JOC*Note*

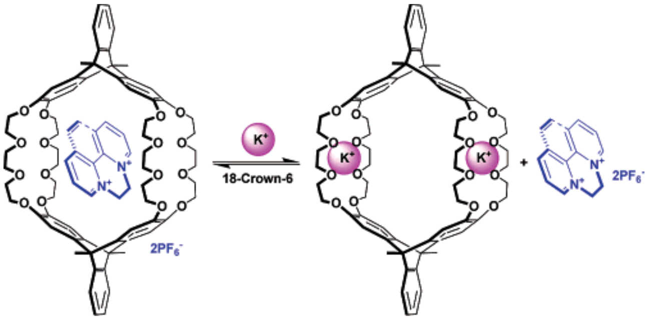
Complexation of Triptycene-Based Cylindrical Macrotricyclic Polyether toward Diquaternary Salts: Ion-Controlled Binding and Release of the Guests

Tao Han,[†,‡] Qian-Shou Zong,[†] and Chuan-Feng Chen*,[†]

Beijing National Laboratory for Molecular Sciences, Laboratory of Chemical Biology, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China, and Graduate School, Chinese Academy of Sciences, Beijing 100049, China

cchen@iccas.ac.cn

Received January 7, 2007



Triptycene-based cylindrical macrotricyclic polyether **1** has been proved to be an efficient host for the complexation with diquaternary salts in solution and in the solid state. Moreover, it was also found that binding and release of the guest molecules could be easily controlled by the addition and removal of potassium ions.

Host−guest complexes,[1] in particular, those in which the binding to substrate could be switched "on" or "off" by external stimuli, have attracted great interest due to their extensive potential applications not only in the construction of artificial molecular machines but also in the development of sensing and controllable drug-delivery systems.[2,3] It was known that diquaternary salts[4] were usually used as herbicides and have played an important role in various biological systems, which also made them some of the most common guests and caused then to be studied intensively in numerous inclusion complexes.[5] Although the controlled binding and release of diquaternary salts as guests would be very useful both in biological and in supramolecular chemistry, little is so far known about their complexes which could be switched between the complex states and uncomplex states by chemical or other external stimuli.

Recently, we[6] became interested in the development of new supramolecular systems based on triptycene with unique three-dimensional rigid structure and electron-rich cavity.[7] As a result, a novel triptycene-based cylindrical macrotricyclic polyether **1**[6b] has been synthesized and proved to be a powerful host for the complexation with paraquat derivatives. Herein we report the efficient complexation of host **1** toward diquat **2** and the diquaternary salt of phenanthroline **3** (Figure 1) in solution and in the solid state. Moreover, since there are two dibenzo[24]crown-8 moieties in the host molecule, we reasoned that the well-established cation−crown interaction could dissociate the host−guest complexes. Consequently, the binding and release of guests **2** and **3** in the complexes can be easily controlled by adding and removing the potassium ions.

First, we investigated the complexation between triptycene-based host **1** and diquaternary guests **2** and **3** in solution. As a result, it was found that when host **1** and diquat **2** (2 mM each) were mixed in 1:1 chloroform/acetonitrile solution at room temperature, they gave an orange solution immediately due to charge transfer between the electron-rich aromatic rings of host **1** and the electron-poor pyridinium rings of guest **2**. Similarly, the mixed solution of **1** and **3** also showed a typical charge-transfer feature but the color was deep red. In the ^{1}H NMR spectrum of a 1:1 mixture (2 mM each) of **1** and **2** in 1:1 chloroform/acetonitrile, only one set of peaks was found, which

---

[†] Institute of Chemistry, Chinese Academy of Sciences.

[‡] Graduate School, Chinese Academy of Sciences.

(1) (a) Vögtle, F. *Supramolecular Chemistry*; John Wiley and Sons: New York, 1991. (b) Cram, D. J.; Cram, J. M. *Container Molecules and Their Guests*; Royal Society of Chemistry: Cambridge, UK, 1994. (c) Lehn, J.-M. *Supramolecular Chemistry*; VCH Publishers: New York, 1995.

