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DIBPillar[*n*]arenes (*n* = 5, 6): Syntheses, X-ray Crystal Structures, and Complexation with *n*-Octyltriethyl Ammonium Hexafluorophosphate

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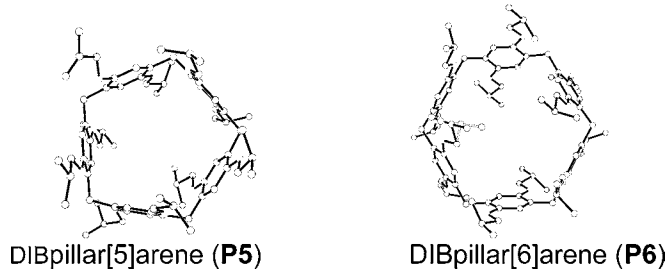
ABSTRACT



DIBPillar[*n*]arenes (*n* = 5, 6) were synthesized. They showed different host−guest properties with *n*-octyltriethyl ammonium hexafluorophosphate G due to their different cavity sizes. DIBpillar[5]arene showed no complexation with G, while DIBpillar[6]arene formed a 1:1 complex with G with an association constant of 334 (±24) M^{-1} in chloroform. In this letter, the first pillar[6]arene crystal structure and the first investigation of the host−guest chemistry of pillar[6]arenes are reported.

The preparation of novel macrocyclic hosts is very important since it is one of the major driving forces to accelerate the development of supramolecular chemistry.[1,2] Pillar[5]arenes, a new kind of macrocyclic hosts, were first synthesized by Ogoshi et al.[2a] by a Lewis acid catalyzed condensation reaction of 1,4-dimethoxybenzene and paraformaldehyde in 22% yield. Then, Cao and co-workers[3] improved the yields of pillararenes to 75−95% using the condensation of 1,4-dialkoxy-2,5-bis(alkoxymethyl)benzene catalyzed by *p*-toluenesulfonic acid with a disadvantage of starting materials

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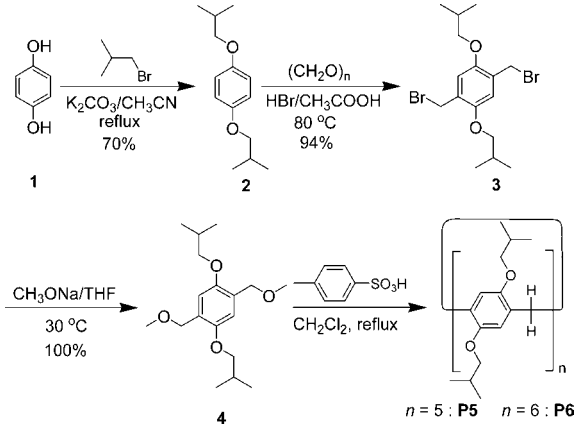
not easily being available. They also obtained a new type of hexameric macrocyclic compounds called pillar[6]arenes. The conformational mobility of pillar[5]arenes with different linear alkyl chains had been fully studied by Ogoshi and co-workers.[2c−e] Later, Li et al. studied the binding of pillar[5]arenes to paraquats and bis(pyridinium) derivatives in detail.[4] Recently, we successfully synthesized a series of copillar[5]arenes from co-oligomerization of different monomers.[5] Pillararenes have some advantages compared with traditional hosts. First, they are highly symmetrical and rigid compared to crown ethers, calixarenes, and cyclodextrins, and this affords their selective binding to guests.[2f,g,4] Second, they are easier to be functionalized by different substituents on the benzene rings than cucurbiturils, which enables tuning of their host−guest binding properties easily. For the investigation and prediction of guest-binding properties of a new host, it is necessary to know its cavity size. However, until now, the exact cavity sizes of pillar[6]arenes are still unknown since their crystal structures have not been reported yet. Furthermore, the host−guest chemistry of pillar[6]arenes has not been explored. Herein, we report the first pillar[6]arene crystal structure and the first exploration of the host−guest chemistry of pillar[6]arenes.

DIBpillar[5]arene (**P5**) and DIBpillar[6]arene (**P6**) were successfully synthesized from the condensation of 1,4-diisobutoxy-2,5-bis(methoxymethyl)benzene using *p*-toluenesulfonic acid as the catalyst (Scheme 1).[3] First, hydroquinone (**1**), 1-bromo-2-methylpropane, and K_2CO_3 in CH_3CN were refluxed to obtain 1,4-diisobutoxybenzene (**2**) in a yield of 70%. After bromomethylation of **2**, 1,4-bis(bromomethyl)-2,5-diisobutoxybenzene (**3**) was obtained (94%). Methoxylation in dry THF using CH_3ONa yielded 1,4-diisobutoxy-2,5-bis(methoxymethyl)benzene (**4**) quantitively. Condensation of **4** catalyzed by *p*-toluenesulfonic acid in CH_2Cl_2 yielded **P5** (73%) and **P6** (4.6%).

