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A cucurbit[7]uril-based supra-amphiphile: Photo-responsive self-assembly and application in controlled release

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ABSTRACT

A photo-responsive host–guest molecular recognition between a cucurbit[7]uril host and an azobenzene-containing guest was investigated. Based on this recognition motif, a photo-responsive supra-amphiphile was constructed. This supra-amphiphile can self-assemble into vesicles in water, which can be destroyed by UV irradiation. Depending on this photo-responsive assembly, its application in controlled release was further performed.

Stimuli-responsive host–guest systems, exhibiting controlled host–guest association/dissociation properties triggered by external stimuli, are one of the major research focuses of supramolecular chemistry.[1] Well-established stimuli-responsive host–guest recognition motifs can be utilized to fabricate supramolecular systems with applications in various fields, such as molecular electronics, compound separation, molecular muscles, biosensors and smart surfaces.[2] External stimuli include, but is not limited to, light, pH-change, temperature-change, enzyme, redox, and a combination of these.[3] Among these stimuli, light is one of the most appealing stimuli-responsive species due to its easy operation, low cost, few by-products and high sensitivity.[4] Azobenzene is a widely used chromophore for the preparation of light-responsive host–guest systems on account of its excellent photoisomerization features including fast response, widely applicable performance and photochemical stability.[5]

Cucurbit[*n*]urils (CB[*n*]s) are an interesting class of macrocyclic receptor molecules consisting of a hydrophobic cavity and two identical carbonyl laced portals.[6] The CB rings have been employed to fabricate robust light-responsive host–guest systems because of their ability to bind a wide array of light-responsive guests with high affinity in water, such as azobenzene and stilbene derivatives.[7] The most relevant to the work described herein is that of Scherman and coworkers who have exploited the ability of CB[8] to promote the formation of heteroternary complexes to construct a supramolecular container system exhibiting light-controlled encapsulation properties in water.[8] Zhang and the coworkers also utilized CB[8]-mediated heteroternary complexes to construct light responsive supramolecular systems for controlled drug release.[9] To date, a variety of examples have demonstrated CB[8]-mediated heteroternary complexes with a light-driven association/dissociation process. However, the related light-controlled system based on CB[7] has been rarely reported.[10] Maybe because the cavity size of CB[7] is relatively small, it's hard to find suitable guests to construct a photo-responsive recognition motif. It is extremely valuable to explore the potential of CB[7] in the fabrication of photo-controlled reversible self-assembly systems.

Herein, we investigate the complexation of an azobenzene-containing guest **M** (Scheme 1) with CB[6] and CB[7]. Because of the different cavity sizes of CB[6] and CB[7], *trans*-**M** cannot complex with CB[6], while it can locate in the cavity of the CB[7]. The photo-responsive threading–dethreading switch between CB[7] and **M** can be reversibly achieved upon UV and visible light irradiation due to the *trans*–*cis* photo-isomerization of **M**. Moreover, based on this novel host–guest recognition motif, a photo-responsive supra-amphiphile was constructed. The disassembly and assembly of the corresponding aggregates could be regulated by UV and visible light irradiation (Scheme 1).

The host–guest complexation between CB[6], CB[7] and **M** was firstly investigated by ^{1}H NMR spectroscopy. As shown in Fig. 1b, after the addition of 1 equiv. of CB[6] into a solution of **M**, the signals from protons on **M** and CB[6] did not show obvious chemical shift changes, indicating that **M** could not complex strongly with CB[6], because **M** was too large to be wrapped by CB[6] completely. In contrast, after the addition of 1 equiv. of CB[7] into the solution