(2) (a) Feringa, B. L. *Molecular Switches*; VCH-Wiley: Weinheim, Germany, 2001. (b) Jeon, Y-M.; Kim, J.; Whang, D.; Kim, K. *J. Am. Chem. Soc.* **1996**, *118*, 9790−9791. (c) Liu, Y.; Flood, H.; Stoddart, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 9150−9151. (d) Sindelar, V.; Silvi, S.; Kaifer, A. E. *Chem. Commun.* **2006**, 2185−2187. (e) Huang, F. H.; Switek, K. A.; Gibson, H. W. *Chem. Commun.* **2006**, 3655−3657. (f) Kaiser, G.; Jarrosson, T.; Otto, S.; Ng, Y.-F.; Bond, A. D.; Sanders, J. K. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 1959−1962. (g) Badjić, J. D.; Balzani, V.; Credi, A.; Silvi, S.; Stoddart, J. F. *Science* **2004**, *303*, 1845−1849. (h) Lin, C.-F.; Liu, Y.-H.; Lai, C.-C.; Peng, S.-M.; Chiu, S.-H. *Angew. Chem., Int. Ed.* **2006**, *45*, 3176−3181. (i) Lin, C.-F.; Liu, Y.-H.; Lai, C.-C.; Peng, S.-M.; Chiu, S.-H. *Chem. Eur. J.* **2006**, *12*, 4594−4599. (j) Chiang, P.-T.; Cheng, P.-N.; Lin, C.-F.; Liu, Y.-H.; Lai, C.-C.; Peng, S.-M.; Chiu, S.-H. *Chem. Eur. J.* **2006**, *12*, 865−876.

(3) (a) Harada, A. *Acc. Chem. Res.* **2001**, *34*, 456−464. (b) Dietrich-Buchecker, C.; Jimenez-Molero, M. C.; Sartir, V.; Sauvage, J.-P. *Pure Appl. Chem.* **2003**, *75*, 1383−1393. (c) Kinbara, K.; Aida, T. *Chem. Rev.* **2005**, *105*, 1377−1400. (d) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72−191.

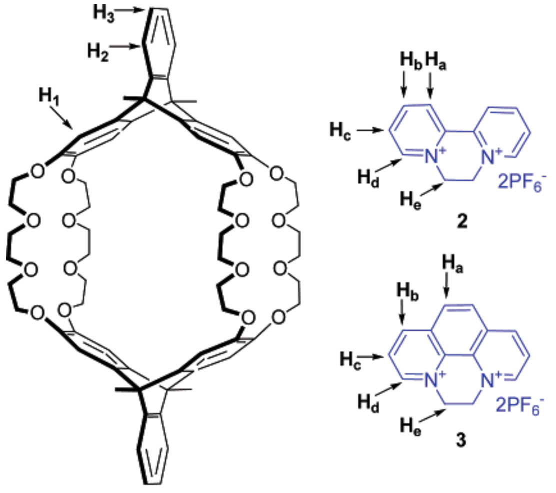
(4) (a) Summers, L. A. *Tetrahedron* **1968**, *24*, 2697−2700. (b) Summers, L. A. *Tetrahedron* **1968**, *24*, 5433−5437. (c) Brigitte, G.; Falk, K.; Horst, K. *Chem. Ber.* **1996**, *129*, 33−38. (d) Fuke, C. *Drugs and Poisons in Humans: A Handbook of Practical Analysis*; Suzuki, O., Wantanabe, K., Eds.; Springer Gmbh: Berlin, Germany, 2005; pp 571−580. (e) Xie, L.; Thrippleton, K.; Irwin, M. A.; Siemering, G. S.; Mekebri, A.; Crane, D.; Berry, K.; Schlenk, D. *Toxicol. Sci.* **2005**, *87*, 391−398. (f) Aramendia, M. A.; Borau, V.; Lafont, F.; Marinas, A.; Marinas, J. M.; Moreno, J. M.; Porras, J. M.; Urbano, F. J. *Food Chem.* **2006**, *97*, 181−188.

(5) (a) Colquhoun, H. M.; Goodings, E. P.; Maud, J. M.; Stoddart, J. F.; Williams, D. J.; Wolstenholme, J. B. *J. Chem. Soc., Chem. Commun.* **1983**, 1140−1142. (b) Colquhoun, H. M.; Goodings, E. P.; Maud, J. M.; Stoddart, J. F.; Wolstenholme, J. B.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **1985**, 607−624. (c) Allwood, B. L.; Kohnke, F. H.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed.* **1985**, *24*, 581−584. (d) Gunter, M. J.; Johnston, M. R. *Tetrahedron Lett.* **1992**, *33*, 1771−1774. (e) Gunter, M. J.; Jeynes, T. P.; Johnston, M. R.; Turner, P.; Chen, Z. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1945−1958. (f) Huang, F. H.; Slebodnick, C.; Switek, K. A.; Gibson, H. W. *Chem. Commun.* **2006**, 1929−1931.

