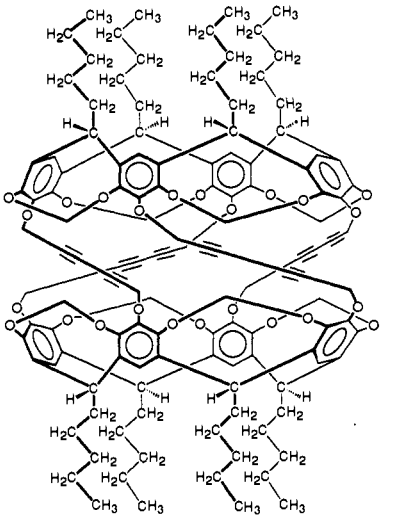
the same method employed in the synthesis of **9** from its corresponding tetrabromide.[9] Tetrol **9** when treated with $HC{\equiv}CCH_2Br$–K_2CO_3–$(CH_3)_2CO$–$CH_3C_6H_5$ gave the tetraacetylenic ether **12** (68%), wheras tetrol **10** similarly produced **13** (79%). The critical oxidative-shell closures involved pure pyridine–$Cu(OAc)_2$–H_2O–O_2 at 60 °C (15 min). The *empty* hemicarcerand was purified by chromatography (CH_2Cl_2–silica gel) to give an 8% yield in the case of **2** and 5.6% for **1**. Several hundred milligrams of material were prepared at one time. Attempts to grow crystals suitable for X-ray crystal structure determination of **1** and **2** failed. Reduction of the eight carbon–carbon triple bonds of **1** with H_2–PdC–C_6H_6 produced **3** (91%) which was characterized, but its complexing properties are not reported here.

Complexation. An examination of the CPK molecular models of **1** indicates that four 30-membered rings compose the sides of the hemicarcerand, which provide portals connecting the inner and outer phases. These openings are largest when the northern and southern hemispheres are untwisted about their common C_4 axis, as drawn in **1a**. The portals are smallest when the northern hemisphere is rotated with respect to the southern hemisphere maximally about that same axis not more than 90°, as is portrayed in **1b**. At about 80°, the eight OCH_2O intrahemispheric bridges start to inhibit further rotation by contacting the acetylenes of the interhemispheric bridges. The rotation decreases the portal size drastically and the cavity size less so, by bringing the polar caps closer together, as was observed in a more severe way in **8**.[7] Molecular models of common solvents such as CH_2Cl_2, $CHCl_3$, C_6H_6, pyridine, $(CH_2)_4O$, and $CH_3C_6H_5$ could be easily inserted into models of **1a**.

Experimentally, *p*-xylene, 1,4-diethylbenzene, hexamethylphosphoramide, adamantane, α-pinene, 1,3,5-trimethylbenzene, 1-aminoadamatane (amantidine), and 2-oxoadamantane failed to be retained by **1** when melts of the compounds were heated and



1a



1b

cooled and the host and potential carceplexes isolated. A solution of **1** in 1,3,5-tri-*tert*-butylbenzene (TTB) was heated for 7 days at 140 °C under argon, the solvent was removed by sublimation under high vacuum, the residue was suspended in methanol, and the product was collected, washed with methanol, and air dried. The product was dissolved in $CDCl_3$, and identified by its 500-MHz ^1H NMR spectrum as empty **1**. Accordingly, molten TTB was used as the solvent for host **1** complexing potential high-melting solid guests present in guest-to-host molar ratios of 27:4. When guests were liquids at temperatures used for incarceration, the solutions of host in guest were heated for various times at 80–140 °C. The mixtures of host and 1:1 complexes were isolated by distilling or subliming the solvent at low pressure and were analyzed by making use of the substantial changes in the ^1H NMR spectrum upon complexation of both the host and guest chemical shifts and their integrals. Table I lists the structures of all the guests successfully incarcerated in **1**, the solvent, the temperature, the time, the extent to which complexation occurred, and a rough half-life at 25 °C for dissociation of the complex dissolved in $CDCl_3$.

Besides the compounds listed in Table I, the following potential guests were examined but failed to provide isolable complexes: *p*-xylene, 1,4-diethylbenzene, 1,4-diisopropylbenzene, 1,4-di-*tert*-butylbenzene, *tert*-butylbenzene, hexamethylphosphoramide, 1-aminoadamantane, α-pinene, 1,3,5-trimethylbenzene, 2-oxoadamantane, [3.4]paracyclophane, ferrocene, ruthenocene, tripiperidylphosphine oxide, 1,3-dicarbomethoxyadamantane, 4,12-dinitro[2.2]paracyclophane, 1,2,3,6,7,8-hexahydropyrene, 1,3-diphenylacetone, *trans*-stilbene, triphenylmethane, 2,6-dimethoxynaphthalene, 9,10-anthraquinone, and cortisone.

Table I shows that empty host **1** when heated at 80–140 °C with large excesses of guests A–M[11] formed 1:1 complexes in yields that ranged from 33 to 90%. The most kinetically stable complex (**1**·B) was separated from the small amount of empty **1** and fully characterized, while the other complexes were characterized by the large upfield shifts of the proton signals in the ^1H NMR spectra of the incarcerated guests ($\Delta\delta$ as high as −2.97 ppm) and the smaller spectral changes in that of the host. No attempt was made to measure rates of complexation. Temperatures of 80–140 °C and 2–7 days were required to produce the observed yields. It was not demonstrated that equilibrium had been reached in any of the experiments.

