

Synthesis of a water-soluble pillar[9]arene and its pH-responsive binding to paraquat†

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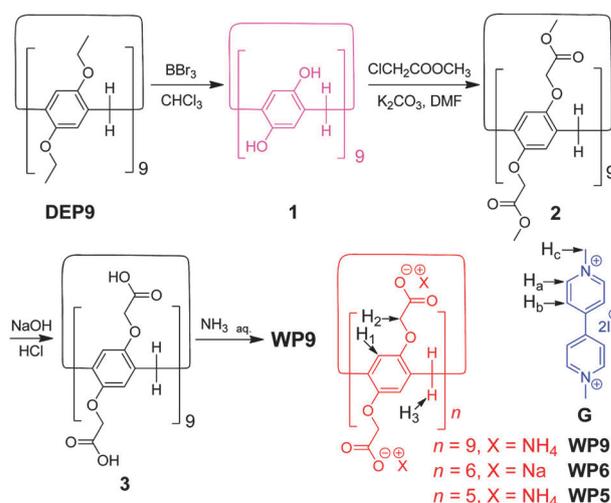
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A water-soluble pillar[9]arene was synthesized. Its pH-responsive host–guest binding to paraquat in water was studied.

The arrival of any novel kind of macrocycles can significantly drive the development of supramolecular chemistry.¹ Pillar[*n*]arenes, mostly including pillar[5]arenes and pillar[6]arenes, are a new type of macrocyclic molecules and have gained increasing attention in recent years.^{2–9} It has been demonstrated that these new host macrocycles and their derivatives have ascendant host–guest properties. Pillararenes have been used to construct a series of fascinating supramolecular systems, such as supramolecular polymers,³ rotaxanes/pseudorotaxanes,⁴ daisy chains,⁵ artificial transmembrane channels⁶ and other advanced functional materials.⁷ Up to now, studies on pillar[*n*]arenes have been almost focused on pillar[5]arenes and pillar[6]arenes. The more advanced pillararenes, which have more than 6 repeating units, are only reported by Cao's group,^{8a} Hou's group^{8b} and our group.^{8c} However, the host–guest chemistry of these advanced pillar[*n*]arenes (*n* = 7, 8, 9, 10) in water has not been reported so far. Herein, we report the synthesis of a water-soluble pillar[9]arene (**WP9** here) and its host–guest complexation with paraquat **G** in water.

The water-soluble pillar[9]arene **WP9** was prepared through four steps in total in our method (Scheme 1), similar to the preparation of analogous water-soluble pillar[5]arene (**WP5**)⁹ and pillar[6]arene (**WP6**).^{7c} Compound **DEP9** was isolated by a one-step way previously reported by Hou's group.^{8b} First, *per*-hydroxylated pillar[9]arene **1** was obtained through dealkylation of **DEP9** by using excess BBr₃. Compound **1** was then processed with excess methyl chloroacetate in dimethyl formamide to gain product **2**. From the ¹H NMR spectrum of **2** in CDCl₃ (Fig. S1, ESI†), four sets of singlets



Scheme 1 Synthetic route to water-soluble pillar[9]arene **WP9** and the chemical structures of compounds used here.

were observed, indicating that the structure of **2** was highly symmetric. Subsequently, the hydrolysis of **2** under the conditions of 40% aqueous sodium hydroxide in ethanol afforded the carboxylic acid-substituted pillar[9]arene **3**. Just like compound **2**, **3** retained the symmetric structure and the signals related to the protons on **3** were still singlets (Fig. S4, ESI†). At last, upon treatment of **3** with ammonium hydroxide, water-soluble pillar[9]arene **WP9**, which contains eighteen carboxylate anion groups at upper and lower rims, was obtained as a white solid. As expected, **WP9** can be dissolved well in water to give a colourless solution.

WP9 was characterized by ¹H NMR, ¹³C NMR and electrospray ionization mass spectrometry (ESI-MS). Fig. S7 (ESI†) shows the ¹H NMR spectrum of **WP9** in D₂O. The resonance peaks related to protons H₁, H₂ and H₃ on **WP9** were still observed as singlets, which indicated the highly symmetric and stereoregular structure. The ¹H NMR spectrum of **WP9** is similar to those of **WP5** and **WP6** but the signals corresponding to phenyl protons H₁ and methylene protons H₂ shifted upfield while signals of bridging methylene protons H₃ shifted downfield (Fig. S10, ESI†).

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Due to the presence of eighteen negative anionic groups, **WP9** can act as a receptor for cationic guests. Consequently, paraquat **G**, which possesses two cationic charges, was chosen as a guest to complex with **WP9**. When **WP9** was mixed with equimolar **G** in water, a bright brown colour appeared immediately (Fig. 2, the inserted photograph), indicating the achievement of charge-transfer interactions between electron-rich aromatic rings of the host molecule and electron-poor pyridinium rings of the guest molecule.

