As shown in Figure 3 and Figure 4, the dependence of autooxidation rate upon ionic strength and ethyl alcohol was more evident in the absence of DTT and the acceleration of the oxidation of Protogen by hydrophobic environment became relatively minor in the presence of DTT. When palmitate was used as the hydrophobic stimulator, the rate enhancement was so large that the counterbalance by DTT was negligible (Figure 5).

Since Proto IX is known to be more hydrophobic than Protogen,[14] the product-like transition state of the oxidation of Protogen would be stabilized by hydrophobic environments and this stabilization is more favourable in the absence of DTT. Therefore, the autooxidation of Protogen would be slow in hydrophilic and reductive condition as in cytosol and fast in hydrophobic and oxidative condition as in plasma membrane. In conclusion, the autooxidation of Protogen initially accumulated by the inhibition of Protox in diphenyl ether treated plants would be hindered in cytosol and the accumulated Protogen would likely be transported to the plasma membrane as an unprocessed form to undergo facilitated enzymatic and/or nonenzymatic autooxidation in the plasma membrane.

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Orthocyclophanes. 6. Hexamethoxy Derivatives of [1$_6$]Orthocyclophane

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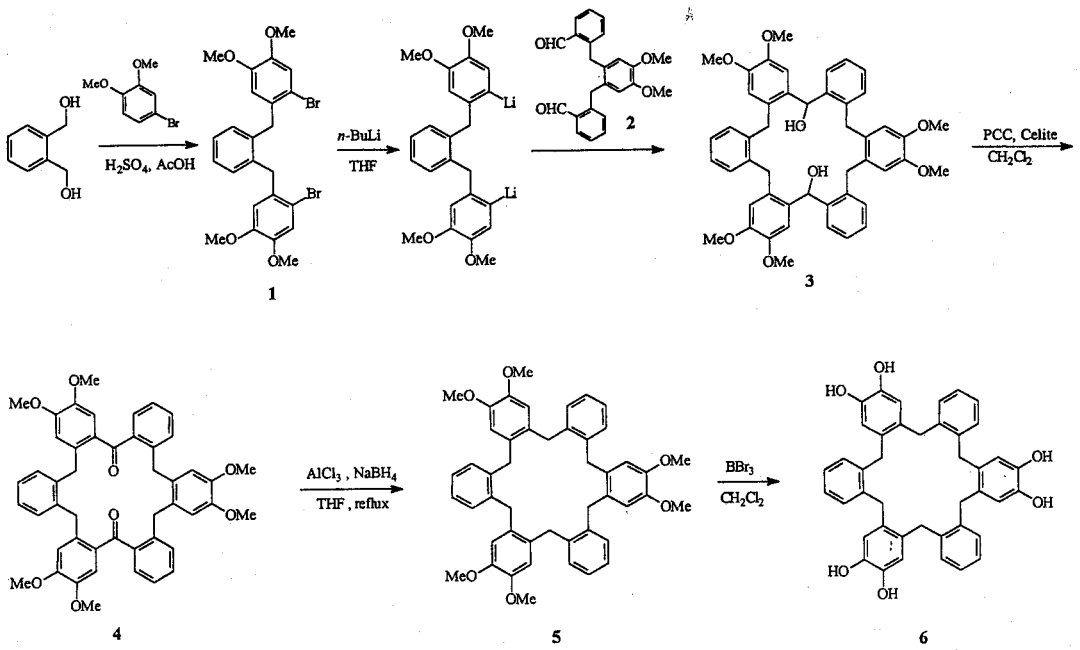
In recent years, we have been involved in developing a new branch of orthocyclophane chemistry, the family of [1$_n$] orthocyclophanes ([1$_n$]OCPs). Since the methylene groups in a bisbenzylic position can be easily transformed into other functionalities, the [1$_n$]OCPs are expected to be precursors to novel macrocyclic ionophores having interesting binding properties.[1] In previous investigations, we developed general synthetic routes[2] to the parent [1$_n$]OCP cycles and their functionalization on the aromatic rings.[3] We also found that the oxidation of the bisbenzylic carbons resulted in new families of crown compounds, either starands[4] or ketonands[5] depending on n. The present paper provides a general synthetic route to further modification of the [1$_6$]OCP by introduction of functional groups to the aromatic rings.

