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Efficient Syntheses of Novel Cryptands Based on Bis(*m*-phenylene)-26-crown-8 and Their Complexation with Paraquat

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High-yielding syntheses of two novel cryptands based on bis(*m*-phenylene)-26-crown-8 are reported. One-step [2+2] cyclization of methyl 3,5-dihydroxybenzoate with tri(ethylene glycol) ditosylate under pseudo-high-dilution conditions gave BMP26C8 (**1**) in 28% yield. Reduction of **1** with LAH, followed by deprotonation (NaH) and alkylation with propargyl bromide, afforded the dialkynated BMP26C8 (**3**) in high yield (two-step 84%). Unimolecular macrocyclization of **3** through copper(II)-mediated Eglinton coupling generated the diacetylene-containing cryptand **4** in 97% yield. Pd/C-catalyzed hydrogenation of **4** yielded the cryptand **5** (93%). Their structures were confirmed by NMR, ESI-MS, and X-ray analysis. The complexation behavior of these new cryptands with paraquat was also studied, and it was found that these cryptands bind paraquat more strongly than the corresponding BMP26C8. The association constants (K_1 and K_2) in acetone solution were determined to be K_1 = 914 M^{-1}, K_2 = 229 M^{-1} for complex **4_2·6** and K_1 = 758 M^{-1}, K_2 = 190 M^{-1} for complex **5_2·6**. Moreover, the two new [3]pseudorotaxane-like complexes **4_2·6** and **5_2·6** were also obtained in the solid state, as confirmed by X-ray analysis.

Introduction

Mechanically interlocked structures such as rotaxanes and catenanes have attracted much attention not only because of the fascinating aspect of their topologies but also thanks to their applicability in the preparation of nanoscale molecular electronic devices.[1] Crown ethers,[2] cucurbit[*n*]urils,[3] calixarenes,[4] cyclodextrins,[5] and other compounds[6] have been widely used as hosts in the preparation of these interlocked structures because they readily allow formation of host–guest complexes with ionic and neutral guest molecules. Recently it has been shown that crown-ether-based cryptands, including those based on bis(*m*-phenylene)-32-crown-10 and on bis(*m*-phenylene)-26-crown-8, are powerful hosts that complex with paraquat, paraquat derivatives, diquats, and secondary ammonium salts much more strongly than the corresponding simple crown ethers.[7] The successful formation of host cryptands has undoubtedly played key roles in the construction of different kinds of complexes with specific structures and properties. During the past decade, Gibson, Huang, and coworkers have made a significant contribution to the syntheses, complexation, and applications of crown-ether-based cryptands.[7,8] However, the preparation of these crown-ether-based cryptands was mostly in yields of only 21–50%.[7a–7h] One possible reason for this is the difficulties inherent in the cyclization of a difunctionalized bisphenylene crown ether with another small molecule.[7b,7i,8b] Consequently, it is still important to improve the synthetic efficiency and to design novel cryptands capable of binding different organic guests, which could provide many opportunities for the development of new specific supramolecular systems. Here we report a high-yielding synthesis of the novel cryptands **4** and **5**, both based on bis(*m*-phenylene)-26-crown-8, by copper(II)-mediated Eglinton coupling[10] and, in the case of **5**, subsequent Pd/C-catalyzed reduction (Scheme 1). Furthermore, the complexation behavior of these new cryptands with paraquat **6** was also investigated and it was found that they can form [3]pseudorotaxane-like complexes with paraquat both in solution and in the solid state.

Results and Discussion

The efficient formation of the crown ether **1** was vital for successful syntheses of these novel cryptands, as depicted in Scheme 1. This compound had previously been prepared by Gibson's group by a one-step method from methyl 3,5-dihydroxybenzoate and tri(ethylene glycol) dichloride in the presence of NaH in DMF.[9d] The yield, however, was reported to be only 6%. In this study we modified the one-step strategy, resulting in a remarkable improvement in the yield. Use of

