Conclusion. These results indicate that the significant decrease in the Brønsted slope β that was observed[2] for catalysis of C(2)-T → D exchange by alkoxide ions and lyoxide ion as the proton-transfer reaction approaches $\Delta pK = 0$ can be explained as (1) a partial change in rate-limiting step, from diffusional separation of the products to proton abstraction by OL^-, (2) a change in transition-state structure with increasing acidity of the C(2) ylide and basicity of the catalyzing base, and (3) a requirement for the removal of water from HO^- and DO^- before reaction. The pK_a values for thiazolium C(2) ylides in the range 17-19 and the small barrier for proton transfer show that the lifetime of the carbanions in aqueous solution is very short.[3] However, the demonstration of internal return in C(2)-hydron exchange proves that the lifetime of thiazolium C(2) ylides is significant. The results provide additional evidence that thiazolium ions undergo proton loss with a small intrinsic barrier and that they are the most normal carbon acids yet identified.[2,3]

Supplementary Material Available: Equations for calculating the propagated error in the calculated values of the Swain-Schaad exponent (y), the extent of internal return (k_{-1}^H/k_2), the primary isotope effect for proton transfer (k_1^H/k_1^T), and the amount of O-T bond formation in the rate-limiting transition state for catalysis of C(2)-T → D exchange by deuterioxide ion (β) (2 pages). Ordering information is given on any current masthead page.

(63) For viscosity at 25 °C, see: Stokes, R. H.; Mills, R. *Viscosity of Electrolytes and Related Properties*; Pergamon Press: New York, 1965; pp 118-123.

Anthraquinone-Based Cyclophane Hosts: Synthesis and Complexation Studies

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Abstract: Synthesis, molecular modeling, and complexation studies of the title compound, **1a-c**, are described. In striking contrast with the behavior of related hosts, they are devoid of guest-binding properties. Possible reasons for this are discussed.

Introduction and Rationale

The design of host molecules with a high specificity for guest molecules is of some current interest.[1-4] We have recently shown[1] that the meso and racemic naphthalene cyclophane-based hosts (Figure 1) show some remarkable properties as hosts: (1) Acidic guests are bound in the host's cavity by formation of a hydrogen bond between the guest's acidic site and the pyridine nitrogen. (2) The hosts are *guest specific*, binding acidic phenols (e.g. *p*-nitrophenol (pNP)) which must be unsubstituted on the C2 and C3 carbons. They are moreover specific for phenolic guests; carboxylic acids do not bind. (3) Remarkably high association constants (K_{assoc}) are observed in *nonaqueous media*. For example the meso host-pNP complex has a K_{assoc} in excess of 1.5×10^4 in chloroform. The design concept of a guest-sticky cavity[1] thus relieves one of dependence on hydrophobic effects as a force affecting guest binding.

Given the above results, we were interested in preparing similar host molecules possessing a larger cavity. Three potential hosts **1a-c** (Figure 2) based on anthraquinone cyclophanes were chosen as potential hosts for the following reasons: (1) The larger cavity size should permit binding of larger aromatic guest molecules, e.g. naphthols, with the possibility of increased K_{assoc} values arising from the increase in π-stacking interactions. (2) The anthraquinone building block would permit testing of the idea that the π-acidic quinone would increase the cavity stickiness toward π-basic guests. This was viewed with some trepidation since Shinmyozu et al.[5] found π acid-π base forces ineffective in a vaguely related cyclophane host.

Table I. Comparison of $\Delta\delta$ between the Diastereotopic CH_2N Protons of Meso and *dl* Host Cyclophanes[a]

	$\Delta\delta$, ppm	
	meso	*dl*
1a	0.51	0.18
1b	0.27	0.12
1c	0.18	0.08
9[a]	1.11	0.6

[a] **9** is the naphthalene analogue of **1a**[6] (Figure 3).

Table II. Cyclization Shifts of Cyclophanes **1a-c** and **9**[a]

	$\Delta\delta$, ppm			
	$H_{2,3}$	H_5	H_8	H_7
dl-**1a**	-0.27	-0.14	-0.08	+0.22
dl-**1b**	-0.17	-0.26	-0.01	+0.07
dl-**1c**	-0.18	-0.18	0.0	-0.09
9	-0.14	-0.15	+0.02	+0.39
meso-**1a**	-0.26	+0.04	-0.17	0
meso-**1b**	-0.21	-0.17	-0.14	-0.03
meso-**1c**	-0.19	-0.14	-0.14	-0.06
9	-0.17	+0.01	-0.06	+0.18

[a] δ **1** - δ precyclophane, negative values mean upfield shifts on cyclization.

Results and Discussion

Synthesis. Host **1a**, based on a bis(tosyl-*p*-phenylenediamine) spacing group, was synthesized as shown in Scheme I. Cyclization of the precyclophane **6** ($Cu(OAc)_2$, pyridine, 40 °C) gave, in 35% yield, an impure (1:1) mixture of meso and racemic isomers of

(1) Sheridan, R. E.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7120-7121. Sheridan, R. E.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 4071-4073.
(2) Rebek, J. E. *Science* **1987**, *235*, 1478-1484.
(3) Schuerman, G.; Diederich, F. *Tetrahedron Lett.* **1986**, *27*(36), 4249-4252.
(4) Cram, D. J.; Doxsee, K. M. *J. Org. Chem.* **1986**, *51*(26), 5068-71.
(5) Shinmyozu, T.; Sakai, T.; Uno, E.; Inazu, T. *J. Org. Chem.* **1985**, *50*, 1959-1963.

