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SHORT COMMUNICATION

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Synthesis of a Difunctionalized Pillar[6]arene and Its Complexation with an Ammonium Salt Coupled to a Weakly Coordinating Counteranion

Chengyou Han,[a] Lingyan Gao,[a] Guocan Yu,[a] Zibin Zhang,[a] Shengyi Dong,[a] and Feihe Huang*[a]

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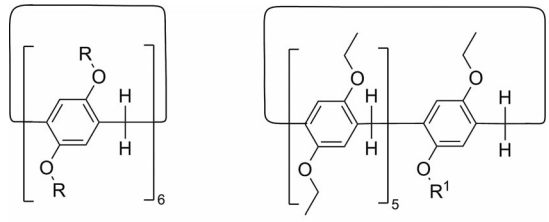
A pillar[5]arene[1]quinone and a difunctionalized pillar[6]arene were synthesized. Their application in host–guest chemistry was investigated by using 1-adamantanylammonium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (**3**), which possesses a weakly coordinating counteranion, as a model guest. These hosts showed different binding affinities for **3** with different association constants.

Introduction

Macrocyclic molecules are one of the hottest topics in supramolecular chemistry because of their interesting host–guest properties that originate from their fascinating topology structures. Pillararenes,[1] as a new kind of host macrocycles after crown ethers,[2] cyclodextrins,[3] calixarenes,[4] and cucurbiturils,[5] have become one of the most popular subjects since their first synthesis in 2008.[6–9] On the basis of their rigid and pillar structures, many interesting host–guest systems have been developed.[6] Pillar[5]arenes, as the first-prepared pillararene homologues of the pillar[*n*]arene family, can complex a long alkyl chain with C–H···π interactions as the main driving force, as reported by us.[7a] This is a very important host–guest property for pillar[5]arenes, as it is the basis of pillar[5]arene-based rotaxanes,[7b,7e,7f,7j] [*c*2]daisy chains,[7c] and supramolecular polymers.[7d,7g–7i] Pillar[6]arenes[8] have different host–guest properties from pillar[5]arenes because they have bigger cavities.[8h,8i] *n*-Octyltriethylammonium hexafluorophosphate was the first guest that was found by us[8b] to have complexation with pillar[6]arenes. After that, some other guests, such as 1,4-diazabicyclo[2.2.2]octane (DABCO)-based ammonium salt[8c] and adamantane-based dialkylammonium salts,[8d] were also proved to complex pillar[6]arenes well. Furthermore, on the basis of the photoresponsive properties of azobenzene, a switch between irregular aggregates and vesicle-like aggregates was developed based on the complexation between an azobenzene-containing guest and a pillar[6]arene.[8e] Recently, we demonstrated that a water-soluble pillar[6]arene could be used both in the dispersion of multiwalled carbon nanotubes into water and in the efficient reduction of paraquat toxicity in vitro.[8f,8g]

Just like pillar[5]arenes, functionalization studies of pillar[6]arenes were all performed on the oxygen atom of the repeating benzene rings. Various methods have been developed to functionalize pillar[5]arenes,[9] but to date only one way is available to functionalize pillar[6]arenes. By dealkylation of dialkylpillar[6]arene with the use of BBr_3, a perhydroxylated pillar[6]arene (i.e., **1a**)[8i] and a monohydroxylated pillar[6]arene (i.e., **2a**)[8c] were obtained (**1b**[8f,8g] and **2b**[8c] were synthesized from **1a** and **2a**, respectively; Figure 1). It is essential and urgent to develop new methods to functionalize pillar[6]arenes considering their interesting host–guest complexation properties and their important applications in different areas. Herein, we report the preparation of the first difunctionalized pillar[6]arene by partial oxidation (Scheme 1) and its application in host–guest chemistry.



1a: R = H
1b: R = CH_2COOH
2a: R^1 = H
2b: R^1 = $(CH_2)_6Br$

Figure 1. Chemical structures of perfunctionalized pillar[6]arenes **1** and partially functionalized pillar[6]arenes **2**.

