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Synthesis of a pillar[5]arene dimer by co-oligomerization and its complexation with *n*-octyltrimethyl ammonium hexafluorophosphate

Binyuan Xia^a, Jiuming He^b, Zeper Abliz^b, Yihua Yu^c, Feihe Huang^{a,*}

^a Department of Chemistry, Zhejiang University, Hangzhou 310027, PR China

^b Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical Colleage, Bejing 100050, PR China

^c Shanghai Key Laboratory of Magnetic Resonance, Department of Physics, East China Normal University, Shanghai 200062, PR China

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ABSTRACT

A pillar[5]arene dimer was successfully prepared by co-oligomerization of 1,4-dimethoxybenzene and 1,6-bis(4-butoxyphenoxy)hexane. It was demonstrated that it forms 1:2 complexes with *n*-octyltrimeth-yl ammonium hexafluorophosphate both in chloroform and the gaseous state. A Scatchard plot indicated that the complexation between them is statistical with an average association constant of 6.0 $(\pm 0.4) \times 10^2 \,\mathrm{M^{-1}}$ in chloroform.

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The discovery of novel macrocyclic hosts with fascinating structures and properties has greatly promoted the development of supramolecular chemistry. These macrocycles, such as crown ethers, cyclodextrins, calixarenes and cucurbiturils, have been investigated in a variety of areas, including molecular recognition,¹ nanotechnology,² fluorescent chemosensors,³ drug delivery systems,⁴ and supramolecular polymers⁵ due to their good host-guest interactions, controllable assembling properties and other interesting abilities. Pillar[5]arene is a new type of macrocyclic host, which was recently prepared by Ogoshi et al.⁶ by the condensation reaction of 1,4-dimethoxybenzene and paraformaldehyde, using $[BF_3 \cdot O(C_2H_5)_2]$ as the catalyst. Later, Cao et al.⁷ firstly obtained pillar[6]arenes by the condensation of 1,4-dialkoxy-2,5-bis(alkoxymethyl)benzene catalyzed by p-toluenesulfonic acid. Then, Li et al.⁸ investigated the host-guest properties of pillar[5]arene with a series of paraquats and bis(pyridinium) derivatives. Recently, our group reported the syntheses of copillar[5]arenes from co-oligomerization⁹ of different repeating units, the first pillar[6]arene crystal structure¹⁰ and the formation of pillararene-based supramolecular polymers driven by C-H $\cdots\pi$ interactions.¹¹ Nowadays, pillararenes have attracted more and more attention not only because their symmetrical and rigid structures make them excellent building blocks in the construction of interesting supramolecular structures, but also due to their good binding abilities and specific binding selectivities for particular organic salts of interest.

In recent years, great efforts have been devoted to the construction of covalently linked macrocycle dimers, such as cyclodextrin dimers¹² and calixarene dimers,¹³ because of their specific applications in carriers, enzyme mimics and supramolecular polymers. However, up to date, the investigations of pillararenes mainly focus on pillararene monomers.¹⁴ Different from pillararene monomers, every one of the pillararene dimers possesses two binding sites so that they have great potential applications in the construction of more sophisticated supramolecular structures, such as [n]rotaxanes and pillararene dimer based A2B2 supramolecular polymers. In order to provide a necessary supplement to the pillararene family, here we designed and successfully synthesized the first pillar[5] arene dimer, which was composed of two pillar[5]arene units linked by a single aliphatic chain, and explored its host-guest binding with *n*-octyltrimethyl ammonium hexafluorophosphate (G). Scheme 1 presents possible complexation geometry between them.

We prepared the pillar[5]arene dimer (**PD**) by co-oligomeri zation of 1,4-dimethoxybenzene and 1,6-bis(4-butoxyphenoxy) hexane. First, 1,6-bis(4-hydroxyphenoxy)hexane (**1**),¹⁵ 1-bromobutane and K₂CO₃ in CH₃CN were heated at reflux to obtain 1,6-bis(4-butoxyphenoxy)hexane (**2**) in 90% yield. Then, a mixture of 8 equiv of 1,4-dimethoxybenzene, 1 equiv of **2**, 10 equiv of paraformalde-hyde and 10 equiv of $[BF_3 \cdot O(C_2H_5)_2]$ was stirred in 1,2-dichloroethane under nitrogen atmosphere at room temperature for 5 h. After purification by preparative thin layer chromatography, **PD** was obtained in 8% yield.

In order to investigate the conformational characteristics of **PD**, variable-temperature ¹H NMR measurements were done in

^{*} Corresponding author. E-mail address: fhuang@zju.edu.cn (F. Huang).

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Scheme 1. The complexation between pillar[5]arene dimer PD and G.

toluene- d_8 (Fig. S7). Neither of the two peaks corresponding to H_4 and H_8 on **PD** were split even at -40 °C because each pillar[5]arene monomer possesses eight relatively small methoxy groups, resulting in a high conformational freedom of the pillar[5]arene dimer.