Discussion

Syntheses. Particularly Whitlock[13] and Breslow,[14] both of whom realized better yields than we were able to obtain, have successfully assembled interesting hosts whose critical ring closures involved the oxidative acetylene–acetylene coupling reactions. In our systems, we appear to get good shell-closure yields only when guests are trapped inside during the reaction,[6] suggesting that templating increases the yields. Host **1** has too large a cavity to make use of this effect with any of the usual solvents.

Driving Forces for Complexation–Decomplexation. Molecular models (CPK) of **1** demonstrate that it contains a large enforced cavity. Dissolution of **1** in 1,3,5-tri-*tert*-butylbenzene introduces large holes into the solution. When dissolved guests enter the cavity, the entropy of dilution of the empty space inside the host increases since it is divided into many small empty spaces dispersed throughout the system characteristically found in liquids. Desolvation of the guest molecules increases the degrees of freedom of liberated solvent molecules which further increases the entropy of the complexation, offsetting the negative entropy associated with collecting and limiting the degrees of freedom of an incarcerated guest. In some cases, the overall result is a net positive entropy of complexation.[6,12] The enthalpy of complexation grows out of the attractive contacts between the incarcerated guest and its host minus the attractive contacts between the solvent and the guest in the starting states for complexation. Additional attractive contacts grow out of the twisting of the northern relative to the southern hemisphere of the host, which undoubtedly occurs.

Operationally, guests are driven into hosts making use of mass law at a high enough temperature so that the portals, in effect, expand just enough to allow guest entrace but which at lower temperatures contract enough to mechanically inhibit guest departure. Thus, binding free energies combined with constrictive binding provide a high enough activation free energy to place decomplexation rates on the human time scale at room temperature.

Guests That Failed To Form Isolable Complexes. Application of the procedure applied successfully to the guests in Table I failed to incarcerate the following compounds, whose numbers of non-hydrogen atoms are listed after their names: *p*-xylene (8), *p*-diethylbenzene (10), *p*-diisopropylbenzene (12), *p*-di-*tert*-butylbenzene (14), ferrocene (11), ruthenocene (11), adamantane (10), 2-oxoadamantane (11), 1-aminoadamantane (11), α-pinene

(11) References for the preparations of the paracyclophanes are as follows: (a) Cram, D. J.; Steinberg, H. *J. Am. Chem. Soc.* **1951**, *73*, 5691–5704. (b) Cram, D. J.; Allinger, N. L.; Steinberg, H. *J. Am. Chem. Soc.* **1954**, *76*, 6132–6141. (c) Dewhirst, K. C.; Cram, D. J. *J. Am. Chem. Soc.* **1958**, *80*, 3115–3125. (d) Singer, L. A.; Cram, D. J. *J. Am. Chem. Soc.* **1963**, *85*, 1080–1084. (e) Cram, D. J.; Day, A. C. *J. Org. Chem.* **1966**, *31*, 1227–1232. (f) Cram, D. J.; Helgeson, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 3515–3521.

(12) Cram, D. J.; Choi, H.-J.; Bryant, J. A.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7748–7765.

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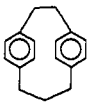
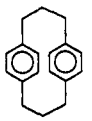
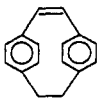
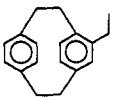
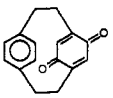
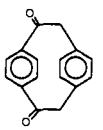
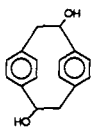
(14) O'Krongly, D.; Denmeade, S. R.; Chiang, M. Y.; Breslow, R. *J. Am. Chem. Soc.* **1985**, *107*, 5544–5545.

Table I. Complexation Conditions, Yields, and Decomplexation Half-Lives in $CDCl_3$ at 25 °C

guest		complxn				
struct	label	solvt[a]	t (h)	T (°C)	complxd (%)[b]	decomplxn $t_{1/2}$ (h)[c]
	A	guest	144	80	33	960
	B	guest	72	90	90	1608
	C	guest	168	80	60	13.5
	D	TBB[d]	48[e]	80	66	5
	E	TBB[d]	168	80	44	0.5
	F	TBB[d]	168	80	82	13
	G	TBB[d]	48	120[f]	90	8
	H	TBB[d]	48	80	90	11
	J	TBB[d]	48	120[f]	48	216
	K	TBB[d]	48	140[f]	80	24
	L	TBB[d]	72	80	61	1
	M	TBB[d]	48	90	57	4

[a] Melts at 80–140 °C. [b] Mixtures of empty host and 1:1 complexes. [c] Calculated from first-order rate constants for decomplexation obtained from ^1H NMR spectral changes with time. [d] 1,3,5-$[(CH_3)_3C]_3C_6H_3$. [e] A large amount of excess insoluble guest was present. [f] Lower temperatures and times gave lower percentages complexed.

