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Complexation between Pillar[5]arenes and a Secondary Ammonium Salt

Chengyou Han, Guocan Yu, Bo Zheng, and Feihe Huang*

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China

fhuang@zju.edu.cn

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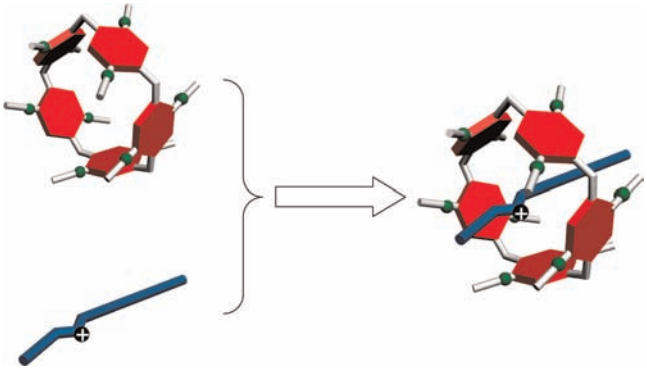
ABSTRACT



We demonstrate that *n*-octylethyl ammonium hexafluorophosphate (G) can thread through the cavity of 1,4-dimethoxypillar[5]arene to form a [2]pseudorotaxane with a binding constant of 1.09 (±0.31) × 10^3 M^{-1} in chloroform. The formation of this threaded structure has been confirmed by proton NMR spectroscopy, electrospray ionization mass spectrometry, and X-ray single crystal analysis. The complexation between 1,4-dimethoxypillar[5]arene and G in chloroform can be switched off by adding Cl^-. For comparison, the complexation between 1,4-bis(*n*-propoxy)pillar[5]arene and G has also been investigated.

The environment-controlled complexation of macrocyclic hosts to organic salt guests has played an important role in the development of supramolecular chemistry and been widely applied in the fabrication of molecular switches,[1] molecular machines,[2] drug delivery materials,[3] supramolecular polymers,[4] and other interesting supramolecular systems.[5] Pillararenes, a new kind of macrocyclic hosts, have attracted more attention since 2008.[6−8] Due to their unique rigid and symmetric pillar structures, pillar[5]arenes have shown interesting host−guest binding properties with different guests. Previously, we demonstrated that alkyl chains could thread through the cavity of pillar[5]arenes to form [2]pseudorotaxanes with C−H···π interactions as

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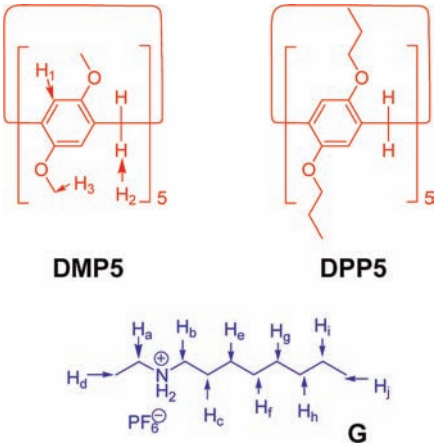
the main driving force.[6b] Later, compounds with different substituents on alkyl chains such as alkanediamines,[6f] bis(imidazole) derivatives,[6g] alkanediacids,[6d] and alkanedinitriles[6j] were proven to be good guests for pillar[5]arenes by Stoddart, Li, and Hou et al. Thanks to these discoveries, rotaxanes,[6f] [*c*2]daisy chains[6h] and supramolecular polymers[6i] have been synthesized to explore the applications of pillar[5]arenes in different areas.[7] The pH control of the threading/dethreading process of pillar[5]arenes was also reported.[8]

On the other hand, although secondary ammonium salts have been extensively used in the preparation of host–guest complexes with many macrocycles including crown ethers,[9a–c] cucurbiturils,[9d] and calixarenes,[9e] the complexation between pillar[5]arenes and secondary ammonium salts have not been explored yet. Herein, we synthesized 1,4-dimethoxypillar[5]arene (**DMP5**)[6a] and 1,4-bis(*n*-propoxy) pillar[5]arene (**DPP5**)[10a] (Scheme 1) as model hosts and *n*-octylethyl ammonium hexafluorophosphate (**G**)[10b] (Scheme 1) as a model guest to investigate the host–guest complexation between pillar[5]arenes and secondary ammonium salts. We found that this host–guest complexation can be switched off by adding chloride anion.

