(2 H, m), 5.16 (1 H, d, J = 5.6 Hz, HC=C), 4.65 (1 H, d, J = 5.6 Hz, HCO), 3.77–2.0 (8 H, m), 2.10 (3 H, s, OAc), 1.91 (3 H, s, OAc), 0.51 (3 H, t, J = 7.0 Hz, CH_3), 1.23 (9 H, s, $Si(CH_3)_3$); IR (KBr) 1600 (m) (C=C), 1680, 1750 (C=O) cm^{-1}.

4a,8a-Dicarbomethoxynaphthalene-1,4,6(5*H*)-trione (31). 2,3-Dicarbomethoxy-1,4-benzoquinone (**12**) (448 mg, 2 mmol) was suspended in 5 mL of dry THF. Butadiene **7** (390 mg, 2.1 mmol) was added. The mixture was stirred for 0.75 h, after which the solvent was evaporated. The NMR spectrum showed the formation of only **28** (R_1 = Et, R_2 = $SiMe_3$).

The crude product was dissolved in 10 mL of THF and stirred for 15 min after the addition of 1 mL of 0.1 N HCl. The product crystallized upon addition of *n*-hexane. Recrystallization from $CHCl_3$/*n*-hexane led to 440 mg (65%) 4a,8a-dicarbomethoxy-8-ethoxy-4a,7,8,8a-tetrahydronaphthalene-1,4,6(5*H*)-trione: 4a,8a-dicarbomethoxy-8-ethoxy-4a,7,8,8a-tetrahydronaphthalene-1-(2*H*),4(3*H*),6(5*H*)-trione: mp 143–145 °C; ^1H NMR δ 6.90 (1 H, A of AB, J = 10 Hz, HC=C), 6.75 (1 H, B of AB, J = 10 Hz, HC=C), 4.45 (1 H, t, J = 2.6 Hz, H(8)), 3.91 (3 H, s, OCH_3), 3.72 (3 H, s, OCH_3), 3.72 (1 H, dd, J = 16 Hz, J = 2 Hz, H(5a)), 3.72–2.98 (2 H, m, CH_2), 2.82 (1 H, d, J = 16 Hz, H(5e)), 2.72 (1 H, ddd, J = 15 Hz, J = 2 Hz, J = 2.6 Hz, H(7a)), 2.28 (1 H, dd, J = 15 Hz, J = 2.6 Hz, H(7e)), 0.98 (3 H, t, J = 7 Hz, CH_3). Elemental Anal. Found: C, 56.63; H, 5.32. $C_{16}H_{18}O_8$ requires: C, 56.80; H, 5.36. MS, m/e 338 (M), 306, 279, 274, 247, 234, 207, 190, 179, 175, 151, 113, 99, 82, 59, 54.

This product (250 mg, 0.74 mmol) was dissolved in 10 mL of methanol and 0.5 mL of concentrated hydrochloric acid. The mixture was refluxed for 3 h, after which the methanol was evaporated. The residue was dissolved in ethyl acetate and washed with brine. After drying over Na_2SO_4, the solvent was evaporated and the residue crystallized from ether/*n*-hexane leaving 200 mg (93%) of **31**: mp 127–129 °C; ^1H NMR δ 6.90 (1 H, A of AB, J = 10 Hz, HC=CH), 6.87 (1 H, d, J = 10 Hz, H(7)), 6.75 (1 H, B of AB, J = 10 Hz, HC=C), 6.12 (1 H, d, J = 10 Hz, H(8)), 3.85 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 3.49 (1 H, d, J = 17.5 Hz, H(5)), 2.81 (1 H, d, J = 17.5 Hz, H(5)). Elemental Anal. Found: C, 57.03; H, 4.32. $C_{14}H_{12}O_7$ requires: C, 57.54; H, 4.14. MS, m/e 292 (M), 261, 233, 205, 179, 151, 113, 82, 59, 54.

2,3-Dicarbomethoxy-1,4,6-trihydroxynaphthalene (30). 2,3-Dicarbomethoxy-1,4-benzoquinone (**12**) (440 mg, 2 mmol) was suspended in 5 mL of dry THF. Butadiene **11** (357 mg, 2.1 mmol) was added and the mixture was stirred at room temperature for 16 h, after which the solvent was evaporated. The residue was dissolved in 10 mL of concentrated HCl and refluxed for 1.5 h. The solvent was evaporated. The residue was dissolved in $CHCl_3$ and crystallized upon addition of *n*-hexane, yielding 280 mg (48%) of **30**: mp 174–177 °C (from ether); ^1H NMR δ 10.51 (1 H, s, ArOH), 10.20 (1 H, s, ArOH), 8.46 (1 H, d, J = 9.0 Hz, H(8)), 8.20 (1 H, d, J = 2.3 Hz, H(5)), 7.73 (1 H, dd, J = 9.0 Hz, J = 2.3 Hz, H(7)), 4.04 (6 H, s, OCH_3), 2.91 (1 H, bs, OH(6)). Elemental Anal.: C, 57.52; H, 4.28. $C_{14}H_{12}O_7$ requires: C, 57.54; H, 4.14. MS, m/e 292 (M), 260, 228, 200, 174, 144, 120, 89.

