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# A water-soluble pillar[10]arene: synthesis, pH-responsive host–guest complexation, and application in constructing a supra-amphiphile†

Cite this: *Org. Chem. Front.*, 2014, **1**, 630

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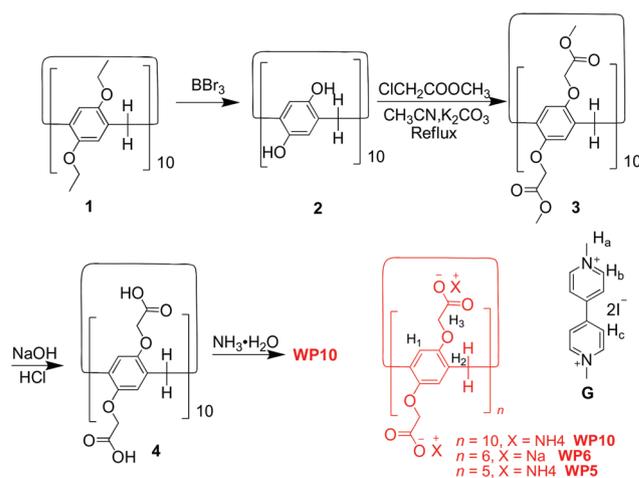
Received 22nd March 2014,  
Accepted 1st May 2014

DOI: 10.1039/c4qo00086b  
rsc.li/frontiers-organic

A water-soluble pillar[10]arene was prepared. Its pH-responsive host–guest complexation with paraquat and application in constructing a supra-amphiphile were investigated.

Supramolecular chemistry has attracted considerable attention in the last decade due to its superiority in the fabrication of artificial molecular machines, supramolecular polymers, supramolecular gels and other functional supramolecular systems.<sup>1</sup> Macrocyclic hosts, such as calixarenes,<sup>2</sup> crown ethers,<sup>3</sup> cyclodextrins,<sup>4</sup> and cucurbiturils,<sup>5</sup> have played prominent roles in the development of supramolecular chemistry. Therefore, it is of continuing interest to design and synthesize novel macrocyclic hosts. Pillar[*n*]arenes, as a kind of emerging macrocyclic hosts, have been studied actively since the first paper published in 2008.<sup>6a</sup> The unique columnar conformation and accessible functionalization of pillararenes gave them an outstanding ability to build various host–guest recognition motifs by selectively binding different kinds of guests and provided a useful platform for the construction of novel supramolecular systems, such as chemosensors,<sup>6n</sup> trans-membrane channels,<sup>6q</sup> supramolecular polymers<sup>6d</sup> and drug delivery systems.<sup>7f</sup> The synthesis and host–guest chemistry of pillar[5,6]arenes have been widely explored. However, limited by the cavity size, research on the host–guest chemistry based on pillar[*n*]arenes was confined to a large extent, so the preparation of advanced pillar[*n* ≥ 7]arenes plays a significant part in the evolution of pillar[*n*]arenes.<sup>8</sup> Herein, we report the synthesis of the first water-soluble pillar[10]arene (**WP10** here) and its pH-responsive binding to paraquat and application in the construction of a supra-amphiphile.

**WP10** was synthesized by introducing carboxylate anionic groups on both rims (Scheme 1). Compound **1** was obtained



Scheme 1 Synthetic route to water-soluble pillar[10]arene **WP10** and chemical structures of other compounds studied here.

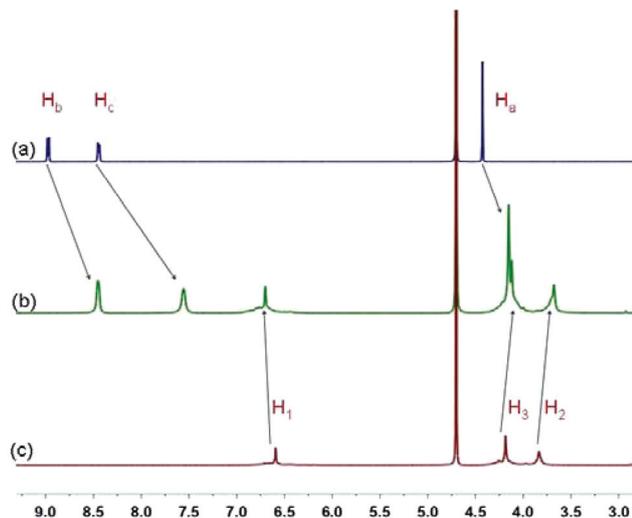
by a one-step method reported by Hou's group.<sup>8b</sup> By dealkylation of **1**, *per*-hydroxylated pillar[10]arene **2** was obtained, and then methoxycarbonylmethoxy-substituted pillar[10]arene **3** was prepared by etherification of **2**. The subsequent acidification after hydrolysis of **3** under basic conditions afforded carboxylic acid-substituted pillar[10]arene **4**. By treatment with excessive ammonium hydroxide, **WP10** was obtained.