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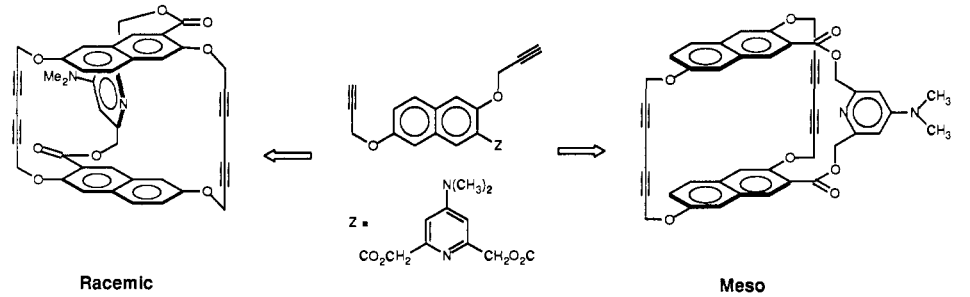


Figure 1.

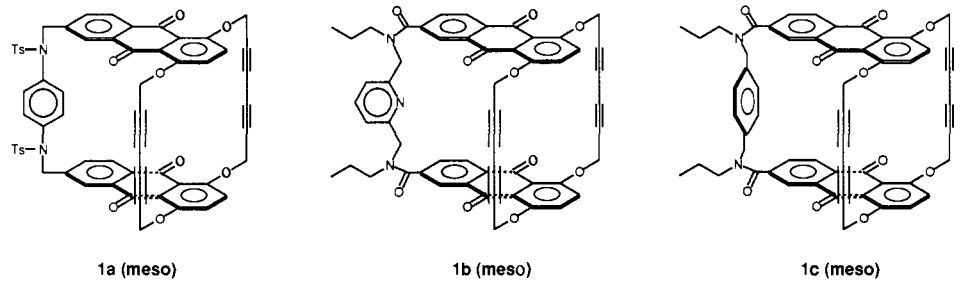
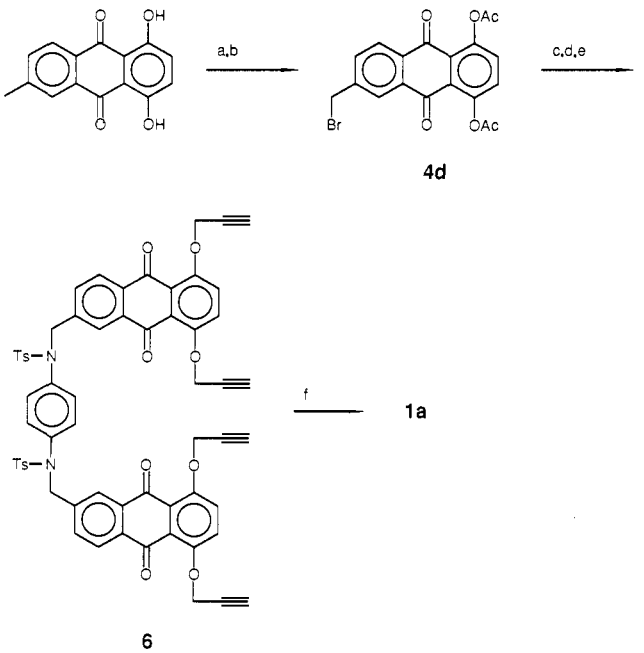


Figure 2.

Scheme I[a]



[a] (a) Ac_2O, pyr; (b) NBS, CCl_4, $h\nu$; (c) $TsNHC_6H_4{\cdot}NHTS$, aqueous NaOH, $Bu_3N^+CH_2C_6H_5Cl^-$; (d) Et_2NH, $CHCl_3$; (e) propargyl bromide, K_2CO_3, acetone, 56 °C; (f) $Cu(OAc)_2$, pyr, 40 °C.

1a. This is common in these cyclophanes,[1,6] as both molecular models and molecular mechanics calculations indicate little steric energy difference between the two diastereoisomeric cyclophanes. Recrystallization of the mixture afforded pure samples of each of the diastereomers.[7] As usual, enantiotopic CH_2 protons, which are singlets in the NMR of precyclophane **6** (CH_2NTs, $ArOCH_2C{\equiv}$), appear as diastereotopic AB quartets in the cyclophanes. To distinguish the isomers, the technique of Miller was used.[6] In the presence of (+)-Eu(hfc)$_3$ the NC_6H_4N protons of the less soluble isomer were split into two singlets. The less soluble isomer is therefore the racemic *dl*-**1a** and the more soluble isomer is *meso*-**1a**.

Synthesis of host **1b**, where the bridging aromatic group is a diamide of 2,6-bis[(propylamino)methyl]pyridine, was carried out in an analogous manner (Scheme II). Cyclization of precyclophane **7** gave a 21% yield of a 1:4 mixture of *meso*-**1b** and *dl*-**1b**, respectively, which were separated by recrystallization.

Similarly, cyclization of precyclophane **8** (Scheme II) afforded an 11% yield of a 5:6 mixture of *dl*-**1c** and *meso*-**1c**. Addition of (+)-Eu(hfc)$_3$ to the minor isomer split its NC_6H_4N protons into two singlets as in the case of **1a**.