2,3-Dicarbomethoxy-6-acetoxy-1,4-dihydroxynaphthalene (29, R_2 = Ac). 2,3-Dicarbomethoxy-1,4-benzoquinone (**12**) (448 mg, 2 mmol) was mixed with butadiene **10** (357 mg, 2.1 mmol) in 5 mL of dry THF. The mixture was stirred for 16 h at room temperature, after which 5 mL of THF and 1 mL of 0.1 N HCl was added. The mixture was stirred for 15 min and evaporated. The residue was crystallized from $CHCl_3$/*n*-hexane, yielding 300 mg (45%) of the pure product: mp 96–98 °C; ^1H NMR δ 10.41 (1 H, s, ArOH), 10.22 (1 H, s, ArOH), 8.37 (1 H, d, J = 8.8 Hz, H(8)), 8.05 (1 H, d, J = 2.4 Hz, H(5)), 7.75 (1 H, dd, J = 2.4 Hz, J = 8.8 Hz, H(7)), 3.92 (6 H, s, OCH_3), 2.37 (3 H, s, OAc). Elemental Anal.: C 57.31; H, 4.24. $C_{16}H_{14}O_8$ requires: C, 57.49; H, 4.22. MS, m/e 334 (M), 302, 260, 228, 200, 174, 173, 119, 89.

Site Selectivity in Reactions of Butadienes with Benzoquinone 12, a Standard Procedure. The butadiene (2.0 mmol) was added to a suspension of dicarbomethoxy-1,4-benzoquinone **12** (448 mg, 2.0 mmol) in 5 mL of THF. The mixture was stirred at room temperature for 16 h. The solvent was evaporated and an NMR spectrum was taken from the residue. The percentage of **28** was evaluated as indicated in the text.

The residue was dissolved in 10 mL of methanol and 0.5 mL of concentrated hydrochloric acid and refluxed for 3 h. The solvent was evaporated leaving a mixture of products **29**, **30**, and **31**. The percentage of **31** was determined from the NMR spectrum as indicated in the text.

Acknowledgment. We are grateful to the Netherlands Cancer Foundation (Koningin Wilhelmina Fonds) for financial support of this research. We thank Professor R. J. F. Nivard for discussing the work and N. L. Agarwal for some valuable contributions.

Registry No. 1, 1709-63-3; 4, 95725-17-0; 7, 84302-38-5; 8, 83352-53-8; 9, 83352-55-0; 10, 95725-18-1; 11, 95725-19-2; 12, 77220-15-6; 13, 63401-20-7; 15, 13945-19-2; 16, 95725-20-5; 17, 95725-21-6; 18, 95783-37-2; 19, 95725-22-7; 20, 95725-23-8; 21, 95783-38-3; 22, 95725-24-9; 23, 95725-25-0; 24, 95725-26-1; 25, 95725-27-2; 26, 66314-42-9; 28 (R_1 = Et, R_2 = TMS), 95725-28-3; 29 (R_2 = Ac), 95725-29-4; 30, 95725-30-7; 31, 95725-31-8; 4a,8a-dicarbomethoxy-8-ethoxy-4a,7,8,8a-tetrahydronaphthalene-1,4,6(5*H*)-trione, 95725-32-9; sodium acetoacetaldehyde, 926-59-0; isopropenyl acetate, 108-22-5.

Syntheses and Inclusion Behavior of 5,8,14,17,23,26,32,35-Octamethoxy[3.3.3.3]paracyclophane and [3.3.3.3](2,5)-*p*-Benzoquinonophane

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Syntheses of 5,8,14,17,23,26,32,35-octamethoxy[3.3.3.3]paracyclophane (**1**)[1] having a π-electron-rich cavity and [3.3.3.3](2,5)-*p*-benzoquinonophane (**2**) having a π-electron-poor cavity are described, and the inclusion behaviors of these hosts are discussed. In principle, a host molecule having a π-electron-rich cavity may include π-electron-poor molecules and vice versa. Unexpectedly, neither π-electron-poor *p*-benzoquinone nor organic solvents were included in the π-electron-rich cavity of **1**. Although the π-electron-poor host **2** did not include π-electron-rich molecules such as hydroquinone and hydroquinone dimethyl ether, **2** was found to retain dioxane or CH_2Cl_2 in a 1:1 (host–guest) ratio, respectively. These results indicate that charge-transfer interaction does not play an important role in the formation of intracavity inclusion complexes between [3.3.3.3]cyclophane host molecules and neutral organic molecules.