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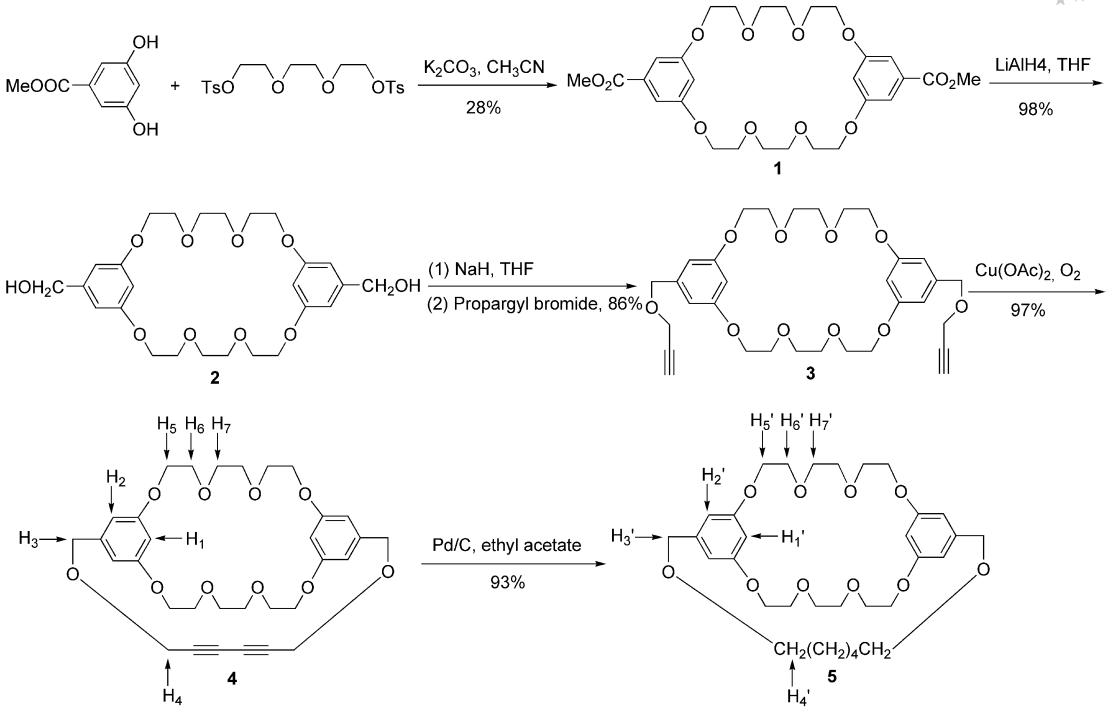


Scheme 1. Syntheses of two cryptands based on bis(*m*-phenylene)-26-crown-8.

tri(ethylene glycol) ditosylate in place of the dichloride in a reaction with methyl 3,5-dihydroxybenzoate in acetonitrile at reflux and in the presence of K_2CO_3 under pseudo-high-dilution conditions generated the desired crown ether **1** in 28% yield, which is much higher than reported.[7m,9d] This modified procedure is practical, easily performed, and high-yielding. The improvement may be accounted for by a number of factors. Firstly, the more soluble potassium tosylate generated in this reaction could have templated the cyclization process. Secondly, the less polar acetonitrile is favorable for cyclization. Thirdly, pseudo-high-dilution conditions can prevent polymer or oligomer formation. After reduction with LAH, followed by deprotonation and alkylation with propargyl bromide, the dialkyne compound **3** (Figure 1, a) was obtained in high yield (Scheme 1).

The final step of the synthesis of a crown-ether-based cryptand usually includes a second cyclization reaction. Although several reactions, such as esterification,[8] have been reported for this purpose, the cyclization yields are often less than 50%. Here we employed the copper(II)-mediated Eglinton coupling for the final cyclization. The cryptand **4** was generated in 97% yield by slow addition of the dialkyne **3** over 2 d (i.e., pseudo-high-dilution conditions) to an acetonitrile/dichloromethane (1:4) solution of $Cu(OAc)_2$ under O_2 at 45–50 °C. From the cryptand **4**, the bis(*m*-phenylene)-26-crown-8-based cryptand **5** was then synthesized in 93% yield by Pd/C-catalyzed reduction under H_2. The yields both for cryptand **4** and for cryptand **5** are much higher than those of analogues reported in the literature previously.[7] We have therefore developed a new and high-yielding approach for syntheses of crown-ether-based cryptands.

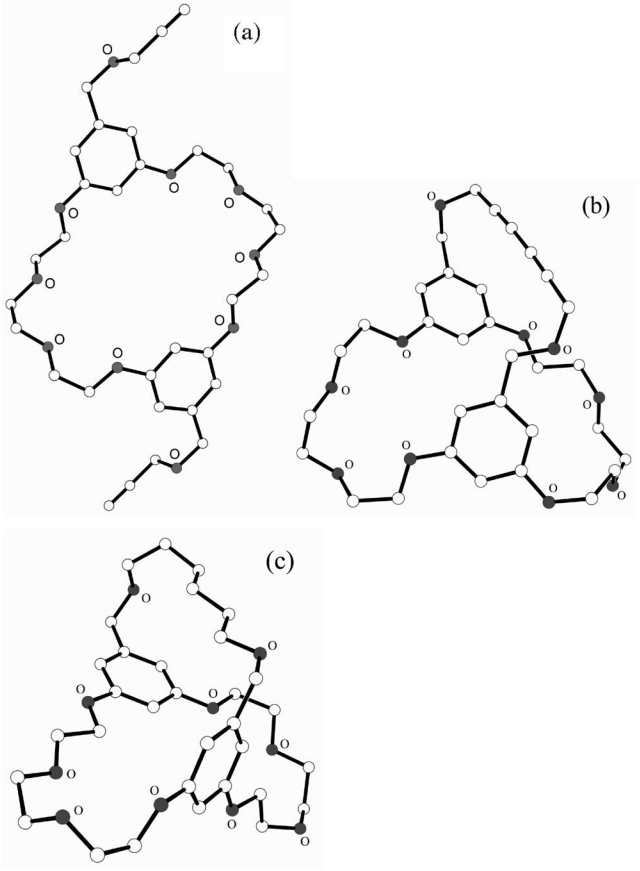


Figure 1. Ball-and-stick views of the X-ray structures of: a) compound **3**, b) cryptand **4**, and c) cryptand **5**. All hydrogen atoms have been omitted for clarity.

