## Supramolecular Polymerization

## Supramolecular Polymerization of a Pillar[5]arene Induced by a Symmetric Biaryl Sulfonate with Dual Binding Sites

Meiling Hong,<sup>[a]</sup> Ying-Ming Zhang,<sup>[a]</sup> Yan-Cen Liu,<sup>[a]</sup> and Yu Liu\*<sup>[a, b]</sup>

Abstract: Macrocycle-based supramolecular polymers have attracted more interest in recent years and found many practical applications with controlled shape and unique physical and chemical properties. In this work, a binary supramolecular polymer is prepared in water by the strong host-guest interactions between a cationic pillar[5]arene and a symmetric sulfonate with dual binding sites. Isothermal titration calorimetry measurements show that the binding process of host-guest complexation is governed in a thermodynamically favorable way with a high stability constant of up to  $10^7 \,\mathrm{m}^{-1}$  order of magnitude. Moreover, spectroscopic and microscopic investigations jointly demonstrate that the resulting stable polymer is multistimuli responsive towards temperature and competitive metal coordination. We anticipate that our obtained multistimuli-responsive supramolecular polymer may offer a new way in the construction of more functionalized pillararene-based nanoassemblies.

The combination of polymer science and nanosupramolecular chemistry has expedited the development of supramolecular polymers,<sup>[1]</sup> in which the same or different kinds of monomers can be held together by reversible and directional noncovalent cooperation.<sup>[2]</sup> In the past two decades, such supramolecular nanostructures have gained increasing attention mainly due to their fascinating chemical and physical properties. Benefiting from the reversible nature of noncovalent interactions, supramolecular polymerization has been utilized as a novel and smart design principle to construct self-healing,<sup>[3]</sup> recycling,<sup>[4]</sup> self-adapting,<sup>[5]</sup> and degradable materials<sup>[6]</sup> that can respond to various external stimuli, and many driving forces have been explored to construct supramolecular polymeris.<sup>[7–10]</sup> In particular,

[a]	Dr. M. Hong, Dr. YM. Zhang, YC. Liu, Prof. Dr. Y. Liu Department of Chemistry					
	State Key Laboratory of Elemento-Organic Chemistry					
	Nankai University					
	Tianjin 300071 (P. R. China)					
	E-mail: yuliu@nankai.edu.cn					
[b]	Prof. Dr. Y. Liu					
	Collaborative Innovation Center of Chemical Science and					
	Engineering (Tianjin)					
	Nankai University					
	Tianjin 300071 (P. R. China)					
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host-guest interaction as a class of fascinating noncovalent driving force has been widely employed to fabricate macrocycle-based supramolecular polymeric materials through multiple noncovalent interactions.<sup>[11]</sup>

Pillararenes, composed of hydroquinone units linked by methylene spacers at the para-position, have stimulated great interest with significant advances in recent years.<sup>[12]</sup> With a highly symmetrical pillar structure, modified pillararenes have distinctive host-quest binding characteristics and find many applications in the field of supramolecular chemistry.<sup>[13-16]</sup> Consequently, a variety of neutral and charged substrates have been utilized in pillararenes-based molecular recognition and supramolecular polymerization.<sup>[17-21]</sup> For example, it has been revealed that hydrophobic and electrostatic interactions play important roles in controlling the unique binding behaviors between cationic pillararenes and sodium 1-octanesulfonate.<sup>[22]</sup> After understanding the basic molecular binding properties of pillararenes and motivated by their unique host-guest recognition with organic sulfonates, we herein utilized a cationic pillar[5]arene with an extended hydrophobic cavity (CP5) and sodium 4,4'-dibutyl-(1,1'-biphenyl)-3,3'-disulfonate with dual binding sites (DBP) to fabricate a multistimuli-responsive supramolecular polymer in water (Scheme 1).



Scheme 1. Molecular structures of CP5 and DBP, and schematic of supramolecular polymer CP5-DBP.

The host compound CP5 was prepared as quaternary ammonium salt according to the reported literature.<sup>[22]</sup> The synthetic route to symmetric guest molecule DBP, which has butyl tails as hydrophobic sites and sulfonate groups as hydrophilic sites, is shown in Scheme S1 in the Supporting Information. 4,4'-Biphenol was alkylated by 1-bromobutane under basic conditions to give the symmetric 4,4'-dibutoxybiphenyl in 47% yield. Subsequent sulfonation of 4,4'-dibutoxybiphenyl with chlorosulfonic acid and neutralization with NaOH afforded disodium DBP in 32% yield.

