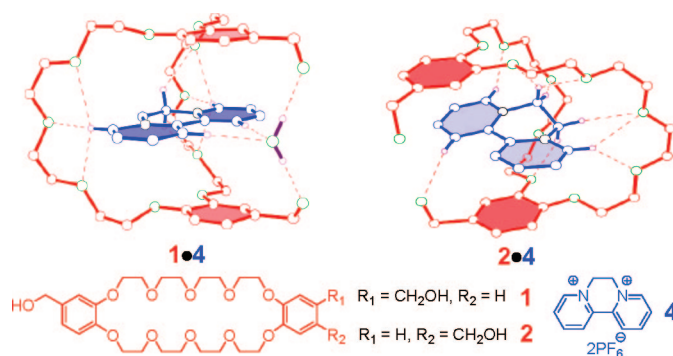# Syntheses of *cis*- and *trans*-Dibenzo-30-Crown-10 Derivatives *via* Regioselective Routes and Their Complexations with Paraquat and Diquat

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cis-Dibenzo-30-crown-10 (*cis*-DB30C10) diester and *trans*-dibenzo-30-crown-10 (*trans*-DB30C10) diester were synthesized regioselectively with reasonable yields. These two isomers were further reduced to *cis*-dibenzo-30-crown-10 diol (**1**) and *trans*-DB30C10 diol (**2**), respectively. The complexations of *cis*- and *trans*-DB30C10 diols with paraquat (**3**) and diquat (**4**) were investigated by ^{1}H NMR, mass spectrometry, UV−vis spectroscopy, and single-crystal X-ray analysis. The reversible control of complexations of **1·3** and **2·3** by adding small molecules (KPF$_6$ and dibenzo-18-crown-6) was demonstrated by ^{1}H NMR. The addition of 2 molar equiv of KPF$_6$ is enough to dissociate **2·3** and **1·3** completely while the subsequent addition of 2 molar equiv of DB18C6 allows the two complexes to reform. However, 2 molar equiv of KPF$_6$ cannot dissociate **1·4** and **2·4** completely. Because the DB30C10 cavity has a better geometry fit with paraquat **3** than with diquat **4**, **4**-based complexes have much higher association constants than the corresponding **3**-based complexes. In the crystal structure of **1·4**, the two hydroxymethyl groups of the crown ether **1** were joined by a "water bridge" to form a "supramolecular cryptand" while this kind of supramolecular cryptand structure was not observed in the crystal structure of **2·4**. This is a possible reason for the increase in association constant from **2·4** (3.3×10^4 M^{-1}) to **1·4** (5.0×10^4 M^{-1}).

Introduction

Since Pederson published his discovery of the alkali metal templated syntheses of crown ethers in 1967,[1] crown ethers have attracted much attention for their interesting binding properties with metal and organic cations and applications in the prepara-

tion of chemosensors, molecular machines, and supramolecular polymers.[2–4] In the recent three decades, several significant recognition motifs based on crown ethers and organic cations, especially the complexations between dibenzo-24-crown-8 (DB24C8) with secondary dialkylammonium salts,[5] between bis(*p*-phenylene)-34-crown-10 (BPP34C10) and paraquat de-

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SCHEME 1. Synthesis of *cis*-DB30C10 Diol 1[a]
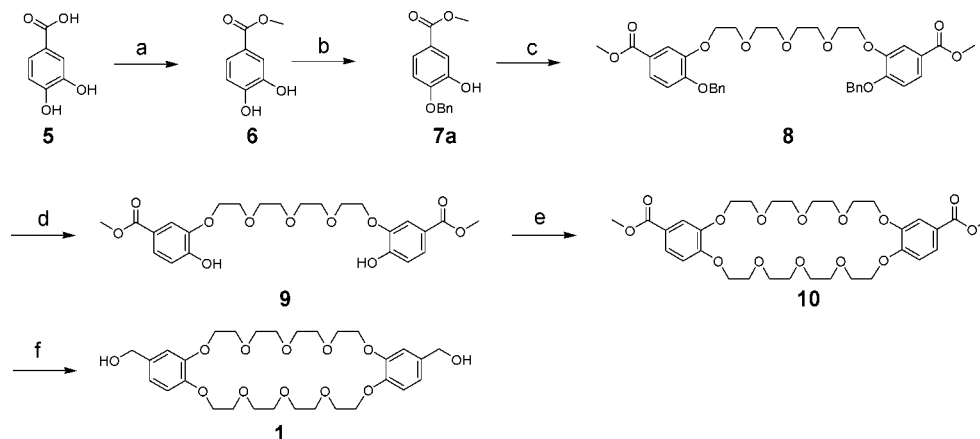
[a] Reagents and conditions: (a) MeOH, SOCl₂, reflux, 12 h, 90%; (b) benzyl bromide, K₂CO₃, N₂, acetone, rt, 24 h, 50%; (c) tetra(ethylene glycol) dichloride, K₂CO₃, N₂, CH₃CN, reflux, 36 h, 87%; (d) H₂, Pd/C (10%), ethyl acetate, 50 °C, 24 h, 92%; (e) tetra(ethylene glycol) ditosylate, K₂CO₃, KPF₆, N₂, DMF, 110 °C, 7 d, 55%; (f) LiAlH₄, N₂, dry THF, rt, 12 h, 95%.

SCHEME 2. Synthesis of Carbomethoxybenzo-15-Crown-5 13[a]
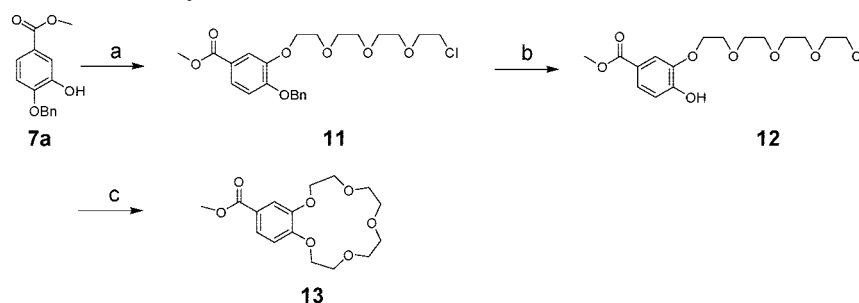
[a] Reagents and conditions: (a) tetra(ethylene glycol) dichloride, K₂CO₃, N₂, CH₃CN, reflux, 36 h, 77%; (b) H₂, Pd/C (10%), ethyl acetate, 50 °C, 24 h, 95%; (c) K₂CO₃, KPF₆, N₂, CH₃CN, reflux, 36 h, 90%.

rivatives,[6] and between bis(*m*-phenylene)-32-crown-10 (BMP32-C10) and paraquat derivatives,[7] have been discovered. These recognition motifs have greatly impelled the development of host−guest chemistry.[8] Paraquat derivatives (*N*,*N*′-dialkyl-4,4′-bipyridinium salts) and diquat (1,1′-ethylene-2,2′-dipyridinium salt) have been widely used in host−guest chemistry.[9,10] However, although host−guest systems based on the recognition motif of dibenzo-30-crown-10 (DB30C10) to metal cations have been widely studied,[11] host−guest systems based on the recognition motif of DB30C10 to organic cations have been relatively scarcely investigated except for several based on the recognition motif of DB30C10 to diquat.[12,13] One possible reason is the difficulty in controlling the regiochemistry of disubstituted dibenzo-type crown ethers and related complexes.[14] Herein, we report syntheses of *cis*- and *trans*-dibenzo-30-crown-10 derivatives *via* regioselective routes, their complexations with paraquat and diquat, and the reversible control of their complexations with paraquat by the addition of small molecules (KPF₆ and dibenzo-18-crown-6).