The structures of these new cryptands have been fully characterized by spectroscopic methods, including ^{1}H NMR, ^{13}C NMR, ESI-MS, HRESI-MS, and MALDI-TOF-MS. Fortunately, single crystals both of cryptand **4** and of cryptand **5** were also obtained.

A single crystal of cryptand **4** suitable for X-ray analysis was grown by slow evaporation of methanol solution. As shown by its crystal structure (Figure 1, b), the catechol rings are not parallel (angle 48.77°) and the centroid–centroid distance between the catechol rings is 5.869 Å.

A single crystal of cryptand **5** was also obtained by slow evaporation of a solution of cryptand **5** in acetone at room temperature. The X-ray structure (Figure 1, c) shows that the angle between the planes of the aromatic rings is 73.54°; the distance between the centroids of the aromatic rings is 5.781 Å. The crystal data and the experimental parameters are summarized in the Supporting Information. The crystal structures of cryptands **4** and **5** show that both of them are slightly collapsed, but the cavities are accessible. Furthermore, the cavity of cryptand **4** is slightly more open than that of cryptand **5** in the solid state (parts b and c in Figure 1).

With these new cryptands to hand, we turned our attention to their application in host–guest chemistry. Complexation between either cryptand **4** or cryptand **5** and paraquat **6** (Scheme 2) was studied. Mole ratio plots[11] (Figure 2) based on proton NMR spectroscopic data demonstrated that both of these complexes were of 2:1 stoichiometry in solution. Equimolar solutions of either cryptand **4** or cryptand **5** and paraquat **6** in [D_6]acetone were yellow as a result of charge transfer between the electron-rich aromatic rings of the cryptands and the electron-poor aromatic ring of paraquat. The ^{1}H NMR spectra of **6** with either **4** or **5** (1:1) in [D_6]acetone solution at room temperature show that the chemical shifts of the protons of the complex are significantly different from those of their free components. Only one set of peaks was found in each of the proton NMR spectra of solutions of **4** or **5** with **6**, indicating that exchange in these two complexation systems was fast on the proton NMR timescale. The chemical shift changes of the protons of **4** and **5** showed almost the same characteristics after complexation with **6**. Partial proton NMR spectra of **4**, **5**, **6**, a mixture of **4** and **6**, and a mixture of **5** and **6** are shown in Figure 3. After complexation, the resonances of the pyridinium protons $\mathbf{H}_\alpha$ and $\mathbf{H}_\beta$ on **6** and the aromatic protons $\mathbf{H_1}$, $\mathbf{H_2}$, $\mathbf{H_1}'$, and $\mathbf{H_2}'$ on **4** and **5** are shifted significantly upfield, which indicates the existence of π-stacking interactions between the π-donors (aromatic rings) and the π-acceptor (bipyridinium). Furthermore, the *N*-methyl protons $\mathbf{H}_\gamma$ on **6** and the benzyl methylene protons $\mathbf{H_3}$ and $\mathbf{H_3}'$ on **4** and **5** and the α-CH_2CH_2O protons $\mathbf{H_5}$ and $\mathbf{H_5}'$ on **4** and **5** were also shifted upfield, whereas the alkyne α-protons $\mathbf{H_4}$, alkane protons $\mathbf{H_4}'$, β-CH_2CH_2O protons $\mathbf{H_6}$ and $\mathbf{H_6}'$, and γ-CH_2CH_2O protons $\mathbf{H_7}$ and $\mathbf{H_7}'$ on **4** and **5** were shifted downfield.

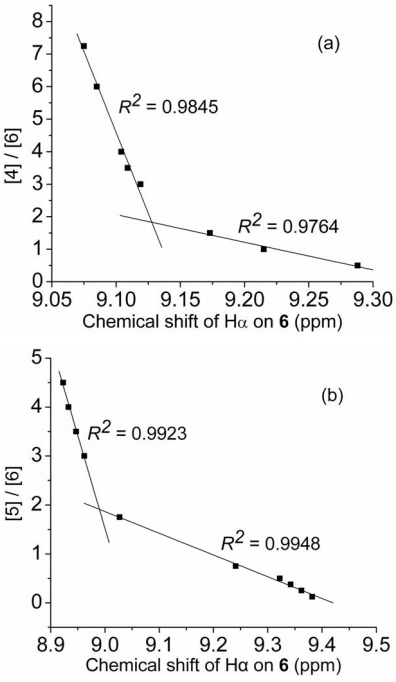
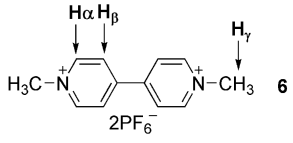


Figure 2. Mole ratio plots for a) cryptand **4** and paraquat **6**, and b) cryptand **5** and paraquat **6** in [D_6]acetone. $[\mathbf{4}]_0$ or $[\mathbf{5}]_0$ = 8.00 mM.