Next, the molecular binding behaviors between CP5 and DBP were investigated by <sup>1</sup>H NMR titration experiments. As shown in Figure 1, the  $\Delta\delta$  values of the alkyl protons on DBP



**Figure 1.** <sup>1</sup>H NMR spectra (400 MHz, D<sub>2</sub>O, 298 K) of (a) free DBP; (b) the CP5-DBP complex; (c) free CP5 ([DBP] = [CP5] = 3 mM). The symbol "**u**" represents the signal of acetone protons as an external reference.

 $(H_{e-g})$  were dramatically broadened and underwent pronounced upfield shifts of -2.02, -1.70 and -1.15 ppm, respectively, which was caused by the strong shielding effect of the aromatic nuclei in CP5. Comparatively, the aromatic protons on DBP  $(H_{a-b})$  were shifted downfield by 0.14 and 0.26 ppm, respectively.<sup>[23]</sup> These contrasting chemical shifts demonstrate that the butyl chains in DBP were deeply immersed into the CP5s cavity, whereas the biphenyl core was located outside.

Besides the proton signals of the guest molecule, it is noteworthy that the peak pattern of methylene protons in CP5  $(H_3)$ was split into two groups, indicating that the molecular conformation of CP5 become more rigid upon complexation with DBP in aqueous solution. Moreover, as shown in Figure S4, the cross-peaks between aromatic protons on DBP (H<sub>c</sub>) and sidechain protons on CP5  $(H_{3-5})$  definitely confirm that the phenyl rings of DBP were accommodated in the extended cavity of CP5 (peaks A). The correlations between the aromatic protons on DBP (H<sub>a,b</sub>) and trimethylammonium protons on CP5 (H<sub>5</sub>) were also detected, corroborating that the phenyl ring in DBP was surrounded by the CP5 hydrophobic side arms (peaks B). Therefore, we can deduce that DBP was readily encapsulated mainly through the hydrophobic interaction of the biphenyl moiety with the CP5 cavity and the electrostatic attraction between sulfonate groups and quaternary ammonium sites.

Isothermal titration calorimetry (ITC) measurements can provide further quantitative information about the thermodynamic parameters in the host-guest binding process, including the complex stability constant ( $K_s$ ) and enthalpy and entropy changes ( $\Delta H^\circ$  and  $\Delta S^\circ$ ). In our case, although the binding stoi-

chiometry between CP5 and DBP could not be ascertained, the asymmetric sodium 1-nonanesulfonate with a single binding site was chosen as a model substrate to simplify the molecular binding process between CP5 and DBP. The binding affinity of CP5 with sodium 1-nonanesulfonate was measured as  $7.3 \times$  $10^7 \,\mathrm{m}^{-1}$  by the two-step competition method using sodium 1butanesulfonate as the competitor guest, indirectly demonstrating the high binding affinity in CP5.DBP complex (Figure S5–S8).<sup>[24]</sup> Such exceptionally strong binding stability would further facilitate the eventual formation of highly degreed supramolecular polymer as described below.<sup>[2c,25]</sup> It can be also seen that the molecular binding process of CP5 with the monoalkylated amphiphilic sulfonate was thermodynamically governed in a favorable way; that is, the main contributions to the negative enthalpy  $(-\Delta H^{\circ} = 46.5 \text{ kJ mol}^{-1})$  are the hydrophobic and electrostatic interactions, whereas the desolvation effect that overwhelms the loss of conformational freedom upon complexation are responsible for the positive entropy change ( $T\Delta S^{\circ} = 7.9 \text{ kJ mol}^{-1}$ ).<sup>[26]</sup>

To investigate the hydrodynamic diameters of 1:1 mixture of the DBP-CP5 complex in aqueous solution, dynamic light scattering (DLS) measurements were performed at different concentrations. A broad size distribution was clearly observed in the range 800–1200 nm at 3.0 mm, corresponding to the formation of highly polymerized supramolecular assemblies (Figure 2a and S9). It is noted that there was a narrow size distribution centered at 40 nm, probably due to supramolecular assemblies with a lower degree of polymerization. As shown in Figure 2b, the hydrodynamic diameter of the supramolecular polymer increased from 394 to 797 nm as the concentration in-



**Figure 2.** (a) Hydrodynamic diameter distribution of the CP5-DBP supramolecular polymer ([CP5] = [DBP] = 3.0 mM); (b) Dependence of the hydrodynamic diameter of the CP5-DBP assembly on the supramolecular polymer concentration at 298 K.