(10), and 1,3,5-trimethylbenzene (9). Molecular model (CPK) examinations of the potential guests and **1** show that these molecules can easily and fully enter the cavity of **1a** and depart without undue distortions of the host or guests.

A second group of potential guests also failed to form isolable complexes of **1** but for a different reason. Models show that the following compounds can easily enter and depart **1** with substantial amounts of their parts protruding through the portals in the complex, thus inhibiting twisting of the two hemispheres of the host relative to one another: 1,3-diphenylacetone (16), triphenylmethane (19), 2,6-dimethoxynaphthalene (14), 9,10-anthraquinone (16), and *trans*-stilbene (14). However, if the long axes of the last three guests in the complex are reoriented to correspond to the polar axis of the host, the guests can be totally encapsulated. However, given these guests' initial perpendicular placement, the host's conformational adaptivity to rotation of the guest with respect to the host is reduced, and the activation energy for constrictively bound placement becomes prohibitively large.

A third group of potential complexes failed to form because the guests are either too large or ill-shaped to pass through the portals and enter the host's cavity. These compounds are as follows: tripiperidylphosphine oxide (20), 1,3,5-tri-*tert*-butylbenzene (18), 1,3-dicarbomethoxyadamantane (18), 4,12-dinitro[2.2]paracyclophane (22), [3.4]paracyclophane (19), 1,2,3,6,7,8-hexahydropyrene (16), and cortisone (26). Molecular model examinations show that these compounds are just too large to enter the interior of **1** through the constrained 30-atom ring portals, even when they are distorted. However, by breaking the bonds of the host molecule, placing the guest model inside the host, and remaking the broken bonds, it is possible to assemble molecular models of complexes of [3.4]paracyclophane, 2,6-dimethoxynaphthalene, and 1,2,3,6,7,8-hexahydropyrene.

Guests That Formed Isolable Complexes. Guests A–M of Table I range in their heavy atoms from 12 for 1,3,5-triethylbenzene (A) and 1,3-dimethyladamantane (C) to 18 for [3.3]paracyclophane (F), 4-ethyl[2.2]paracyclophane (J), and the three disubstituted [2.2]paracyclophanes (K–M). All of these guests either are rigid or have very few degrees of freedom of rotation of their parts. In CPK molecular modeling experiments, these guests either are very difficult to force into the capity of **1** or can *not quite* be forced into the cavity of **1** without breaking the host's bonds. Once inside the host model, the guest models do not inhibit the rotation of the two hemispheres of the host relative to one another, thus increasing the number of host-to-host and host-to-guest contacts.

Experimentally, for the paracyclophane guests for which TTB served as the solvent, the following gross order was observed with respect to the increasing temperature (80–140 °C) and time (48–168 h) required to produce 44–90% complexation: H ~ D ~ E ~ L ~ F < M < G < J < K. Not surprisingly, the wider guests were qualitatively more diffcult to intoduce into the cavity than the narrower ones.

Host **1** was able to distinguish between the complexation of [3.3]paracyclophane (F) and the lack of complexation of [3.4]-paracyclophane. Thus, the presence of an additional single methylene in the bridge of [3.3]paracyclophane was enough to destroy its ability to enter **1**. A less dramatic example of structural recognition in complexation was the ability of 1,3,5-triethylbenzene (A) to be incarcerated by **1** at high temperatures, but 1,3,5-trimethylbenzene was too small to be similarly incarcerated, although it undoubtedly was weakly complexed.

Correlation of Decomplexation Rates with Guest Structures. The decomplexation rates for the 12 complexes of Table I were estimated at 25 °C in $CDCl_3$ to provide an impression of their half-lives, which decrease in the following order ($t_{1/2}$ in h): B (1608); A (960); J (216); K (24); C (13.5); F (13); H (11); G (8); D (5); M (4); L (1); and E (0.5). Guest shape appears to be a much more important factor contributing to this order than the number of heavy atoms. For example, the $t_{1/2}$ for 1,3,5-triethylbenzene (A, 960 h) having 12 heavy atoms is about 3 powers of 10 greater than that for 2,9-dioxo[2.2]paracyclophane (L, 1 h) having 18 heavy atoms. The 30-membered ring through which a guest must pass to enter the cavity of **1** in its open form (**1a**) is roughly rectangular in shape, much longer in the axial compared to the equatorial dimension. Thus, 1,4-disubstituted benzene derivatives also possessing rectangular cross sections easily enter and exit the cavity, and only when they become extended in the third dimension as in the paracyclophanes is constrictive binding visible in the exit rates. In contrast, the 1,3,5-trisubstituted benzenes possess much more square cross sections, one of whose dimensions is noncomplementary to the narrow rectangular portal by the time the substituents are ethyls as in A or

isopropyls as in B. Model examinations show that although A and B might enter or depart the portals of **1a** if the guest's best plane is roughly perpendicular to the rectangular entrace, the guest on entry will pass out the opposite portal unless it rotates about its axis of entry when it is part way in, a motion resisted by the walls of the cavity. The same type of rotation is required of the paracyclophanes, but resistance to this rotation is markedly pronounced only with 4-ethyl[2.2]paracyclophane (J), whose cross sections that include the ethyl group become quite broad compared to the shorter dimension of the 30-membered rings of **1a**. Consequently for **1**·J, $t_{1/2}$ = 216 h.