(6) (a) Zhu, X. Z.; Chen, C. F. *J. Am. Chem. Soc.* **2005**, *127*, 13158−13159. (b) Zong, Q. S.; Chen, C. F. *Org. Lett.* **2006**, *8*, 211−214. (c) Han, T.; Chen, C. F. *Org. Lett.* **2006**, *8*, 1069−1072. (d) Zhu, X. Z.; Chen, C. F. *Chem. Eur. J.* **2006**, *12*, 5603−5609. (e) Zong, Q. S.; Zhang, C.; Chen, C. F. *Org. Lett.* **2006**, *8*, 1859−1862.

(7) (a) Zhu, X. Z.; Chen, C. F. *J. Org. Chem.* **2005**, *70*, 917−924. (b) Zhang, C.; Chen, C. F. *J. Org. Chem.* **2006**, *71*, 6626−6629.

10.1021/jo070035i CCC: $37.00



1

FIGURE 1. The structures and proton designations of the host **1** and guests **2** and **3**.

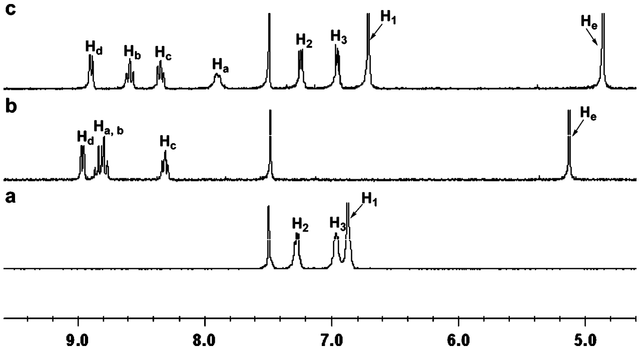


FIGURE 2. Partial ^{1}H NMR spectra (300 MHz, CD_3CN:$CDCl_3$ 1:1, 295 K) of (a) free host **1**, (b) free guest **2**, and (c) **1** plus 1.0 equiv of **2**. $[\mathbf{1}]_0 = 2$ mM.

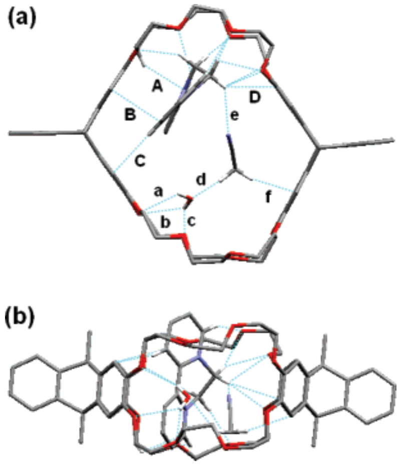


FIGURE 3. Top view (a) and side view (b) of the crystal structure of the complex **1·2**. The distances of the noncovalent interactions between the complex **1·2** and the solvents are the following: $a = 2.34$ Å, $b = 2.45$ Å, $c = 2.23$ Å for O−H···O; $d = 2.43$ Å for C−H···O; $e = 2.58$ Å for C−H···N; $f = 2.59$ Å for C−H···π. Two PF_6^- counterions, other solvent molecules, and hydrogen atoms not involved in the noncovalent interactions are omitted for clarity.

indicated the fast-exchange complexation between the host and the guest. As shown in Figure 2c, the H_a, H_b, and H_e proton signals of the pyridinium ring and the H_1 proton signal of **1** showed significant upfield shifts, which might be due to the strong shielding effect of the aromatic rings. In addition, a slight downfield shift of the proton H_c was observed, which might be attributed to the deshielding effect of the host's aromatic rings. These observations suggested that a new complex **1·2** was formed. Similarly, host **1** could also form a stable complex with guest **3**, which has been confirmed by the ^{1}H NMR spectral studies of a 1:1 mixture of host **1** and guest **3**.[8]

