

Photo-responsive self-assembly based on a water-soluble pillar[6]arene and an azobenzene-containing amphiphile in water†

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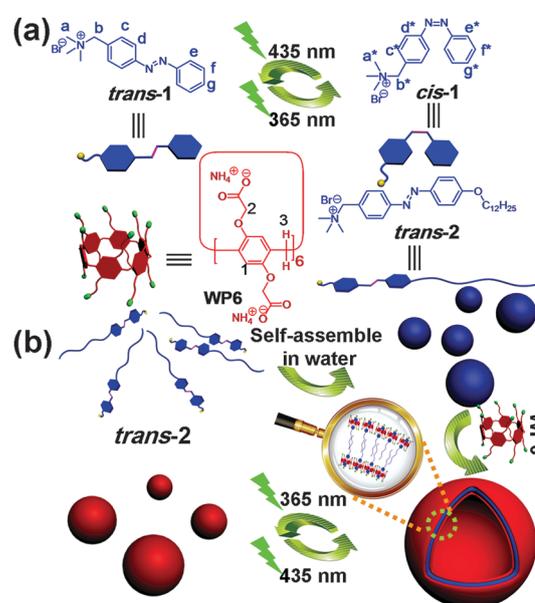
Photo-responsive self-assembly in water based on the molecular recognition motif between a water-soluble pillar[6]arene host and an azobenzene-containing amphiphilic guest in water was investigated.

Stimuli-responsive self-assembly has attracted considerable attention from the scientific community as it can be used to make various functional nanostructures which can be used in the areas of drug delivery,¹ controlled release,² nanoreactors,³ supramolecular polymers⁴ and detection.⁵ Many external stimuli such as light, pH-change, temperature-change, ions, enzymes, and gases have been used to construct responsive self-assembly systems.⁶ Among them, light is remarkably attractive due to its cleanness, controllability, rapidness, and handiness.⁷

Pillararenes, a new class of macrocyclic hosts next to crown ethers,^{4,8} cyclodextrins,⁹ calixarenes¹⁰ and cucurbiturils,¹¹ have been widely studied since 2008. The repeating units of pillararenes are connected by methylene bridges at the *para* positions, forming a unique rigid pillar architecture. Their syntheses, conformational mobility, functionalizations, host-guest chemistry, and self-assemblies have recently been actively explored.¹² Pillararenes can selectively bind various guests and have provided a useful platform for the construction of diverse and interesting supramolecular systems, such as explosive detectors, transmembrane channels, drug delivery systems, selective separation, cell glue, green catalysis, supramolecular polymers and liquid crystals.¹³ From our previous work, we know that the size of pillar[6]arene is suitable for *trans*-azobenzene while it is too small for *cis*-azobenzene.¹⁴ A photo-controllable threading–dethreading switch can be achieved due to the photoisomerization of the azobenzene group. Herein, we constructed a photo-responsive supramolecular self-assembly system in water on the basis of the molecular

recognition motif between a water-soluble pillar[6]arene host (WP6) and an azobenzene-containing guest (1). The azobenzene-based amphiphilic guest (2) itself self-assembled into solid nanoparticles before complexation with WP6. Upon addition of WP6, vesicles were obtained, which were sensitive to UV and visible light irradiation. Reversible transitions between vesicles and solid nanoparticles were achieved due to the photo-responsiveness of the guest (Scheme 1).

First, ¹H NMR spectroscopy was used to study the host-guest complexation between WP6 and 2 by using 1 as the model compound because of the relatively poor water-solubility of 2. Compared with free *trans*-1 (Fig. 1a), significant chemical shift changes of the signals for the protons on *trans*-1 occurred in the presence of an equimolar amount of WP6 (Fig. 1b).



Scheme 1 (a) Chemical structures of 1, 2, and WP6. (b) Cartoon representation of the photo-responsive self-assembly between WP6 and 2 in water.

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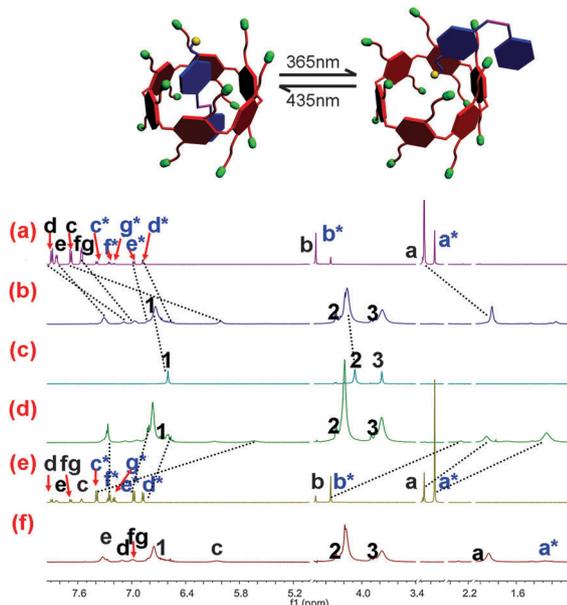