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creased from 0.2 to 3 mM, indicating that the size of the supramolecular polymer was intrinsically concentration-dependent and could be formed in a very low concentration region. In contrast, the light scattering intensity of CP5 alone was undetectable at 3.0 mM, suggesting that supramolecular assemblies could not be formed without the assistance of the guest molecule (Figure S10). Viscosity is one of important parameters to directly characterize the rheological properties of supramolecular polymers in aqueous solution. It can be seen that the viscosity of the CP5-DBP assembly gradually increased, compared with the individual components CP5 or DBP (Figure 3). This



Figure 3. Specific viscosity of CP5, DBP, and the CP5-DBP assembly versus monomer concentration in aqueous solution at 298 K.

specific viscosity of the CP5-DBP assembly varied exponentially with its monomer concentration, further corroborating the existence of large-sized supramolecular polymer in solution.

Furthermore, atomic force microscopy (AFM) was employed to confirm the morphology of the obtained supramolecular architecture. As shown in Figure 4a, AFM images showed several fine, curved structures with lengths on the micron scale, and the average height of these 1D nanostructures was around 1.0 nm, which was basically consistent with the outer diameter of one pillararene molecule. Accordingly, the length of regular







**Figure 5.** Hydrodynamic diameter distribution of the CP5-DBP supramolecular polymer at 298 and 358 K respectively ([CP5]=[DBP]=2.5 mM).

linear assemblies measured in transmission electron microscopy (TEM) images was ca. 20 nm, jointly confirming the formation of binary supramolecular polymer (Figure 4b and S18).

The responsiveness to various stimuli, including pH, light, and temperature, is known as one of major advantages of supramolecular assemblies, which can lead to the generation of more reversible and adaptable smart materials. In our case, the average hydrodynamic diameter of the CP5-DBP assembly decreased from 663 to 341 nm with temperature ascending from 298 to 358 K, which shows that the polymer was disassembled into oligomers with a lower degree of polymerization (Figure 5 and S11–S12). In addition, the diameters increased from 341 nm to 576 nm with temperature descending from 358 to 298 K. This indicates the regeneration of the polymeric nanostructure with decreasing temperature (Figure 5 and S13). This capability of responding to temperature mainly originates from the enthalpy-driven host-guest complexation between CP5 and DBP, which would be weakened upon heating.

Moreover, considering that DBP has two sulfonate groups that can be neutralized and precipitated by BaCl<sub>2</sub>, it was anticipated that the CP5·DBP supramolecular polymer could be disrupted by the addition of BaCl<sub>2</sub>. As expected, the average diameter makredly increased to micron level and precipitate immediately formed upon addition of BaCl<sub>2</sub>, suggesting that the DBP was expelled from the cavity of CP5 by the competitive metal coordination with BaCl<sub>2</sub> in aqueous solution (Figure 6 and S14). After the removal of insoluble Ba-DBP by centrifugation, no obvious DLS signal was detected in the resulting solution (Figure S15). Therefore, we can infer that the polymer was completely disassembled by BaCl<sub>2</sub>. More interestingly, the assembly/disassembly process was reversibly controlled by the alternate addition of BaCl<sub>2</sub> and ethylenediaminetetraacetic acid (EDTA). Upon addition of Ba<sup>2+</sup>, the optical transmittance sharply decreased because of the formation of large-sized Ba-DBP precipitates. Then, the optical transmittance was largely recovered to the original state in the presence of EDTA, indicating that the supramolecular polymer reassembled through the chelation of Ba<sup>2+</sup> by adding excess EDTA (Figure 6 and S16 and S17).

In conclusion, we successfully prepared a linear binary supramolecular polymer, CP5·DBP, the formation of which is driven by the favorable host-guest interactions of the positively charged pillar[5]arene with the negatively charged symmetric



**Figure 6.** Optical transmittance of (a) the CP5-DBP assembly; (b) the CP5-DBP assembly in the presence of BaCl<sub>2</sub>; (c) the CP5-DBP assembly in the presence of BaCl<sub>2</sub> and EDTA; and (d) the CP5-DBP assembly in the presence of EDTA in aqueous solution at 298 K ([CP5]=[DBP]=0.8 mm, [BaCl<sub>2</sub>]=1.8 mm, and [EDTA]=3.2 mm).

guest in water. The large binding constant further endows the water-soluble polymer with strong binding stability and a high degree of polymerization. Benefiting from the reversible noncovalent connection and multiple sulfonate groups in the obtained supramolecular assembly, this polymer can be readily disrupted by increasing temperature and the action of an inorganic salt. We envision that this water-soluble supramolecular polymer with satisfactory multistimuli responsiveness may provide a new and feasible method to fabricate more advanced pillararene-containing nanostructures in aqueous solution.

## **Experimental Section**

General methods and characterizations are provided in the supporting information.

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**Keywords:** cationic pillar[5]arenes · multistimuli responsiveness · self-assembly · supramolecular polymers · sulfonates

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