Results and Discussion

A. Synthesis of *cis*-Dibenzo-30-Crown-10 Diol 1. Syntheses of *cis*- and *trans*-DB24C8, *cis*- and *trans*-BPP34C10, and their derivatives were reported previously.[15–17] *cis*-DB30C10 diol was synthesized by the Stoddart group using an aldehyde derivative as the starting material.[18,19] To avoid the difficult control of deprotection of the benzylated aldehyde in the Stoddart's method,[17–19] we synthesized *cis*-DB30C10 diester **10** in a similar

way to prepare a *cis*-DB24C8 diester reported by the Gibson group[17] and reduced it to the aimed diol product **1** (Scheme 1).

B. Synthesis of *trans*-Dibenzo-30-Crown-10 Diol 2. We also attempted to synthesize the *trans*-DB30C10 diester using a similar route to that of *trans*-DB24C8 diester reported by the Gibson group (Scheme 2).[17] However, only carbomethoxy-benzo-15-crown-5 (**13**) was obtained.

Then we tried another method to synthesize **2** (Scheme 3). **7b**, the side product obtained in the preparation of **7a**, was reacted with **11** to give **14** (90%), a regiospecific isomer of **8**. The hydrogenolysis of **14** afforded diphenolic product **15** in a high yield (95%). Then *trans*-DB30C10 diester **16** was obtained by the cyclization reaction of **15** with tetra(ethylene glycol) dichloride in the presence of potassium hexafluorophoaphate as a template reagent (45%). The reduction of **16** was carried out in dry THF to afford **2** in a high yield (93%).

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SCHEME 3.   Synthesis of *trans*-DB30C10 Diol 2*a*
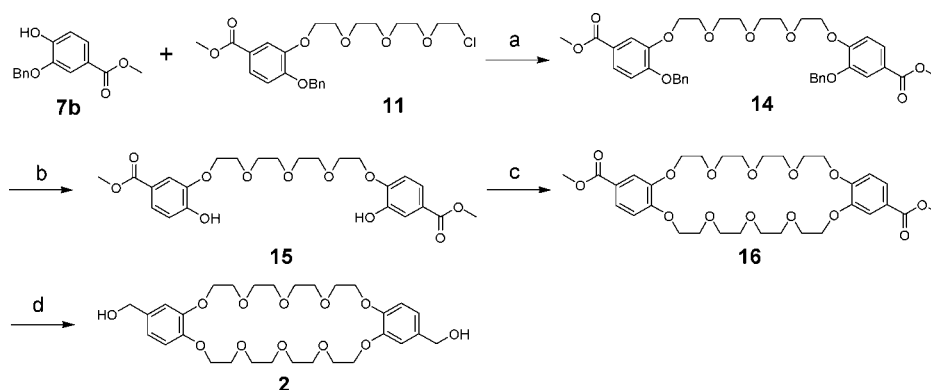
a Reagents and conditions: (a) **7b**, K_2CO_3, N_2, CH_3CN, reflux, 36 h, 90%; (b) H_2, Pd/C (10%), ethyl acetate, 50 °C, 24 h, 95%; (c) tetra(ethylene glycol) dichloride, K_2CO_3, KPF_6, N_2, DMF, 110 °C, 7 d, 45%; (d) $LiAlH_4$, N_2, dry THF, rt, 12 h, 93%.
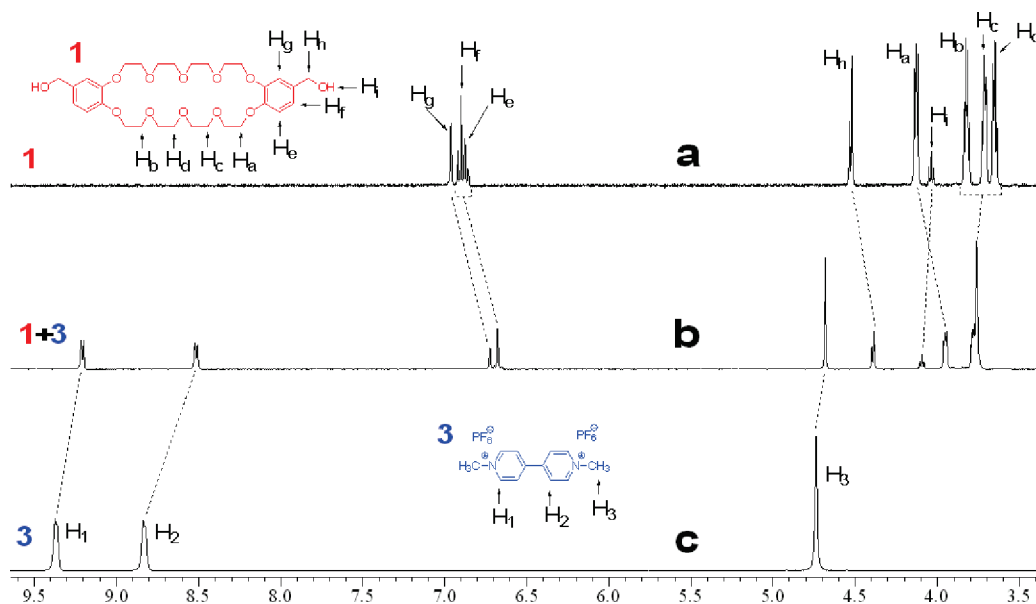

FIGURE 1. Partial ^1H NMR spectra (400 MHz, 22 °C) of 4.00 mM crown ether **1** (a), 4.00 mM crown ether **1** and paraquat **3** (b), and 4.00 mM paraquat **3** (c) in acetone-d_6.

C. The ^1H NMR Study of the Complexation of *cis*-DB30C10 Diol 1 with Paraquat. As shown in Figure 1, the 1:1 mixture of **1** and **3** in acetone-d_6 at 22 °C had significant

chemical shift changes in the ^1H NMR signals compared with the free crown ether host and paraquat guest under the same condition.[18] The pyridinium protons (H_1 and H_2) on paraquat **3** and phenyl protons (H_e, H_f, and H_g) of crown ether **1** moved upfield sharply (Figure 1), indicating the formation of strong $\pi-\pi$ stacking interaction between the two pyridinium rings of

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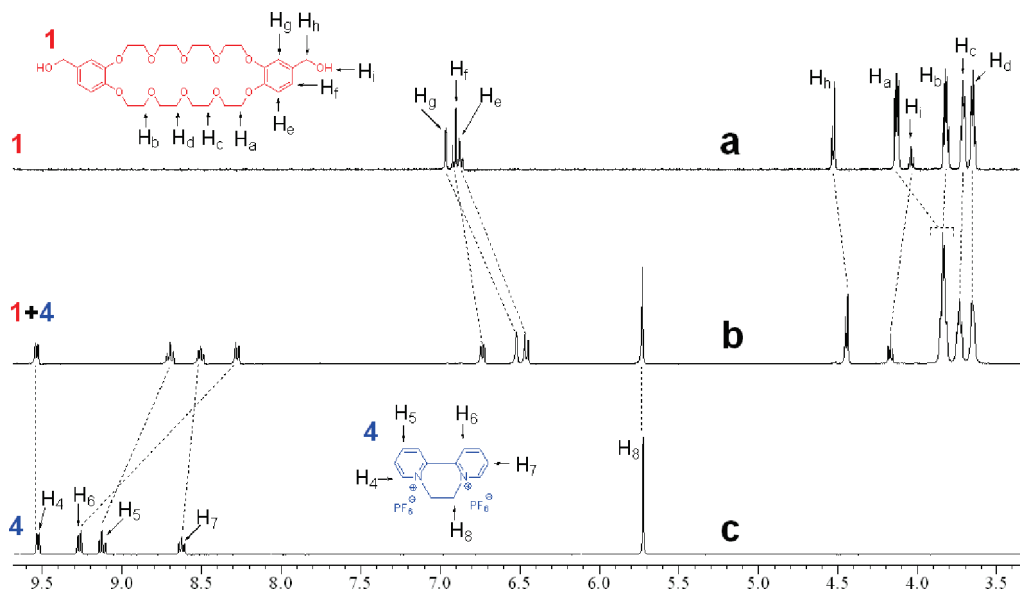
FIGURE 2. Partial ^{1}H NMR spectra (400 MHz, 22 °C) of 4.00 mM crown ether **1** (a), 4.00 mM crown ether **1** and diquat **4** (b), and 4.00 mM diquat **4** (c) in acetone-d_6.