One of the starting materials, dibromide **1** was prepared from acid-catalyzed Friedel-Crafts alkylation[6] of 4-bromoveratrole with 1,2-benzenedimethanol in AcOH/H_2SO_4. The other key compound, an aromatic dialdehyde **2**, was prepared according to the literature procedure.[3] Generation of the [1$_6$] OCP cycle was accomplished by treatment of of an aromatic dibromide **1** in dry THF with n-BuLi at -13 ℃ to give the corresponding dilithio reagent, followed by condensation with an aromatic dialdehyde (**2**, 1,2-dimethoxy-4,5-bis(2′-formylbenzyl)benzene) and succesive hydrolytic workup, to give a cyclic diol **3**. Because it turned out difficult to isolate and purify, crude diol **3** was oxidized directly with PCC to the corresponding cyclic dione, hexamethoxy[1$_6$]OCPdione **4**. Clemmensen reduction of **4** did not give the hexamethoxy [1$_6$]OCP **5**, though dimethoxy- and tetramethoxy[1$_6$]OCPs[3] could be obtained by Clemmensen reduction. The reduction of **4** was successfully carried out by the literature procedure of Ono *et al.*,[7] heating at reflux temperature with a mixture of $NaBH_4$ and $AlCl_3$ in THF to give rise to the hexamethoxy [1$_6$]OCP **5**. Whereas the even-numbered [1$_n$]OCPs are generally insoluble in conventional organic solvents presumably due to the molecular symmetry, the hexamethoxy derivative **5** could be extracted into EtOAc without difficulty from the reaction mixture to give crystalline solid after chromatographic purification. The structure of both **4** and **5** was unambiguously confirmed by HRMS, ^{1}H NMR, ^{13}C NMR, and IR spectroscopy. (see experimental section)

Treatment of a solution of **5** in CH_2Cl_2 with BBr_3 at 0 ℃, followed by stirring at rt, provided hexahydroxy[1$_6$]OCP (**6**). Since the phenolic OH functions can be easily modified, the hexahydroxy cyclophane (**6**) could serve as a precursor to other classes of novel crown compounds.

In summary, we developed a convenient route to the synthesis of hexamethoxy[1$_6$]OCP (**5**). Since the methoxy functions in **5** can be demethylated to provide the corresponding



hexaphenolic analog (**6**), various other side chains can be introduced at the phenolic sites.

Experimental

1,2-Bis(2-bromo-4,5-dimethoxybenzyl)benzene (1). To a stirred solution of 4-bromoveratrole (2.02 g, 9.22 mmol) in AcOH (1.8 mL) was added bis(1,2-hydroxymethyl) benzene (630 mg, 4.61 mmol) at 0 ℃, followed by addition of conc H_2SO_4 (2.7 mL) with stirring. The mixture was stirred at rt for 2 d, diluted with water (200 mL), and extracted with CH_2Cl_2. The organic layer was washed successively with aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and evaporated under reduced pressure. The crude product was chromatographed on silica gel eluting with CH_2Cl_2/*n*-hexane (3 : 2, v/v) to give 1.05 g (1.96 mmol, 42.5%) of crystalline dibromide **1**.

Mp 111.5-113.0 ℃; IR (KBr) 3070, 2950, 2850, 1610, 1510, 1470, 1450, 1390, 1348, 1265, 1230, 1170, 1050, 1035, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.21-7.16 (m, 2H, Ar*H*), 7.06-6.95 (m, 2H, Ar*H*), 7.04 (s, 2H. Ar*H*), 6.45 (s, 2H, Ar*H*), 3.98 (s, 4H, ArCH_2), 3.86 (s, 6H, OCH_3), 3.69 (s, 6H, OCH_3); ^{13}C NMR ($CDCl_3$, 50.29 MHz) δ 148.46, 148.11, 137.95, 131.45, 129.62, 126.73, 115.56, 114.88, 113.49, 56.19, 55.94, 38.74; EIMS m/z (rel intensity) 538 (4.0), 536 (6.2), 534 (2.8), 331 (14), 243 (20), 239 (13), 118 (88); HRMS (EI) calcd for $C_{24}H_{24}O_4Br_2$ 534.0041, found 534.0053.