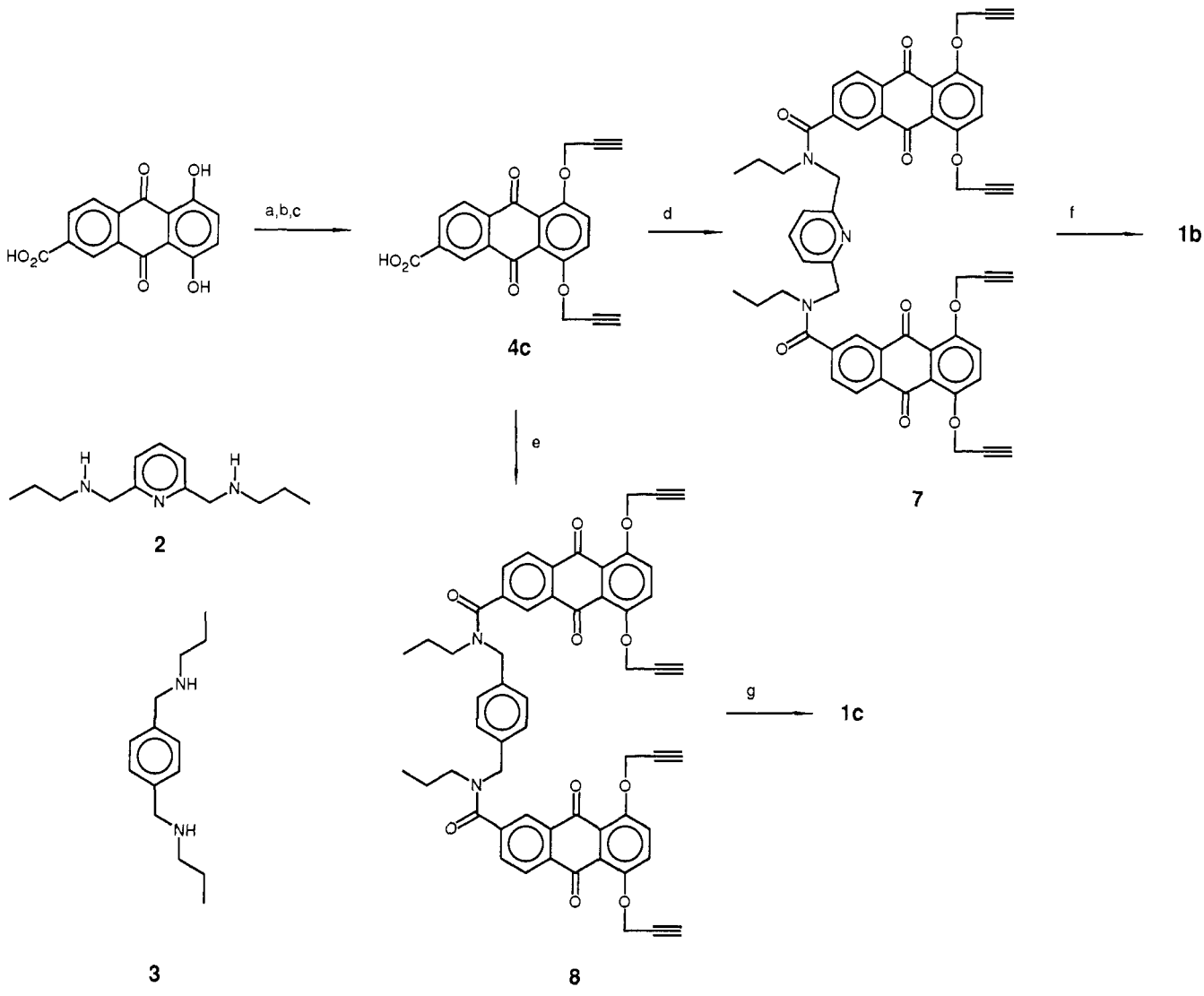
Certain interesting trends are seen on comparing the NMR spectra of **1a–c** and cyclophane **9** (Figure 3), the naphthalene analogue of **1a**.[6] In all cases, the chemical shift difference between the diastereotropic CH_2N protons is greater for the *meso*- than for the *dl*-cyclophanes (Table I). This may be reasonably interpreted to be due to a greater rigidity of the "crisscross" *dl* isomers. Cyclization of the precyclophanes **1a–c** generally results in *upfield* shifts of the aromatic protons' signals (Table II). We interpret this as partial collapse of the cavity in the hosts.

All of these cyclophanes tenaciously retain solvent of recrystallization (see the Experimental Section). While this causes some difficulties in obtaining reproducible elemental analyses, we ascribe this to the large sheetlike shape of these molecules rather than to any interesting intrinsic incavitation behavior. This property seems characteristic of this class of potential hosts and goes back to Stetter and Ross's original work on benzidine related hosts.[17]

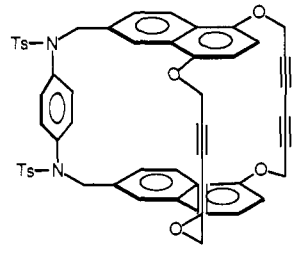
Complexation. Despite the design predictions discussed in the introduction, the complexation behavior of hosts **1a–c** (meso and *dl*) can be described succinctly: they do not complex. The basic experimental protocol as previously described[1,8] involves titration of the host with guest and the use of ^1H NMR to follow the movement of the various protons' signals. The titration curve (δ_{Hx} vs host/guest ratio) is then subjected to nonlinear regression which ejects K_{assoc} and the chemical shift of the proton in question *in the complex*. We emphasize that a third step is also important: visual inspection of the experimental/calculated titration curves to assure that the latter "makes sense". It is our experience that this method works well for this type of π-stacking complex when $200 \lesssim K_{assoc} \lesssim 1.5 \times 10^4$. In several cases UV–visible spectra were used.

(6) Miller, S. P.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 1492–1494.
(7) That the isolated hosts are "monomeric", i.e. have two anthraquinones per molecule, is assumed on the basis of earlier work[1,6] and the isolation of only two diastereomers rather than the four expected for the "dimeric" hosts. We have been unable to get mass spectra on any of the present cyclophanes.
(8) Sheridan, R. E., Ph.D. Thesis, University of Wisconsin, 1988.
(9) Zimmerman, S. C.; VanZyl, C. M. *J. Am. Chem. Soc.* **1987**, *109*, 7894–7896.
(10) MacroModel, Professor C. Still, Columbia University.
(11) Sorm, F.; Sdeivy, L. *Collect. Czech. Chem. Commun.* **1948**, *13*, 288.
(12) Wenner, W. *J. Org. Chem.* **1952**, *17*, 523.

Scheme II[a]



[a](a) MeOH, H_2SO_4, 65 °C; (b) propargyl bromide, K_2CO_3, acetone, 56 °C; (c) LiOH, H_2O, THF; (d) $(COCl)_2$, THF, Et_3N, diamine **2**; (e) Et_3N, ClCOOEt, THF, 0 °C, diamine **3**; (f) $Cu(OAc)_2$, pyr, 40 °C; (g) CuCl, $CuCl_2$, pyr, −5 °C.



9

Figure 3.