3 and the two phenyl rings of **1**. The methyl protons (H$_3$) of **3** and methylene protons (H$_h$), α-ethyleneoxy protons (H$_a$), and β-ethyleneoxy protons (H$_b$) of **1** also had upfield chemical shift changes after complexation (Figure 1). However, γ-ethyleneoxy protons (H$_c$), δ-ethyleneoxy protons (H$_d$), and hydroxyl protons (H$_i$) of **1** had downfield chemical shift changes after complexation (Figure 1).

D. The ^{1}H NMR Study of the Complexation of *trans*-DB30C10 Diol 2 with Paraquat 3. Chemical shift changes of protons on *trans*-DB30C10 diol **2** and paraquat **3** after their complexation in acetone-d_6 are similar to chemical shift changes of protons on *cis*-DB30C10 diol **1** and paraquat **3** after their complexation in acetone-d_6 (Figure 1, as well as Figure S40 in the Supporting Information). Two common characteristics are worth noting. First, either the multiplet peak corresponding to phenyl protons H$_e$ and H$_f$ of crown ether **1** (Figure 1a) or the multiplet peak corresponding to phenyl protons H$_o$ and H$_p$ of crown ether **2** (Figure S40a, Supporting Information) merged to become a sharp peak after host−guest complexation (Figure 1b as well as Figure S40b in the Supporting Information). Second, either the three peaks corresponding to β- (H$_b$), γ- (H$_c$), and δ-ethyleneoxy protons (H$_d$) of **1** (Figure 1a) or the three peaks corresponding to β- (H$_k$), γ- (H$_l$), and δ-ethyleneoxy protons (H$_m$) of **2** (Figure S40a, Supporting Information) merged to become a multiplet peak after host−guest complexation (Figure 1b as well as Figure S40b in the Supporting Information).

E. The ^{1}H NMR Study of the Complexation of *cis*-DB30C10 Diol 1 with Diquat 4. Chemical shift changes of protons of **1** after complexation of crown ether **1** with diquat **4** were far different from those after complexation of crown ether **1** with paraquat **3**. First, phenyl protons H$_e$, H$_f$, and H$_g$ of **1**

had about the same chemical shift changes (Figure 1, spectra a and b) after complexation of **1** with paraquat **3** while the chemical shift changes of H$_e$ and H$_g$ were obviously bigger than that of H$_f$ after complexation of **1** with diquat **4** (Figure 2, spectra a and b). Second, the signals corresponding to phenyl protons H$_e$ and H$_f$ were together after complexation of **1** with paraquat **3** (Figure 1, spectra a and b) while the signals corresponding to phenyl protons H$_e$ and H$_g$ were together after complexation of **1** with diquat **4** (Figure 2, spectra a and b). Third, the three peaks corresponding to β- (H$_b$), γ- (H$_c$), and δ-ethyleneoxy protons (H$_d$) of **1** (Figure 1a) merged to become a multiplet peak after complexation of **1** with paraquat **3** (Figure 1b) while they were still three separate peaks after complexation of **1** with diquat **4** (Figure 2b). Fourth, the peak corresponding to β-ethyleneoxy protons (H$_b$) of **1** moved upfield after complexation of **1** with paraquat **3** (Figure 1, spectra a and b) while this peak moved downfield after complexation of **1** with diquat **4** (Figure 2, spectra a and b). These differences occurred possibly due to the difference in host−guest geometries of the complexes between **1** and paraquat **3** and between **1** and diquat **4** since both **3** and **4** are bipyridinium salts. γ-Pyridinium protons H$_5$, δ-pyridinium protons H$_6$, and β-pyridinium protons H$_7$ of diquat **4** moved upfield after the complexation between crown ether **1** and diquat **4**, but the peak corresponding to δ-pyridinium protons H$_6$ has the biggest upfield shift (Figure 2, spectra b and c). However, α-pyridinium protons H$_4$ and *N*-methylene protons H$_8$ of diquat **4** have no obvious chemical shift changes (Figure 2, spectra b and c).

F. The ^{1}H NMR Study of the Complexation of *trans*-DB30C10 Diol 2 with Diquat 4. Chemical shift changes of protons on *trans*-DB30C10 diol **2** and diquat **4** after their complexation in acetone-d_6 are similar to chemical shift changes of protons on *cis*-DB30C10 diol **1** and diquat **4** after their complexation in acetone-d_6 (Figure 2 as well as Figure S41 in the Supporting Information).

G. The Determination of Stoichiometries of the Complexations between Either of Hosts 1 and 2 and Either of Guests 3 and 4. Equimolar (0.500 mM) acetone solutions of either of two crown ethers **1** and **2** with either of two guests **3**

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(15) Li, X.-Q.; Feng, D.-J; Jiang, X.-K.; Li, Z.-T. *Tetrahedron* **2004**, *60*, 8275–8284.

and **4** are yellow or orange due to charge transfer between the electron-rich aromatic rings of the crown ether hosts and the electron-poor pyridinium rings of the bipyridinium guests. Job plots[20] (Figure S39, Supporting Information) based on UV−vis absorption spectroscopy data demonstrated that all four complexes were of 1:1 stoichiometry in acetone.

H. Electrospray Ionization Mass Spectrometry. The 1:1 stoichiometries of complexations between either of hosts **1** and **2** and either of guests **3** and **4** were further confirmed by electrospray ionization mass spectrometry in acetone. Three relevant peaks were found for **1·3**: m/z 927.2 $[\mathbf{1·3} - \mathrm{PF_6}]^+$ (79%), 781.3 $[\mathbf{1·3} - \mathrm{PF_6} - \mathrm{HPF_6}]^+$ (29%), and 391.4 $[\mathbf{1·3} - 2\mathrm{PF_6}]^{2+}$ (25%) with the base peak at m/z 619.5 for $[\mathbf{1} + \mathrm{Na}]^+$.

Two peaks were observed for **2·3**: m/z 927.2 $[\mathbf{2·3} - \mathrm{PF_6}]^+$ (32%) and 391.5 $[\mathbf{2·3} - 2\mathrm{PF_6}]^{2+}$ (25%) with the base peak at m/z 635.4 for $[\mathbf{2} + \mathrm{K}]^+$.

One relevant peak was detected for **1·4**: m/z 925.2 $[\mathbf{1·4} - \mathrm{PF_6}]^+$ (42%) with the base peak at m/z 635.2 for $[\mathbf{1} + \mathrm{K}]^+$.

Also one relevant peak was observed for **2·4**: m/z 925.2 $[\mathbf{2·4} - \mathrm{PF_6}]^+$ (18%) with the base peak at m/z 635.2 for $[\mathbf{2} + \mathrm{K}]^+$.

No peaks were found for complexes with other stoichiometries.