Scheme 1. Syntheses of DIBpillar[5]arene (**P5**) and DIBpillar[6]arene (**P6**)



P5 and **P6** are well soluble in common organic solvents such as dichloromethane, chloroform, *n*-hexane, and acetone. The melting point of **P6** (142 °C) is higher than **P5** (139 °C) because of the better crystallinity of **P6** resulting from its higher symmetry. The UV−vis spectra of **P5** and **P6** in chloroform are almost the same with a common peak at 295 nm due to the same aromatic rings.

According to the ^{1}H NMR spectra of **P5** and **P6** in $CDCl_3$ at 22 °C (Figure 1), we found that phenylene protons H_1 upshifted from 6.85 ppm for **P5** to 6.72 ppm for **P6** because of the shielding of more aromatic rings of **P6**. Methylene protons H_3 on **P5** were observed to split into two overlapped doublets, indicating that the mobility of H_3 was suppressed and slow on the NMR time scale at 22 °C caused by the bulky isobutyl substituents on the benzene rings. Protons H_3 located in the inner and outer spaces were shielded and deshielded, respectively, by the electron-rich cyclic structure, leading to the 1:1 split.[2d] However, **P6** had a more flexible structure and larger cavity. The mobility of H_3 was relatively faster so no splitting was observed at 22 °C in $CDCl_3$. To further investigate the conformational characteristics of **P5** and **P6**, variable-temperature ^{1}H NMR measurements were done in toluene-d_8 (Figure 2). Methylene protons H_3 on **P5** were not coalescent even at 50 °C. Methyl protons H_5 of the methyl groups at the end of the isobutyl groups had synchronized changes with H_3, which was not observed for previously reported linear-alkyl-substituted pillar[5]arenes.[2d] Upon heating to 75 °C, H_3 and H_5 were all coalescent into one peak, indicating that the thermal motions of H_3 and H_5 were fast enough to overcome the suppression at this temperature. The mobility of H_3 on **P6** was so fast that no splitting was observed even at −70 °C. These demonstrated that the protons on **P6** had more mobility than those of **P5** at the same temperature.

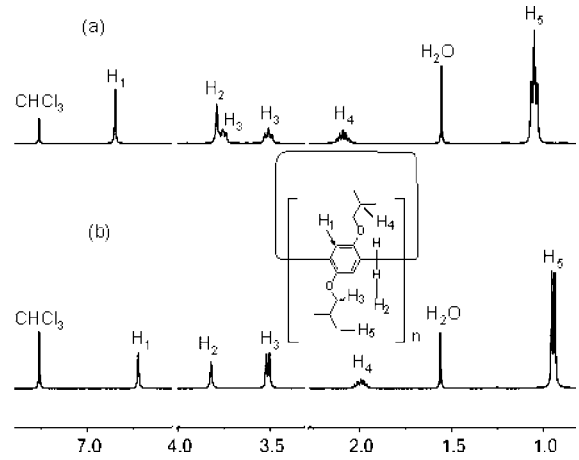


Figure 1. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 22 °C) of (a) **P5** and (b) **P6**.

Single crystals of **P5** and **P6** were obtained by slow evaporation of their respective solutions in a mixture of dichloromethane and acetonitrile (1:2, *v*/*v*). Though **P5** and

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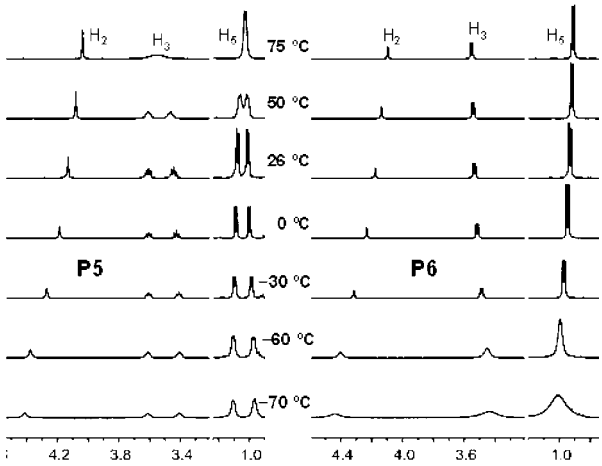


Figure 2. Partial variable-temperature ^{1}H NMR spectra (500 MHz, toluene-d_8) of **P5** (left) and **P6** (right).