Resistance to the screwlike motion required for entry or exit (same transition states) of guests also increases in the order **1**·[2.2]paracyclophane (**1**·D, 5) < **1**·[3.3]paracyclophane (**1**·F, 13) < [3.4]paracyclophane (off scale). The interesting observation that **1**·[2.3]paracyclophane (**1**·E, 0.5) decomplexes by a power of 10 faster than either **1**·[2.2]paracyclophane or **1**·[3.3]-paracyclophane is explained by the fact that because of the unlike bridge lengths in [2.3]paracyclophane, the molecule possesses a *preorganized screwlike structure along its long axis and thus is better preorganized to complement the transition state for exit or entry into the cavity of* ***1***. In other words, [2.3]paracyclophane can worm its way into the cavity. However, [3.4]paracyclophane is just too large to be accommodated in the cavity of **1** without shell distortion. As expected, the complexes of the dehydro derivatives of [2.2]paracyclophane (**1**·G and **1**·H) exhibit $t_{1/2}$ values within a factor of 2 to that of **1**·[2.2]paracyclophane (5 h).

Adamantane is roughly spherical, and model examinations show that entry and exit of this potential guest are sterically uninhibited. The same is true of oxoadamantane and 1-amino-adamantane but not of 1,3-dimethyladamantane, which extends the molecule in two dimensions. A further extension as in 1,3-dicarbomethoxyadamantate (18 heavy atoms) made the compound's shape incompatible with the cavity portal of **1**. On the other hand, dioxoparacyclophanes and dihydroxyparacyclophanes K, L, and M are composed of 18 heavy atoms, but they are arranged to possess shapes complementary to the portal and the cavity of **1** (molecular model examination).

On the basis of CPK molecular model examination, 9,10-anthraquinone and 2,6-dimethoxynaphthalene were predicted to form hemicarceplexes. To do so, the long axis of each guest would have to coincide with the long polar axis of the host. In models, each guest can easily enter conformation **1a** with its long axis *perpendicular* to the long axis of the host. Apparently, rotation of these guests 90° once inside is too inhibited sterically to occur at temperatures under which the host is stable.

Comparison of 1 with Other Hemicarcerands. The hemicarcerand containing the largest cavity studied previously was **6**, whose two polar hemispheres were bridged with (m-CH=NC$_6$H$_4$N=CH)$_4$ groups, thereby separating the two hemispheres by seven atoms. Guests entering and departing the cavity of **6** must pass through a 28-membered ring. The largest guests incarcerated in **6** were [2.2]paracyclophane and 9,10-anthraquinone, while ferrocene and amantidine were easily retained at room temperature.[5] This contrasts with **1** whose (OCH$_2$C≡CC≡CCH$_2$O)$_4$ bridges provided eight-atom chains separating the hemispheres and 30-membered ring portals. These portals appeared to be too large to retain ferrocene or 9,10-anthraquinone, but [2.2]-paracyclophane and even [3.3]paracyclophane with a molecular weight of 236 were readily incarcerated. The latter compound was too large to be complexed by **6** (CPK models).

In general, the hemicarceplexes of **1** released their guests faster than those of **6**, probably because the CH=NC$_6$H$_4$N=CH bridges contain kinks while the OCH$_2$C≡CC≡CCH$_2$O bridges are much more linear.

Summary. We have reported the syntheses of three hemicarcerands (**1–3**) and the results of a survey of guests subject to constrictive binding by **1**. By heating **1** in liquid 1,3,5-triethylbenzene, 1,3,5-triisopropylbenzene, or 1,3-dimethyladamantane, 1:1 complexes were formed which were manipulable at ambient temperatures. When **1** was heated in 1,3,5-tri-*tert*-butylbenzene solutions of nine [*mn*]paracyclophanes, nine hemicarceplexes were formed whose stabilities are due largely to constrictive binding. The largest guest thus far encapsulated is [3.3]paracyclophane. The ^{1}H NMR signals of incarcerated guests were moved upfield by several parts per million, whereas those of the host most sensitive to the presence of guests gave $\Delta\delta$ values that ranged from 0.07 to –0.35 ppm. The half-lives for decomplexation of the 12 carceplexes at 25 °C in CDCl$_3$ ranged from a low of 0.5 to a high of 1608 h. Both the shape and the size of the guest control the complexability of potential guests.

Experimental Section

General. Tetrahydrofuran (THF) was distilled from sodium–benzophenone, and pure pyridine was dried over molecular sieves. Cupric acetate was purified by refluxing in acetic anhydride and drying under vacuum. The Pd–C catalyst was dried over P_2O_5 at 25 °C under vacuum. The ^{1}H NMR spectral signals were referenced against (CH$_3$)$_4$Si and obtained in CDCl$_3$ solutions on a Brucker AM-500 instrument unless otherwise indicated.