I. Determination of Association Constants. The association constants (K_a) of **1·3**, **1·4**, **2·3**, and **2·4** were determined by probing the charge-transfer bands of the complexes by UV−vis spectroscopy and employing a titration method. Progressive addition of an acetone solution with high guest salt (**3** or **4**) concentration and low host (**1** or **2**) concentration to an acetone solution with the same concentration of host results in an increase of the intensity of the charge-transfer band of the complex. Treatment of the collected absorbance data at $\lambda = 403$ nm with a nonlinear curve-fitting program afforded the corresponding K_a values: $1.1(\pm 0.1) \times 10^3$ M^{-1} for **1·3**, $1.7(\pm 0.1) \times 10^3$ M^{-1} for **2·3**, $5.0(\pm 1.3) \times 10^4$ M^{-1} for **1·4**, and $3.3(\pm 1.0) \times 10^4$ M^{-1} for **2·4**. The K_a value of **1·4** is about 44 times higher than that of **1·3** and the K_a value of **2·4** is about 18 times higher than that of **2·3**. Since both paraquat **3** and diquat **4** are bipyridinium salts, the obvious increase in K_a from **3**-based complexes to **4**-based complexes should be due to the better geometry fit between diquat **4** (it has a relatively shorter $N^+ \cdots N^+$ distance) and the DB30C10 cavity (its two ethylene glycol chains of the DB30C10 cavity are at two neighboring positions of its phenylene rings) than that between paraquat **3** (it has a relatively longer $N^+ \cdots N^+$ distance) and the DB30C10 cavity (Figure 3). It should be noted that due to the two positive charges that the two pyridinium rings of paraquat **3** or diquat **4** have, all hydrogens of **3** and **4** are acidic (electron-poor) so they want to form hydrogen bonds with basic (electron-rich) ether oxygen atoms of the DB30C10 cavity. The two ethylene glycol chains of the DB30C10 cavity are at two neighboring positions of its phenylene rings, making it easier for their basic aliphatic ether oxygen atoms to form hydrogen bonds with N-methylene hydrogens and α-pyridinium hydrogens of diquat **4** together (this is allowed based on their positions on diquat **4**, see Figure 3) than with N-methyl hydrogens and
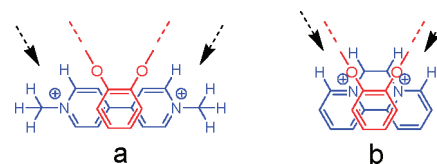

FIGURE 3. Stacking diagrams of (a) paraquat **3** (blue) and a part of the DB30C10 cavity (red) and (b) diquat **4** (blue) and a part of the DB30C10 cavity (red) showing how the DB30C10 cavity can bind paraquat and diquat driven by π-stacking and charge transfer interactions between the electron-rich catechol rings of the DB30C10 cavity and the electron-poor pyridinium rings of paraquat **3** or diquat **4**, electrostatic interaction between electron-rich ethyleneoxy oxygens of the DB30C10 cavity and the positive-charged nitrogen atoms of paraquat **3** or diquat **4**, and hydrogen bonding between ethyleneoxy oxygen atoms of the DB30C10 cavity and pyridinium hydrogens of paraquat **3** or diquat **4**. Black dashed arrows show the best places for ethylene glycol chains where the total noncovalent interaction between the host and guest can be maximized.

α-pyridinium hydrogens of paraquat **3** together (this is allowed based on their positions on paraquat **3**, see Figure 3).

The K_a value of **1·3** is a little lower than that of **2·3** while the K_a value of **1·4** is a little higher than that of **2·4**, indicating that host−guest geometries of paraquat **3**-based complexes are different from those of diquat **4**-based complexes, in accordance with the notable differences between the chemical shift changes of protons of crown ether host **1** or **2** that occurred when it complexes **3** and those that occurred when it complexes **4** (Figures 1a, 1b, 2a, and 2b or Figures S40a, S40b, S41a, and S41b in the Supporting Information).

J. Influence of the Addition of Small Molecules KPF$_6$ and Dibenzo-18-Crown-6 (DB18C6) on the Complexations of Either of *cis*- and *trans*-Dibenzo-30-Crown-10 Diols 1 and 2 with Either of Paraquat 3 and Diquat 4. When 1 molar equiv of KPF$_6$ was added to an equimolar solution of 4.00 mM *cis*-DB30C10 diol **1** and paraquat **3**, the chemical shifts of protons on paraquat **3** returned to almost their uncomplexed values (Figure 4a,b,c,f) and correspondingly the yellow color of the solution turned very weak. When one more molar equiv of KPF$_6$ was added, the chemical shifts of protons on paraquat **3** returned to their uncomplexed values (Figure 4d,f) and correspondingly the yellow color of the solution totally disappeared, indicating the total dissociation of complex **1·3**. However, when 2 molar equiv of DB18C6 was subsequently added, chemical shift changes of protons on paraquat **3** were observed again (Figure 4e,f) and correspondingly the yellow color of the solution recovered, indicating the reformation of complex **1·3**. The same phenomena were observed for the complexation between *trans*-DB30C10 diol **2** and paraquat **3** (Figure S42, Supporting Information). These demonstrated that the complexations between *cis*- and *trans*-DB30C10 diols **1** and **2** with paraquat **3** can be reversibly controlled by adding small molecules KPF$_6$ and DB18C6 (Figure 5). Considering that the stoichiometry of the complexation between the DB30C10 cavity and KPF$_6$ is also 1:1,[21] these also indicated that the K_a value of complex **1·3** (or **2·3**) is much lower than that of complex **1·KPF$_6$** (or **2·KPF$_6$**) and that the K_a values of complexes **1·KPF$_6$** (or **2·KPF$_6$**) and DB18C6·**3** are much lower than that of complex DB18C6·KPF$_6$.

When 1 molar equiv of KPF$_6$ was added to an equimolar solution of 4.00 mM *cis*-DB30C10 diol **1** and diquat **4**, the