To improve understanding of the complexation behavior of the cryptands **4** or **5** with paraquat **6**, proton NMR characterization was carried out with a series of acetone solutions in which the initial concentration of guest **6** was kept constant at 0.5 mM while the initial concentrations of hosts **4** or **5** were systematically varied. From these proton NMR spectroscopic data, the extent of complexation (ρ) was determined by the Benesi–Hildebrand method[12] and Scatchard plots[13] were made (Figure 4). The linear natures of these plots demonstrated that the two *N*-methylpyridinium binding sites in paraquat **6** are independent of each other during the complexation between **6** and either **4** or **5**. From the slope of the top plot we determined the association constants K_1 and K_2 for **4** and **6** to be 914 ± 13 M^{-1} and 229 ± 3 M^{-1}, respectively (Figure 4, a).[14] From the slope of the bottom plot (Figure 4, b), the association constants $K_1 = 758 \pm 7$ M^{-1} and $K_2 = 190 \pm 2$ M^{-1} were estimated for **5** and **6**. The average association constants (K_{av}) for the complexes $\mathbf{4_2}\cdot\mathbf{6}$ and $\mathbf{5_2}\cdot\mathbf{6}$ are $K_{av1} = 572 \pm 8$ M^{-1} and $K_{av2} = 474 \pm 5$ M^{-1}, respectively. The value of K_{av} is higher for the complex $\mathbf{4_2}\cdot\mathbf{6}$ than for the complex $\mathbf{5_2}\cdot\mathbf{6}$. Both of these average association constants K_{av1} and K_{av2} are higher than the K_a value for BMP26C8·**6** (390 M^{-1} in [D_6]acetone[7f]), indicating that the binding affinities of cryptands **4** and **5** for paraquat are higher than that of the corresponding crown ether.[7]



Scheme 2. Structure of paraquat **6**.

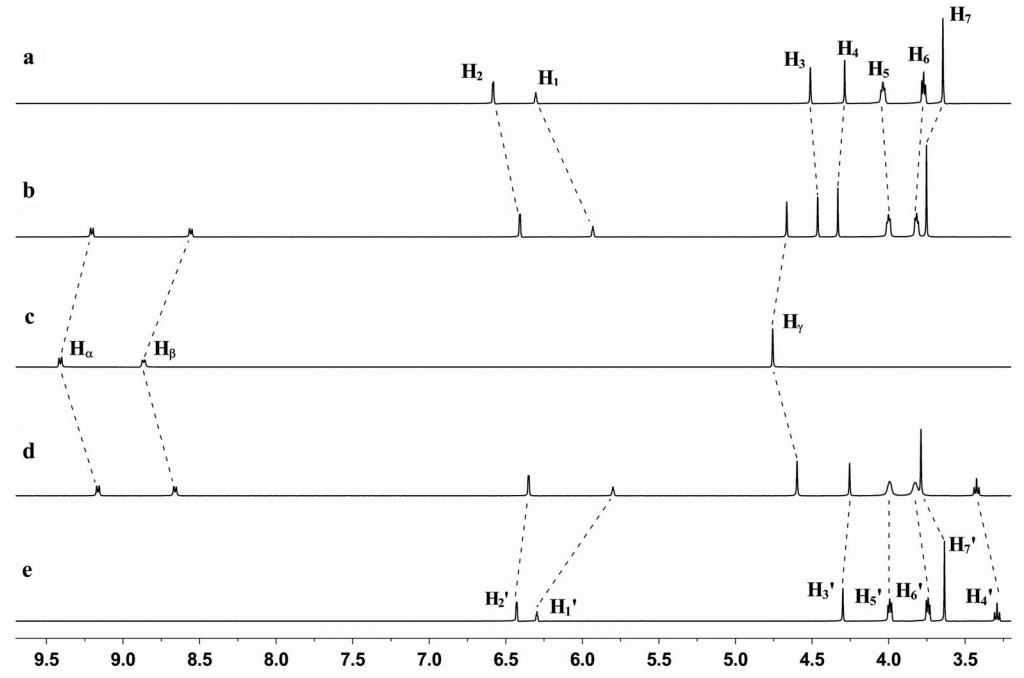


Figure 3. Partial proton NMR spectra (400 MHz, [D$_6$]acetone, 22 °C) of a) cryptand **4**, b) **4** (5.00 mM) with **6** (5.00 mM), c) paraquat **6**, d) **5** (5.00 mM) with **6** (5.00 mM), and e) cryptand **5**.

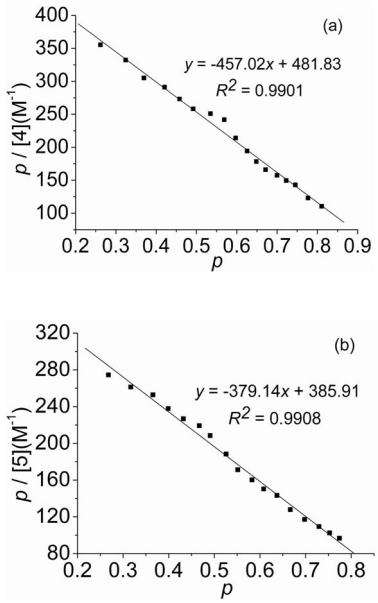


Figure 4. Scatchard plots for the complexation of **6** with a) **4**, and b) **5** in [D$_6$]actone at 22 °C; p = fraction of cryptand unit bound.