Scheme 1. Chemical Structures of Hosts **DMP5** and **DPP5** and Guest *n*-Octylethyl Ammonium Hexafluorophosphate (**G**)



The ^{1}H NMR spectrum (spectrum b in Figure 1) of an equimolar solution of **DMP5** and **G** in chloroform-*d* shows only one set of peaks, showing fast-exchange complexation between **DMP5** and **G** on the ^{1}H NMR time scale at 22 °C. After complexation, phenyl protons H_1 on **DMP5** shifted downfield (spectra a and b in Figure 1) from 6.80 to 6.89 ppm. No chemical shift changes were observed for bridging methylene protons H_2. The methyl protons H_3 on **DMP5** shifted downfield from 3.68 to 3.76 ppm and overlapped with the peak of H_2. The chemical shift changes of protons on **G** were calculated: −0.68, −1.23, −0.89, and −0.75 ppm for methylene protons H_a, H_b, and H_c and methyl protons H_d, respectively. The methylene protons H_e shifted upfield to 0.99 ppm. The significant chemical shift upfield changes for H_{a-e} indicated these methylene protons are located in the shielding region of the cyclic pillar structure. H_f, H_g, H_h, and H_i that overlapped together before complexation shifted upfield about 0.43, 0.29, 0.07, and 0.07 ppm, respectively. However, the methyl protons H_j showed downfield chemical shift changes from 0.88 to 0.92 ppm, which indicated these protons are located in the deshielding region of the cyclic pillar structure. These phenomena indicated that the linear guest **G** was threaded through the cavity of cyclic host **DMP5** to

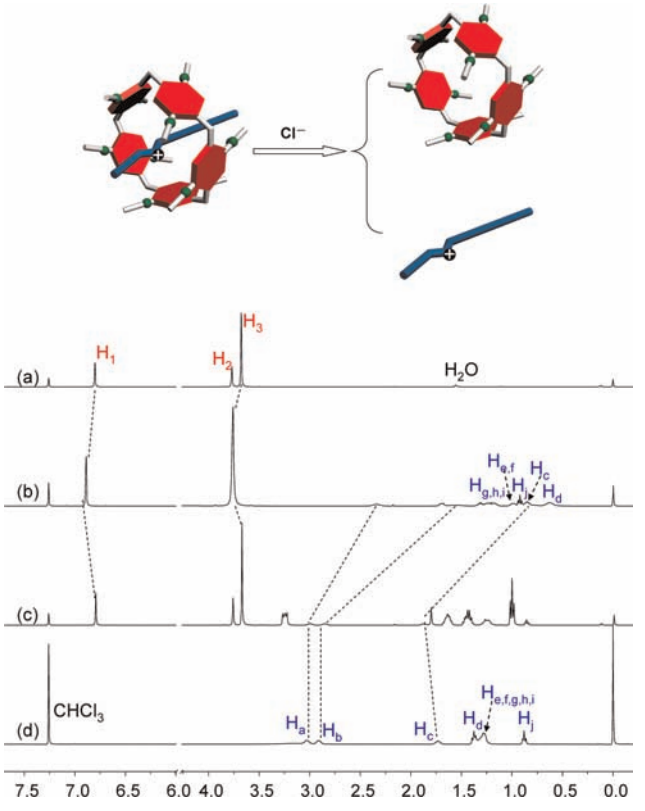


Figure 1. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 22 °C) of (a) 10 mM **DMP5**, (b) 10 mM **DMP5** and **G**, (c) 10 mM **DMP5** and **G** + 18 mM TBACl, (d) 10 mM **G**.

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form a [2]pseudorotaxane in solution with the methylene protons H_{a-e} in the cavity of **DMP5** and the methyl protons H_j out of the cavity of **DMP5**. The 2D NOESY also confirmed this complexation model (Figure S12). Correspondingly, the ^1H NMR spectrum (spectrum b in Figure S1) of an equimolar solution of **DPP5** and **G** in chloroform-*d* shows similar chemical shift changes (Figure S1), and the same conclusion can be made (Figure S1).