[a] MOE Key Laboratory of Macromolecular Synthesis and Functionalization, Department of Chemistry, Zhejiang University,
Hangzhou 310027, P. R. China
Fax: +86-571-8795-3189
E-mail: fhuang@zju.edu.cn
Homepage: http://www.chem.zju.edu.cn/~huangfeihe/

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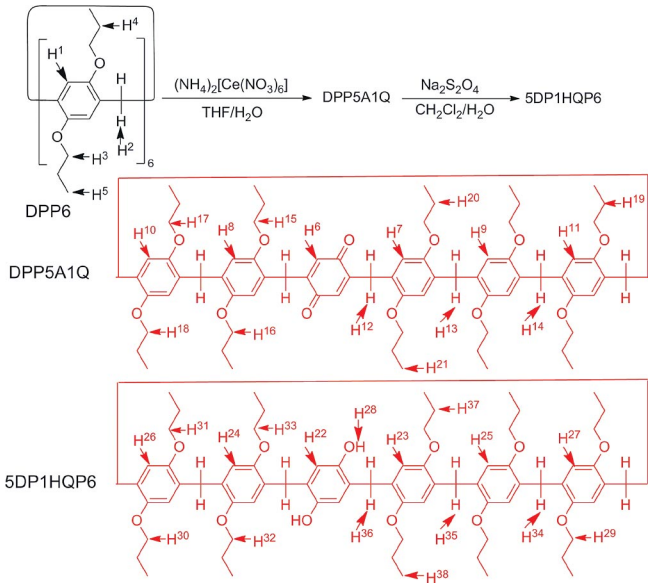

Scheme 1. Synthetic routes to a pillar[5]arene[1]quinone (DPP5A1Q) and a difunctionalized pillar[6]arene (5DP1HQP6).

Results and Discussion

First, a pillar[5]arene[1]quinone (DPP5A1Q), a macrocycle with a benzoquinone unit replacing a dipropoxybenzene unit in the structure of pillar[6]arene (DPP6), was prepared by partial oxidation with $(NH_4)_2[Ce(NO_3)_6]$ as the oxidizing agent. Then, after reduction with $Na_2S_2O_4$, a difunctionalized pillar[6]arene (5DP1HQP5) with a hydroquinone repeating unit was prepared quantitatively.

The ^{1}H NMR spectra of DPP6, DPP5A1Q, and 5DP1HQP6 are shown in Figure 2. When DPP6 was partially oxidized to DPP5A1Q, a new peak corresponding to the H^6 protons on the benzoquinone unit appeared, which indicated the successful oxidation of pillar[6]arene. The protons on the benzene rings (H^{7-11}), especially those on the same benzene rings (H^7 and H^8, H^9 and H^{10}), split well enough to be identified, and this indicated the loss of symmetry. The bridging methylene H^{12-14} protons and the methylene H^{15-19} protons next to the oxygen atoms showed similar phenomena. All the methylene H^{20} protons and the methyl H^{21} protons did not split well enough to be identified because of their minor chemical environmental differences, as they were far from the benzoquinone unit. 5DP1HQP6 has the same symmetry as that of DPP5A1Q, and the splittings of the protons on the benzene rings were better than the splittings of the protons of DPP5A1Q; only one new peak corresponding to the H^{28} protons on the hydroxy groups of the hydroquinone moiety appeared.

We obtained single crystals of DPP5A1Q by slow evaporation of its petroleum ether/ethyl acetate (50:1 v/v) solution at room temperature. The X-ray crystal structure (Figure 3) of DPP5A1Q not only confirmed its chemical structure but also demonstrated that the oxidation did not destroy the pillar structure of DPP6.