Due to the existence of twenty carboxylate anionic groups on both rims, **WP10** can be a wonderful host for cationic guest molecules. The complexation between paraquat **G** and **WP10** was firstly studied by <sup>1</sup>H NMR spectroscopy. As shown in Fig. 1, when equimolar **WP10** was added into a solution of **G** (1.00 mM), the signals related to the protons on paraquat shifted upfield significantly. Additionally, an extensive broadening effect occurred when paraquat interacted with **WP10** due to complexation dynamics. The reason is that these protons were located within the cavity of **WP10** and were

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†Electronic supplementary information (ESI) available: Synthesis, characterization, stoichiometry and association constant determination, UV-vis data and other materials. See DOI: 10.1039/c4qo00086b



**Fig. 1** Partial  $^1\text{H}$  NMR spectra (400 MHz,  $\text{D}_2\text{O}$ , 293 K): (a) **G** (1.00 mM); (b) **G** (1.00 mM) and **WP10** (1.00 mM); (c) **WP10** (1.00 mM).  $\text{H}_a$ – $\text{H}_c$  and  $\text{H}_1$ – $\text{H}_3$  are the related protons on **G** and **WP10**, respectively, displayed in Scheme 1.

shielded by the electron-rich cyclic structure upon forming a threaded structure between **G** and **WP10**. The peak for proton  $\text{H}_a$  shifted upfield slightly (from 4.42 to 4.15 ppm) compared with protons  $\text{H}_b$  and  $\text{H}_c$  on the pyridinium units ( $\Delta\delta = -0.51$  and  $-0.88$  ppm), for the reason that when **G** penetrated into the cavity of **WP10**, protons  $\text{H}_b$  and  $\text{H}_c$  were located in the electron-rich cavity of **WP10**, while protons  $\text{H}_a$  were outside the cavity. On the other hand, protons on **WP10** also exhibited slight chemical shift changes due to the interactions with paraquat **G**.

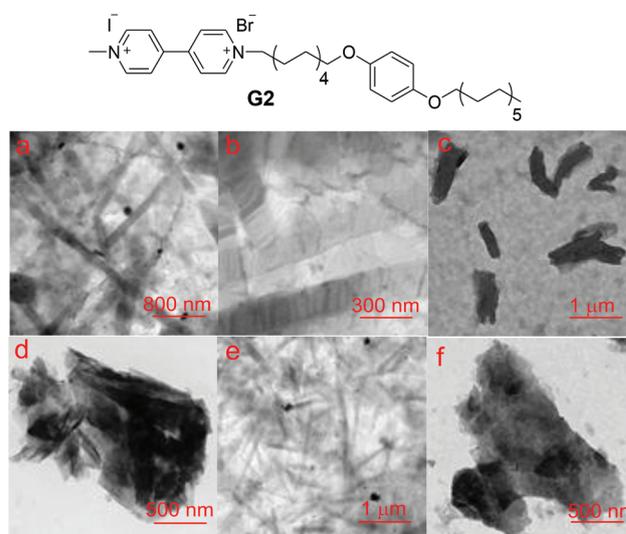
Further evidence for the complexation between **WP10** and **G** was obtained from UV-vis absorption spectroscopy and NOESY. When **G** and **WP10** were mixed in water with a 1 : 1 molar ratio, the color of the resulting solution turned red immediately, and the spectrum exhibited a broad absorption above 400 nm, which corresponded to the characteristic absorption of the charge-transfer complex between electron-rich **WP10** and electron-deficient **G** (Fig. S16, ESI $^\dagger$ ).<sup>9</sup> Additionally, a NOESY study of a solution of 5.00 mM **WP10** and **G** was conducted to investigate the relative spatial positions of this host-guest complex. As shown in Fig. S17, $^\dagger$  correlations between protons  $\text{H}_b$  and  $\text{H}_c$  on **G** and protons  $\text{H}_1$  on **WP10** were observed, suggesting that paraquat **G** was threaded into the cavity of **WP10**.

For the estimation of the binding constant, fluorescence titration experiments of **WP10** with **G** were conducted in aqueous solution at room temperature. As shown in Fig. S13, $^\dagger$  the decrease of fluorescence intensity was found upon gradual addition of **G**. A mole ratio plot (Fig. S14, ESI $^\dagger$ ) based on the fluorescence titration experiments demonstrated that the complex between **WP10** and **G** has a 1 : 1 stoichiometry. Further evidence for the formation of the 1 : 1 complex between **WP10** and **G** was obtained by the electrospray ionization mass spectrum. A peak was observed at  $m/z$  1392.3 corresponding to  $[\text{WP10} \supset \text{G} - 2\text{I} - 7\text{NH}_4 + 3\text{H}]^{2-}$  (Fig. S21, ESI $^\dagger$ ).