Further investigation of the complexation between **DMP5** and **G** was carried out by proton NMR titration. A mole ratio plot was made based on the chemical shift changes of H_1 on **DMP5** (Figure S2). A 1:1 stoichiometry was obtained from it (Figure S4). The electrospray ionization mass spectrometry also confirmed the 1:1 complexation of **DMP5** with **G**. A peak was found at *m*/*z* 908.8 (100%), corresponding to $[\mathbf{DMP5}\supset\mathbf{G} - PF_6]^+$ (Figure 2). The association constant was calculated to be 1.09 (±0.31) × 10^3 M^{-1} based on the proton NMR data of H_1 (Figure S3). The complexation of **DMP5** with other secondary ammonium salts, such as *n*-octylbenzyl ammonium hexafluorophosphate and di(*n*-octyl) ammonium hexafluorophosphate, have also been investigated (Figures S13−S18). They have lower association constants with **DMP5**, caused by the increase of the guest size. For comparison, we investigated the stoichiometry and association constant of the complexation between **DPP5** and **G**. A 1:1 stoichiometry was also obtained (Figure S7). The association constant was determined to be 2.40 (±0.20) × 10^3 M^{-1} based on the proton NMR titration (Figure S6). This value is higher than the corresponding association constant value of **DMP5**⊃**G**. A possible reason is the introduction of van der Waals forces between the propyl groups of **DPP5** and the long alkyl chain of **G**.[6h]

We obtained the crystal structure of **DMP5**⊃**G** using a single crystal grown by slow diffusion of isopropyl ether to a chloroform solution of **DMP5** and **G** at room temperature (Figure 3). This helps us to investigate the host−guest

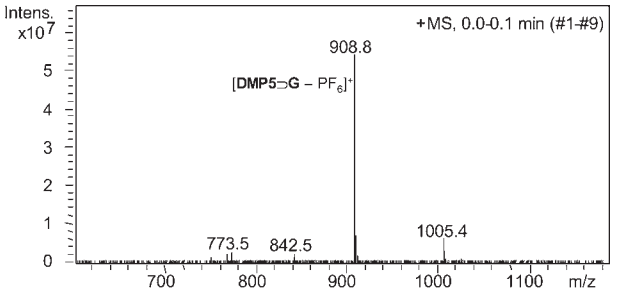

Figure 2. Electrospray ionization mass spectrum of a solution of **DMP5** and **G**.

complexation of **DMP5** and **G** in the solid state. The formation of the [2]pseudorotaxane between **DMP5** and **G** was confirmed by the crystal structure. The host **DMP5** is a regular pentagon in the solid state. Interestingly, the guest **G** is divided into two parts: one part that contains the cation is in the cavity of **DMP5** and the other part, the long alkyl chain, is out of the cavity. This is consistent with the above proton NMR investigation result that the protons H_{a-d} are in the cavity of **DMP5** while protons H_j are out of the cavity after the complexation between **DMP5** and **G**. Two ammonium hydrogen atoms and two methyl hydrogen atoms have H···π-plane distances, 2.58−2.91 Å (Figure 3, **a**−**e**), indicating the existence of the N−H···π interactions and C−H···π interactions.[6b,i] The three N−H···π interactions and two C−H···π interactions should be the main driving forces to form the [2]pseudorotaxane between **DMP5** and **G**.

We then focused on environmental control of the binding of **DMP5** to **G**. pH control did not work very well since the *n*-octylethyl amine, the neutralized form of **G**, can complex **DMP5** although the complexation is weak (Figure S20).[6f] Luckily, we found that chloride anion could control the complexation between **DMP5** and **G** (Figure 1). After excess tetrabutylammonium chloride was added to an equimolar solution of **DMP5** and **G**, a disassembly process between **DMP5** and **G** occurred. Correspondingly, protons H_1 on **DMP5** shifted from 6.89 to 6.79 ppm, close to the chemical shift of H_1 (6.80 ppm) on uncomplexed **DMP5** (spectra a−c in Figure 1). The chemical shift of H_2 changed synchronously. Compared with the hexafluorophosphate anion, the chloride anion is smaller and charge-convergent and forms an intimate ion pair with the *n*-octylethyl ammonium cation in chloroform. This ion pair is too big for the cavity of **DMP5**. In other words, *n*-octylethyl ammonium chloride cannot complex with **DMP5** or has weak complexation (Figure S9). On the other hand, the hexafluorophosphate anion is bigger and charge-divergent and forms a relatively loose ion pair with the *n*-octylethyl ammonium cation in chloroform. Therefore, the ion pairing between the *n*-octylethyl ammonium cation and the hexafluorophosphate anion is not strong enough to prevent the complexation between **DMP5** and the *n*-octylethyl ammonium cation from happening.