Since Stetter's proposal[2] of the concept that cyclophane host molecules and uncharged organic molecules could form "intracavity inclusion complexes",[3] a few examples of the intracavity inclusion in the crystalline state have

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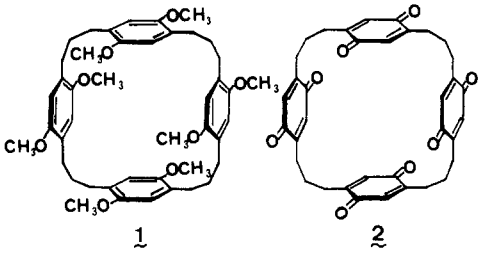
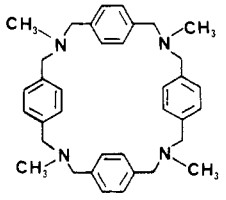
been reported so far.[4] The first example of a crystalline complex of water soluble 1,6,20,25-tetraaza[6.1.6.1]paracyclophane with a hydrophobic substrate, durene, was reported by Odashima and Koga[4c] in 1980. They clearly demonstrated that the guest molecule was fully included in the cavity of the host molecule by X-ray structure analysis. In this case hydrophobic interaction may play an important role.



1 2

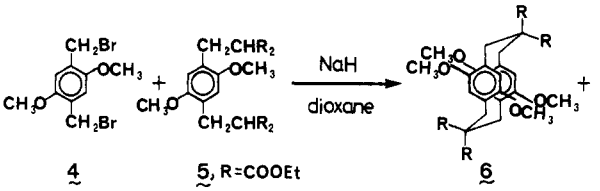
Two years later, Barrett et al.[4d] reported the second example. They performed X-ray structure analysis of *N,N',N'',N'''*-tetramethyl-2,11,20,29-tetraaza[3⁴]PC (**3**)–dioxane (1:1) complex and confirmed that dioxane was actually included in the cavity of the host molecule. The host molecule **3** was first synthesized by Urushigawa et al. of our laboratory in 1971.[5] At that time they found that **3** formed 1:1 complexes with benzene and dioxane and suggested the possibility of intramolecular inclusion. However the X-ray structure analysis of the day was not sufficiently advanced to allow direct structure determination of the complex. The structure remained unproved. Tabushi et al. also reported the X-ray structure analysis of the 1:1 complexes of **3** with $CHCl_3$ and CH_2Cl_2.[6] The host molecule **3** and its water soluble derivatives have been extensively used as enzyme models.[7] The number of examples of the intracavity inclusion in the crystalline state has been increasing.[8]



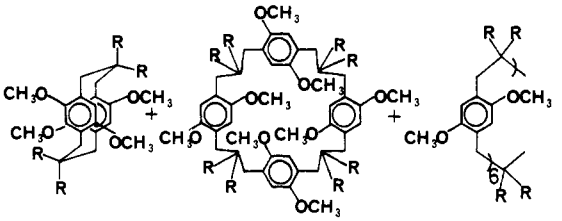
3

In our efforts along these lines, we have synthesized the host molecules having π-electron-rich cavity,

Scheme I

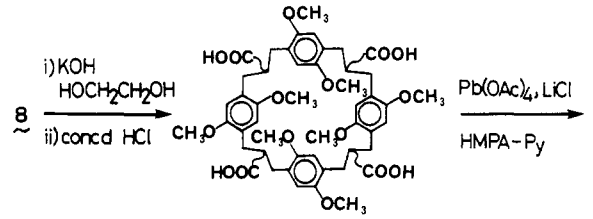


4 5, R=COOEt 6



7 8 9

Scheme II



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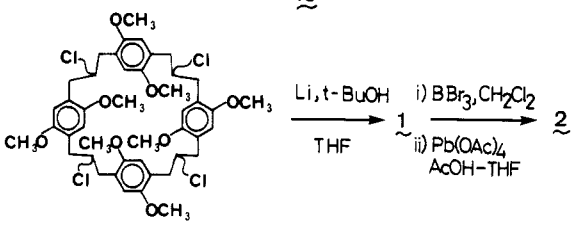

11

5,8,14,17,23,26,32,35-octamethoxy[3⁴]PC (**1**), and π-electron-poor cavity, [3⁴](2,5)-*p*-benzoquinonophane (**2**). As described above, the [3⁴]PC system has been proved to have a suitable cavity for inclusion of uncharged organic molecules such as benzene, dioxane, and $CHCl_3$. It is our idea that charge-transfer (CT) interaction should enhance inclusion complex formation and stabilize the complex. The host molecule having a π-electron-poor cavity should include π-electron-rich guest molecules more strongly and vice versa. CT interaction may serve as a driving force in the complex formation. In this paper we describe the syntheses and inclusion behaviors of **1** and **2**.

Results and Discussion

Synthesis. The synthetic routes to **1** and **2** are shown in Schemes I and II. The dibromide **4** was coupled with the ester **5** in the presence of sodium hydride in refluxing dioxane under high dilution conditions.[9] The crude products were separated by silica gel column chromatography with 10% EtOH in $CHCl_3$ to afford the pseudogeminal and pseudoortho tetramethoxy[3⁴]PC tetraesters **6** and **7** (1:1 mixture, 23%),[10] octamethoxy[3⁴]PC octaester **8** (33%), and the hexamer **9** (15%). The pseudogeminal and pseudoortho isomers, **6** and **7**, were separated by

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(9) Shinmyozu, T.; Inazu, T.; Yoshino, T. *Chem. Lett.* **1976**, 1405.
(10) The first synthesis of pseudogeminal and pseudoortho tetramethoxy[3.3]paracyclophanes was reported by Staab et al.: Staab, H. A.; Herz, C. P. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 799.

fractional recrystallization from $CHCl_3$–EtOH.