The stoichiometries of these complexes were determined to be 1:1 in solution by mole ratio plot[9] with use of proton NMR data, which is different from that of a 1:2 complex between dibenzo[24]-crown-8 and diquat in acetone solution.[5a,b] Furthermore, ^{1}H NMR spectroscopic titrations afforded a quantitative estimate for the apparent association constant (K_a) of the two complexes.[10] Consequently, $K_{a\mathbf{1\cdot2}}$ and $K_{a\mathbf{1\cdot3}}$ for the 1:1 complexes were calculated to be 3.5(±0.3) × 10^3 and 4.6(±0.4) × 10^3 M^{-1}, respectively, by the Scatchard plots.[11] As we can see that $K_{a\mathbf{1\cdot3}}$ is slightly bigger than $K_{a\mathbf{1\cdot2}}$, this is probably due to the stronger $\pi-\pi$ stacking interaction between the host and guest **3**. The 2D-NMR spectrum technique was also used to investigate the noncovalent interaction between the host and the guests. As a result, NOE effects between *N*-methylene protons and crown ether protons were all observed in the ROSY spectra of the complexes **1·2** and **1·3**.[8] Moreover, NOE effects between the aromatic protons of phenanthroline and crown ether protons could also be observed, which might indicate that the phenanthroline ring is adjacent to the crown ether moieties of the host molecule.

The electrospray ionization mass spectra (ESI MS) provided more evidence for the formation of the 1:1 complexes.[8] Consequently, the strongest peak at *m/z* 666.5 for $[\mathbf{1\cdot2}-2PF_6]^{2+}$ was found by using the solution of **1** and **2** in 1:1 chloroform and acetonitrile. Similarly, the peak at *m/z* 678.6 for $[\mathbf{1\cdot3}-2PF_6^-]^{2+}$ was also observed at the same condition.

Further support for the formation of the complex **1·2** came from its X-ray diffraction results. It was noted that the structural feature of the complex **1·2** was quite different from those of paraquat-based complexes we reported previously.[6b] As shown in Figure 3, the diquat molecule threaded the cavity from the central ring of the cylindrical macrotricyclic host and the two pyridinium rings of the guest were non-coplanar with the dihedral angle of 19.19°. Moreover, the proton H_c of the diquat molecule extend out of the shielding region of the triptycene aromatic ring, which is consistent with the result in solution. It was further found that there existed not only multiple ·C−H···O hydrogen bonding interactions between the hydrogen atoms of the guest and polyether oxygen atoms, but also a $\pi-\pi$ stacking ($d_{\pi\cdots\pi} = 3.26$ Å for B) and C−H···π interactions ($d_{H\cdots\pi} = 2.71$ Å for A, 2.81 Å for C, and 2.75 Å for D) between the host and the guest. These multiple noncovalent interactions played an important role in the stability of the complex.

---

(8) See the Supporting Information.

(9) Tsukube, H.; Furuta, H.; Odani, A.; Takeda, Y.; Kudo, Y.; Inoue, Y.; Liu, Y.; Sakamoto, H.; Kimura, K. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Lehn, J. M., Eds.; Elsevier: New York, 1996.

(10) The complexation between the host and guests was determined to be not concentration dependent,[8] indicating that the complexes are essentially ion paired.[6c]

(11) Connors, K. A. *Binding Constants*; J. Wiley and Sons: New York, 1987.

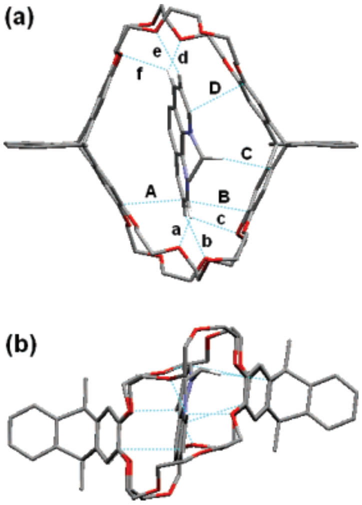


FIGURE 4. Top view (a) and side view (b) of the crystal structure of the complex **1·3**. The C−H···O hydrogen-bonding distances (Å) are the following: $a = 2.48$; $b = 2.53$; $c = 2.57$; $d = 2.51$; $e = 2.54$; and $f = 2.62$. Two PF_6^- counterions, the solvent molecules, and hydrogen atoms not involved in the noncovalent interactions are omitted for clarity.

Interestingly, we also found that a water molecule and an acetonitrile were included in the cavity of host **1**, which acted as a noncovalent force bridge to connect the diquat and the host.