Electrospray ionization mass spectra of solutions of **4** and **6** and of **5** and **6** in acetonitrile confirmed the 2:1 stoichiometries of these complexes. For the mass spectrum of a solution of **4** and **6** with molar ration 2:1, the base peak was at *m*/*z* 331.12, corresponding to [**6** – PF_6]$^+$. Three peaks were found for **4$_2$·6** at *m*/*z* 807.20 (24%) [**4$_2$·6** – 2 CH_3 + 3 H]$^{2+}$, 675.45 (42%) [**4$_2$·6** – 2 PF_6]$^{2+}$, and 384.56 (69%) [**4$_2$·6** – PF_6 + Na + H_2O + H]$^{4+}$. Moreover, one peak was found for **4·6** at *m*/*z* 913.21 (37%) [**4·6** – PF_6]$^+$. For the mass spectrum of a mixture of **5** and **6** with molar ration 2:1, the base peak was at *m*/*z* 331.14, corresponding to [**6** – PF_6]$^+$. Four peaks for **5$_2$·6** were observed at *m*/*z* 683.69 (84%) [**5$_2$·6** – 2 PF_6]$^{2+}$, 505 [**5$_2$·6** – PF_6 + 4 H]$^{2+}$, 473.53 (42%) [**5$_2$·6** – 2 PF_6 + 3 H_2O]$^{3+}$, and 388.64 (83%) [**5$_2$·6** – PF_6 + Na + H_2O + H]$^{4+}$. In addition, one peak was observed for **5·6** at *m*/*z* 921.27 (53%) [**5·6** – PF_6]$^+$. However, no peaks corresponding to other stoichiometries were found in complexation of **6** either with **4** or with **5**.

Further evidence from X-ray analysis unambiguously confirmed the complex formation. X-ray analysis was carried out with a yellow crystal of **4$_2$·6** grown by slow evaporation of an acetone solution of **6** with excess **4**, which confirmed the 2:1 stoichiometry of the complexation between **4** and **6** in solution (Figure 5). The complex **4$_2$·6**, a [3]pseudorotaxane-like structure,[7f] is stabilized in the solid state by hydrogen bonding between host and guest and face-to-face π-stacking interaction between the aromatic rings of **4** and the pyridinium rings of **6**. It has recently been reported that a different bis(*m*-phenylene)-26-crown-8-based cryptand, with a tri(ethylene glycol) third chain, can also form a 2:1 complex with **6** in the solid state, as confirmed by single-crystal analysis.[7e] As in that complex, the *N*-methyl hydrogen atoms of **6** are not involved in hydrogen bonding between the host and the guest, and the two cryptand host molecules of the complex are also connected by two hydrogen bonds (**F** in Figure 5). However, there are some different characteristics because of the different structures of the two cryptand hosts. In the previous complex,[7e] four α-pyridinium hydrogen atoms of **6** form six hydrogen bonds directly with -CH_2CH_2O oxygen atoms of the cryptand host. Here, in the crystal structure of **4$_2$·6**, two α-pyridinium

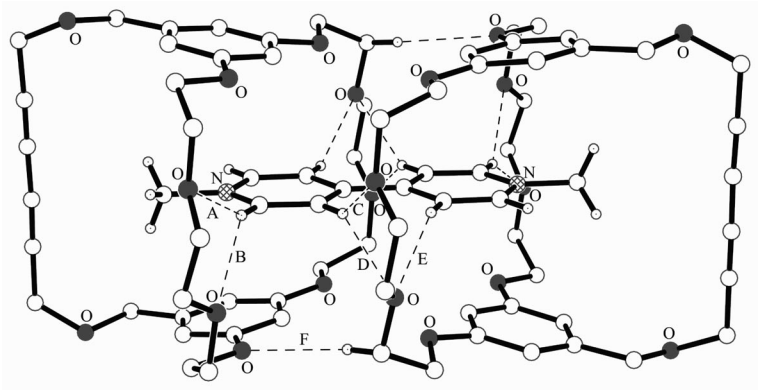


Figure 5. Ball-and-stick views of the X-ray structure of complex $\mathbf{4_2 \cdot 6}$. The PF_6 counterions, solvent molecules, and hydrogen atoms have been omitted for clarity, except for those on **6** or involved in hydrogen bonding. Hydrogen bond parameters: H···O distances [Å], C–H···O angles (degrees), C···O distances [Å] for **A**) 2.70, 153.42, 3.53; **B**) 2.71, 142.75, 3.50; **C**) 2.37, 143.86, 3.17; **D**) 2.48, 145.25, 3.29; **E**) 2.53, 147.68, 3.35; **F**) 2.58, 160.34, 3.51. Face-to-face π-stacking parameters: centroid–centroid distances [Å] 3.79, 3.77; ring plane/ring plane inclinations (degrees): 7.72, 8.75.

hydrogen atoms of **6** are directly connected to the host through four hydrogen bonds (**A** and **B** in Figure 5), and four β-pyridinium hydrogen atoms of **6** are directly hydrogen-bonded to ethylenoxy oxygen atoms of **4**, forming six hydrogen bonds (**C**, **D**, and **E** in Figure 5), unlike in the case of the analogous complex connected by four hydrogen bonds with β-pyridinium hydrogen atoms of **6**.[7e] Unlike in analogous cryptands reported in the literature,[7c,7e–7h,7l] there are no water molecules serving as hydrogen bonding bridges in the crystal structure of $\mathbf{4_2 \cdot 6}$ (Figure 5).