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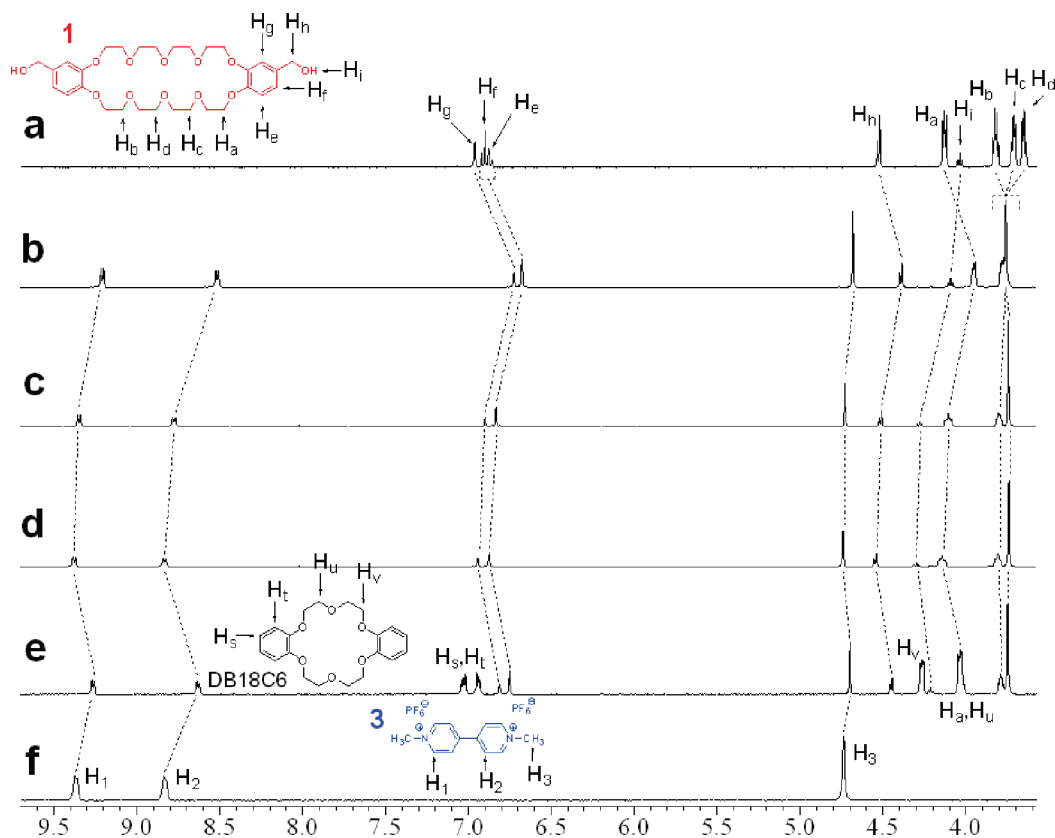
FIGURE 4. Partial 400 MHz ^{1}H NMR spectra of (a) 4.00 mM **1**, (b) 4.00 mM **1** and **3**, (c) 4.00 mM **1**, **3**, and KPF$_6$, (d) 4.00 mM **1** and **3** and 8.00 mM KPF$_6$, (e) 4.00 mM **1** and **3** and 8.00 mM KPF$_6$ and DB18C6, and (f) 4.00 mM **3** in acetone-d_6.
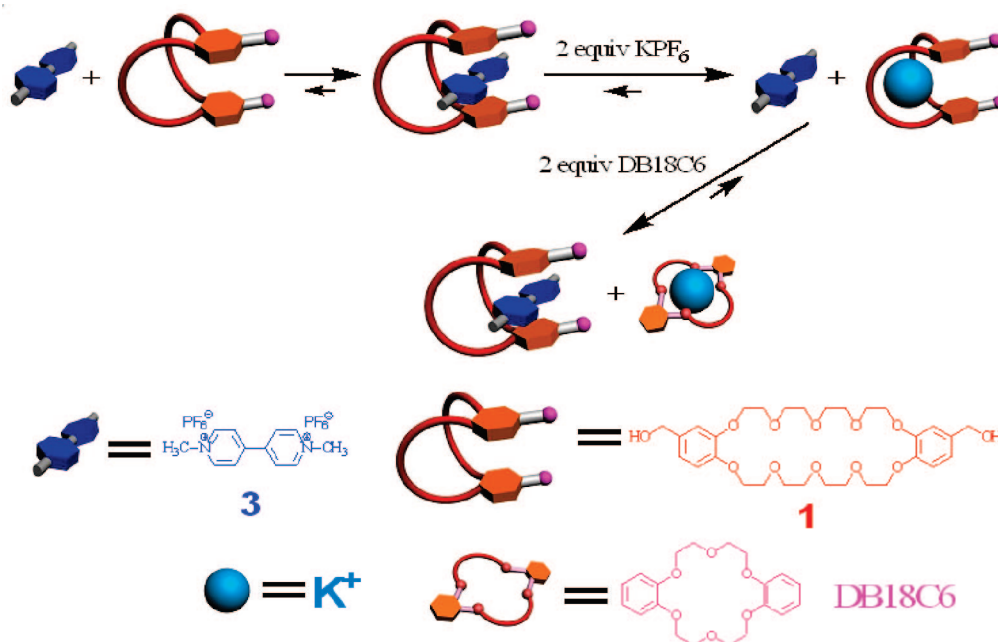

FIGURE 5. Reversible control of the complexation of *cis*-DB30C10 diol (**1**) with paraquat (**3**) brought about by displacement with the potassium cation from KPF$_6$ and the subsequent rebinding of **3** by **1** as K$^+$ is bound by added DB18C6.

chemical shift changes of protons on diquat **4** caused by its complexation with **1** decreased (Figure 6a,b,c,f) and correspondingly the orange color of the solution turned weak. When one more molar equiv of KPF$_6$ was added, the chemical shift changes of protons on diquat **4** decreased further (Figure 6d,f) and correspondingly the orange color of the solution turned a little weaker but did not disappear, indicating that the com-

plexation between **1** and **4** was not completely prohibited. When 2 molar equiv of DB18C6 was subsequently added, chemical shift changes of protons on diquat **4** were increased but not to the degree when neither KPF$_6$ nor DB18C6 were added (Figure 6b,e,f) and correspondingly the orange color of the solution became stronger, indicating the increase of the complex **1·4** concentration. The same phenomena were observed for the
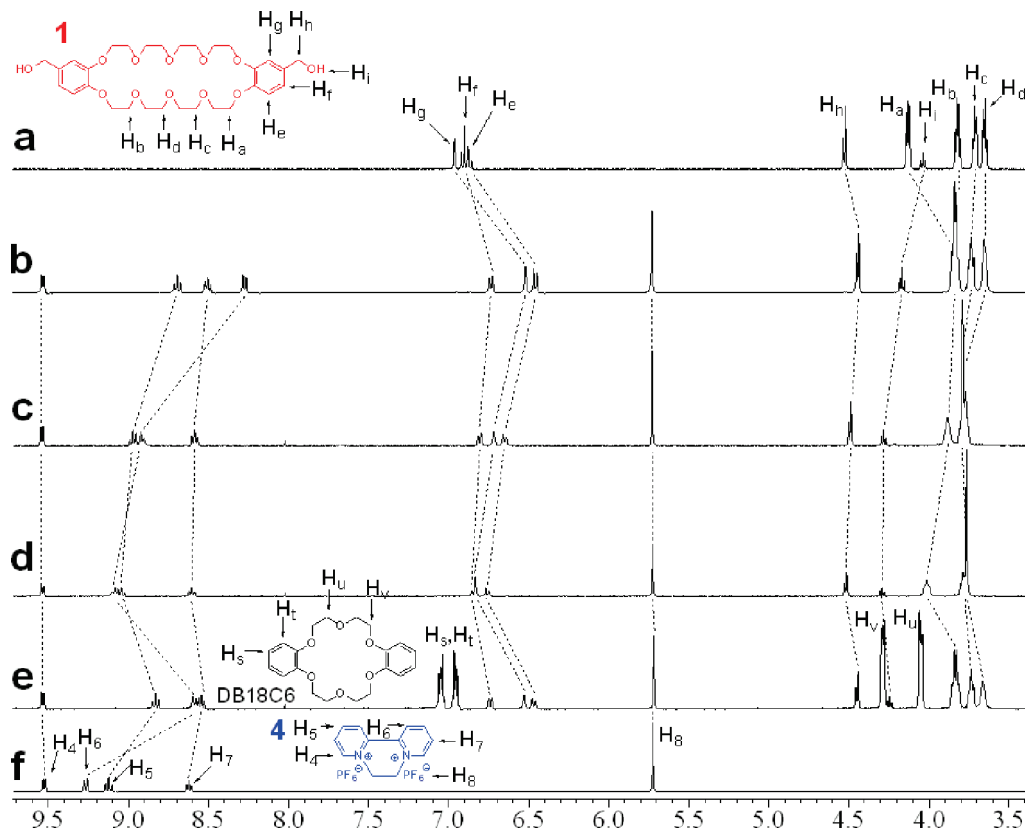
FIGURE 6. Partial 400 MHz ^{1}H NMR spectra of (a) 4.00 mM **1**, (b) 4.00 mM **1** and **4**, (c) 4.00 mM **1**, **4**, and KPF$_6$, (d) 4.00 mM **1** and **4** and 8.00 mM KPF$_6$, (e) 4.00 mM **1** and **4** and 8.00 mM KPF$_6$ and DB18C6, and (f) 4.00 mM **4** in acetone-d_6.

complexation between *trans*-DB30C10 diol **2** and diquat **4** (Figure S43, Supporting Information). These demonstrated that the complexations between *cis*- and *trans*-DB30C10 diols **1** and **2** with diquat **4** cannot be controlled by adding small molecules KPF$_6$ and DB18C6. These also indicated that the K_a value of complex **1·4** (or **2·4**) is comparable to that of complex **1·**KPF$_6$ (or **2·**KPF$_6$).