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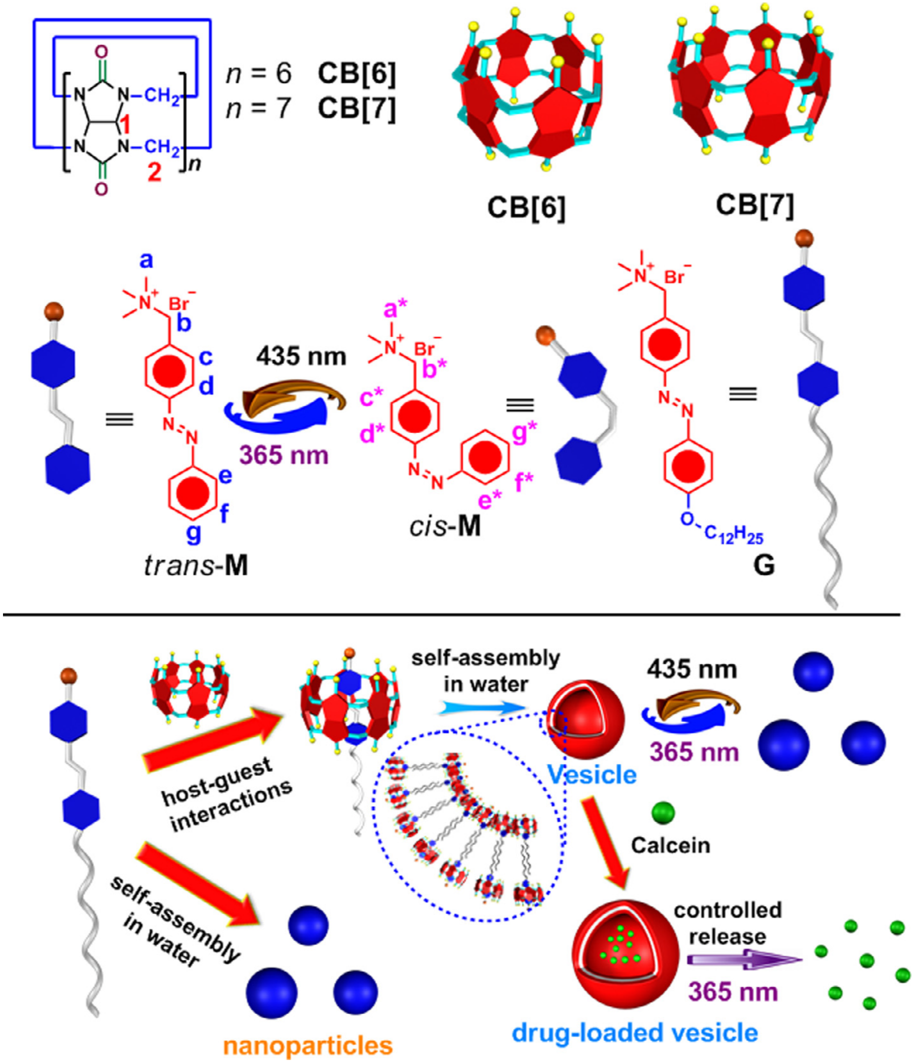

Scheme 1. Chemical structures of CB[*n*]s, **G** and **M**, and cartoon representation of the photo-responsive self-assembly between them in water.

of **M**, the chemical shift changes of signals related to the protons on **M** and CB[7] appeared (Fig. 1d). The signals related to protons H_{a-g} of **M** shifted upfield slightly ($\Delta\delta = -0.054$, -0.124, -0.097, -0.015, -0.036, -0.049 and -0.049 ppm, respectively) and all the peaks corresponding to the protons on CB[7] shifted downfield slightly, which was ascribed to the ion-dipole interactions between **M** and CB[7].[7c] Moreover, the peaks corresponding to the protons on **M** and CB[7] all exhibited broadening effect, owing to the interactions between **M** and CB[7]. A 2D NOESY NMR experiment was conducted to investigate the relative positions of the components in the host–guest inclusion complex (Fig. 2a). NOE correlation signals were observed between protons $H_{1,2}$ on CB[7] and $H_{c,d,e,f,g}$ on **M**, which indicated that the azobenzene part of **M** located in the cavity of CB[7] upon forming a [2]pseudorotaxane.

After irradiation with UV light at 365 nm (8 W medium-pressure Hg lamp using a UV filter) for 30 min, the new peaks of the protons on *cis*-**M** appeared (Fig. 1f). As shown in Fig. 1g, the signals related to the protons on *cis*-**M** did not exhibit obvious upfield chemical shift changes, neither did the protons on CB[7]. These phenomena indicated that the photo-induced *E*/*Z* isomerization of azobenzene group of **M** occurred upon UV irradiation, resulting in the azobenzene part threading out of the cavity of CB[7], as shown in the cartoon representation of Fig. 1g. Upon further irradiation with visible light at 435 nm for 30 min, *cis*-**M** transformed into the *trans* form. The proton signals related to the mixed solution of CB[7] and *trans*-**M** went back to the original state (Fig. 1h), indicating the azobenzene unit threading into the cavity of CB[7] again. The 2D NOESY NMR experiment was conducted again to demonstrate the complex model after the UV irradiation. As shown in Fig. 2b, no NOE correlation signals was observed between the protons on CB[7] and the benzene part of *cis*-**M**, confirming that the azobenzene part of *cis*-**M** was out of the cavity of CB[7].

Moreover, isothermal titration calorimetry (ITC) experiments were conducted to measure the association constant between CB[7] and **M**. As shown in Fig. S1, the association constant between CB[7] and *trans*-**M** was measured to be $(1.87 \pm 0.14) \times 10^6\ M^{-1}$, while the association constant between CB[7] and *trans*-**M** after UV irradiation at 365 nm for 30 min decreased to $(1.21 \pm 0.07) \times 10^5\ M^{-1}$ (Fig. S2). It is notable that even though the azobenzene group threaded out of the cavity of CB[7], the association constant was still very high. The reason was that the main driving force of this host–guest complexation was ion-dipole interactions. After UV irradiation, the ion-dipole interactions were still very strong, thus the trimethylammonium group on the *cis*-**M** was bound by a rim of CB[7].

After the establishment of this photo-responsive host–guest complex model, we further applied it to construct a photo-responsive supra-amphiphile between CB[7] and **G**. From the work