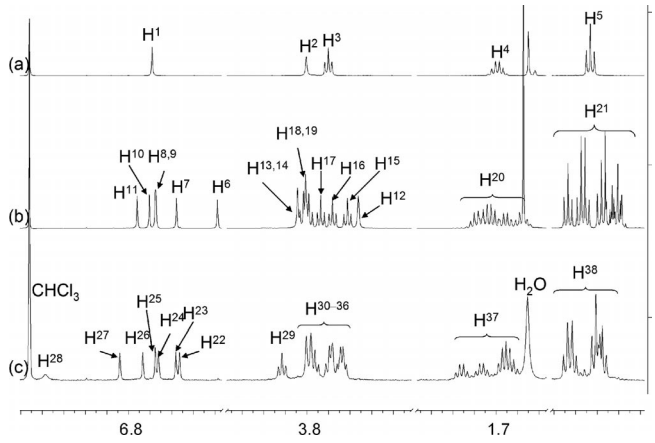

Figure 2. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 22 °C) of (a) DPP6 (2.00 mM), (b) DPP5A1Q (2.00 mM), and (c) 5DP1HQP6 (2.00 mM).

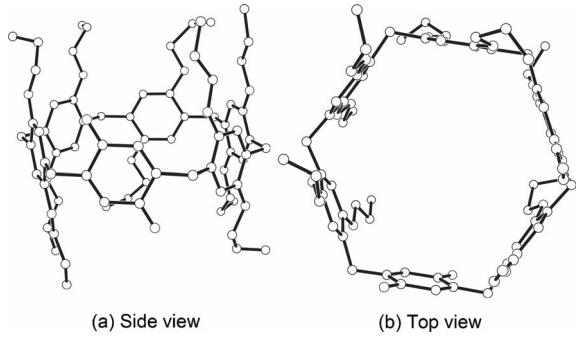

Figure 3. Ball-and-stick view of the crystal structure of DPP5A1Q. Hydrogen atoms are omitted for clarity.

We further explored the differences of the host–guest binding properties among DPP6, DPP5A1Q, and 5DP1HQP6. It was recently reported[8d,10] that a weak coordinating counteranion, such as tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ($BArF^-$), can improve host–guest complexation, so we chose 1-adamantylammonium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (**3**) as a model guest to do our host–guest complexation investigation.

First, the complexation of DPP6 with **3** was investigated for comparison. In the ^{1}H NMR spectrum, the protons on the guest shifted upfield dramatically after complexation. The association constant in chloroform was determined to be $(2.00 \pm 0.63) \times 10^4$ M^{-1} by NMR titration (Figure S11, Supporting Information). According to the ^{1}H NMR spectra of DPP5A1Q and **3** (Figure 4, a and c), the ^{1}H NMR spectrum (Figure 4, b) of an equimolar solution of DPP5A1Q and **3** showed only one group of peaks, and this indicates fast-exchange complexation on the ^{1}H NMR timescale at 22 °C. The chemical shift changes of the protons on DPP5A1Q were not big, whereas the chemical shift changes of the protons on **3** were impressive. The protons on **3** were all shifted upfield significantly, especially the methylene H^c protons and the methine H^d protons, which indicates that these protons located in the shielding region of the cyclic pillar structure and **3** formed an inclusion com-