K. Crystal Structures of Complexes 2·4 and 1·4. Single crystals of **1·4** were obtained by diffusion of isopropyl ether into a solution of **1** and **4** in acetone at room temperature. The X-ray crystal structure of complex **1·4** confirmed the 1:1 stoichiometry and demonstrated that *cis*-DB30C10 diol **1** and diquat **4** formed a taco complex in the solid state (Figure 7). Because of the formation of a so-called "supramolecular cryptand" structure,[22] complex **1·4** is stabilized by not only the hydrogen bonding between the host and guest and $\pi-\pi$ stacking between the catechol rings of the crown ether host and the pyridinium rings of the diquat guest but also the hydrogen bonding between the "water bridge" and **1** and **4** (Figure 7). Interestingly, the same kind of water-assisted formation of supramolecular cryptand structure was also observed in a previously reported complex based on an isomeric bis(*m*-phenylene)-32-crown-10 diol and diquat.[10h] Two *N*-methylene hydrogens H$_8$ (**f** and **j** in Figure 7) and two α-pyridinium hydrogens H$_4$ (**e, g, h, i, k,** and **l** in Figure 7) are directly hydrogen bonded to ethyleneoxy oxygen atoms of the crown ether host. Two δ-pyridinium hydrogens H$_6$ are indirectly connected to the two terminal alcohol groups of host **1** by a hydrogen-bonding water bridge (**a, b, c,** and **d** in Figure 7) to form the supramolecular cryptand structure. None of the β-pyridinium hydrogens H$_7$ and γ-pyridinium hydrogens H$_5$ of **4** are involved
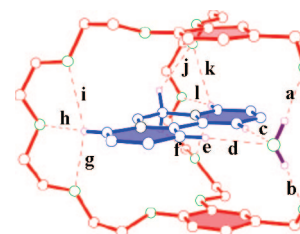

FIGURE 7. A ball-stick view of the X-ray structure of **1·4**. **1** is red, **4** is blue, hydrogens are pink, oxygens are green, nitrogens are black, and the water molecule is magenta. PF$_6$ counterions, solvent molecules, and hydrogens except the ones involved in hydrogen bonding between **1** and **4** were omitted for clarity. Hydrogen bond parameters: H···O distance (Å), C(O)–H···O angle (deg), C(O)···O distance (Å)—**a**, 1.90, 177, 2.75; **b**, 1.90, 177, 2.75; **c**, 2.70, 180, 3.63; **d**, 2.54, 170, 3.46; **e**, 2.70, 113, 3.19; **f**, 2.65, 141, 3.46; **g**, 2.63, 108, 3.04; **h**, 2.26, 166, 3.17; **i**, 2.63, 108, 3.04; **j**, 2.65, 141, 3.46; **k**, 2.70, 113, 3.19; **l**, 2.50, 166, 3.41. Face-to-face π-stacking parameters: centroid–centroid distances (Å) 4.04, 4.36, 4.04, 4.36; ring plane/ring plane inclinations (deg) 3.3, 3.3, 3.3, 3.3.

in interactions between the host and guest in complex **1·4** in the solid state.

The two phenylene rings of **1** are not parallel to each other but exhibit a twist angle of 6.7°. The centroid—centroid distance

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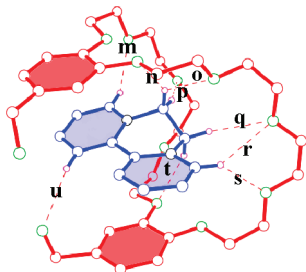
FIGURE 8. A ball-stick view of the X-ray structure of **2·4**. **2** is red, **4** is blue, hydrogens are pink, oxygens are green, and nitrogens are black. PF$_6$ counterions, solvent molecules, and hydrogens except the ones involved in hydrogen bonding between **2** and **4** were omitted for clarity. Hydrogen bond parameters: H···O distance (Å), C−H···O angle (deg), C···O distance (Å)—**m**, 2.27, 140, 3.04; **n**, 2.49, 146, 3.34; **o**, 2.68, 130, 3.39; **p**, 2.40, 166, 3.35; **q**, 2.69, 157, 3.60; **r**, 2.62, 146, 3.43; **s**, 2.32, 140, 3.09; **t**, 2.49, 150, 3.36; **u**, 2.57, 161, 3.47. Face-to-face π-stacking parameters: centroid−centroid distances (Å) 3.66, 4.99, 4.87, 3.65; ring plane/ring plane inclinations (deg): 8.3, 8.3, 10.2, 6.2.

between them is 6.84 Å. The two pyridium rings of diquat **4** were twisted in the solid state for all previously reported diquat-based complexes,[10a,g−i,12,18] but the crystal structure shown in Figure 7 demonstrates that here the two pyridium rings of diquat **4** are exactly coplanar in the solid state for complex **1·4**, presumably to maximize face-to-face π-stacking and charge transfer interactions between the electron-rich catechol rings of crown ether **1** and electron-poor pyridinium rings of diquat **4**.

Single crystals of **2·4** were obtained by diffusion of isopropyl ether into a solution of **2** and **4** in acetonitrile at room temperature. The X-ray crystal structure of complex **2·4** also confirmed the 1:1 stoichiometry and demonstrated that *trans*-DB30C10 diol **2** and diquat **4** also formed a taco complex in the solid state (Figure 8). Just like complex **1·4**, complex **2·4** is also stabilized by hydrogen bonds between the host and guest and π−π stacking interactions between the two catechol rings of the crown ether host and the two pyridinium rings of the diquat guest (Figure 8), two α-pyridinium hydrogens H$_4$ (**m**, **r**, and **s** in Figure 8) are directly hydrogen bonded to ethyleneoxy oxygen atoms of the crown ether host, and none of β-pyridinium hydrogens H$_7$ and γ-pyridinium hydrogens H$_5$ of **4** are involved in interactions between the host and guest in complex **2·4** in the solid state.

However, there are some differences. First, the formation of a supramolecular cryptand structure is not observed for complex **2·4** in the solid state (Figure 8) and one δ-pyridinium hydrogen H$_6$ is directly connected to a terminal alcohol group of host **2** (**i** in Figure 8). This is a possible reason for the increase in association constant from **2·4** (3.3 × 10^4 M$^{−1}$) to **1·4** (5.0 × 10^4 M$^{−1}$). Second, all four *N*-methylene hydrogens H$_8$ are directly hydrogen bonded to ethyleneoxy oxygen atoms of the crown ether host (**n**, **o**, **p**, **q**, and **t** in Figure 8) for complex **2·4** in the solid state while only two *N*-methylene hydrogens H$_8$ do so (**f** and **j** in Figure 7) for complex **1·4** in the solid state. Third, the two catechol rings of the crown ether host in **2·4**, with a twist angle of 2.3°, are more parallel in the solid state (Figure 8) than those in **1·4**, with a twist angle of 6.7°, in the solid state (Figure 7). Fourth, the centroid−centroid distance, 7.23 Å, between the two catechol rings of the crown ether host in **2·4** is bigger (Figure 8) than the corresponding value, 6.84 Å, in **1·4** (Figure 7). Fifth, the two pyridium rings of diquat **4**, with a twist angle of 16.3°, are not coplanar in the crystal structure of complex **2·4** (Figure 8).