1,21,23,25-Tetrapentyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin-7,11,15,28-tetrol, Stereoisomer (10). To a solution of 21.0 g (18.6 mmol) of tetrabromide **11**[10] dissolved in 1.3 L of dry THF stirred at –78 °C under dry N_2 was added 60 mL of a 2.5 M solution of n-BuLi in pentane (150 mmol) over a 15-min period. After an additional minute, 25 mL of B(OCH$_3$)$_3$ (262 mmol) was added over 2 h. The solution was warmed to 25 °C and stirred for 1 h. The mixture was cooled to –78 °C, and 300 mL of a 1.5 N NaOH solution in 15% aqueous H_2O_2 was added over 10 min. The solution was warmed to 25 °C and stirred for 15 h. Careful addition of 50 g of $Na_2S_2O_5$ to the mixture followed by evaporation of THF under vacuum gave a yellow solid that was collected and air dried. This material was dry loaded onto a 1-L silica gel gravity column using a minimum of THF, and the product was eluted with 2:1 EtOAc:CHCl$_3$ to give 10.3 g (63%) of **10** as a white solid, mp 240 °C dec: MS (FAB$^+$, NOBA) m/e 880 (M$^+$, 100) 881 (M$^+$ + 1, 75) 882 (M$^+$ + 2, 28); ^{1}H NMR (200 MHz, (CD$_3$)$_2$CO), δ 0.99 (t, 12H, CH$_2$CH_3, J = 7.1 Hz), 1.3–1.5 (m, 24H, CH_2CH_2CH$_3$), 2.19 (m, 8H, CHCH_2CH$_2$), 4.38 (d, 4H, inward-turned Hi of OCH_2O, J = 7.2 Hz), 4.69 (t, 4H, CHCH$_2$, J – 2.9 Hz), 5.80 (d, 4H, outward-turned Ho of OCH_2O, J = 7.3 Hz), 7.04 (s, 4H, ArH), 7.86 (s, 4H, OH). Anal. Calcd for C$_{52}$H$_{64}$O$_{11}$: C, 70.89; H, 7.32. Found: C, 71.01; H, 7.30.

1,21,23,25-Tetrapentyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin-7,11,15,28-tetrakis(propargyloxy-, Stereoisomer (13). Procedure A. A mixture of 600 mL of acetone, 5 g of tetrol **10** (6 mmol), 10 g of K_2CO_3 (72.4 mmol), and 10 mL of 80% propargyl bromide in toluene (88 mmol) was heated to reflux for 20 h. The solvent was evaporated under reduced pressure. That part of the solid residue soluble in CH_2Cl_2 was filtered and chromatographed on 300 mL of silica gel with a CH_2Cl_2–20% EtOAc/CH_2Cl_2 gradient as the mobile phase. The eluted product was dried at 10^{-2} Torr to give 4.2 g (68%) of **13**, mp 229 °C, after recrystallization from EtOH: MS (FAB$^+$, NOBA) m/e 1032 (M + H$^+$, 100); ^{1}H NMR, δ 0.92 (t, 12H, CH$_2$CH_3, J = 6.5 Hz), 1.3–1.5 (m, 24H, CH_2-CH_2CH$_2$CH$_3$), 2.18 (m, 8H, CHCH_2CH$_2$), 2.46 (t, 4H, C≡CH, J = 2.4 Hz), 4.39 (d, 4H, Hi of OCH_2O, J = 7.2 Hz), 4.60 (d, 8H, OCH_2C≡C, J = 2.4 Hz), 4.71 (t, 4H, CHCH$_2$, J = 7.6), 5.89 (d, 4H, Ho of OCH_2O, J = 7.2 Hz), 6.81 (s, 4H, Ho of OCH_2O, J = 7.2 Hz). Anal. Calcd for C$_{64}$H$_{72}$O$_{12}$: C, 74.39; H, 7.02. Found: C, 74.03; H, 7.15.

36,51-(Epoxy[2,4]hexadiynoxy)-22,26:61,65-dimethano-2,56:19,31-dimetheno-3,55,18,32-(methynoxy[2,4]hexadiynoxymethyno)-1*H*,20*H*,28*H*,30*H*,57*H*,59*H*-bis[1,3]benzodioxocino[9,8-*d*:9′,8′-*d*′]bis[1,3]benzodioxocino[9′,10′:19,20;10″,9‴:29,30][1,3,6,13,16,18,21,28]octaoxacyclotriacontino[4,5-*j*:15,14-*j*′]bis[1,3]benzodioxocin, 9,10,11,12,42,43,44,45-Octadehydro-8,13,41,46-tetrahydro-1,20,28,30,57,59,67,88-octapentyl-, Stereoisomer (1). Procedure B. To a mixture of 200 mL of dry pure pyridine, stirred at 60 °C, containing 10 g of Cu(OAc)$_2$ (55 mmol) through which O_2 was bubbled was added 2.5 g (2.5 mmol) of solid tetraacetylene **13** over 5 min. The reaction mixture was stirred an additional 10 min at 60 °C and then poured into 500 mL of water. The white solid that separated was filtered, washed, and air dried. This material was dissolved in a minimum amount of CH_2Cl_2 and chromatographed on 600 mL of silica gel (initially dry column) with CH_2Cl_2 as the mobile phase to provide after drying at 10^{-2} Torr 0.107 g (8%) of host **1**, mp 240

°C dec: MS (FAB$^+$, NOBA) m/e 2059 (M + H$^+$, 100); ^{1}H NMR δ 0.91 (t, 24H, CH_2CH_3, J = 6.8 Hz), 1.3–1.5 (m, 48 H, $CH_2CH_2CH_2CH_3$), 2.15 (m, 16H, $CHCH_2$), 4.43 (d, 8H, *Hi* of OCH_2O, J = 7.6 Hz), 4.68 (t, 8H, $CHCH_2$, J = 7.9 Hz), 4.74 (s, 16H, $CH_2C{\equiv}C$), 5.94 (d, 8H, *Ho* of OCH_2O, J = 7.6 Hz), 6.77 (s, 8H, Ar*H*); R_f 0.59 ($CHCl_3$, silica gel). Anal. Calcd for $C_{128}H_{136}O_{24}$: C, 74.66; H, 6.66. Found: C, 74.55; H, 6.50.