Complexation of **1a** (in $CDCl_3$) was studied with benzene, pyridine, and naphthalene as guests. Complexation of **1b**, the host with a pyridine-sticky cavity, was studied with *p*-nitrophenol, *m*-nitrophenol, 2,4-dinitrophenol, β-naphthol, benzoic acid, *p*-nitrobenzoic acid, and *p*-toluenesulfonic acid (HOTs). There was no appreciable upfield movement of the host's protons at up to 2 equiv of guest. In the case of HOTs, the pyridine was protonated but the tosylate was clearly not in the cavity.

Complexation of **1c** was studied with *p*-nitrophenol, tetramethyl-*p*-phenylenediamine, *p*-phenylenediamine, β-methoxynaphthalene, and 2,4,7-trinitrofluorenone as guests. Only the latter (K_{assoc} = 30 M^{-1}) was significantly greater than zero.[9]

Why is K_{assoc} so small? We suggest two possible reasons.

(1) We have shown in several related cases[6,18,19] with benzo- and naphthalenophanes connected by dioxaoctadiyne spacers that the aromatic rings are magnetically isolated from one another. Cyclization shifts, the difference in chemical shifts of aromatic protons before and after cyclization, of cyclophanes **1a–c** are appreciably larger than those found in an earlier series studied by us (Table II), but of course they are much smaller than those found in flexible systems susceptible to intracavity collapse.[17,20] We interpret this as being due to the rigid spacers holding the aromatic faces approximately 9 Å apart, with a cavity of ~4.5 Å. This is, of course, a consequence of the particular structural theme employed and is not to be expected for all cyclophanes. An

(13) Mori, S.; Kitao, T.; Kuroki, N.; Konishi, K. *Chem. Abstr.* **1968**, *69*, 20393.
(14) Mayer, F.; Gunther, H. *Chem. Ber.* **1930**, *63*, 1455.
(15) Stetter, H.; Roos, E.-E. *Chem. Ber.* **1954**, *87*, 566.
(16) O'Krongly, D.; Denmeade, S. R.; Chiang, M. Y.; Breslow, R. *J. Am. Chem. Soc.* **1985**, *107*, 5544.
(17) Stetter, H.; Roos, E. E. *Chem. Ber.* **1955**, *88*, 1390–1395.
(18) Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1983**, *105*, 838–844; **1985**, *107*, 1325–1329.
(19) Jarvi, E. T.; Whitlock, H. W. *J. Am. Chem. Soc.* **1982**, *104*, 7196–7204.
(20) Loncharich, R. J.; Seward, E.; Ferguson, S. B.; Brown, F. K.; Diederich, F.; Houk, K. N. *J. Org. Chem.* **1988**, *53*, 3479–3491.

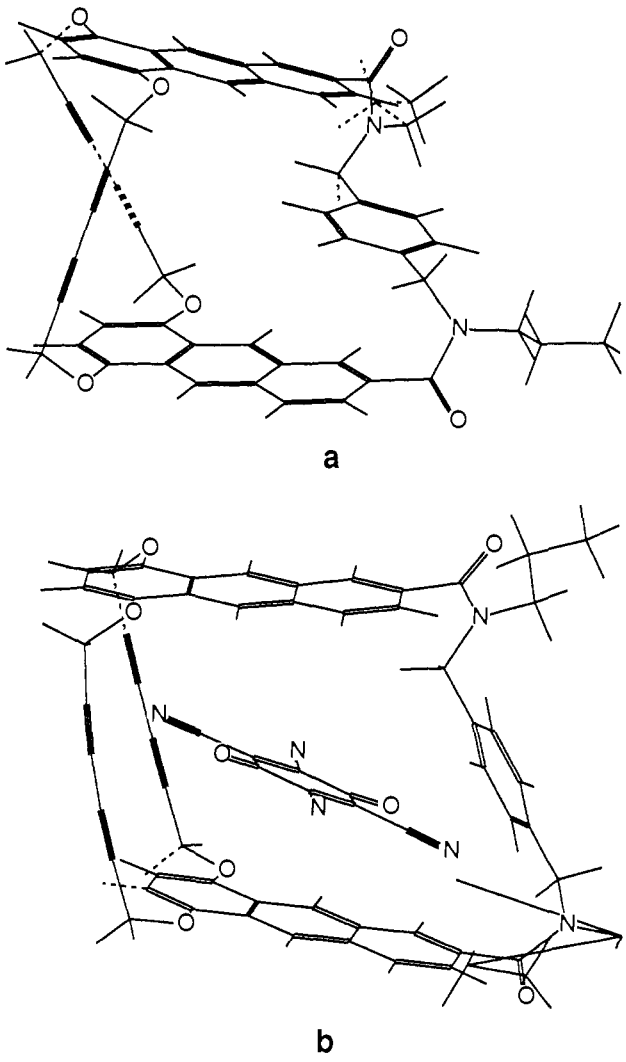


Figure 4.

interesting example to the contrary has been reported recently by Diederich and Houk[20] wherein intracavity collapse[6] occurs, accompanied by upfield shifts of 0.5–1.2 ppm.

The rather substantial upfield shifts on cyclization suggests a considerable diminution in the ring–ring distance in cyclophanes **1a–c**. We have pointed out[6] that a rigidly maintained cavity is a necessary prerequisite for incorporation of guests. Molecular mechanics[10] calculations are consistent with this idea. Figure 4a shows a typical minimized structure of *meso*-**1c** (as anthracene). The bridging phenyl is almost parallel with the anthracenes and the dioxaoctadiyne units are wildly skewed. The result is a dislocation, tipping, and approach of the anthracenes toward to one another, with a partial filling of the cavity by the bridging C_6H_4 unit. The difficulty seems to arise from a combination of proximity between the dioxaoctadienes and the flexibility of the $CONCH_2$ connectors. Figure 4b shows the corresponding TCNQ–intracavity complex.