Conclusion

In summary, isomeric *cis*- and *trans*-DB30C10 diols **1** and **2** were successfully synthesized regiospecifically with good yields, avoiding the difficult problem of separation of the two isomers' precursors diesters. Because *trans*-DB30C10 diester has 6 more atoms in its polyether macroring than *trans*-DB24C8 diester has, the reported method for the preparation of *trans*-DB24C8 diester fell in the trouble of the exclusive formation of smaller macrocycle carbomethoxybenzo-15-crown-5 when it was used for the synthesis of *trans*-DB30C10 diester. The synthetic routes of the two hosts **1** and **2** as a whole have atomic economy because the side product, **7b**, of benzylation of methyl 3,4-dihydroxybenzoate was used in the preparation of *trans*-DB30C10 diester **16**.

The big difference (44 or 18 times) between the K_a value of the **1·3** (or **2·3**) and **1·4** (or **2·4**) in acetone suggested high selectivity of **1** (or **2**) to bind diquat **4** against paraquat **3**. This indicated that the DB30C10 cavity can be used for the preparation of chemical sensors which can selectively detect diquat against paraquat.[23]

From the investigation of the influence of the addition of small molecules KPF$_6$ and DB18C6 on the complexations of either of hosts **1** and **2** with either of guests paraquat **3** and diquat **4**, we found that the addition of KPF$_6$ could dissociate the complexes **1·3** and **2·3** completely and the subsequent addition of DB18C6 could reform these complexes completely. This reversible control makes DB30C10 derivatives and paraquat derivatives good candidate components for constructing molecular machines driven by adding small molecules.

Experimental Section

α,ω-**Bis(2′-benzyloxy-5′-carbomethoxyphenoxy)-3,6,9-trioxaundecane (Dimethyl 4,4′-Bis(benzyloxy)-3,3′-oxytetra(ethyleneoxy)dibenzoate) (8).** A suspension of methyl 4-benzyloxy-3-hydroxybanzoate **7a** (5.16 g, 20.0 mmol), tetra(ethylene glycol) dichloride (1.96 g, 8.50 mmol), and K$_2$CO$_3$ (7.60 g, 55.0 mmol) in CH$_3$CN (100 mL) was heated under N$_2$ atmosphere at reflux for 48 h. After the mixture was filtered, the solvent of the filtrate was removed. The residue was dissolved in CH$_2$Cl$_2$ and washed twice with saturated Na$_2$CO$_3$ solution and the organic layer was dried over anhydrous Na$_2$SO$_4$. CH$_2$Cl$_2$ was removed. The crude product was absorbed on silica gel and purified by flash column chromatography (ethyl acetate/petroleum ether = 2/3) to give **8** as a light yellow liquid (4.98 g, 87%). ^{1}H NMR (400 MHz, CDCl$_3$, 22 °C) δ 7.62 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 2H), 7.57 (d, J = 2.0 Hz, 2H), 7.43−7.26 (m, 10H), 6.90 (d, J = 8.4 Hz, 2H), 5.16 (s, 4H), 4.21 (t, J = 5.2 Hz, 4H), 3.88 (t, J = 5.2 Hz, 10H), 3.71 (t, J = 5.2 Hz, 4H), 3.62 (t, J = 5.2 Hz, 4H). Anal. Calcd for C$_{38}$H$_{42}$O$_{11}$: C, 67.64; H, 6.27. Found: C, 67.68; H, 6.28.

α,ω-**Bis(2′-hydroxy-5′-carbomethoxyphenoxy)-3,6,9-trioxaundecane (Dimethyl 4,4′-Dihydroxy-3,3′-oxytetra(ethyleneoxy)dibenzoate) (9).** A suspension of **8** (10.0 g, 14.8 mmol) and Pd/C (10%, 1.00 g) in ethyl acetate (200 mL) was stirred at room temperature under H$_2$ atmosphere for 24 h. After filtration, the filtrate was concentrated to give **9** as a white solid (6.72 g, 92%). Mp 62−63 °C. ^{1}H NMR (400 MHz, CD$_3$COCD$_3$, 22 °C) δ 8.46 (br, 2H), 7.51 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 2H), 6.86 (d, J = 8.4

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Hz, 2H), 4.17 (t, J = 4.2 Hz, 4H), 3.80 (t, J = 4.2 Hz, 4H), 3.77 (s, 6H), 3.65−3.58 (m, 8H). Anal. Calcd for $C_{24}H_{30}O_{11}$: C, 58.29; H, 6.12. Found: C, 58.30; H, 6.14.

cis-Bis(carbomethoxybenzo)-30-crown-10 (10). To a suspension of tetrabutylammonium bromide (80.0 mg) and K_2CO_3 (20.7 g, 150 mmol) in DMF (800 mL) under N_2 atomsphere at 110 °C was added a solution of 9 (9.01 g, 18.2 mmol) and tetra(ethylene glycol) dichloride (4.20 g, 18.2 mmol) in DMF (50 mL) with a syringe pump at 0.80 mL/h. The mixture was further stirred at 110 °C for 5 days. After filtration, the solvent of the filtrate was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed twice with water. The solvent was removed to afford a crude product, which was absorbed on silica gel and purified by flash column chromatography (ethyl acetate/acetone =3/1) to give 10 as a light yellow solid (6.50 g, 55%). Mp 149−150 °C; ^{1}H NMR (400 MHz, CD_3COCD_3, 22 °C) δ 7.61 (dd, J_1 = 4.8 Hz, J_2 = 1.6 Hz, 2H), 7.49 (d, J = 1.6 Hz, 2H), 7.06 (d, J = 4.8 Hz, 2H), 4.30−4.28 (m, 4H), 4.24−4.22 (m 4H), 3.89−3.86 (m, 14H), 3.80−3.70 (m, 16H). Anal. Calcd for $C_{32}H_{44}O_{14}$: C, 58.89; H, 6.79. Found: C, 58.82; H, 6.79.

cis-Bis(hydroxymethylbenzo)-30-crown-10 (1). To a suspension of $LiAlH_4$ (76.0 mg, 2.00 mmol) in dry THF (10 mL) was added dropwise a solution of 10 (0.650 g, 1.00 mmol) in dry THF (20.0 mL) under N_2 atmosphere at 0 °C. The mixture was further stirred for 12 h at room temperature. The excess $LiAlH_4$ was quenched with ethyl acetate. The resulting mixture was filtered and the filtrate was concentrated to give a white solid, which was dissolved in CH_2Cl_2 and washed with saturated NaCl solution. The solvent was removed to give 1 as a white solid (0.57 g, 95%). Mp 89−90 °C; ^{1}H NMR (400 MHz, CD_3COCD_3, 22 °C) δ 6.91 (d, J = 2.0 H, 2H), 6.87−6.82 (m, 4H), 4.47 (d, J = 6.0 Hz, 4H), 4.07 (t, J = 4.4 Hz, 8H), 3.99 (t, J = 6.0 Hz, 2H), 3.78−3.75 (m, 8H), 3.67−3.65 (m, 8H), 3.61−3.58 (m, 8H). Anal. Calcd for $C_{30}H_{44}O_{12}$: C, 60.39; H, 7.43. Found: C, 60.39; H, 7.43.