36,51-(Epoxy[2,4]hexadiynoxy)-22,26:61,65-dimethano-2,56:19,31-dimetheno-3,55,18,32-(methynoxy[2,4]hexadiynoxymethyno)-1*H*,20*H*,28*H*,30*H*,57*H*,59*H*-bis[1,3]benzodioxocino[9,8-*d*:9′,8′-*d*′]bis[1,3]benzodioxocino[9′,10′:19,20;10″,9‴:29,30][1,3,6,13,16,18,21,28]octaoxacyclotriacontino[4,5-*j*:15,14-*j*′]bis[1,3]benzodioxocin, 9,10,11,12,42,43,44,45-Octadehydro-8,13,41,46-tetrahydro-1,20,28,30,57,59,67,88-octakis(2-phenylethyl)-, Stereoisomer (2). Application of procedure A to tetrol **9** on a 4.9-g (4.8-mmol) scale produced the tetrapropargyloxy compound **12** (4.4 g, 78%) which after purification by chromatography but without characterization was converted on a 2.9-mmol- of-**12** scale by procedure B to host **2** (0.330 g, 5%): MS (FAB$^+$, NOBA) m/e 2331 (M$^+$ + 1, 100); ^{1}H NMR δ 2.45–2.49 (m, 16H, CH_2CH_2), 2.64–2.67 (m, 16H, CH_2CH_2), 4.50 (d, 8H, *Hi* of OCH_2O, J = 7.2 Hz), 4.78 (s, 16H, $CH_2C{\equiv}C$), 4.81 (t, 8H, $CHCH_2$, J = 7.8 Hz), 5.98 (d, 8H, *Ho* of OCH_2O, J = 7.2 Hz), 6.83 (s, 8H, Ar*H*), 7.13–7.24 (m, 40H, ArH of C_6H_5); R_f 0.20 ($CHCl_3$, silica gel). Anal. Calcd for $C_{152}H_{120}O_{24}$: C, 78.33; H, 5.19. Found: C, 78.09; H, 5.24.

36,51-(Epoxyhexanoxy)-22,26:61,65-dimethano-2,56:19,31-dimetheno-3,55,18,32-(methynoxyhexanoxymethyno)-1*H*,20*H*,28*H*,30*H*,57*H*,59*H*-bis[1,3]benzodioxocino[9,8-*d*:9′,8′-*d*′]bis[1,3]benzodioxocino[9′,10′:19,20;10″,9‴:29,30][1,3,6,13,16,18,21,28]octaoxacyclotriacontino[4,5-*j*:15,14-*j*′]bis[1,3]benzodioxocin, 8,9,10,11,12,13,41,42,43,44,45,46-Dodecahydro-1,20,28,30,57,59,67,88-octapentyl-, Stereoisomer (3). A mixture of 80 mg (0.040 mmol) of **1**, 150 mL of benzene, and 100 mg of 10% P–C was shaken in a Parr hydrogenation apparatus under a hydrogen pressure of 10 psi for 4 h. The mixture was filtered through Celite and the solvent evaporated under vacuum. The residue was dissolved in 5 mL of CH_2Cl_2, and the resulting solution was added dropwise to 20 mL of pentane. The white solid that separated was collected and air dried to give 75 mg (91%) of **3**, mp > 280 °C: MS (FAB$^+$, NOBA) m/e 2091 (M + H$^+$, 100); ^{1}H NMR δ 0.91 (t, 24H, CH_2CH_3, J = 6.8 Hz), 1.3–1.5 (m, 48H, $CH_2CH_2CH_2CH_3$), 1.41 (m, 16H, $OCH_2CH_2CH_2$), 1.67 (m, 16H, OCH_2CH_2), 2.16 (m, 16H, $CHCH_2$), 3.90 (t, 16H, OCH_2CH_2, J = 5.5 Hz), 4.33 (d, 8H, *Hi* of OCH_2O, J = 7.2 Hz), 4.68 (t, 8H, $CHCH_2$, J = 7.8 Hz), 5.74 (d, 8H, *Ho* of OCH_2O, J = 7.2 Hz), 6.74 (s, 8H, Ar*H*); R_f 0.25 ($CHCl_3$, silica gel). Anal. Calcd for $C_{128}H_{168}O_{24}{\cdot}CH_2Cl_2$: C, 71.22; H, 7.88. Found: C, 70.85; H, 7.70.