2,23-Dioxo-5,6,19,20,33,34-hexamethoxyheptacyclo[36.4.0.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}.0^{31,36}] dotetraconta-1(38),3(8),4,6,10(15),11,13,17(22),18,20,24(29),25,27,31(36),32,34,39,41-octadecaene. Hexamethoxy-[1$_6$]OCP-1,4-dione (4). To a solution of dibromide **1** (1.56 g, 2.92 mmol) in THF (100 mL) was added *n*-BuLi (2.7 mL, 2.5 M in hexane) dropwise at −78 ℃ under nitrogen, and the mixture was stirred at −40 ℃ for 30 min, whereupon the solution turned red and then finally to pale yellow to give the corresponding dilithio reagent. To this reagent was added a solution of dialdehyde **2** (0.91 g, 2.43 mmol) in THF (100 mL) dropwise, and the mixture was allowed to warm to rt followed by refluxing overnight. After being cooled, the reaction was quenched with aqueous NH_4Cl followed by removal of the solvent *in vacuo*. The mixture was extracted with CH_2Cl_2. The organic layer was washed successively with aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated to give a crude cyclic diol **3**, which was oxidized directly without purification.

To a solution of the crude diol **3** in CH_2Cl_2 (100 mL) containing Celite (4 g) was added PCC (3.0 g) and the mixture was stirred at rt for 5 h. The reaction mixture was filtered on silica gel in a glass filter, followed by washing the silica gel with CH_2Cl_2/Et_2O (1 : 1, v/v). The solvent was evaporated *in vacuo*, and the crude product was chromatographed on silica gel eluting with Et_2O/*n*-hexane (1 : 1, v/v), followed by recrystallization from EtOAc/*n*-hexane (1 : 1, v/v) to give 200 mg (9.1%) of crystalline dione **4**.

Mp 190-192 ℃; IR (KBr) 2910, 2940, 2910, 1650, 1600, 1555, 1510, 1450, 1350, 1260, 1200, 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.30-7.01 (m, 12H, Ar*H*), 6.77 (s, 2H, Ar*H*), 6.43 (s, 2H, Ar*H*), 6.42 (s, 2H, Ar*H*), 3.99 (s, 4H, ArCH_2Ar), 3.89 (s, 4H, ArCH_2Ar), 3.70 (s, 6H, OCH_3), 3.68 (s, 6H, OCH_3), 3.67 (s, 6H, OCH_3); ^{13}C NMR ($CDCl_3$, 50.29 MHz) δ 199.54, 151.62, 147.27, 146.39, 140.30, 139.60, 138.99, 135.21, 130.74, 130.61, 130.47, 130.29, 128.91, 126.53, 125.71, 118.42, 113.47, 113.09, 55.89, 55.79, 55.74, 36.59, 35.63; FABMS m/z 749 (M^++1), 735, 705, 675, 625, HRMS calcd for $C_{48}H_{44}O_8$ 748.3036, found 748.3036.

5,6,19,20,33,34-Hexamethoxyheptacyclo[36.4.0.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}.0^{31,36}] dotetr-aconta-1(38),3(8),4,6,10(15),11,13,17(22),18,20,24(29),25,27,31(36),32,34,39,41-octadecaene. Hexamethoxy-[1$_6$]OCP (5). A mixture of hexamethoxy-[1$_6$]OCP-1,4-dione (**4**) (80 mg, 111 mmol), anhydrous $AlCl_3$ (1 g, 7.4 mmol), $NaBH_4$ (0.5 g, 2.7 mmol) in THF (25 mL) was refluxed for 6 h. After being cooled, the reaction was quenched with H_2O (50 mL), and the mixture extracted with EtOAc. The extract was dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was

chromatographed on silica gel eluting with CH_2Cl_2 to afford 70 mg (87%) of crystalline hexamethoxy[1$_6$]OCP **5**.

Mp 238-240 ℃; IR (KBr) 3030, 2940, 1610, 1515, 1450, 1280, 1240, 1210, 1100 cm^{-1}; ^1H NMR ($CDCl_3$ 200 MHz) δ 7.05-7.00 (m, 6H, Ar*H*), 6.79-6.75 (m, 6H, Ar*H*), 6.63 (s, 6H, Ar*H*), 3.80 (s, 18H, OCH_3), 3.67 (s, 12H, ArCH_2); ^{13}C NMR ($CDCl_3$ 50.29 MHz) δ 147.54, 138.50, 130.40, 128.33, 126.13, 114.02, 55.90, 35.59; EIMS m/z 720 (M^+), 687, 476, 355, 239, HRMS (EI) calcd for $C_{48}H_{48}O_6$ 720.3450, found 720.3431.