P6 have the same repeating unit and are cyclic molecules, their X-ray crystal structures (Figure 3) have an obvious

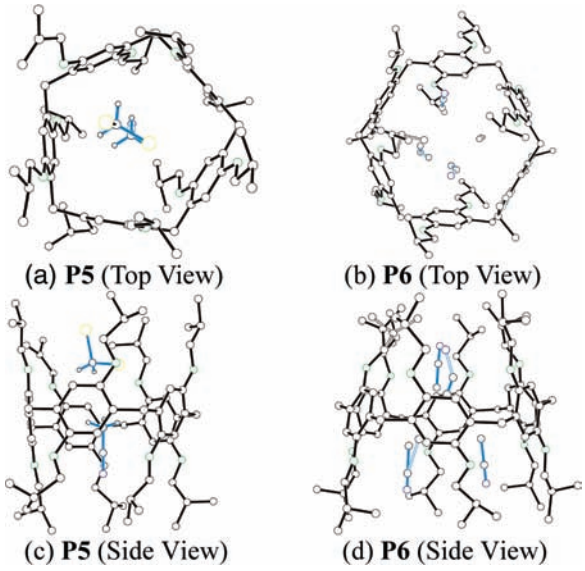


Figure 3. Ball-stick views of the crystal structures of **P5**⊃(CH_2Cl_2)(CH_3CN) (a and c) and **P6**⊃$(CH_3CN)_4$ (b and d). Hydrogens except the ones on the solvent molecules included in **P5** were omitted for clarity. Carbon atoms are black; oxygen atoms are green; chlorine atoms are yellow; and nitrogen atoms are deep blue.

difference. **P5** has a pentagon-like cyclic structure with one dichloromethane molecule and one acetonitrile molecule included in its cavity, while **P6** has a hexagon-like cyclic structure with four acetonitrile molecules included in its cavity. From a capped stick view of the crystal structure of **P5** (Figure 4), it can be observed that the methyl groups on the isobutyl groups are divided into two sets in the solid state, one shielded set inside the electron-rich cyclic space and the other deshielded set outside the cyclic space.[2c] This

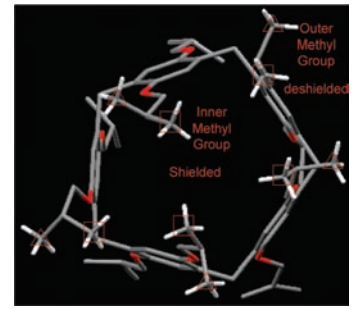
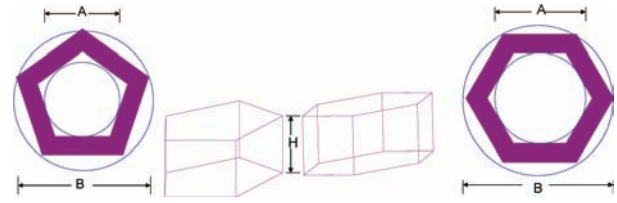


Figure 4. Capped stick top view of the crystal structure of **P5**. Hydrogens except the ones on the methyl groups at the top side were omitted for clarity. The methyl groups in the red squares are inside the cyclic space, while the methyl groups in the red triangles are outside the cyclic space.

is consistent with the above-mentioned variable-temperature ^{1}H NMR measurement results.

By the treatment of **P5** and **P6** as a regular pentagonal pillar and a regular hexagonal pillar, respectively, and ignorance of the substituents on the oxygen atoms of the repeating units, we calculated the structural parameters of **P5** and **P6** (Table 1). In terms of the cavity size, the diameter

Table 1. Calculated Structural Parameters for **P5** and **P6**[a]



	A (Å)	**B** (Å)	**H** (Å)[d]	**V** (Å^3)[e]
P5	5.6[b]	13.0[b]	7.8	225
P6	7.7[c]	14.5[c]	7.8	400

[a] Based on X-ray crystal structures reported here. [b] Based on the diameter of the inscribed circle or the circumcircle of the regular pentagon. [c] Based on the diameter of the inscribed circle or the circumcircle of the regular hexagon. [d] Based on the distance between the two oxygen atoms on the same benzene ring. [e] Based on the volume of the regular pentagonal pillar or hexagonal pillar.

of the internal cavity of **P5** is ∼5.6 Å, analogous to cucurbit[6]uril (∼5.8 Å)[6] and α-cyclodextrin (∼4.7 to ∼5.3 Å).[7] The diameter of the internal cavity of **P6** is ∼7.7 Å, analogous to cucurbit[7]uril (∼7.3 Å)[6] and *β*-cyclodextrin (∼6.0 to ∼6.6 Å).[7] Cucurbiturils and cyclodextrins are usually insoluble in organic solvents. The organic solvent soluble pillararenes are good and necessary supplements to the corresponding cucurbiturils and cyclodextrins with the similar cavity sizes.