The 2:1 stoichiometry of complexation between **5** and **6** in solution was also confirmed by its solid-state structure (Figure 6). X-ray quality,[15] yellow, single crystals of $\mathbf{5_2 \cdot 6}$ were grown by slow evaporation of an acetone solution of **6** with excess **5**. As in the 2:1 complex between cryptand **4** and paraquat **6**, the complex $\mathbf{5_2 \cdot 6}$, a [3]pseudorotaxane-like structure, is stabilized by hydrogen bonding and face-to-face π-stacking interaction between host and guest in the solid state. Also as in complex $\mathbf{4_2 \cdot 6}$, none of the *N*-methyl hydrogen atoms of **6** is involved in hydrogen bonding between the host and the guest, and two α-pyridinium hydrogen atoms of **6** are directly hydrogen-bonded to ethylenoxy oxygen atoms of **5** through four hydrogen bonds (**A** and **B** in Figure 4). In addition, no hydrogen-bonding water bridges between cryptand host and paraquat guest are observed in the crystal structure of $\mathbf{5_2 \cdot 6}$ either (Figure 6). Interestingly, four β-pyridinium hydrogen atoms of **6** are directly connected to the host through eight hydrogen bonds, unlike in the complex $\mathbf{4_2 \cdot 6}$ and analogous cryptands.[7c,7e–7h,7l] Also as in complex $\mathbf{4_2 \cdot 6}$ (Figure 5), the distances between each pyridinium ring of **6** and the phenylene rings of **5** are mostly equal, presumably in order to maximize face-to-face π-stacking interaction between the electron-rich cryptand host and the electron-poor pyridinium paraquat guest (Figure 6). The centroid–centroid distance between the phenylene rings of the cryptand host in $\mathbf{4_2 \cdot 6}$ is 6.91 Å, whereas in $\mathbf{5_2 \cdot 6}$ this distance is 6.93 Å, indicating slightly weaker charge-transfer interactions between cryptand hosts and pyridinium binding sites in $\mathbf{5_2 \cdot 6}$. This result is consistent with the weaker average association constant for the com-

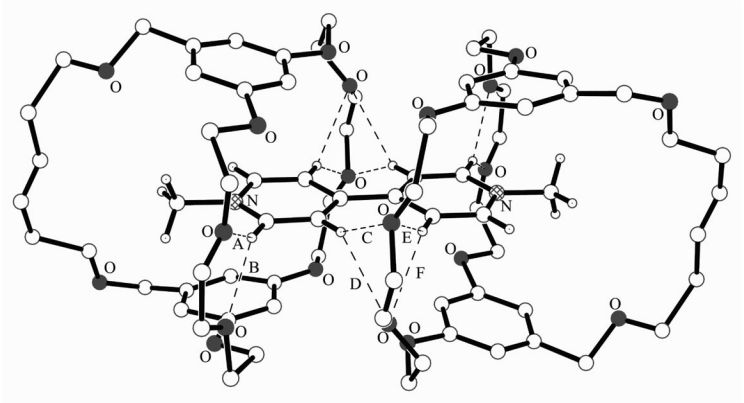


Figure 6. Ball-and-stick representations of the X-ray structure of complex $\mathbf{5_2 \cdot 6}$. The PF_6 counterions, solvent molecules, and hydrogen atoms have been omitted for clarity, except for those on **6** or involved in hydrogen bonding. Hydrogen-bond parameters: H···O distances [Å], C–H···O angles (degrees), C···O distances [Å] for **A**) 2.45, 149.41, 3.29; **B**) 2.47, 145.09, 3.28; **C**) 2.48, 151.57, 3.33; **D**) 2.63, 141.70, 3.41; **E**) 2.68, 151.17, 3.52; **F**) 2.68, 145.54, 3.49; Face-to-face π-stacking parameters: centroid–centroid distances [Å] 3.96, 3.83; ring plane/ring plane inclinations (degrees): 7.74, 8.30.

plexation between cryptand **5** and paraquat **6** than for cryptand **4** and paraquat **6**.

Conclusions

We have synthesized two novel crown-ether-based cryptands in high yield, by use of a modified one-step [2+2] cyclization (to crown ether) and a alkyne coupling reaction for the key steps. It is believed that this methodology might find more extensive applications in the preparation of new macrocycles. It has also been demonstrated by means of NMR techniques, ESI-MS, and X-ray analysis that these new cryptands can bind paraquat more strongly than the corresponding crown ether. In view of the easy availabilities and binding capabilities of these cryptands, this approach might be expected to be extendable to the construction of mechanically interlocked structures, such as rotaxanes and catenanes. Furthermore, one can envisage polymerization of diacetylene components to generate unique π-conjugated polymer materials and mechanically interlocked polymers with π-conjugated backbones either by direct utilization of diacetylene-containing cryptand or after formation of interlocked structures. We now intend to explore these possibilities.