(2) At the other extreme is the possibility that the cavities are *too* large. Naphthalene hosts having sticky cavities (Figure 1) are remarkably efficient binders ($K_{assoc} \sim 10^4$ M^{-1}) of phenols. The cavities here are *exactly* the right size to accommodate guests. Naphthalenophane **9**, on the other hand,[6] has an appreciably smaller nonsticky cavity and binds guests (e.g. pyridine) much more weakly ($K_{assoc} \sim 10^2$).[21] We thus were surprised at the present results, especially with the concave pyridine host **1b**, since previous results were consistent with the idea that cavity size is important only in the simple steric minimum size sense. A requirement for an exact fit "parking effect" may be extent and unavailable in hosts **1a–c**.

It is possible but unlikely that electronic effects are at the root of this. The anthracene analogues (meso and *dl*, M. E. Haeg, unreported results) also show no complexation ($K_{assoc} < 100$ M^{-1}) behavior. In this respect, the review by Herbstein[22] makes some interesting observations as to the favored positioning of the aromatic rings in charge-transfer complexes. This positioning is observed in the naphthalenophane complexes (Figure 1)[1] and may not be possible in hosts **1a–c**.

Experimental Section

2,6-Bis[(propylamino)methyl]pyridine (2). A mixture containing 2.3 g (16.5 mM) of 2,6-pyridinedimethanol (Aldrich), 30 mL of 48% hydrobromic acid, and 150 mL of acetic anhydride was heated at 100 °C overnight.[11] Upon cooling, crystals formed, which were separated and washed with ethyl acetate to give 5.2 g of 2,6-bis(bromomethyl)pyridine hydrobromide as a colorless solid: mp 205 °C dec; ^{1}H NMR (DMSO-d_6) δ 7.88 (2 H, t, J = 8 Hz), 7.52 (2 H, d, J = 8 Hz), 4.70 (4 H, s).

A solution of the hydrobromide in 200 mL of methanol at −20 °C was treated with 20 mL of *n*-propylamine. Upon standing overnight at 25 °C, the mixture was concentrated to give 8.9 g of colorless solid. A solution of this solid in methanol was converted to diamine **2** by passage through a column of Amberlite 400 (OH^-). After purification via the hydrobromide salt, mp 222–224 °C (MeOH–Et_2O), diamine **2** was obtained in 56% yield: MS, m/e 222.1970 ($C_{13}H_{24}N_3$ (P + 1)); ^{1}H NMR ($CDCl_3$) δ 7.57 (1 H, t, J = 8 Hz), 7.15 (2 H, d, J = 8 Hz), 3.87 (4 H, s), 2.61 (4 H, t, J = 7 Hz), 2.0 (2 H, br s), 1.55 (4 H, sextet, J = 7 Hz), 0.92 (6 H, t, J = 7 Hz); *N,N'*-bis(acetyl), MS, m/e 306.2181 ($C_{17}H_{28}N_3O_2$ (P + 1)); *N,N'*-bis(benzoyl), MS m/e 429.2411 ($C_{27}H_{31}N_3O_2$); ^{1}H NMR δ ($CDCl_3$, 70 °C) 7.63 (1 H, t, J = 8 Hz, H-4), 7.3–7.4 (10 H, m, C_6H_5), 7.16 (2 H, br, H-3,5), 4.7 (4 H, br, $PyCH_2$), 3.36 (4 H, br, CH_2N), 1.6 (4 H, br, CH_2), 0.82 (6 H, br, CH_3).

1,4-Bis[(propylamino)methyl]benzene (3). A mixture containing 11.4 g (43 mmol) of α,α'-dibromo-*p*-xylene[12] in 280 mL of ether, 21 mL (258 mmol) of *n*-propylamine in 170 mL of water, and 27 g of Na_2CO_3 was stirred for 19 h. After workup, the crude oil was distilled to give, in 44% yield, diamine **3**: MS, m/e 220.1943 ($C_{14}H_{24}N_2$); ^{1}H NMR (acetone-d_6) δ 7.27 (4 H, s), 3.72 (4 H, s), 2.54 (4 H, t, J = 7 Hz), 1.48 (4 H, sextet, J = 7 Hz), 0.90 (6 H, t, J = 7 Hz).

6-Carbomethoxy-1,4-dihydroxyanthraquinone (4a). A solution of 8.5 g (30 mM) of 1,4-dihydroxy-6-anthraquinonecarboxylic acid[13] in 250 mL of methanol and 12 mL of sulfuric acid was refluxed for 23 h. The solution was concentrated under reduced pressure and filtered. The resulting solid was recrystallized from benzene to give 4.5 g (51% yield) of the methyl ester (**4a**) as reddish needles: mp 187–189 °C; MS, m/e 298.0463 ($C_{16}H_{10}O_6$); ^{1}H NMR ($CDCl_3$) δ 12.9 (1 H, s), 12.8 (1 H, s), 8.99 (1 H, d, J = 1 Hz), 8.46 (2 H, d, J = 8 Hz), 7.36 (2 H, s), 4.03 (3 H, s).

6-Carbomethoxy-1,4-bis(propargyloxy)anthraquinone (4b). A mixture of 1.7 g (5.7 mmol) of methyl ester **4a**, 8.8 mL (116 mmol) of propargyl bromide, and 8 g of potassium carbonate in 165 mL acetone was refluxed for 18 h. After workup, the product was crystallized from $CHCl_3$–hexane to give 1.7 g (80% yield) of the bis(propargyl ether) (**4b**) as a yellow powder: mp 128–130 °C; MS, m/e 374.0791 ($C_{22}H_{14}O_6$); ^{1}H NMR ($CDCl_3$) δ 8.82 (1 H, d, J = 2 Hz), 8.36 (1 H, dd, J = 8, 2 Hz), 8.24 (1 H, d, J = 8 Hz), 7.55 (2 H, s), 4.98 (4 H, d, J = 2.3 Hz), 3.99 (3 H, s), 2.58 (2 H, t, J = 2.4 Hz).