plex with DPP5A1Q. This complex formation was confirmed by a LRMS (ESI) with a peak at *m*/*z* = 1302.7, corresponding to [DPP5A1Q⊃**3** – BArF]$^+$ (Figure S16, Supporting Information). The association constant of DPP5A1Q⊃**3** in chloroform was determined to be $(2.44 \pm 1.44) \times 10^3$ M^{-1} (Figure S15, Supporting Information). The complexation of 5DP1HQP6 with **3** in [D]-chloroform was similar to that of DPP5A1Q with **3**. Fast-exchange complexation was also observed. The protons on 5DP1HQP6 showed slight chemical shift changes, whereas clear chemical shift changes were observed for the protons of **3**. The protons on **3** showed larger chemical shift changes. Specifically, the signal for the H^c proton shifted upfield, even below 0 ppm, to –0.388 ppm, which is indicative of the formation of an inclusion complex between 5DP1HQP6 and **3**. The association constant of 5DP1HQP6⊃**3** in chloroform was determined to be $(3.33 \pm 0.99) \times 10^4$ M^{-1} (Figure S19, Supporting Information) with a 1:1 complexation stoichiometry, which was confirmed by a LRMS (ESI) peak at *m*/*z* = 1304.6 corresponding to [5DP1HQP6⊃**3** – BArF]$^+$ (Figure S20, Supporting Information). The association constant of 5DP1HQP6⊃**3** in chloroform was higher than that of DPP5A1Q⊃**3**. This could be attributed to the electron-deficient benzoquinone unit of DPP5A1Q, which may have repulsion interactions with the ammonium salt. This association constant was also higher than that of DPP6⊃**3**. A possible reason is that the steric hindrance became smaller after the loss of the two propyl groups from DPP6 to 5DP1HQP6.

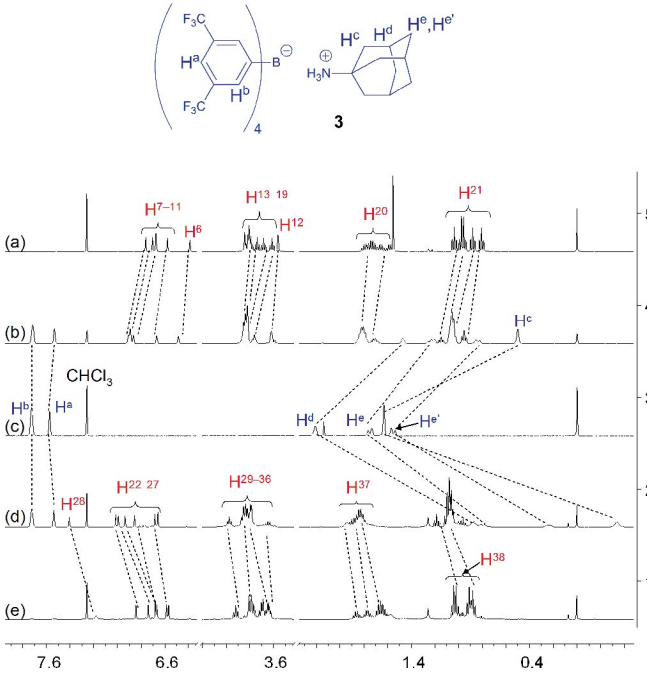

Figure 4. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 22 °C) of (a) 10.0 mM DPP5A1Q, (b) 10.0 mM DPP5A1Q and **3**, (c) 10.0 mM **3**, (d) 10.0 mM 5DP1HQP6 and 10.0 mM **3**, and (e) 10.0 mM 5DP1HQP6.

Conclusions

In summary, we synthesized a pillar[5]arene[1]quinone and a difunctionalized pillar[6]arene by partial oxidation and subsequent reduction. This difunctionalized pillar[6]-arene is the first difunctionalized pillar[6]arene. The X-ray crystal structure of the pillar[5]arene[1]quinone was obtained. The differences in the host–guest binding properties of DPP6, DPP5A1Q, and 5DP1HQP6 were investigated by using a 1-adamantanylammonium salt with the weakly coordinated tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (**3**) counteranion as the model guest. We found that the difunctionalized pillar[6]arene had a higher association constant with **3** in chloroform than the pillar[5]arene[1]quinone and DPP6. With this new functionalization method and the new host–guest system, functionalized pillar[6]arenes can be applied in various research areas, such as molecular sensors and supramolecular polymers, to promote the development of pillararene supramolecular chemistry.

Supporting Information (see footnote on the first page of this article): Synthetic procedures, characterizations, ^{1}H NMR titrations.

Acknowledgments

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