Fig. 1 Partial ^1H NMR spectra (500 MHz, D_2O , room temperature): (a) **trans-1** (2.50 mM); (b) **trans-1** (2.50 mM) and **WP6** (2.50 mM); (c) **WP6** (2.50 mM); (d) **trans-1** (2.50 mM) and **WP6** (2.50 mM) after irradiation at 365 nm for 10 min; (e) **trans-1** (2.50 mM) after irradiation at 365 nm for 10 min; (f) **trans-1** (2.50 mM) and **WP6** (2.50 mM) after further irradiation at 435 nm for 10 min.

The peaks related to H_a , H_c , H_d , H_e , H_f and H_g shifted upfield remarkably ($\Delta\delta = -1.20, -1.68, -0.82, -0.52, -0.59$ and -0.59 ppm, respectively). The reason for the extensive changes of the chemical shifts is that these protons are located within the cavity of **WP6** and are shielded by the electron-rich cyclic structure upon forming a threaded structure between **WP6** and **trans-1**. Moreover, these peaks became broad and H_b disappeared owing to complexation dynamics.^{12d} In addition, the protons on **WP6** also exhibited slight chemical shift changes. The peak related to H_1 shifted downfield from 6.59 to 6.75 ppm, and the signal corresponding to H_2 shifted upfield slightly. These phenomena provided convincing evidence for the formation of an inclusion complex between **WP6** and **trans-1** (Fig. 1), mainly driven by hydrophobic and electrostatic interactions.

After irradiation with UV light at 365 nm for 10 min, the molar ratio of the *trans* to *cis* form of **1** changed to 30 : 70 (Fig. 1e) and the chemical shift of proton H_{c^*} of *cis-1* shifted upfield from 7.38 to 5.64 ppm in the presence of equimolar **WP6** (Fig. 1d). Furthermore, the peaks related to H_{a^*} and H_{b^*} shifted upfield dramatically, from 2.96 to 1.26 ppm and 4.34 to 2.29 ppm, respectively, and exhibited a broadening effect, suggesting the complexation between **WP6** and *cis-1*. Moreover, the chemical shifts of protons H_{d^*} , H_{e^*} , H_{f^*} , and H_{g^*} on the benzene rings of *cis-1* changed slightly, indicating that the benzene ring containing protons H_{c^*} , H_{f^*} and H_{g^*} of guest *cis-1* was outside the cavity of **WP6**. Upon irradiation with light at 435 nm for 10 min, *cis-1* went back to *trans-1*, and the proton signals related to the mixed solution of **WP6** and **1** went back to the original state (Fig. 1f), suggesting that the photo-controllable threading–dethreading switch between **WP6** and **1** was achieved. UV-vis absorption

spectroscopy was also employed to confirm the photo-controllable threading–dethreading switch (Fig. S10–S12, ESI†). Additionally, a 2D NOESY NMR experiment was also conducted to confirm the ^1H NMR results (Fig. S7, ESI†). Moreover, isothermal titration calorimetry (ITC) experiments were used to determine the association constant (K_a) and stoichiometry of this host–guest complex. The K_a value was estimated to be $(4.13 \pm 0.19) \times 10^5 \text{ M}^{-1}$ for **WP6** \supset *trans-1* in the 1 : 1 complexation mode (Fig. S8, ESI†). Similarly, upon irradiation with UV light at 365 nm the molar percentage of the *cis*-azobenzene increased to 70%, accompanied with a decrease of K_a to $(5.89 \pm 0.33) \times 10^4 \text{ M}^{-1}$ (Fig. S9, ESI†). This indicated a sharp decrease in binding strength when *trans-1* changed to *cis-1*.