1,4-Bis(propargyloxy)-6-anthraquinonecarboxylic Acid (4c). A solution of 2.4 g (6.4 mmol) of bis(propargyl) methyl ester **4b** in 52 mL of tetrahydrofuran (THF) and 26 mL of 10% lithium hydroxide was stirred at room temperature for 22 h. The THF was removed under reduced pressure; the residue dissolved was in water and acidified with hydrochloric acid. The resultant solid was dried, giving 2.2 g (96% yield) of the acid **4c** as a yellow-brown powder: mp 210–220 °C dec; MS m/e 360.0627 ($C_{21}H_{12}O_6$); ^{1}H NMR (DMSO-d_6) δ 8.52 (1 H, d, J = 1.3 Hz), 8.29 (1 H, dd, J = 8, 1.7 Hz), 8.11 (1 H, d, J = 8 Hz), 7.66 (2 H, s), 4.96 (4 H, d, J = 2 Hz), 3.63 (2 H, t, J = 2 Hz).

1,4-Diacetoxy-6-(bromomethyl)anthraquinone (4d). A mixture containing 12.1 g (36 mM) of 1,4-diacetoxy-6-methylanthraquinone[14] and 6.1 g (34 mM) of *N*-bromosuccinimide in 300 mL of refluxing carbon tetrachloride was irradiated for 21 h with a 500-W light bulb. The product obtained after workup was crystallized from benzene to give bromide **4d** (47% yield) as a yellow powder: mp 177–178 °C; ^{1}H NMR

(21) The X-ray structure of the **9**–pyridine complex (S. P. Miller, personal communication) shows that the pyridine is only partially inserted into the cavity.

(22) Herbstein, F. H. In *Perspectives in Structural Chemistry*; Dunitz, J. D., Ibers, J. A., Eds.; Wiley: New York, 1971; Vol. 4.

(23) Partial support of this work by the National Science Foundation is acknowledged.

(acetone-d_6) δ 8.29 (1 H, d, J = 1.7 Hz, H-5), 8.15 (1 H, d, J = 8 Hz, H-8), 8.0 (1 H, dd, J = 8.1, 1.8 Hz, H-7), 7.6 (2 H, s, H-2,3), 4.8 (2 H, s, CH_2Br), 2.46 (6 H, s, $OCOCH_3$).

Precyclophane 6. A mixture containing 3.4 g (8.2 mM) of bromide **4d** in 135 mL of CH_2Cl_2, *N,N'-bis*(*p*-tolylsulfonyl)-*p*-phenylenediamine,[15] and 0.44 g of sodium hydroxide in 14 mL of water was stirred under nitrogen for 90 min with 0.2 equiv of tri-*n*-butylbenzylammonium chloride. After workup, crystallization from chloroform–hexane gave 2.1 g (70% yield) of tetraacetate **5** as an orange powder: mp 238–240 °C; ^{1}H NMR ($CDCl_3$) δ 8.1 (2 H, d, J = 8 Hz, H-8), 8.0 (2 H, d, J = 1.5 Hz, H-5), 7.6 (2 H, dd, J = 8, 1.5 Hz, H-7), 7.41 (4 H, s, H-2,3), 7.3 (8 H, AB q, J = 8 Hz, tosyl), 6.85 (4 H, s, C_6H_4), 4.75 (4 H, s, CH_2N), 2.45 and 2.47 (12 H, s, $OCOCH_3$), 2.39 (6 H, s, CH_3).

A suspension of 2.1 g (1.9 mM) of tetraacetate **5** in 50 mL of $CHCl_3$ was stirred for 2 days with 1 mL of diethylamine. The product, isolated as a red solid in 90% yield, was treated without purification with excess propargyl bromide–potassium carbonate in refluxing acetone for 1 day. After workup, the product was chromatographed on silica gel to give 1.0 g (45% yield) of precyclophane **6** as a yellow solid: mp 200 °C dec (CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$) δ 8.1 (2 H, d, J = 8 Hz, H-8), 7.91 (2 H, d, J = 2 Hz, H-5), 7.65 (2 H, dd, J = 8,2 Hz, H-7), 7.49 (4 H, s, H-2,3), 7.29 (8 H, AB q, J = 8 Hz, tosyl), 6.9 (4 H, s, NC_6H_4N), 4.85 (8 H, d, J = 2 Hz, $CH_2C{\equiv}C$), 4.77 (4 H, s, CH_2N), 2.55 (4 H, t, J = 2 Hz, $C{\equiv}CH$), 2.40 (6 H, s, CH_3).

Cyclophane 1a. To a stirred solution containing 3.8 g (14 mM) of cupric acetate in 45 mL of pyridine at 40 °C was added dropwise 1.8 g of precyclophane **6** in 70 mL of pyridine. After 2 h the mixture was treated with cold 6 N HCl and the resulting solid was separated by filtration. After extraction with acetone at 25 °C, 0.72 g of yellow solid was obtained. From the NMR spectrum of this solid, the expected meso and *dl* isomers of **1a**, contaminated with polymeric material, were present in equal amounts. Repeated crystallization from CH_2Cl_2 afforded a pure sample of the less soluble isomer, *dl*-**1a**: dec >220 °C; ^{1}H NMR ($CHCl_3$) δ 8.02 (2 H, d, J = 8 Hz, H-8), 7.87 (2 H, dd, J = 8,1 Hz, H-7), 7.77 (2 H, d, J = 1 Hz, H-5), 7.38 (8 H, AB q, J = 8 Hz, tosyl), 7.22 (4 H, br s, H-2,3), 6.93 (4 H, s, NC_6H_4N), 4.99 (4 H, AB q, J = 17 Hz, $CH_2C{<<}tbdC$), 4.92 (4 H, AB q, J = 17 Hz, $CH_2C{<<}tbdC$), 4.83 (4 H, AB q, J = 16 Hz, CH_2N), 2.48 (6 H, s, CH_3). This isomer was identified as *dl*-**1b** since two singlets, δ 6.96 and 7.00, were observed for the protons (NC_6H_4N) of the diamide bridge in the presence of (+)-Eu(hfc)$_3$. Anal. Calcd for $C_{62}H_{40}N_2S_2O_{12}{\cdot}CH_2Cl_2$: C, 65.56; H, 3.67. Found: C, 66.01; H, 3.72. From the mother liquors, the more soluble isomer, *meso*-**1a**, dec >190 °C, was isolated: ^{1}H NMR ($CDCl_3$) δ 7.93 (2 H, s, H-5), 7.92 (2 H, d, J = 8 Hz, H-8), 7.65 (2 H, dd, J = 8,1 Hz, H-7), 7.37 (4 H, AB q, J = 8 Hz, tosyl), 7.21 (4 H, s, H-2,3), 7.00 (4 H, s, NC_6H_4N), 4.98 (4 H, AB q, J = 17 Hz, $CH_2C{\equiv}C$), 4.97 (4 H, AB q, J = 17 Hz, $CH_2C{\equiv}C$), 4.87 (4 H, AB q, J = 16 Hz, CH_2N), 2.51 (6 H, s, CH_3). Anal. Calcd for $C_{62}H_{40}N_2S_2O_{12}{\cdot}CH_2Cl_2$: C, 65.56; H, 3.67. Found: C, 66.01; H, 3.57.