The [3⁴]PC octaester 8 was hydrolyzed by refluxing with KOH in ethylene glycol, and the cooled mixture was acidified with concentrated HCl to give the tetraacid **10** in 93% yield. The tetraacid **10** was treated with lead tetraacetate and lithium chloride in pyridine–HMPA (4:1 v/v)[11] at 100 °C for 1 h to give the tetrachloride **11** in 27% yield. Efforts to increase the yield by varying the reaction conditions (solvent, temperature, reaction time) failed. Probably the low yield is attributable to the acetoxylation of the activated benzene nuclei[12] and incomplete decarboxylative chlorination of the carboxyl groups. The reduction of the tetrachloride **11** with lithium and 2-methyl-2-propanol in refluxing THF afforded the octamethoxy[3⁴]PC **1** in 86% yield. Over all yield of **1** from the tetraester **5** was 7.1%.

The methyl ether **1** was demethylated with boron tribromide in CH_2Cl_2 at room temperature, followed by oxidation with lead tetraacetate in AcOH–THF in the dark to afford [3⁴](2,5)-*p*-benzoquinonophane (**2**) in 44% yield. The tetraquinone **2** was sensitive to light in the crystalline state as well as in solution; when yellow crystals of **2** were left standing, they slowly converted into a brownish yellow substance. Upon exposure to daylight, the intensity of the carbonyl stretching absorption band of **2** occurring at 1656 cm^{-1} decreased, while the new absorption due to aliphatic carbonyl stretching appeared at 1700 cm^{-1}. Presumably this photochemical reaction[13] is an intermolecular [2 + 2] cycloaddition reaction.

Spectroscopic Properties. The ^1H NMR spectra suggest that the benzene rings of **8** and **9** rotate freely at room temperature, for both the benzylic and aromatic protons of each cyclophane appear as singlets. The aromatic protons of pseudogeminal and pseudoortho [3²]PC derivatives, **6** and **7**, [3⁴]PC derivative **8**, and [3⁶]PC derivative **9** appear as singlets at 6.31, 6.76, 6.45, and 6.60 ppm, respectively. The absorptions show downfield shifts as the size of the macroring increases except those of **7**. This phenomenon is commonly observed in [2ⁿ]PC[14] systems[15] and ascribed to a gradual decrease in the magnitude of the shielding effects of other benzene rings. But the aromatic protons of pseudoortho isomer **7** show unusual downfield shifts as compared with those of the pseudogeminal isomer **6** due to a steric compression effect of the methoxy groups[13] as well as a deshielding effect of the ethoxycarbonyl groups.[16] The aromatic protons of **1** and the olefinic protons of **2** appear as singlets at 6.44 and 6.53 ppm, respectively. Moreover the trimethylene chains of both compounds show averaged spectral patterns, suggesting free rotation of the benzene and bezoquinone rings at room temperature. The tetraquinone **2** shows the carbonyl stretching absorption at 1656 cm^{-1} and the characteristic mass spectral fragmentation pattern near the molecular ion peak (M^+), where we can observe M^+ (592), $M^+ + 2$, $M^+ + 4$, $M^+ + 6$, and, $M^+ + 8$ with relative intensities of 11, 21, 67, 100, and 45%, respectively.

The electronic spectra of **1**, 1,4-dimethoxy-2,5-dimethylbenzene (**12**), **2**, and 2,5-dimethyl-*p*-benzoquinone (**13**) are shown in Figure 1. The compound **1** shows an

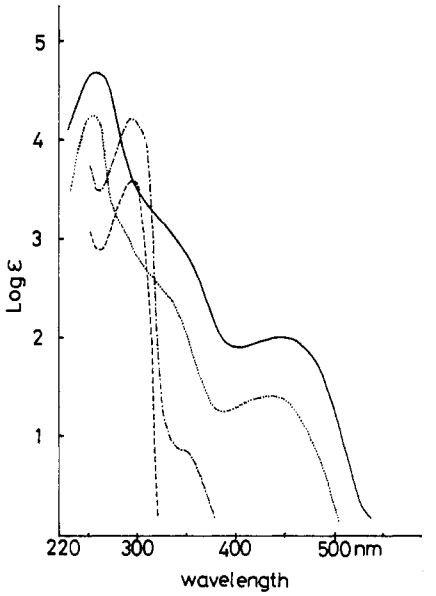

Figure 1. Electronic spectra of **1** (–·–), 1,4-dimethoxy-2,5-dimethylbenzene (**12**) (– –), **2** (—), and 2,5-dimethyl-*p*-benzoquinone (**13**) (···).

absorption maximum at 292 nm (ε, 16 600) and a shoulder at about 345 nm (ε, 7.6) in $CHCl_3$. The weak but new absorption at about 345 nm may be attributed to the transannular π-electronic interaction of the benzene rings. In the whole region the absorption intensity of **1** is higher by a factor of about four than that of the reference compound **12**. The tetraquinone **2** shows a strong absorption maximum at 253 nm (ε, 52 300) with a weak band at 446 nm (ε, 107) in dioxane. The absorption curve of **2** is similar to that of the reference compound **14** but the absorption bands of **2** exhibit weak bathochromic shifts and significant hyperchromic effects (about 4-fold) as compared with those of **13**.