Complexes of 1. All complexations–decomplexations were carried out in an argon atmosphere. Table I records the structures and the labels of the guests, the solvent, the time, the temperature, the percent complexed, and the half-lives for the decomplexations in $CDCl_3$ at 25 °C. In each complexation, 10 mg of host dissolved in 2 mL of either neat guest or pure 1,3,5-tri-*tert*-butylbenzene in the presence of the following specified molar excesses of guest were heated to the specified times and temperatures. The solvent was removed by distillation–sublimation at low pressure. The resulting residue was added to 10 mL of CH_3OH, and the precipitate was filtered, washed, and air dried and its ^{1}H NMR spectrum in $CDCl_3$ taken at 25 °C. In a separate experiment, the ^{1}H NMR of the pure guest was taken under the same conditions. The amounts of complexed vs uncomplexed host were determined by integrations of ^{1}H NMR signals of free host and complexed guest. Relevant ^{1}H NMR spectral peak changes upon complexation are listed for each of the guests and the host.

Guest A. The guest was used as the solvent: free guest ^{1}H NMR δ 1.33 (t, 9H, CH_3, J = 7.5 Hz), 2.70 (q, 6H, CH_2, J = 7.5 Hz), 6.96 (s, 3H, Ar*H*); $\Delta\delta$ guest signals in the complex, CH_3 –1.33, Ar*H* –0.41; $\Delta\delta$ host signals in the complex, *Hi* –0.07, $CHCH_2$ 0.00, OCH_2 0.11, *Ho* –0.08, Ar*H* –0.01; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 2.0 × 10^{-7} s^{-1}.

Guest B. The guest was used as the solvent. The complex was purified by thick-layer chromatography on silica gel–$CHCl_3$: free guest ^{1}H NMR δ 1.35 (d, 18H, CH_3, J = 6.9 Hz), 2.97 (sp, 3H, $CH(CH_3)_2$, J = 6.9 Hz), 7.01 (s, 3H, Ar*H*); $\Delta\delta$ guest signals in the complex, CH_3 –0.73, $(CH_3)_2CH$ –0.64, Ar*H* –0.29; $\Delta\delta$ host signals in the purified complex, *Hi* –0.04, $CHCH_2$ –0.01, OCH_2 –0.07, *Ho* 0.01, Ar*H* 0.01; MS of the complex (FAB$^+$, NOBA) m/e 2263 (80, complex), 2059 (100, free host); partial decomplexations of hemicarceplexes while getting them into the gas phase is typical;[4-6] decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 1.2 × 10^{-7} s^{-1}. Anal. Calcd for $C_{143}H_{160}O_{24}$: C, 75.90; H, 7.13. Found: C, 75.92; H, 7.20.

Guest C. The guest was used as the solvent: free guest ^{1}H NMR δ 0.78 (s, 6H, CH_3), 1.16 (s, 2H, $(CH_3C)_2CH_2$), 1.30–1.45 (m, 8H, CH_2), 1.55 (s, 2H, C_3CH), 1.98 (t, 2H, CH_2 remote from methyls, J = 2.7 Hz); $\Delta\delta$ guest signals in the complex, CH_3 –1.12, $(CH_3C)_2CH_2$ –0.65, CH_3CCH_2CH –0.70, C_3CH –0.75, CH_2 remote from methyls is under host peaks; $\Delta\delta$ host signals in the complex, *Hi* –0.19, CH_2CH 0.00, OCH_2 –0.11, *Ho* –0.01, Ar*H* 0.02; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 1.4 × 10^{-5} s^{-1}.

Guest D. TTB was the solvent, 48 molar excess of the guest,[11a] much insoluble: free guest ^{1}H NMR δ 3.09 (s, 8H, CH_2), 6.49 (s, 8H, Ar*H*); $\Delta\delta$ guest signals in the complex, CH_2 –1.24, Ar*H* –0.43; $\Delta\delta$ host signals in the complex, *Hi* –0.13, CH_2CH 0.00, OCH_2 –0.08, *Ho* 0.03, Ar*H* –0.01; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 3.8 × 10^{-5} s^{-1}.

Guest E. TTB as the solvent, 18 molar excess of the guest:[11a] free guest ^{1}H NMR δ 2.03–2.14 (m, 2H, $CH_2CH_2CH_2$), 2.68–2.74 (m, 4H, $CH_2CH_2CH_2$), 2.98 (s, 4H, CH_2CH_2), 6.38 (d, 4H, Ar*H*, J = 7.9 Hz), 6.57 (d, 4H, Ar*H*, J = 7.9 Hz); $\Delta\delta$ guest signals in the complex, $CH_2CH_2CH_2$ –0.92, $CH_2CH_2CH_2$ –0.72, CH_2CH_2 –1.05, Ar*H* –0.56; $\Delta\delta$ host signals in the complex, *Hi* –0.17, CH_2CH 0.00, OCH_2 –0.08, *Ho* –0.06, Ar*H* 0.02; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 3.8 × 10^{-4} s^{-1}.