Precyclophane 7. To a suspension of 1.5 g (4.17 mM) of 1,4-bis(propargyloxy)-6-anthraquinonecarboxylic acid (**4c**) in 50 mL of dry tetrahydrofuran was added dropwise 1.6 mL (19 mM) of oxalyl chloride. After stirring of the mixture for 2 h, a clear solution resulted. Concentration of this solution at reduced pressure gave the acid chloride of **4c** as a light orange solid. To a solution of the chloride in THF was added 0.9 mL (6.4 mM) of triethylamine, followed by the addition of 0.44 g (2.0 mM) of diamine **2** in 2 mL of methylene chloride. After stirring of the mixture for 18 h, the solvents were separated, and the residue was extracted with $CHCl_3$ to give 1.7 g of brown solid. Chromatography on silica gel gave, upon elution with 3% methanol in chloroform, 1.2 g (64% yield) of precyclophane **7**: IR ($CHCl_3$) 3300, 1670, 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 °C) δ 8.20 (2 H, br s, H-5), 8.16 (2 H, d, J = 8 Hz, H-8), 7.75 (2 H, dd, J = 8, 1.5 Hz, H-7), 7.67 (1 H, t, J = 8 Hz, H-4′), 7.48 (4 H, s, H-2,3), 7.23 (2 H, m, H-3′,5′), 4.85 and 4.83 (each 4 H, d, J = 2.4 Hz, $CH_2C{\equiv}C$), 4.75 (4 H, m, $pyCH_2N$), 3.4 (4 H, m, CH_2N), 2.52 (4H, t, J = 2.4 Hz, $C{\equiv}CH$), 1.6 (4 H, m, $CH_2CH_2CH_3$), 0.84 (6 H, m, CH_3).

Hexadecahydro 7. Catalytic hydrogenation of precyclophane **7** (5% Rh on alumina, ethyl acetate) gave hexadecahydro **7** (38% yield) as an orange oil: MS *m/e* 921.4192 ($C_{55}H_{59}N_3O_{10}$); ^{1}H NMR ($CDCl_3$, 80 °C) δ 8.21 (2 H, br s, H-5), 8.16 (2 H, d, J = 8 Hz, H-8), 7.72 and 7.65 (3 H, overlapping dd, J = 8,2 Hz, H-7 and t, J = 8 Hz, H-4′), 7.2 (2 H, m, H-3′,5′), 7.62 (4 H, s, H-2,3), 4.75 (4 H, m, $pyCH_2$), 3.4 (4 H, m), 1.64 (4 H, m) and 0.84 (6 H, m) (*N*-propyl), 4.05 and 4.04 (8 H, t, J = 7 Hz), 1.91 and 1.90 (8 H, sextet, J = 7 Hz) and 1.11 and 1.10 (12 H, t, J = 7 Hz) (*O*-propyl).

Cyclophane 1b. To a solution of 4.8 g (24 mM) of cupric acetate in 76 mL of pyridine at 40 °C was added 1.5 g (1.66 mM) of precyclophane **7** in 76 mL of pyridine. After 2 h, the solvent was distilled at reduced pressure and the solid obtained was extracted with acetone to give 0.6 g of soluble product. Chromatography (silica gel, $CHCl_3$) afforded 317 mg of **1b**, as a 1:4 mixture of meso and *dl* isomers. Crystallization from $CHCl_3$ gave 32 mg (2% yield) of *dl*-**1b**, the less soluble isomer: dec >200 °C; ^{1}H NMR ($CDCl_3$) δ 8.15 (2 H, d, J = 8 Hz, H-8), 7.94 (2 H, br s, H-5), 7.82 (H, dd, J = 8, 1.5 Hz, H-7), 7.64 (1 H, t, J = 8 Hz, H-4′), 7.31 (4 H, s, H-2,3), 6.93 (2 H, d, J = 8 Hz, H-3′,5′), 5.13 and 5.11 (4 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.95 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.72 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.44 (4 H, AB q, J = 17 Hz, $pyCH_2N$), 3.46 (4 H, m, NCH_2), 1.7 (4 H, m, $CH_2CH_2CH_3$), 0.99 (6 H, t, J = 7 Hz, CH_3). Crystallization of the mother liquor from ethyl acetate gave 156 mg (10% yield) of *meso*-**1b**: dec >240 °C; ^{1}H NMR ($CDCl_3$) δ 8.03 (2 H, br s, H-5), 8.015 (2 H, d, J = 8 Hz, H-8), 7.72 (2 H, dd, J = 8, 1.5 Hz, H-7), 7.27 (4 H, s, H-2,3), 7.67 (1 H, t, J = 8 Hz, H-4′), 6.96 (2 H, d, J = 8 Hz, H-3′,5′), 5.15 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 5.11 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.83 (4 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.50 (4 H, AB q, J = 17 Hz, $pyCH_2N$), 3.54 and 3.26 (4 H, m, NCH_2), 1.72 (4 H, sextet, J = 7 Hz, $CH_2CH_2CH_3$), 0.99 (6 H, t, J = 7 Hz, CH_3).