In order to estimate the association constant (K_a) of the complexation between **WP9** and **G**, fluorescence titration experiments (Fig. S11–S13, ESI[†]) were conducted with aqueous solutions which had a constant concentration of **WP9** (1.00×10^{-5} M) and varying concentrations of **G** (0 – 6.10×10^{-5} M) at room temperature. The fluorescence intensity corresponding to **WP9** was quenched significantly upon gradual addition of **G** (Fig. S11, ESI[†]). A mole ratio plot (Fig. S12, ESI[†]) based on the fluorescence spectroscopic data showed that the stoichiometry of the complexation between **WP9** and **G** was 1 : 1, which was further confirmed by ESI-MS (Fig. S17, ESI[†]). ESI-MS revealed a clear peak at m/z 1164.4 for $[\text{WP9} \supset \text{G} - 2\text{I} - 18\text{NH}_3]^{2+}$, and no peaks related to other complexation stoichiometry were observed. By a non-linear curve-fitting method, the K_a value for **WP9** \supset **G** was calculated to be $(2.27 \pm 0.24) \times 10^6 \text{ M}^{-1}$ (Fig. S13, ESI[†]), which is lower than the corresponding K_a value for the complex between **WP6** and **G** ($1.02 \times 10^8 \text{ M}^{-1}$),^{2e} while higher than that for the complex between **WP5** and **G** ($8.20 \times 10^4 \text{ M}^{-1}$).⁹ We speculated that the molecule of **WP9** developed into one relatively larger cavity than those of **WP5** and **WP6** due to the presence of strong electrostatic repulsion between the negative anionic groups. Therefore, only part of the repeating units on **WP9** participated in the complexation with **G** upon addition of the guest. However, due to the suitable cavity size of **WP6**, the guest **G** can interact with **WP6** sufficiently.^{2e} Additionally, the internal cavity of **WP5** is smaller than the width of paraquat, the interaction between **WP5** and **G** was insufficient.^{2e} We thought that the cavity size played an important role in the complexation between the host and the guest.

Furthermore, we carried out ¹H NMR experiments to explore the interaction between **WP9** and **G** (Fig. 1). The ¹H NMR spectrum of an equimolar (1.00 mM) D₂O solution of **WP9** and **G** (Fig. 1b) indicated that the complexation between **WP9** and **G** is fast exchange on the ¹H NMR time scale. When equimolar **WP9** was added into a D₂O solution of **G**, pronounced upfield shifts in the signals related to the protons of **G** occurred. In addition, the peaks corresponding to protons H_a and H_b became broad, which was mainly resulted from complexation dynamics when **WP9** interacted with **G**. On the other hand, slight chemical shift changes were also observed for the protons of **WP9**. Further evidence for the complexation between **WP9** and **G** was obtained from UV-vis absorption spectroscopy. The spectrum of an equimolar aqueous solution of **WP9** and **G** displays a clear charge-transfer band that exhibits the charge-transfer interaction between electron-rich **WP9** and electron-deficient **G** (Fig. 2). In addition, we can also observe a noticeable red-shift (Fig. 2 and Fig. S15, ESI[†]), suggesting the electronic interaction between **WP9** and **G**.

A 2D NOESY NMR study of an aqueous solution of **WP9** (5.00 mM) and **G** (5.00 mM) was carried out to investigate the relative spatial positions of this host–guest complex. As shown in Fig. 3,

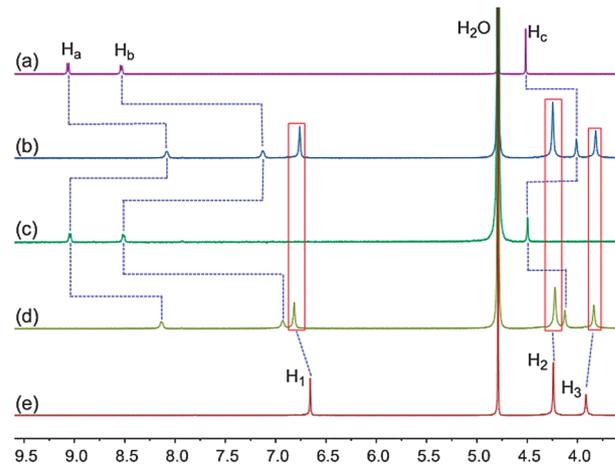


Fig. 1 Partial ¹H NMR spectra (400 MHz, D₂O, 293 K): (a) **G** (1.00 mM); (b) **WP9** (1.00 mM) and **G** (1.00 mM); (c) after addition of 2.0 μL of aqueous DCl solution (20%) to b; (d) after addition of 1.0 μL of aqueous NaOD solution (30%) to c; (e) **WP9** (1.00 mM).