Experimental Section

General: Unless specified otherwise, all reagents were purchased from commercial suppliers and used as received. THF was distilled from sodium/acetophenone; CH_3CN was distilled from CaH_2. All reactions were carried out under N_2. Melting points were determined with an Electrothermal x-5 melting point apparatus and are uncorrected. Thin-layer chromatography was performed on Qing-Dao silica gel. NMR spectra were recorded at ambient temperature with a Varian NMR system (400 MHz) with use of the deuterated solvent as the lock and the residual solvent or TMS as the internal reference. Low-resolution electrospray ionization mass spectra were recorded with a Thermo Finnigan LCQ Deca XP Max LC/MSn instrument. High-resolution electrospray ionization mass spectra were recorded with a Bruker Apex IV FTMS instrument at Peking University. Elemental analysis were obtained with a FlaskEA 1112 Series CHNS-O analyzer. MALDI-TOF MS were provided by Nankai University. X-ray crystallographic analyses were performed with a Bruker SMART APEX II machine.

Synthesis of Compound 1: A solution of tri(ethylene glycol) ditosylate (3.21 g, 7 mmol) and methyl 3,5-dihydroxybenzoate (1.18 g, 7 mmol) in CH_3CN (25 mL) was added at 1 mL h^{-1} and at 90–100 °C to a suspension containing K_2CO_3 (4.83 g, 35 mmol) in CH_3CN (75 mL). After the completion of the addition, the solution was stirred at 90–100 °C for 2 d, allowed to cool, filtered, and concentrated to give a pale yellow, viscous oil. This crude compound was purified by column chromatography [SiO_2, CH_2Cl_2/Et_2O 1:4, v/v]. After the solvent had been removed, the resulting pale yellow solid was recrystallized from acetone to give compound **1** (0.53 g, 28%) as a white powder; m.p. 128.3–129.3 °C (ref.[9d] m.p. 131.2–133.2 °C). ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C): δ = 7.16 (s, 4 H, Ar-H), 6.68 (s, 2 H, Ar-H), 4.12 (t, J = 4.0 Hz, 8 H, α-OCH_2), 3.87 (s, 6 H, –COOMe), 3.86 (t, J = 4.0 Hz, 8 H, β-OCH_2), 3.74 (s, 8 H, γ-OCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C): δ = 166.68, 15969, 131.72, 107.83, 107.00, 70.90, 69.46, 67.63, 52.13 ppm. MS (ESI): m/z (%) = 582.31 [M + NH_4]$^+$.

Synthesis of Compound 2: $LiAlH_4$ (0.31 g, 8 mmol) was added under N_2 at 0 °C to a suspension of compound **1** (1.13 g, 2 mmol) in dry THF (50 mL). The mixture was further stirred for 12 h at room temperature. The excess $LiAlH_4$ was quenched with ethyl acetate and the resulting mixture was neutralized with HCl (2 M). The system was extracted with ethyl acetate and $CHCl_3$, and the organic fractions were combined, dried with $MgSO_4$, and concentrated to give compound **2** (0.99 g, 98%) as a white solid; m.p. 139.0–140.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C): δ = 6.50 (s, 4 H, Ar-H), 6.36 (s, 2 H, Ar-H), 4.56 (s, 4 H, –CH_2OH), 4.05 (d, J = 4.0 Hz, 8 H, α-OCH_2), 3.85 (t, J = 4.0 Hz, 8 H, β-OCH_2), 3.73 (s, 8 H, γ-OCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C): δ = 159.97, 143.30, 105.25, 100.89, 70.84, 69.60, 67.37, 65.10 ppm. MS (ESI): m/z (%) = 531.60 [M + Na]$^+$.

Synthesis of Compound 3: Sodium hydride (60% in mineral oil, 0.19 g, 3.9 mmol) was added under N_2 at 0 °C to a suspension of compound **2** (0.76 g, 1.5 mmol) in dry THF (15 mL). The mixture was stirred for 0.5 h. Propargyl bromide (80% in toluene, 1.1 mL, 1.06 mmol) was added at 1 mL h^{-1}. The reaction mixture was stirred for 1 h at 0 °C and for 4 d at room temperature. The excess NaH was quenched with ice water, and the mixture was extracted with ethyl acetate and $CHCl_3$, combined, dried with $MgSO_4$, and concentrated to give a yellow powder. This crude compound was purified by column chromatography [SiO_2, ethyl acetate/CH_2Cl_2 1:1, v/v] and solvent removal to give compound **3** (0.75 g, 86%) as a light yellow powder; m.p. 103.7–104.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C): δ = 6.51 (s, 4 H, Ar-H), 6.44 (s, 2 H, Ar-H), 4.51 (s, 4 H, benzyl-H), 4.13 (s, 4 H, α-CH_2), 4.08 (d, J = 4.0 Hz, 8 H, α-OCH_2), 3.86 (d, J = 4.0 Hz, 8 H, β-OCH_2), 3.73 (s, 8 H, γ-OCH_2), 2.45 (s, 2 H, –C≡CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C): δ = 159.98, 139.40, 106.50, 101.31, 79.60, 74.61, 71.33, 70.88, 69.57, 67.41, 56.88 ppm. MS (ESI): m/z (%) = 602.25 [M + NH_4]$^+$. $C_{32}H_{40}O_{10}$ (584.65): calcd. C 65.74, H 6.90; found C 65.70, H 7.10.