Guest F. TBB as the solvent, 27 molar excess of the guest:[11b] free guest ^{1}H NMR δ 2.01–2.13 (m, 4H, $CH_2CH_2CH_2$), 2.69–2.75 (m, 8H, $CH_2CH_2CH_2$), 6.69 (s, 8H, Ar*H*); $\Delta\delta$ guest signals in the complex, $CH_2CH_2CH_2$ signals hidden behind guest signals, $CH_2CH_2CH_2$ –0.38, Ar*H* –0.82; $\Delta\delta$ host signals in the complex, *Hi* –0.33, CH_2CH –0.02, OCH_2 –0.10, *Ho* –0.12, Ar*H* 0.03; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 1.5 × 10^{-5} s^{-1}.

Guest G. TBB as the solvent, 7 molar excess of the guest:[11c] free guest ^{1}H NMR δ 3.04 (s, 8H, CH_2CH_2), 6.41 and 6.49 (AB system, 8H, Ar*H*, J = 8.1 Hz), 7.25 (s, 2H, $CH{=}CH$); $\Delta\delta$ guest signals in the complex, CH_2CH_2 –1.93, Ar*H* –0.39, $CH{=}CH$ –2.74; $\Delta\delta$ host signals in the complex, *Hi* 0.02, CH_2CH 0.07, OCH_2 –0.12, *Ho* 0.02, Ar*H* 0.03; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 2.4 × 10^{-5} s^{-1}.

Guest H. TBB as the solvent, 9 molar excess of the guest:[11c] free guest ^{1}H NMR δ 6.50 (s, 8H, Ar*H*), 7.19 (s, 4H, $CH{=}CH$); $\Delta\delta$ guest signals in the complex, Ar*H* –0.39, $CH{=}CH$, –2.68; $\Delta\delta$ host signals in the complex, *Hi* 0.07, CH_2CH 0.08, OCH_2 –0.13, *Ho* 0.01, Ar*H* 0.5; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 1.8 × 10^{-5} s^{-1}.

Guest J. TBB as the solvent, 9 molar excess of the guest:[11d] free guest ^{1}H NMR δ 1.10 (t, 3H, CH_3, J = 7.6 Hz), 2.26–2.37 (m, 1H, CH_2CH_3), 2.57–2.86 (m, 2H, CH_2CH_2), 3.00–3.07 (m, 6H, CH_2CH_2), 3.29–3.41 (m, 1H, CH_2CH_3), 6.15 (s, 1H, Ar*H*), 6.38–6.55 (m, 5H, Ar*H*), 6.66 and 6.70 (dd, 1H, Ar*H*, J = 1.7 Hz); $\Delta\delta$ guest signal in the complex, only one assignable, CH_3 –2.97; $\Delta\delta$ host signals in the complex, *Hi* –0.25, CH_2CH 0.00, OCH_2, –0.13, *Ho* –0.07, Ar*H* 0.00; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 8.9 × 10^{-7} s^{-1}.

Guest K. TBB as the solvent, 6 molar excess of the guest:[11e] free guest ^{1}H NMR δ 2.24–2.38 (m, 2H, CH_2CH_2), 2.98–3.30 (m, 6H, CH_2CH_2), 5.82 (s, 2H, Ar*H*), 6.73 and 6.85 (AB, 4H, Ar*H*, J = 23.2, 7.8 Hz); $\Delta\delta$ guest signals in the complex, CH_2-quinone –0.60, CH_2-quinone –1.25, CH_2Ar –1.18, $CH{=}C$ –0.45, Ar*H* –0.54, Ar*H* –0.57; $\Delta\delta$ host signals in the complex, *Hi* –0.16, CH_2CH –0.04, OCH_2 –0.08, *Ho* 0.02, Ar*H* 0.05; decompexation rate constant estimate in $CDCl_3$ at 25 °C, 8.0 × 10^{-6} s^{-1}.

Guest L. TBB as the solvent, 6 molar excess of the guest:[11e] free guest ^{1}H NMR δ 3.88 (s, 4H, CH_2), 6.69 (s, 4H, Ar*H*), 6.80 (s, 4H, Ar*H*); $\Delta\delta$ guest signals in the complex, CH_2 –1.01, Ar*H* –0.39, Ar*H* –0.47; $\Delta\delta$ host signals in the complex, *Hi* –0.16, CH_2CH 0.00, OCH_2 –0.07, *Ho* 0.02, Ar*H* –0.02; decomplexation rate constant estimate in $CDCl_3$ at 25 °C, 1.9 × 10^{-4} s^{-1}.

Guest M. TBB as the solvent, 4 molar excess of the guest:[11e] free guest ^{1}H NMR δ 2.84–2.97 (m, 2H, CH), 3.61 and 3.68 (dt, 2H, CH_2, J = 8.8, 13.7 Hz), 5.27–5.39 (m, 2H, CH), 6.41 (s, 4H, Ar*H*), 6.45–6.62 (m, 2H, Ar*H*), 6.71 (d, 1H, Ar*H*, J = 8.0 Hz), 6.94 (t, 2H, Ar*H*, J = 8.2 Hz); $\Delta\delta$ guest identifiable signal in the complex, $CHOH$ –0.27; $\Delta\delta$ host signals in the complex, *Hi* –0.35, CH_2H –0.07, OCH_2 –0.09, *Ho* 0.05, Ar*H* –0.13; decomplexation rate constant estimate, 4.8 × 10^{-5} s^{-1}.