5,6,19,20,33,34-Hexahydroxyheptacyclo[36.4.0.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}.0^{31,36}] dotetr-aconta-1(38),3(8),4,6,10(15),11,13,17(22),18,20,24(29),25,27,31(36),32,34,39,41-octadecaene. Hexahydroxy-[1$_6$]OCP (6). To a solution of hexamethoxy[1$_6$]OCP (**5**) (50 mg, 69.4 μmol) in CH_2Cl_2 (5 mL) was added BBr_3 (0.21 g 840 μmol) at 0 ℃ under nitrogen. The mixture was stirred at rt for 5 h. The reaction mixture was quenched with water, extracted with EtOAc, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was triturated with *n*-hexane to give 42 mg (96%) of crystalline hexahydroxy-[1$_6$]OCP **6**.

Mp >230 ℃ dec; IR (KBr) 3648-3000, 2912, 1600, 1507, 1437, 1283, 1177, 1132, 870, 736 cm^{-1}; ^1H NMR (acetone-d_6, 200 MHz) δ 7.60 (s, 6H, O*H*), 7.15-6.95 (m, 6H, Ar*H*), 6.40 (s, 6H, Ar*H*), 3.64 (s, 12H, ArCH_2); ^{13}C NMR (acetone-d_6 50.29 MHz) δ 144.10, 140.02, 130.51, 126.96, 117.49, 35.81; FABMS m/z 606 (M^+).

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A Facile Preparation, Structure, and Some Reactions of *trans*-PdPhI(PMe$_3$)$_2$

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Aryl halides are converted into amides or esters on treatment with carbon monoxide and amine (or alcohol and amine) in the presence of palladium catalysts.[1] Throughout these catalytic reactions arylpalladium halide complexes, PdAr(X)L$_2$ (X=Cl, Br, I and L=tertiary phosphine) are believed as a key intermediate. Furthermore, these complexes are considered as indispensable starting materials or intermediates for the mechanistic study of Pd-catalyzed organic synthesis such as Heck arylation or Stille's C-C coupling reaction.[2] Arylpalladium iodide complexes, PdAr(I)L$_2$ are more widely used than the corresponding chloride and bromide complexes in related studies of Pd-catalyzed synthetic organic reactions.

The arylpalladium halide complexes are usually formed through oxidative addition of aryl halide to Pd(O) species.[3] *Trans*-PdPhI(PMe$_3$)$_2$ is isolated from the reaction of PhI with Pd(PMe$_3$)$_4$[4]. Oxidative addition of PhI to Pd(PPh$_3$)$_4$, followed by ligand diplacement reaction by PMe$_3$ might produce the same complex also. On the other hand, reaction of PhI with *trans*-PdEt$_2$(PMe$_3$)$_2$ also gives *trans*-PdPhI(PMe$_3$)$_2$.[1] However, these reactions have a limitation because of air-sensitivity or thermal lability of both Pd(0) and Pd(II) complexes as a starting material.

In this work we have easily prepared *trans*-PdPhI(PMe$_3$)$_2$ and related complexes, *trans*-PdPhIL$_2$ (L=PMePh$_2$ and L$_2$ =Ph$_2$PCH$_2$PPh$_2$) in high yield at room temperature from the ligand exchange reaction of PdPhI(tmeda) (tmeda=*N,N,N′,N′*-tetramethylethlenediamine) with equimolar amounts of phosphine ligands. We here report preparation and structure of *trans*-PdPhI(PMe$_3$)$_2$ and its reactions with isocyanides.

Experimental

All manipulations of air-sensitive compounds were performed under N_2 or argon atmosphere with use of standard Schlenk technique. Solvents were distilled from Na-benzophenone. PdCl$_2$, PMe$_3$, PMePh$_2$, Ph$_2$PCH$_2$PPh$_2$, isocyanides (*tert*-butyl, clclohexyl, 2,6-dimethylphenyl), and tmeda were commercial grade reagents and used without further purification. PdPhI(tmeda) was prepared by the literature method.[5]

Elemental analyses were carried out by Korea Basic Science Center, Seoul. IR spectra were recorded on a Hitachi 270-30 spectrophotometer. NMR (^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$) spectra were obtained by a Bruker 300 and 500 MHz spectrometers. ^1H and ^{13}C NMR spectra were referred to solvent