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To investigate the differences in host−guest binding properties between **P5** and **P6**, we studied their binding to *n*-octyltriethyl ammonium hexafluorophosphate (**G**). Compared with the ^{1}H NMR spectra (spectra a and c in Figure 5) of **P5** and **G**, the ^{1}H NMR spectrum (spectrum b in Figure 5) of an equimolar solution of **P5** and **G** shows no chemical shift changes and no signal doubling, indicating no complexation between **P5** and **G** in chloroform-*d*. The ^{1}H NMR spectrum (spectrum d in Figure 5) of an equimolar solution of **P6** and **G** in chloroform-*d* shows only one set of peaks, showing fast-exchange complexation between **P6** and **G** on the ^{1}H NMR time scale at 22 °C. After complexation, phenyl protons H_1, methylene protons H_3, methine protons H_4, and methyl protons H_5 on **P6** shifted downfield (spectra d and e in Figure 5). No chemical shift changes were observed for bridging methylene protons H_2. The peaks corresponding to methyl protons H_d and H_j at the two ends of **G** could be observed after complexation (spectrum d in Figure 5), while the peaks corresponding to methylene protons H_a, H_b, H_c, and $H_{e,f,g,h,i}$ could not be found. These missing peaks could not be found even in the higher field that is below 0 ppm. A possible reason for this is that these methylene protons are located in the cavity of **P6** and shielded by its electron-rich cyclic structure after the formation of a threaded structure between **P6** and **G**.[4,8] Another possible reason is the complexation-induced broadening effect. The variable-temperature ^{1}H NMR and EXSY spectra of a mixture of **P6** and **G** at −2 °C also confirmed the complexation between them. A mole ratio plot indicated that the complexation stoichiometry between **P6** and **G** was 1:1. This was confirmed by a low-resolution electrospray ionization mass spectroscopy peak at *m*/*z* 1618.0 corresponding to $[\mathbf{P6}\supset\mathbf{G}-PF_6]^+$. The association constant of the 1:1 complex **P6**⊃**G** in chloroform-*d* was determined to be 334 (±24) M^{-1} by an NMR titration method. These experiments demonstrated that **G** fits the cavity of **P6**, but it is too big for the cavity of **P5**.

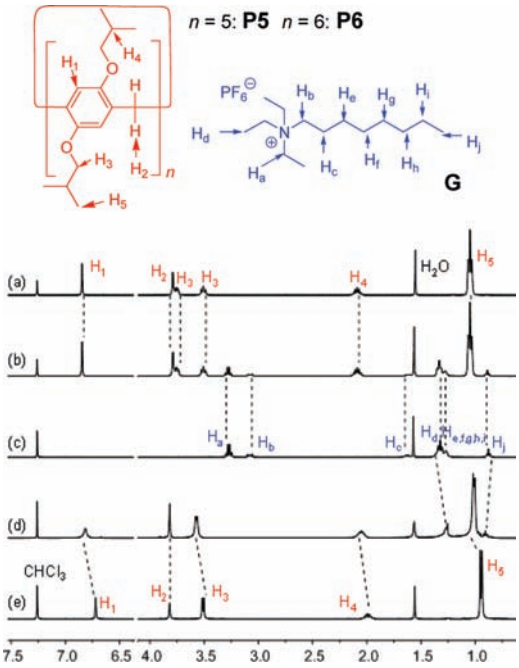

Figure 5. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 22 °C) of (a) 7.5 mM **P5**; (b) 7.5 mM **P5** and **G**; (c) 7.5 mM **G**; (d) 7.5 mM **P6** and **G**; and (e) 7.5 mM **P6**.

In summary, we successfully synthesized two new hosts DIBpillar[5]arene **P5** and DIBpillar[6]arene **P6**. Despite their same repeating unit, they have different melting points, different proton NMR chemical shifts for the same protons, and different conformational mobilities. We reported the first pillar[6]arene crystal structure. It was found that the cavity size of **P5** is analogous to cucurbit[6]uril and α-cyclodextrin, while that of **P6** is analogous to cucurbit[7]uril and *β*-cyclodextrin. The host−guest binding property of **P6** was investigated for the first time with *n*-octyltriethyl ammonium hexafluorophosphate **G** as a model guest. **P6** shows complexation with **G**, while no complexation was observed between **G** and **P5**. With their unique symmetric pillar structures, pillararenes are good and necessary supplements to the existing widely used macrocycles and will be widely used in molecular recognition and material chemistry to construct novel fascinating supramolecular structures.

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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.

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