We also obtained the single crystals of complex **1·3** suitable for X-ray analysis. As shown in Figure 4, it was found that guest **3** positioned in almost the center of the cavity of host molecule, which is different from that of complex **1·2**, and the host molecule had a big distortion to maximize the face-to-face $\pi-\pi$ interactions. There existed multiple C−H···O hydrogen bonds between aromatic hydrogen atoms in the guest molecule and oxygen atoms in the polyether chains of host **1**. Moreover, $\pi-\pi$ stacking interactions between the phenanthroline ring and the aromatic rings of the host with the distances of 3.37 (A), 3.31 (B), and 3.35 Å (D), and a C−H···π interaction between the *N*-methylene proton and the aromatic ring of the host with the distance of 2.74 Å (C) were also observed. These multiple noncovalent interactions resulted in the stable complex **1·3**, which is consistent with that in solution.

Since host **1** contains two dibenzo[24]-crown-8 moieties, we speculated that it could form a complex with cations, and the consequent complexation of cations would introduce extra electrostatic repellent force to the cationic diquaternary guest molecules and dissociate the previously formed host−guest complex. It was found that a solution of **1** and 2 equiva of KPF_6 showed a single strong peak at *m*/*z* 613.8 in the ESI-MS spectrum,[8] which indicated that two potassium ions could bind to the crown ether moieties to form the complex **1·2KPF₆**. Moreover, 18-crown-6 is known to be a very strong sequestering agent[12] for potassium ion, which encouraged us to further investigate the potassium ion-controlled binding and release of the guest molecules in the above complexes.[13] Consequently, a series of ^1H NMR experiments were carried out. As shown in Figure 5c, the ^1H NMR spectrum of a 1:1 mixture of **1** and guest **3** showed a well-defined resonance, which was consistent with formation of the 1:1 complex **1·3**. When excess KPF_6 salts were added to the above solution, it was found that the proton signals of the complex **1·3** totally disappeared, while the proton signals of guest **3** shifted downfield almost to the original positions (Figure 5d). Moreover, the aromatic proton signals of host molecule had a little downfield shift while the peak shape of the crown ether region had a big change. These observations indicated that the potassium ions bond to the crown ether moieties, which resulted in the release of the guest **3** from the cavity of the host molecule probably due to the extra electrostatic repellent force. When 18-crown-6 was added into the above system, it was further found that the proton signals of complex **1·3** recovered (Figure 5e), which suggested that the complex **1·3** formed again. Thus, the ion-controlled binding and release of the guest **3** could be easily performed by adding and removing the potassium ions. Similarly, it was found that the binding and release of the guest **2** in the complex **1·2** could also be efficiently controlled by the potassium ions.[8]

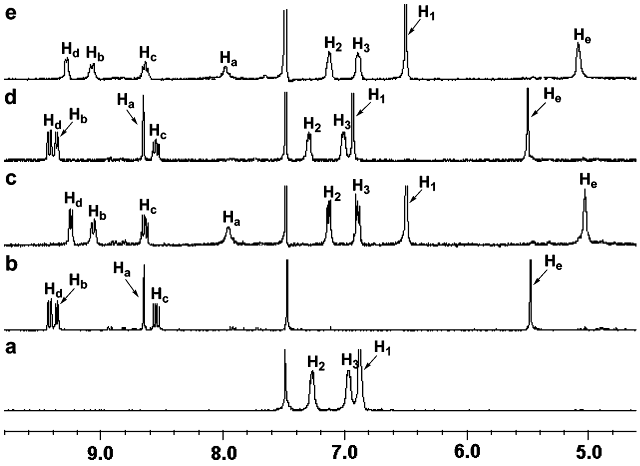


FIGURE 5. Partial ^1H NMR spectra (300 MHz, CD_3CN:$CDCl_3$ 1:1, 295 K) of (a) free host **1**, (b) free guest **3**, (c) **1** plus 1.0 equiv of **3**, (d) the mixture obtained after adding KPF_6 (4 equiv) to the solution in part c, and (e) the mixture obtained after adding 18-crown-6 (6 equiv) to the solution in part d. $[\mathbf{1}]_0 = 2$ mM.

In conclusion, the triptycene-based cylindrical macrotricyclic polyether has been proved to be an efficient host for the complexation with the diquaternary salts. They could form 1:1 stable complexes in solution and in the solid state, in which the multiple noncovalent interactions played an important role in the stabilities of the complexes. Moreover, it was also found that the binding and release of the diquaternary salts could be easily controlled by adding and removing the potassium ions, which would have many potential applications in the development of controllable drug-delivery systems or complicated switchable supramolecular systems.