Inclusion Behavior. The tetramethoxy[3⁴]PC **1** has an electron-rich cavity, so it may strongly bind π-electron-poor molecules such as *p*-benzoquinone. A mixture of **1** and *p*-bezoquinone was dissolved in THF and the solvent was allowed to evaporate at room temperature and ambient pressure. The resulting crystals were washed with MeOH, air-dried at room temperature, and characterized by ^1H NMR spectrum, but *p*-benzoquinone could not be detected. The cyclophane **1** was also recrystallized from other organic solvents such as CH_2Cl_2, MeOH, benzene, and THF. However none of these solvents were included.

A similar result was obtained when a mixture of the tetraquinone **2** having a π-electron-poor cavity and hydroquinone (π-donor) were recrystallized from THF. The resulting crystals were characterized by ^1H NMR, but no hydroquinone molecule could be detected. However surprising results were obtained when **2** and hydroquinone were recrystallized from dioxane in place of THF. A ^1H NMR analysis of the resulting crystals revealed the presence of dioxane. Dioxane molecules alone were retained in the host molecules in a 1:1 ratio on the basis of the ^1H NMR. Moreover, when **2** and *p*-dimethoxybenzene were recrystallized from CH_2Cl_2, again, only CH_2Cl_2 molecules were retained in a 1:1 ratio. The complexation behavior of **1** and **2** in solution were also studied by the use of electronic spectra. But neither a $CHCl_3$ solution of a mixture of **1** and *p*-benzoquinone nor a dioxane solution of a mixture of **2** and hydroquinone showed marked CT bands. Probably the CT bands of these complexes may be submerged in the π–π* band or n–π* band of the *p*-benzoquinone moiety itself.

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(16) The chemical shift difference of the aromatic protons between tetraethyl [3²]PC-2,2,11,11-tetracarboxylate (6.6 ppm) and [3²]PC (6.60 ppm) is 0.09 ppm in $CDCl_3$.

These results lead to the following conclusion. Although currently we do not have direct evidence that dioxane and CH_2Cl_2 molecules are included in the cavity of the host molecule **2**, CT interaction does not play an important role in the formation of intracavity inclusion complexes between [3⁴]cyclophane host molecules and neutral organic guest molecules. The X-ray structure analysis of the **2**–dioxane complex is in progress.

In order to test further the basic concept that an electron-poor host would prefer the electron-rich guest and vice versa, we plan to synthesize the host molecules having a tetraaza[3⁴]PC system, 5,8,14,17,23,26,32,35-octamethoxy-2,11,20,29-tetraaza[3⁴]PC and 2,11,20,29-tetraaza-[3⁴](2,5)-*p*-benzoquinonophane, and study their inclusion phenomena in solid state as well as in solution.

Experimental Section

General Comments. All melting points were uncorrected. The ^1H NMR spectra were recorded on either a Hitachi R-20B (60MHz) or a JEOL FX-90Q (90MHz) spectrometer. Chemical shifts are reported as δ values (ppm) relative to internal Me_4Si. Mass spectra were obtained on a Hitachi RMU-6MG mass spectrometer at an ionization energy of 70 ev; m/z values reported include the parent ion peak and other significantly large peaks. Infrared spectra were obtained on a Hitachi 125 spectrophotometer as KBr disks. Electronic spectra were obtained with a Shimadzu UV-240 spectrometer. Elemental analyses were performed by the Service Center of the Elemental Analysis of Organic Compounds in Kyushu University.

Dioxane and tetrahydrofuran (THF) were distilled from the sodium ketyl of benzophenone and EtOH from magnesium ethoxide. Hexamethylphosphoric triamide (HMPA), benzene, 2-methyl-2-propanol, pyridine, and CH_2Cl_2 were distilled from calcium hydride. Silica gel chromatography utilized Wako gel C-200 for column chromatography and Merck siilica gel PF_{254} for preparative TLC.

Tetramethyl 1,4-Diethyl-2,5-dimethoxybenzene-ω,ω,ω',ω'-tetracarboxylate (5). To 200 mL of EtOH was added 5.29 g (0.23 mmol) of freshly cut sodium in small pieces under N_2. After the sodium was completely dissolved, 54 g (0.34 mol) of diethyl malonate was added in one portion and the mixture was stirred for 1 h under reflux. To the mixture was added 32.4 g (0.10 mmol) of 1,4-bis(bromomethyl)-2,5-dimethoxybenzene (**4**) in 500 mL of THF at such a rate that the mixture refluxed gently. After the addition, stirring was continued for an additional 4 h under reflux. The solvent was evaporated in vacuo and the resultant oil was extracted with benzene (600 mL). The combined benzene extracts were washed with water, dried over $MgSO_4$, and filtered, and the filtrate was concentrated on a rotary evaporator. EtOH (300 mL) was added to the concentrate and the resultant precipitate was collected by filtration. Recrystallization from benzene afforded colorless crystals (29 g, 60% yield): mp 100–101 °C; ^1H NMR (δ, $CDCl_3$) 6.68 (s, 2, aromatic), 3.81 (t, 2, J = 7 Hz, methine), 3.77 (s, 6, methoxy), 3.17 (d, 4, J = 7 Hz, benzylic).