Based on the photo-controllable threading–dethreading switch between **WP6** and **1**, we further explored whether it could be used to construct a photo-responsive self-assembly system by introducing the azobenzene-containing amphiphile **2**. First, the critical aggregation concentrations were measured to be $2.19 \times 10^{-5} \text{ M}$ and $2.85 \times 10^{-5} \text{ M}$ for *trans-2* and **WP6** \supset *trans-2*, respectively, by using the concentration-dependent conductivity measurements (Fig. S14, ESI†). The self-assembly morphologies of *trans-2* and **WP6** \supset *trans-2* in water were then investigated *via* transmission electron microscopy (TEM). As shown in Fig. 2a, *trans-2* formed solid nanoparticles with an average diameter of ~ 30 nm, while **WP6** \supset *trans-2* formed vesicles with an average diameter of ~ 200 nm (Fig. 2b). Notably, the wall thickness of the observed fully collapsed vesicles¹⁵ was ~ 16 nm (Fig. 2c), which was twice as large as in the “normal” vesicles. This indicated that the actual

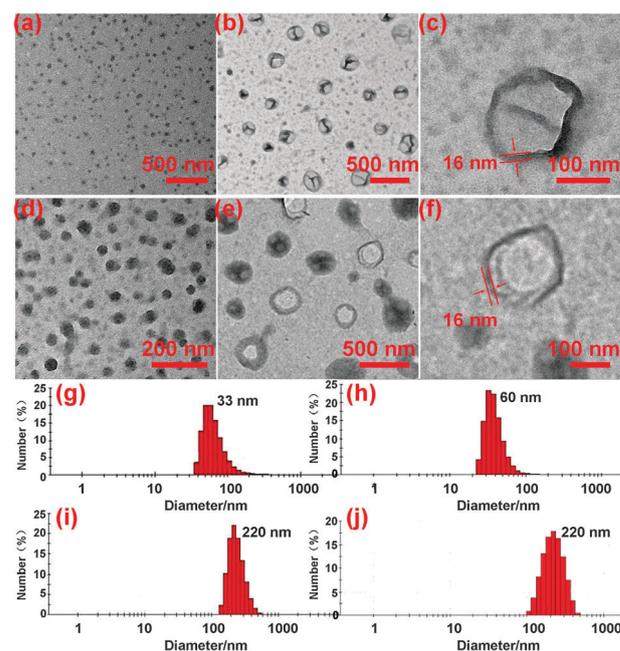


Fig. 2 TEM images: (a) *trans-2* ($2.50 \times 10^{-4} \text{ M}$) aggregates in water; (b) **WP6** with *trans-2* aggregates ($2.50 \times 10^{-4} \text{ M}$ for both) in water; (c) enlarged image of (b); (d) after irradiation with UV light at 365 nm of (b); (e) after further irradiation with visible light at 435 nm of (d); (f) enlarged image of (e). (g) DLS result of (a); (h) DLS result of (d); (i) DLS result of (b); (j) DLS result of (e).

wall thickness was ~ 8 nm, which was about the extended length of two **WP6** \supset *trans*-**2** complexes with antiparallel packing, suggesting that the vesicles had a bilayer wall. When the solution was irradiated with UV light, complex **WP6** \supset *cis*-**2** formed and the vesicles changed into solid nanoparticles with an average diameter of ~ 60 nm (Fig. 2d). Moreover, upon irradiation with visible light at 435 nm, the solid nanoparticles turned back to vesicles (Fig. 2e and 2f). Dynamic light scattering (DLS) was utilized to monitor the size changes of the self-assemblies formed by **2** and **WP6** \supset **2** (Fig. 2g–j), which were in accordance with the TEM results.

A possible mechanism is proposed to explain the morphological changes of the photo-responsive self-assemblies. The amphiphilic azobenzene **2** forms solid nanoparticles in water. Upon addition of **WP6**, *trans*-**2** threads into the hydrophobic cavity of **WP6** to form an inclusion complex **WP6** \supset *trans*-**2**, resulting in the formation of vesicles with lower curvature due to the steric hindrance and the electrostatic repulsion generated.^{6g,16} Upon UV irradiation, *cis*-**2** dethreads from the cavity of **WP6** and the positive trimethylammonium groups of *cis*-**2** interact with the negative carboxylic groups of **WP6**, causing the change of the packing arrangement of the amphiphilic building blocks and resulting in the self-assembly morphology turning to solid nanoparticles.¹⁷ Then upon further irradiation with visible light, the azobenzene unit returns to the *trans* state and threads into **WP6** again and the complex self-assembles into vesicles.

In conclusion, photo-responsive self-assembly in water was achieved based on the photo-responsive recognition motif between a water-soluble pillar[6]arene host and an azobenzene-containing amphiphilic guest. The guest itself self-assembled into solid nanoparticles before complexation with the host. Upon addition of the host, vesicles were obtained. Reversible transitions between vesicles and solid nanoparticles were controlled by UV and visible light irradiation due to the photo-responsiveness of the guest. This photo-responsive self-assembly can be used to fabricate nanostructures which can be applied in various fields such as drug delivery, controlled release, nano-reactors, supramolecular polymers, and detection.

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