By a non-linear curve-fitting method, the  $K_a$  value for **WP10**  $\supset$  **G** was calculated to be  $(1.25 \pm 0.21) \times 10^7 \text{ M}^{-1}$  (Fig. S15, ESI $^\dagger$ ), which is higher than that for the complex between **WP5** and **G** ( $8.20 \times 10^4 \text{ M}^{-1}$ ),<sup>10</sup> but lower than the corresponding  $K_a$  value for the complex between **WP6** and **G** ( $1.02 \times 10^8 \text{ M}^{-1}$ ).<sup>7e</sup> A reasonable explanation for this binding constant difference was proposed. **WP10** tends to form a much larger cavity than **WP5** or **WP6** due to the strong electrostatic repulsion generated by the negative anionic groups on both rims in solution. Therefore, the cavity of **WP10** is too large for paraquat to form a more stable host-guest complex, resulting in a lower  $K_a$  value than that of **WP6**. While for the relatively stronger electrostatic interaction generated by the twenty carboxylate anionic groups, the  $K_a$  value is larger than that of **WP5**.

To investigate the pH-responsiveness of **WP10**,  $^1\text{H}$  NMR spectroscopy was utilized (Fig. S18, ESI $^\dagger$ ). When the water-soluble pillar[10]arene precipitated from  $\text{D}_2\text{O}$  after acidification of the solution by adding DCl, proton signals of **WP10** disappeared accompanied by the proton signals of paraquat **G** returning to the positions before complexation with **WP10**. These indicated that no interactions existed between **WP10** and **G** after **WP10** was acidified. When the solution was made basic again by addition of NaOD, the precipitated host redissolved, the proton signals of **WP10** reappeared, and the protons of paraquat **G** shifted upfield again. These results demonstrated that the host-guest complexation between **WP10** and **G** could be easily controlled by changing the pH of the solution.

After the investigation of this new molecular recognition motif, we constructed a supra-amphiphile based on the host-guest complexation between **WP10** and an amphiphilic guest **G2** derived from the 4,4'-bipyridinium unit (Fig. 2). By using the concentration-dependent conductivity, the critical aggregation concentration (CAC) of **G2** was determined to be  $8.87 \times 10^{-6} \text{ M}$



**Fig. 2** Top: chemical structure of **G2**; bottom: TEM images: (a) **G2**; (b) enlarged image of **G2**; (c) **WP10**  $\supset$  **G2**; (d) enlarged image of **WP10**  $\supset$  **G2**; (e) **WP10**  $\supset$  **G2** when the pH of the solution is 6.0; (f) **WP10**  $\supset$  **G2** when the pH of the solution is 7.4.

(Fig. S19<sup>†</sup>). As revealed by TEM, the typical amphiphilic **G2** itself self-assembled in water to form nanoribbons (Fig. 2a). Upon addition of **WP10**, the CAC value increased to  $4.06 \times 10^{-5}$  M (Fig. S20<sup>†</sup>), which was about 4 times higher than that of **G2**, confirming the host–guest complexation between **WP10** and **G2**. From the TEM images, nanosheets were observed (Fig. 2c), drastically different from the nanoribbons formed by **G2** alone.

A mechanism was proposed to explain the change in the shape of **G2** aggregates which transformed from nanoribbons to nanosheets after complexation with **WP10**. The micro-assembled structure of the aggregates formed by amphiphiles is determined by the curvature of the membrane.<sup>11</sup> The hydrophobic parts of amphiphiles favor aggregation while the hydrophilic parts are prone to stay in water, so **G2** self-assembled in solution with the hydrophobic alkyl chains in the interlayer of the nanoribbons. After complexation with **WP10**, the anionic hosts were introduced into the hydrophilic membrane of nanoribbons; because of the steric hindrance and electrostatic repulsion generated upon insertion of **WP10** molecules, the formation of a nanosheet structure with lower curvature was spontaneous.

The above discussed pH-responsiveness of the **WP10** ⊃ **G** complex was utilized to control the reversible aggregation nanostructure transition by changing the solution pH. As shown in Fig. 2e, nanoribbons appeared again by adjusting the solution pH to 6.0. As expected, when the pH was adjusted to 7.4, the nanosheets could be regained (Fig. 2f). As demonstrated above, **WP10** precipitated when the solution pH decreased, leading to the destruction of **WP10** ⊃ **G2**, so nanoribbons were observed. Therefore, self-assembly of this host–guest system can be easily controlled by changing the solution pH.

In conclusion, we reported the synthesis of the first water-soluble pillar[10]arene and its pH-responsive host–guest complexation with paraquat. Furthermore, a supra-amphiphile based on this new host–guest recognition motif was constructed. Compared to the nanoribbon aggregates built by amphiphilic molecule **G2**, the host–guest complex **WP10** ⊃ **G2** self-assembled into nanosheets instead. By changing the solution pH, the reversible transformation from nanoribbons to nanosheets could be controlled easily. This novel recognition motif based on the water soluble pillar[10]arene in aqueous media will be helpful for the fabrication of functional architectures and definitely bring about many promising applications, such as supramolecular polymers, nanoelectronics, drug-delivery and controlled release.

This work was supported by the National Basic Research Program (2013CB834502) and the National Natural Science Foundation of China (21125417).

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