Experimental Section

Materials. Host molecule **1** was synthesized according to the previous publication.[6b] Diquaternary bromic salts **2** and **3** were prepared according to the literature,[4b] and the corresponding

---

[12] (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495−2496. (b) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017−7036. (c) Inoue, Y.; Liu, Y.; Tong, L.-H; Ouchi, M.; Hakushi, T. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1947−1950.

[13] More reasons why the potassium ion was used are (1) the cavity size of dibenzo[24]-crown-8 is known to be appropriate for the cesium ion, and the potassium ion has a similar radius as that of the cesium ion ($R_{K^+} = 1.33$ Å, $R_{Cs^+} = 1.67$ Å), and (2) the potassium hexafluorophosphate used in the experiments has good solubility in acetonitrile.

hexafluorophosphate salts were obtained by ion exchange with saturated aqueous NH_4PF_6.

Complexation Studies by Proton NMR. Since host **1** could not dissolve in acetonitrile and guests **2** and **3** could not dissolve in chloroform, a 1:1 chloroform/acetonitrile solution was chosen as the NMR solvent to dissolve the host and guests. In the NMR measurements, the deuteriated acetonitrile (CD_3CN) was used as the lock, while the TMS was employed as the internal standard. Chemical shifts were reported in parts per million (ppm). ^1H NMR characterization was done on solutions with a constant $[\mathbf{1}]_0$ and varied $[\mathbf{2}]_0$ or $[\mathbf{3}]_0$. All solutions were prepared as follows. Precisely weighted amounts of dried host and guests were added into separate screw cap vials. The NMR solvents were added with to-deliver volumetric pipets. Then specific volumes of each fresh solution were mixed to yield the desired concentration. Δ is the observed chemical shift change relative to uncomplexed species, Δ_0 is the difference between the uncomplexed and fully complexed species, and is determined by extrapolation of a plot of Δ vs $1/[\text{guest}]_0$ in the high initial concentration range of guest. The complex fraction p value was calculated from $p = \Delta/\Delta_0$, and [guest] values were calculated from $[\text{guest}]_0 - p[\mathbf{1}]_0$. A plot of $p/[\text{guest}]$ vs p was used to determine the association constant K_a, which was obtained from the average value of the slope and the intercept.[6c]

Single-Crystal Analyses. Single crystals of the complexes **1·2** and **1·3** suitable for X-ray analysis were obtained by slow diffusion of ether into an equimolar mixture of the two relevant components in a 1:1 $CHCl_3/CH_3CN$ solution. Crystallographic data for **1·2·**5.25CH_3CN·H_2O: $C_{90.50}H_{105.75}F_{12}N_{7.25}O_{17}P_2$, FW 1857.01, monoclinic, space group $P21/c$, $a = 20.2750(10)$ Å, $b = 19.9664(8)$ Å, $c = 24.5497(10)$ Å, $\beta = 114.0130(10)°$, $V = 9077.4(7)$ Å^3, $Z = 4$, $d = 1.359$ g cm^{-3}, $T = 113(2)$ K, $\mu = 0.143$ mm^{-1}. $R_1 = 0.0880$, $wR_2 = 0.2006$ (all data); $R_1 = 0.0681$, $wR_2 = 0.1824$ $[I > 2\sigma(I)]$. Crystallographic data for **1·3·**6CH_3CN: $C_{94}H_{106}F_{12}N_8O_{16}P_2$, FW 1893.81, monoclinic, space group $P21/c$, $a = 17.996(3)$ Å, $b = 18.364(3)$ Å, $c = 28.784(3)$ Å, $\beta = 91.452(7)°$, $V = 9509(2)$ Å^3, $Z = 4$, $d = 1.323$ g cm^{-3}, $T = 113(2)$ K, $\mu = 0.137$ mm^{-1}. $R_1 = 0.1534$, $wR_2 = 0.3444$ (all data); $R_1 = 0.1259$, $wR_2 = 0.3263$ $[I > 2\sigma(I)]$.

Acknowledgment. We thank the National Natural Science Foundation of China, National Basic Research Program (2007CB808004), and the Chinese Academy of Sciences for financial support. We also thank Dr. H. B. Song for determining the crystal structures of the complexes.

Supporting Information Available: Experimental procedures and charaterization for the complexes, determination of the association constants for the complexes, and the crystal structures for complexes **1·2** and **1·3** and their CIF data. This material is available free of charge via the Internet at http://pubs.acs.org.

JO070035I