Methyl 4-Benzyloxy-3-(chloroethoxy{ethoxy[ethoxy(ethoxy)]})-benzoate (11). A solution of 7a (2.00 g, 7.70 mmol), K_2CO_3 (3.20 g, 23.2 mmol), and tetra(ethyleneglycol) dichloride (5.50 g, 20.0 mmol) in CH_3CN (250 mL) was stirred under N_2 atmosphere at reflux for 3 days. After filtration, the solvent of the filtrate was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed twice with water. CH_2Cl_2 was removed. The crude product was absorbed on silica gel and purified by column chromatography (ethyl acetate/petroleum = 1/8) to give 11 as a light yellow liquid (2.61 g, 75%). ^{1}H NMR (400 MHz, CD_3COCD_3, 22 °C) δ 7.63−7.60 (m, 2H), 7.54 (d, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.34 (t, J = 6.8 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 5.24 (s, 2H), 4.23 (t, J = 4.8 Hz, 2H), 3.86 (t, J = 4.8 Hz, 2H), 3.84 (s, 3H) 3.72−3.57 (m, 12H). Anal. Calcd for $C_{23}H_{29}ClO_7$: C, 60.99; H, 6.45. Found: C, 60.94; H, 6.49.

Methyl 4-Hydoxy-3-(chloroethoxy{ethoxy[ethoxy(ethoxy)]})-benzoate (12). A suspension of 11 (0.109 g, 0.240 mmol) and 10% Pd/C (92.0 mg) in $CH_3OH/CHCl_3$ (25.0/25.0 mL) was stirred under H_2 atmosphere at 50 °C for 48 h. After filtration, the filtrate was concentrated to give 12 as a light yellow oil (2.75 g, 100%). This compound was used in the next step without further purification. ESIMS (negative) *m/z* 361.2 [M − H]⁻. ESIMS (positive) *m/z* 385.2 [M + Na]⁺, 401.2 [M + K]⁺. ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C) δ 7.79 (br, 1H), 7.66 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.59 (d, J = 2.4 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.23−4.21 (m, 2H), 3.87(s, 3H), 3.86−3.84 (m, 2H), 3.78−3.62 (m, 12H). Anal. Calcd for $C_{16}H_{23}ClO_7$: C, 52.97; H, 6.39. Found: C, 52.96; H, 6.38.

α-(2′-Benzyloxy-5′-carbomethoxyphenoxy)-ω-(5′-benzyloxy-2′-carbomethoxyphenoxy)-3,6,9-trioxaundecane (Dimethyl 3,4′-Bis(benzyloxy)-4,3′-oxytetra(ethyleneoxy)dibenzoate) (14). A suspension of 7b (0.517 g, 2.00 mmol), 12 (0.810 g, 1.80 mmol), and K_2CO_3 (0.790 g, 5.00 mmol) in CH_3CN (25.0 mL) was stirred under N_2 atmosphere at reflux for 36 h. After filtration, the solvent was removed. The resulting residue was dissolved in CH_2Cl_2 and washed

twice with saturated Na_2CO_3 solution. CH_2Cl_2 was removed. The crude product was absorbed on silica gel and purified by flash column chromatography (ethyl acetate/petroleum ether = 1/2) to give 14 as a yellow liquid (1.09 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C) δ 7.66−7.58 (m, 4H), 7.46−7.26 (m, 10H), 6.90 (d, J = 8.4 Hz, 2H), 5.16 (s, 2H), 5.13 (s, 2H), 4.22−4.20 (m, 4H), 3.89−3.87 (m, 10H), 3.72−3.70 (m, 4H), 3.62−3.60 (m, 4H). Anal. Calcd for $C_{38}H_{42}O_{11}$: C, 67.64; H, 6.27. Found: C, 67.65; H, 6.31.

α-(2′-Hydroxy-5′-carbomethoxyphenoxy)-ω-(5′-hydroxy-2′-carbomethoxyphenoxy)-3,6,9-trioxaundecane (Dimethyl 3,4′-Bis(hydroxy)-4,3′-oxytetra(ethyleneoxy)dibenzoate) (15). A suspension of 14 (1.00 g, 1.48 mmol) and Pd/C (0.10 g, 10%) in ethyl acetate (20.0 mL) was stirred under H_2 atmosphere at 50 °C for 24 h. After filtration, the filtrate was concentrated to give 15 as a light yellow liquid (0.70 g, 96%). ^{1}H NMR (400 MHz, CD_3COCD_3, 22 °C) δ 7.70 (br, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.58−7.54 (m, 3H), 7.05 (br, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 4.21−4.20 (br, 4H), 3.88−3.84 (m, 10H), 3.73−3.71 (m, 8H). Anal. Calcd for $C_{24}H_{30}O_{11}$: C, 58.29; H, 6.12. Found: C, 58.29; H, 6.20.

trans-Bis(carbomethoxybenzo)-30-crown-10 (16). To a stirred suspension of tetrabutylammonium bromide (60.0 mg, 0.186 mmol) and K_2CO_3 (20.7 g, 150 mmol) in DMF (800 mL) at 110 °C under N_2 atmosphere was added a solution of 15 (8.00 g, 16.2 mmol) and tetra(ethyleneglycol) dichloride (3.74 g, 16.2 mmol) in DMF (50 mL) with a syringe pump at 0.80 mL/h. The mixture was further stirred at 110 °C for 5 days. After filtration, the solvent of the filtrate was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed twice with water. The solvent was removed to afford a crude product, which was absorbed on silica gel and purified by flash column chromatography (ethyl/acetone = 3/1) to give 16 as a light yellow solid (4.75 g, 45%). Mp 170−171 °C; ^{1}H NMR (400 MHz, CD_3COCD_3, 22 °C) δ 7.62 (dd, J_1 = 4.8 Hz, J_2 = 1.6 Hz, 2H), 7.48 (d, J = 1.6 Hz, 2H), 7.08 (d, J = 4.8 Hz, 2H), 4.32−4.30 (m, 4H), 4.22−4.20 (m, 4H), 3.92−3.90 (m, 4H), 3.85 (s, 6H), 3.83−3.80 (m, 4H), 3.78−3.70 (m, 16H). Anal. Calcd for $C_{32}H_{44}O_{14}$: C, 58.89; H, 6.79. Found: C, 58.84; H, 6.77.

trans-Bis(hydroxymethylbenzo)-30-crown-10 (2). To a suspension of $LiAlH_4$ (57.0 mg, 1.50 mmol) in THF (10.0 mL) was added a solution of 15 (0.500 g, 0.770 mmol) in dry THF (20.0 mL) dropwise under N_2 atmosphere at 0 °C. The reaction was further stirred for 12 h at room temerature. The excess $LiAlH_4$ was quenched with ethyl acetate. The resulting mixture was filtered and the filtrate was concentrated to give a solid. The solid was washed with saturated NaCl solution and water and dried over anhydrous Na_2SO_4. The solvent was removed to give 2 as a white solid (0.43 g, 94%). Mp 106−107 °C; ^{1}H NMR (400 MHz, CD_3COCD_3, 22 °C) δ 6.92 (s, 2H), 6.86−6.80 (m, 4H), 4.47 (d, J = 6.0 Hz, 4H), 4.09−4.06 (m, 8H), 3.98 (t, J = 6.0 Hz, 2H), 3.79−3.75 (m, 8H), 3.67−3.65 (m, 8H), 3.60−3.58 (m, 8H). Anal. Calcd for $C_{30}H_{44}O_{12}$: C, 60.39; H, 7.43. Found: C, 60.39; H, 7.44.

Supporting Information Available: The X-ray crystallographic files (CIF) for 1·4 and 2·4, determination of association constants of complexes 1·3, 1·4, 2·3, and 3·4, proton NMR spectra of compounds, electrospray ionization mass spectra of equimolar acetone solutions of either of hosts 1 and 2 with either of guests 3 and 4, and X-ray analysis data of 1·4 and 2·4, and other materials. This material is available free of charge via the Internet at http://pubs.acs.org.

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