Partial ¹H NMR spectra of **PD**, a mixture of **PD** and **G**, and **G** in chloroform-*d* at 22 °C are shown in Figure 1. The spectrum of the mixture (spectrum b of Fig. 1) shows only one set of peaks, indicating fast-exchange complexation between **PD** and **G** on the ¹H NMR time scale at 22 °C. After complexation, phenyl protons H₁, methylene protons H₄, H₅, H₆, H₈, H₉, H₁₀ and methyl protons H₃, H₇ on

PD shifted downfield. Large chemical shifts were observed for methyl protons H_a and methylene protons H_b , H_c , H_d , H_e , and H_f on **G** due to the shielding effect of the electron-rich cavities of **PD**. Methylene protons H_c , H_d , and H_e shifted upfield even below 0 ppm. The peaks corresponding to H_g on **G** exhibited a small upfield shift, while methyl protons H_i shifted downfield obviously. From these phenomena, a reasonable conclusion was that the linear guest **G** was threaded through the two cyclic host cavities of **PD**. Two COSY spectra of a solution of 10.0 mM **PD** in chloroform-*d* (Fig. S8) and a solution of 16.0 mM **PD** and 18.0 mM **G** in



Figure 1. Partial ¹H NMR spectra (400 MHz, chloroform-d, 22 °C) of (a) 8.00 mM PD; (b) 8.00 mM PD and 9.00 mM G; (c) 9.00 mM G.

chloroform-*d* (Fig. S10) were obtained to confirm the peak assignments. The host–guest complexation between **PD** and **G** was also verified by a 2D NOESY study (Fig. S11). A cross-peak was observed between phenyl protons H_1 on **PD** and methylene protons H_f on **G**. NOEs were also found between methyl protons H_3 on **PD** and methyl protons H_a and methylene protons H_c , H_d , and H_f on **G**. These evidences further supported that **PD** and **G** can form a threaded structure in chloroform. A job plot¹⁶ based on proton NMR data demonstrated that the complexation between **PD** and **G** was of 1:2 stoichiometry in chloroform-*d* at room temperature (Fig. 2).

Further evidence for the formation of the 1:2 complex between **PD** and **G** was obtained by cold spray ionization mass spectrometry. A peak was observed at m/z 992.08 (Fig. 3), corresponding to $[\mathbf{PD} \supset \mathbf{G}_2 - 2\mathbf{PF}_6]^{2+}$.

To investigate how the two pillar[5]arene binding sites of PD influence each other during its complexation with **G**, proton NMR characterizations were done on a series of chloroform solutions for which the initial concentration of PD was kept constant at 1.50 mM while the concentration of G was systematically varied. On the basis of these data, the extent of complexation, p, of pillar[5]arene units was determined and a Scatchard plot was made (Fig. 4). The linear nature of this plot demonstrated that the complexation between PD and G was statistical, that is, the two pillar[5]arene binding sites behaved independently. From the intercept and the slope of the Scatchard plot, the average association constant (K_{av}) was determined to be 6.0 (±0.4) × 10² M⁻¹ for **PD** \supset **G**₂. Since $K_1/K_2 = 4:1$ for statistical systems $(K_1 = [\mathbf{PD} \supset \mathbf{G}]/$ $\{[\mathbf{PD}][\mathbf{G}]\}$ and $K_2 = [\mathbf{PD} \supset \mathbf{G}_2] / \{[\mathbf{PD} \supset \mathbf{G}][\mathbf{G}]\}$, K_1 and K_2 were calculated to be 9.6 (±0.6) \times 10² M⁻¹ and 2.4 (±0.2) \times 10² M⁻¹, respectively. The value of K_{av} is lower than the association constant $(K = 1695 \pm 115 \text{ M}^{-1})$ for the complexation between 1,4-dimethoxypillar[5]arene (P5) and G (see the Supplementary data). This is understandable considering that a bigger steric hindrance exists for the complexation between PD and G.

In conclusion, we have successfully synthesized a pillar[5]arene dimer, which is composed of two pillar[5]arene units linked by a single aliphatic chain. As a necessary supplement to the pillararene family, pillar[5]arene dimer showed good host–guest binding properties with *n*-octyltrimethyl ammonium hexafluorophosphate. These investigations open up a way for the studies of pillararene dimers. Future works will focus on the syntheses of new kinds of pillararene dimers, such as the ones linked by functional groups, and their applications in the construction of more sophisticated supramolecular systems such as [*n*]rotaxanes, the formation of



Figure 2. Job plot showing the 1:2 stoichiometry of the complex between **PD** and **G** in chloroform-*d* using proton NMR data for H_a of **G**. [**G**]_c is the concentration of complexed **G**. [**PD**]₀ + [**G**]₀ = 2.00 mM.



Figure 3. CSI-TOF mass spectrum of a mixture of PD and G.



Figure 4. Scatchard plot for the complexation of host **PD** with guest **G** in chloroform-*d* at 22 °C. *p* = fraction of monopillar[5]arene units bound. Error bars in *p*: ± 0.03 absolute; error bars in *p*/[**G**]: ± 0.06 relative.

supramolecular polymers, and even the fabrication of organic nanotubes with ion conductance properties.

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Supplementary data

Supplementary data (synthetic procedures, characterizations, and other materials) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.06.065.

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