Pseudogeminal and Pseudoortho Tetraethyl 5,8,14,17-Tetramethoxy[3.3]paracyclophane-2,2,11,11-tetracarboxylate (Dimers, 6 and 7) and Their Tetramer (8) and Hexamer (9). A 3-L, four-necked, round-bottomed Morton flask was equipped with a sealed stirrer, a nitrogen inlet tube, and a 200-mL dilution head[17] to which was attached a reflux condenser topped with a 500-mL pressure-equalizing Hershberg type dropping funnel protected with a $CaCl_2$ tube. After the system had been thoroughly purged with N_2, the flask was charged with oil-free sodium hydride (20 g of commercially available 50% sodium hydride was washed with dioxane) and 1.5 L of dioxane. To the refluxing mixture was added dropwise a solution of 7.0 g (22 mmol) of the dibromide **4** and 10 g (21 mmol) of the tetraester **5** in 600 mL of dioxane over a period of 7 h. The mixture was stirred under reflux for an additional 4 h and then allowed to cool to room temperature. The excess sodium hydride was removed by filtration and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel with 10% EtOH in $CHCl_3$ to afford the dimers (**6** and **7**, ratio 1:1), tetramer **8**, and hexamer **9** in 23%, 33%, and 15% yields, respectively. R_f values (silica gel, $CHCl_3$–EtOH, 19:1) are as follows: 0.58 for **6**, 0.57 for **7**, 0.45 for **8**, and 0.46 for **9**.

Two isomers of the dimers were successfully separated by fractional crystallization from a mixture of $CHCl_3$ and EtOH. The dimer **6** (pseudogeminal): colorless prisms from benzene–cyclohexane; mp 217.5–218 °C; ^1H NMR (δ, $CDCl_3$) 6.31 (s, 4, aromatic), 3.60 (s, 12, methoxy), 3.60 (d, 4, J = 15.3 Hz, benzylic), 3.34 (d, 4, J = 15.3 Hz, benzylic); m/z M^+ found 644. Anal. Calcd for $C_{34}H_{44}O_{12}$: C, 63.34; H, 6.89. Found: C, 63.50; H, 6.75. The dimer **7** (pseudoortho): colorless prisms from MeOH; mp 155.6–158.8 °C; ^1H NMR (δ, $CDCl_3$) 6.76 (s, 4, aromatic), 3.66 (s, 12, methoxy), 3.48 (d, 4, J = 15 Hz, benzylic), 3.31 (d, 4, J = 15 Hz, benzylic); m/z found 644. Anal. Found: C, 63.60; H, 6.96. The tetramer **8**: colorless powder from benzene–cyclohexane; mp 247–248 °C; ^1H NMR (δ, $CDCl_3$) 6.45 (s, 8, aromatic), 3.46 (s, 24, methoxy), 3.24 (br s, 16, benzylic); m/z M^+ found 1288. Anal. Calcd for $C_{68}H_{88}O_{24}$: C, 63.34; H, 6.89. Found: C, 63.50; H, 6.92. The hexamer **9**: colorless powder from benzene–cyclohexane; mp 190.8–191.6 °C; ^1H NMR (δ, $CDCl)_3$ 6.60 (s, 12, aromatic), 3.59 (s, 36, methoxy), 3.23 (brs, 24, benzylic); m/z M^+ found 1932. Anal. Calcd for $C_{120}H_{132}O_{36}$: C, 63.34; H, 6.89. Found: C, 63.31; H, 6.81.

5,8,14,17,23,26,32,35-Octamethoxy[3.3.3.3]paracyclophane-2,11,20,29-tetracarboxylic Acid (10). A mixture of 4.7 g (3.6 mmol) of the tetramer **8**, 8.3 g (148 mmol) of KOH, and 140 mL of ethylene glycol was heated to reflux with stirring. After all the tetramer **8** had been dissolved, stirring was continued for 30 h at 130–140 °C. The mixture was allowed to cool to room temperature and acidified with concentrated HCl, and then water (200 mL) was added. The resultant precipitate was collected by filtration and dried in vacuo over P_2O_5 to afford 3.0 g (93%) of crude acid **10** as light brown solid: ^1H NMR (δ, $CDCl_3$–MeOH-d_4) 6.36–6.53 (aromatic), 3.48–3.75 (methoxy), 2.5–3.1 (benzylic); IR (KBr) $\nu_{c=o}$ 1700 cm^{-1}. The sample was used in the following reaction without further purification.