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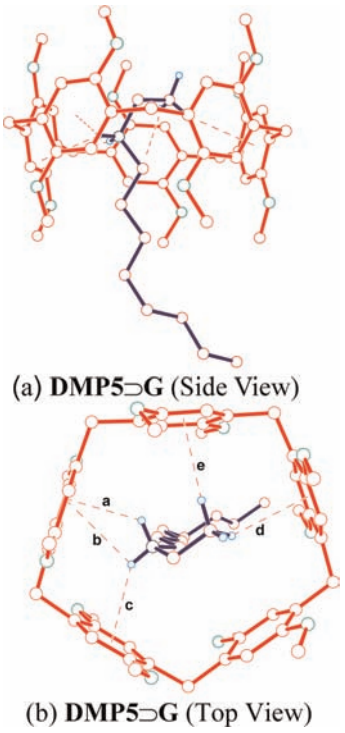

Figure 3. Ball-stick views of the crystal structures of **DMP5**⊃**G**. One PF_6 counterion, solvent molecules, and hydrogen atoms on **DMP5** have been omitted for clarity. Hydrogens except the ones that have interactions with **DMP5** on the guest **G** were omitted for clarity. Carbon atoms are red, oxygen atoms are green, hydrogen atoms are blue, and the nitrogen atom is black. The dashed lines indicate N−H···π interactions and C−H···π interactions. N−H···π interaction parameters: N−H···π distance (Å), N−H···π angle (deg) **a**, 2.58, 122; **b**, 2.89, 98.9; **c**, 2.64, 144. C−H···π interaction parameters: C−H···π distance (Å), C−H···π angle (deg) **d**, 2.89, 135; **e**, 2.91, 160.

In this "on−off" process, the protons on **G** show more obvious changes. The methylene protons H_a and H_b, next to the cation NH_2^+, exhibit chemical shift changes from 2.34 ppm for the complexed state to 3.00 ppm, close to 3.02 ppm for the uncomplexed state, and from 1.68 ppm for the complexed state to 2.85 ppm, close to 2.91 ppm for the uncomplexed state, respectively. Other protons on **G** consistently have similar changes. That the chemical shifts could not recover fully may be the result of the combination of the ionic strength change of the solution after the addition of tetrabutylammonium chloride and the strength change of ion pairing between the positive ammonium part and the negative counterion. The complexation between **DPP5** and **G** could also be switched off by adding Cl^- (Figure S10). Surprisingly, the uncomplexed solution of **DMP5**, **G**, and TBACl cannot be switched back by adding Ag^+ to remove the Cl^- (Figure S11) while that of **DPP5**, **G**, and TBACl can be switched back by adding Ag^+ (Figure S10). A possible reason is that **DMP5** can complex with Ag^+ much more strongly than **DPP5**. This was supported by bigger and more complicated chemical shift changes when $AgPF_6$ was added to **DMP5** (Figures S19 and S20).

In summary, we synthesized two model pillar[5]arene hosts **DMP5** and **DPP5** and studied their anion-controlled complexation with the model secondary ammonium salt guest **G**. We found that these two pillar[5]arenes can bind **G** in chloroform. More importantly, we demonstrated that this host−guest complexation could be switched off by adding the chloride anion. This anion-responsive host−guest binding property is a novel feature about the host−guest properties of pillar[5]arenes. This new host−guest molecular recognition motif can be used in the fabrication of mechanically interlocked structures such as rotaxanes and catenanes. Furthermore, the anion-responsive binding of pillar[5]arenes to secondary dialkylammonium salts can be employed in the fabrication of advanced functional supramolecular systems such as molecular switches, molecular machines, controlled-release systems, and supramolecular polymers.

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Supporting Information Available. Synthetic procedures, characterizations, crystal data, and other materials. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.