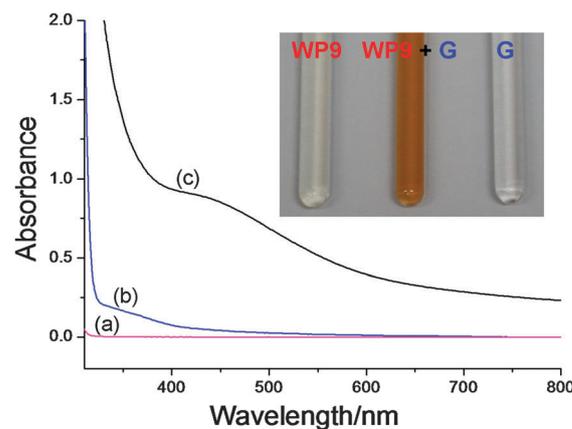


Fig. 2 UV-vis spectra of (a) 1.00 mM **G**, (b) 1.00 mM **WP9**, and (c) 1.00 mM **WP9** with equimolar **G** in water at room temperature. The inserted photograph exhibits the color changes of aqueous solutions upon complexation between **WP9** and **G**.

clear correlation signals were observed between protons H_a, H_b or H_c on **G** and protons H_{1–3} on **WP9**, respectively, indicating that **G** penetrated through the cavity of **WP9**. Therefore, according to the ¹H NMR and 2D NOESY investigations, we can draw a conclusion that the guest molecule **G**, as an axis, was threaded through the cavity of the cyclic host **WP9** to form a 1 : 1 inclusion complex. In this complex system, protons H_a and H_b were located in the electron-rich cavity of **WP9**, while protons H_c were at the portal of the cavity.

Moreover, the assembly and disassembly between **WP9** and **G** can be reversibly controlled by sequential addition of DCl and NaOD aqueous solutions, that is to say, the complexation is pH-responsive. When aqueous DCl solution was added into a brown solution containing **WP9** and **G**, the brown colour disappeared immediately and precipitates appeared simultaneously (Fig. S16, ESI[†]), which was observed by the naked eye clearly. The reason is apparent: when the solution became acidic by adding an

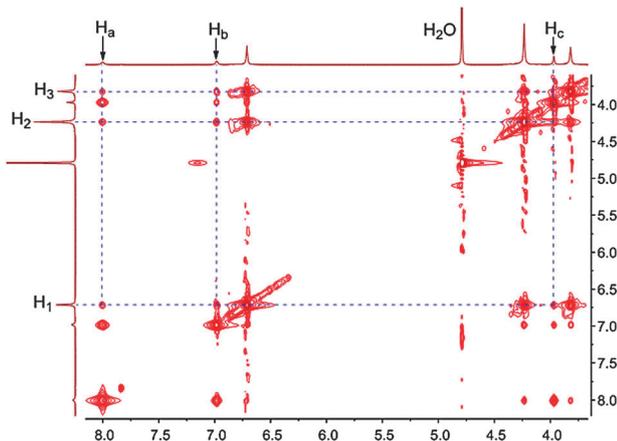


Fig. 3 2D NOESY NMR (500 MHz, D₂O, 293 K) spectrum of a solution of **WP9** (5.00 mM) and **G** (5.00 mM).

aqueous DCl solution, the carboxylate groups on **WP9** were changed into carboxylic acid groups, resulting in the precipitation of water-insoluble protonated **WP9**. However, as we expected, the bright brown colour appeared again upon addition of NaOD (Fig. S16, ESI[†]), resulting from the deprotonation of the carboxylic acid groups and the recovery of water-soluble **WP9**. In order to testify this reversible process, ¹H NMR spectroscopy was conducted (Fig. 1). Compared with the spectrum of **WP9** and **G** in D₂O (Fig. 1b), the signals for the protons on **WP9** disappeared after adding DCl to the solution (Fig. 1c). Meanwhile, the chemical shifts and the split of H_{a-c} on **G** got back to the original states as the individual **G**, suggesting that the guest dethreaded from the cavity of **WP9**. On the other hand, the signals corresponding to protons on **G** shifted upfield remarkably and the peaks of H_{a-b} became broad again by deprotonating the carboxylate groups on both rims of **WP9** upon addition of NaOD (Fig. 1d), indicating the reformation of the complex between **WP9** and **G**. In a word, the complexation between **WP9** and **G** is pH-responsive and its reversible property can be used to offer a simple on-off switch that is of great importance in the construction of controllable molecular switches.

In summary, we synthesized water-soluble pillar[9]arene **WP9** and studied its pH-responsive binding to paraquat **G**. We found that **WP9** and **G** formed a stable 1 : 1 inclusion complex in water with a considerably high association constant. More interestingly, we demonstrated that the assembly and disassembly of this host-guest system could be reversibly controlled by changing the solution pH. Our present efforts are focused on expanding this new pH-responsive recognition motif to fabricate molecular switches, responsive supramolecular polymers and smart supramolecular materials in aqueous media.

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