2,11,20,29-Tetrachloro-5,8,14,17,23,26,32,35-octamethoxy-[3.3.3.3]paracyclophane (11). A mixture of 620 mg (0.70 mmol) of the tetracarboxylic acid **10**, 145 mg (3.4 mmol) of anhydrous lithium chloride, 20 mL of pyridine, 5 mL of HMPA, and 20 mL of benzene was heated to 100 °C with stirring. Trace amounts of water in the system were removed by azeotropic distillation with benzene. When the mixture was cooled to 80 °C, the flask was purged with N_2 and 1.92 g (3.9 mmol) of 90% lead tetraacetate was added under a positive pressure of N_2. The solution was stirred at 100 °C for 1 h and then allowed to cool. Ethylene glycol (4 mL) was added and the mixture was extracted with Et_2O (200 mL). The combined ether extracts were washed successively with 1 N HCl, saturated aqueous $NaHCO_3$ solution, and water and dried over $MgSO_4$. Filtration and removal of the solvent on a rotary evaporator provided a semisolid which was purified by chromatography on silica gel with CH_2Cl_2 as an eluent to afford 158 mg (27%) of the chloride **12**: colorless crystals from EtOAc; mp 213–226 °C; ^1H NMR (δ, $CDCl_3$) 6.42–6.54 (aromatic), 4.1–4.6 (methine), 3.55–3.63 (methoxy), 2.96–3.09 (benzylic); IR (KBr) ν_{CCl} 718 cm^{-1}; m/z M^+ 848 ($C_{44}H_{52}O_8{}^{35}Cl_4$), $M^+ + 2$ 850, $M^+ - {}^{35}Cl$ 813, $M^+ - 2{}^{35}Cl$ 778, $M^+ - 3{}^{35}Cl$ 743, $M^+ - 4{}^{35}Cl$ 708. Anal. Calcd for $C_{44}H_{52}O_8Cl_4$: C, 62.12; H, 6.16. Found: C, 62.20; H, 6.19.

5,8,14,17,23,26,32,35-Octamethoxy[3.3.3.3]paracyclophane (1). To a mixture of 413.9 mg (0.49 mmol) of the chloride **11**, 0.7 mL of 2-methyl-2-propanol, and 50 mL of THF was added 100 mg of freshly cut lithium under N_2. The stirred reaction mixture was refluxed for 9 h and then allowed to cool to room temperature. After removal of the excess lithium, the solvent was evaporated in vacuo. The residue was extracted with benzene (100 mL), the combined benzene solution was washed with water, dried over $MgSO_4$, and filtered. Removal of the solvent on a rotary evaporator afforded crystalline solid, which was purified by chromatography on silica gel with CH_2Cl_2 as an eluent. Recrystallization from CH_2Cl_2 and 2-propanol afforded 297 mg (86%) of **1**. The analytically pure sample was obtained by recrystallization from THF as colorless crystals: mp 184–185 °C; ^1H NMR (δ, $CDCl_3$) 6.44 (s, 8, aromatic), 3.60 (s, 24, methoxy), 2.56 (t, 16, benzylic), 1.68 (m, 8, methylene); m/z M^+ 712. Anal. Calcd for

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$C_{44}H_{56}O_8$: C, 74.13; H, 7.92. Found: C, 74.04; H, 7.86.

[3.3.3.3](2,5)-*p*-Benzoquinonophane (2). To a stirred mixture of 152 mg (0.21 mmol) of 1 and 15 mL of CH_2Cl_2 was added 4 mL of 2 M BBr_3 in CH_2Cl_2 and the mixture was stirred overnight at room temperature. Water (10 mL) was added and the mixture was extracted with Et_2O (150 mL) containing small amounts of MeOH. The combined extracts were washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and filtered. Removal of the solvent afforded the crude hydroquinonophane: ^1H NMR (δ, $CDCl_3$–MeOH-d_4) 6.42 (s, 8, aromatic) 1.5–2.7 (m, 24, methylene).

To a mixture of the crude hydroquinonophane, 18 mL of AcOH, and 6 mL of THF was added 650 mg of 90% lead tetraacetate with stirring at room temperature. The solution immediately turned yellow. The flask was covered with aluminum foil to intercept daylight. The mixture was refluxed for 3 h with stirring. A small amount of ethylene glycol was added and the mixture was extracted with $CHCl_3$ (100 mL). The combined $CHCl_3$ solution was washed successively with saturated aqueous $NaHCO_3$ solution and water, dried over $MgSO_4$, and filtered. The filtrate was concentrated to dryness on a rotary evaporator to give brownish yellow solid, which was purified by preparative TLC on silica gel with using $CHCl_3$ and EtOAc (5:1 v/v); 55.6 mg (44% from 1) of the yellow solid was obtained: yellow crystals from benzene; mp 212 °C dec; ^1H NMR (δ, $CDCl_3$) 6.53 (s, 8, olefinic), 2.42 (t, 16, $CH_2CH_2CH_2$), 1.70 (m, 8, $CH_2CH_2CH_2$); IR (KBr) $\nu_{C=O}$ 1656 cm^{-1}, $\nu_{C=C}$ 1610 cm^{-1}; *m/z* (relative intensity) M^+ 592 (11%), $M^+ + 2$ 594 (21%), $M^+ + 4$ 596 (67%), $M^+ + 6$ 598 (100%), and $M^+ + 8$ 600 (45%). Anal. Calcd for $C_{36}H_{32}O_8$: C, 72.96; H, 5.44. Found: C, 73.12; H, 5.54.