Synthesis of Compound 4: A solution of compound **3** (584.7 mg, 1.0 mmol) was slowly added under O_2 at 45–50 °C to a solution of $Cu(OAc)_2$·H_2O (199.7 mg, 1.0 mmol) in dry CH_3CN (10 mL) and CH_2Cl_2 (40 mL). The solvent was then removed, and the crude bluish solid was dissolved in aq. ammonia (0.5 mol mL^{-1}) and extracted with CH_2Cl_2. After drying and removal of solvent, the crude product was purified by column chromatography [SiO_2, ethyl acetate/CH_2Cl_2 1:1, v/v] and the solvent was removed to give a light yellow powder, which was recrystallized from CH_3OH to give compound **4** (565.2 mg, 97%) as a white solid; m.p. 105.6–106.8 °C. ^{1}HNMR (400 MHz, $CDCl_3$, 22 °C): δ = 6.58 (s, 4 H, Ar-H), 6.30 (s, 2 H, Ar-H), 4.50 (s, 4 H, benzyl-H), 4.23 (s, 4 H, α-CH_2), 4.03 (s, 8 H, α-OCH_2), 3.81 (t, J = 4.0 Hz, 8 H, β-OCH_2), 3.70 (s, 8 H, γ-OCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C): δ = 159.94, 140.00, 106.85, 101.35, 75.78, 72.72, 70.99, 70.88, 69.86, 67.44, 58.53 ppm. MS (ESI): m/z (%) = 600.32 [M + NH_4]$^+$. MALDI-TOF-MS: m/z (%) calcd. for [M + Na]$^+$, 605.2363; found 605.2441.

Synthesis of Compound 5: Pd/C (10%, 12 mg) was added to a solution of compound **4** (116.5 mg, 0.2 mmol) in ethyl acetate (10 mL). The suspension was stirred under H_2 at room temperature. After 24 h, TLC showed complete conversion to product. The catalyst was removed by filtration and the filtrate was concentrated to give a white oil. This crude compound was purified by column chromatography [SiO_2, ethyl acetate/CH_2Cl_2 1:1, v/v] and the solvent was removed to give compound **5** (109 mg, 93%) as a white powder; m.p. 88.2–89.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 22 °C): δ

= 6.42 (s, 4 H, Ar-H), 6.27 (s, 2 H, Ar-H), 4.30 (s, 4 H, benzyl-H), 3.95 (s, 8 H, α-OCH_2), 3.79 (t, J = 4.0 Hz, 8 H, β-OCH_2), 3.70 (s, 8 H, γ-OCH_2), 3.27 (t, J = 8.0 Hz, 4 H, α-CH_2), 1.46 (t, J = 4.0 Hz, 4 H, β-CH_2), 1.13 (s, 4 H, γ-CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C): δ = 159.81, 140.76, 106.73, 100.79, 72.77, 70.96, 69.70, 68.80, 67.25, 29.25, 24.86 ppm. MS (ESI): m/z (%) = 608.44 $[M + NH_4]^+$. HR-MS (ESI): calcd. for $[M + H]^+$ 591.3169; found 591.3162; calcd. for $[M + Na]^+$ 613.2989; found 613.2978.

CCDC-752976 (for **4_2·6**), -752977 (for **5_2·6**), -752978 (for **3**), -752979 (for **4**) and -752980 (for **5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK [Fax: (+44)1223-336-033; or E-mail: deposit@ccdc.cam.ac.uk].

Supporting Information (see also the footnote on the first page of this article): ^1H NMR and ^{13}C NMR spectra of all compounds, low-resolution electrospray ionization mass spectra of complexes **4_2·6** and **5_2·6**, and crystal data and structure refinement data for the compounds and complexes.

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[14] In a system possessing two identical binding sites for its complementary partner, with association constants K_1 and K_2, respectively, $K_1 = 4K_2$ if the binding sites operate independently. The value of the slope is –457, which equals the values of both $-2K_2$ and $2K_2 - K_1$ simultaneously. We calculated the errors of the association constants on the basis of the error of the slope; see: a) K. A. Connors, *Binding Constants*, Wiley, New York, **1987**; b) ref.[13]

[15] The crystal data for complex $\mathbf{5_2 \cdot 6}$ are imperfect. We tried our best, including growing crystals in different solvent systems and performing data collection on different single crystals at low temperature, but no better data set could be obtained. Although this data set is not good, the framework can be clearly solved and the crystallographic data strongly support the spectroscopic characterization.

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