Anal. Calcd for $C_{55}H_{39}N_3O_{10}{\cdot}CH_3COOCH_2CH_3$: C, 71.57; H, 4.79. Found: C, 71.94; H, 4.85.

Precyclophane 8. To a mixture of 554 mg (1.54 mmol) of acid **4c** and 0.21 mL (1 equiv) of triethylamine in 15 mL THF at 0 °C was added dropwise 0.16 mL (1.6 mmol) of ethyl chloroformate. The reaction mixture was stirred at 0 °C for 30 min and then 11 mg (0.52 mmol) of diamine **3** in 3 mL of THF was added. The mixture was allowed to warm to room temperature and stirred for 3 days. After workup, the product was chromatographed to give 43 mg (9% yield) of precyclophane **8** as yellow-orange powder: mp 110–112 °C; ^{1}H NMR (DMSO-d_6, 110 °C) δ 8.10 (2 H, d, J = 8 Hz, H-8), 7.99 (2 H, d, J = 2 Hz, H-5), 7.80 (2 H, dd, J = 8,2 Hz, H-7), 7.62 (4 H, s, H-2,3), 7.29 (4 H, s, C_6H_4), 4.90 (8 H, m, $CH_2C{\equiv}C$), 4.63 (4 H, s, CH_2Ar), 3.32 (4 H, m, $C{\equiv}C$-*H*), 3.27 (4 H, t, J = 7 Hz, CH_2N), 1.56 (4H, sextet, J = 7 Hz, CH_2CH_2CH3), 0.78 (6 H, t, J = 7 Hz, CH_3).

Anal. Calcd for $C_{56}H_{44}N_2O_{10}{\cdot}0.5\ CHCl_3$: C, 70.35; H, 4.65; N, 2.90. Found: C, 70.08; H, 5.20; N, 2.75.

Hexadecahydro 8. Catalytic hydrogenation (5% Rh on alumina, ethyl acetate) of **5** gave hexadecahydro **8**, (48% yield) as an orange powder: mp 98–101 °C; MS, *m/e* 920.4251 ($C_{56}H_{60}N_2O_{10}$); ^{1}H NMR (DMSO-d_6, 126 °C) δ 8.09 (2 H, d, J = 8 Hz, H-8), 7.98 (2 H, d, J = 2 Hz, H-5), 7.77 (2 H, dd, J = 8,2 Hz, H-7), 7.50 (4 H, s, H-2,3), 7.29 (4 H, s, C_6H_4), 4.62 (4 H, s, CH_2Ar), 4.08 (4 H, t, J = 6.3 Hz, OCH_2), 4.07 (4 H, t, J = 6.3 Hz, OCH_2), 3.27 (4 H, t, J = 7.3 Hz, NCH_2), 1.82 (4 H, sextet, J = 6.7 Hz, $OCH_2CH_2CH_3$), 1.81 (4 H, sextet, J = 6.7 Hz, $OCH_2CH_2CH_3$), 1.56 (4 H, sextet, J = 7.5 Hz, $NCH_2CH_2CH_3$), 1.07 (6 H, t, J = 7 Hz, $OCH_2CH_2CH_3$), 1.06 (6 H, t, J = 7 Hz, $OCH_2CH_2CH_3$), 0.78 (6 H, t, J = 7 Hz, $NCH_2CH_2CH_3$).

Cyclophane 1c. A mixture of 0.22 g (0.25 mmol) of precyclophane **8**, 2.41 g (24.3 mmol) of anhydrous CuCl, and 0.45 g (3.32 mmol) of anhydrous $CuCl_2$ in 245 mL of dry, deoxygenated pyridine[16] was kept at −5 °C for 49 h with occasional swirling. The pyridine was evaporated under reduced pressure without heating. The residue was purified by chromatography through a short column (silica gel, 5% MeOH in $CHCl_3$). Anal. Calcd for $C_{56}H_{40}N_2O_{10}{\cdot}0.5CHCl_3$: C, 70.64; H, 4.25; N, 2.92. Found: C, 69.92; H, 4.72; N, 2.76.

Both meso, mp 225–230 °C dec, and *dl* isomers of **1c**, 170–180 °C dec, were isolated as yellow powders in 5% and 6% yield, respectively, by preparative thin-layer chromatography. Identification of the *dl* isomer of **1c** followed from the observation of two singlets (NC_6H_4N) in the presence of (+)-Eu(hfc)$_3$.

meso-**1c**: ^{1}H NMR ($CDCl_3$) δ 8.06 (2 H, s, H-5), 8.02 (2 H, d, J = 8 Hz, H-8), 7.69 (2 H, dd, J = 8, 1.5 Hz, H-7), 7.29 (4 H, s, H-2,3), 6.87 (4 H, s, C_6H_4), 5.16 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 5.10 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.83 (4 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.37 (4 H, AB q, J = 16.6 Hz, CH_2Ar), 3.44 (4 H, m, CH_2N), 1.68 (4 H, sextet, J = 7 Hz, $CH_2CH_2CH_3$), 0.988 (6 H, t, J = 7 Hz, CH_3).

dl-**1c**: ^{1}H NMR ($CDCl_3$) δ 8.16 (2 H, d, J = 8 Hz, H-8), 8.02 (2 H, s, H-5), 7.66 (2 H, d, J = 7 Hz, H-7), 7.30 (4 H, s, H-2,3), 7.02 (4 H, s, C_6H_4), 5.11 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 5.06 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.97 (2 H, J = 17 Hz, $CH_2C{\equiv}C$), 4.66 (2 H, d, J = 17 Hz, $CH_2C{\equiv}C$), 4.32 (4 H, AB q, J = 16.5 Hz, CH_2Ar), 4.09 and 2.79 (4 H, m, CH_2N), 1.70 (4 H, m, $CH_2CH_2CH_3$), 0.98 (6 H, t, J = 7 Hz, CH_3).