Inclusion Behavior of 1 and 2. (1) 1 (5.6 mg, 7.9 μmol) and 8.6 mg (80 μmol) of *p*-benzoquinone were dissolved in 1 mL of THF. The solvent was allowed to evaporate at room temperature and ambient pressure. The resultant crystals were washed with MeOH, air-dried, and characterized by ^1H NMR. But neither *p*-benzoquinone nor THF was detected.

(2) 2 (3.0 mg, 5.0 μmol) and 5.7 mg (52 μmol) of hydroquinone were dissolved in 1 mL of THF. The solution was allowed to evaporate at room temperature and ambient pressure. The resultant precipitate was washed with MeOH, air-dried, and characterized by ^1H NMR. But neither hydroquinone nor THF was detected.

(3) 2 (709 μg, 1.2 mol) was dissolved in 0.25 mL of dioxane (solution A). Hydroquinone (199 μg, 1.8 μmol) was dissolved in 0.25 mL of dioxane (solution B). Solutions A and B were mixed. The color of the mixed solution did not change. The mixed solution was allowed to stand at room temperature for a day. The resultant precipitate was collected by filtration, washed with MeOH, and air-dried. ^1H NMR spectrum of the precipitate showed the presence of dioxane in a 1:1 (host–guest) ratio: ^1H NMR (δ, $CDCl_3$) 6.50 (s, 8, olefinic), 3.67 (s, ca 8, dioxane). The sample for the elemental analysis was recrystallized from dioxane. Anal. Calcd for $C_{36}H_{32}O_8 \cdot 1.1C_4H_8O_2$: C, 70.37; H, 5.96. Found: C, 69.98; H, 5.66.

(4) 2 (3.0 mg, 5.1 μmol) and 7.0 mg (50.7 μmol) of *p*-dimethoxybenzene was dissolved in 1.5 mL of CH_2Cl_2. The resulting crystals were characterized by ^1H NMR. The ^1H NMR spectrum showed the presence of CH_2Cl_2 in a 1:1 host–guest ratio: ^1H NMR (δ, $CDCl_3$) 6.50 (s, 8, olefinic), 5.27 (s, ca 2 H, CH_2Cl_2). The sample for elemental analysis was recrystallized from CH_2Cl_2. Anal. Calcd for $C_{36}H_{32}O_8 \cdot 0.8CH_2Cl_2$: C, 66.91; H, 5.12. Found: C, 67.10; H, 5.41.

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Registry No. 1, 95865-80-8; 2, 95865-81-9; 2 (hydroquinone), 95865-82-0; 2·dioxane, 95865-83-1; 2·CH_2Cl_2, 95865-84-2; 4, 50874-27-6; 5, 13949-89-8; 6, 95865-76-2; 7, 95976-15-1; 8, 95865-77-3; 9, 95892-08-3; 10, 95865-78-4; 11, 95865-79-5; diethyl malonate, 105-53-3.

A Useful Synthon Approach to Bicyclic Enols: Acid-Catalyzed and Base-Catalyzed Rearrangements of Diels–Alder Adducts of 2-Methoxy-5-methyl-1,4-benzoquinone

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Acid- and base-catalyzed reactions of Diels–Alder adducts of the title compound 1 have been investigated. Bicyclic adducts **6**, **9**, and **11** isomerized to the corresponding enols **8**, **10**, and **13** on treatment with base followed by rapid acidification. However, thermal reactions of 1 with sorbic acid esters afforded the enol products **3** directly. Similar base treatment of tricyclic adducts **15** and **17** resulted in ether cleavage to α-keto enols **16** and **18**. The bicyclic enols suffered facile aerial oxidation to the *cis*- or *trans*-hydroperoxides **31** or **33**, depending on the substituent at the C-5 position. The *trans*-hydroperoxides **33** were reduced to the alcohols **34** on treatment with silica gel; however, the *cis*-hydroperoxides **31** underwent a novel decarbonylation to afford β-keto esters **32**. Acid treatment of adducts **6** gave α-keto enols **35**, but the ester-substituted adducts **4** were stable to acid. These interesting structure–reactivity relationships are summarized in Scheme I.

The successful synthesis of vinyl alcohol, the simplest enol,[1] in the gas phase[2] strikingly indicates that enols are not inherently unstable, although they are usually thermodynamically less stable than their corresponding keto forms.[3,4] Several ways of producing enols, including photoenolization[5] and metal coordination,[6] have been reported.[7–9] However, a systematic study of their chemistry has never been undertaken and might be worthwhile.

Recently, we found that a stable enol was formed as the major product in the Diels–Alder reaction of 2-methoxy-

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