

Organic & Supramolecular Chemistry

Photoinduced Assembly/Disassembly of Supramolecular Nanoparticle Based on Polycationic Cyclodextrin and Azobenzene-Containing Surfactant

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The assembly of molecular induced aggregation and photo-response has gradually evolved into one of the valuable topics in supramolecular chemistry and other important fields. In this work, a shrinkable nanoparticles with two opposite charges has been successfully constructed, i.e. polycationic cyclodextrin (H) and anionic azobenzene-containing surfactant (G). Herein, polycationic cyclodextrins were able to induce the incorporation of azobenzene-containing anionic surfactants into nano-

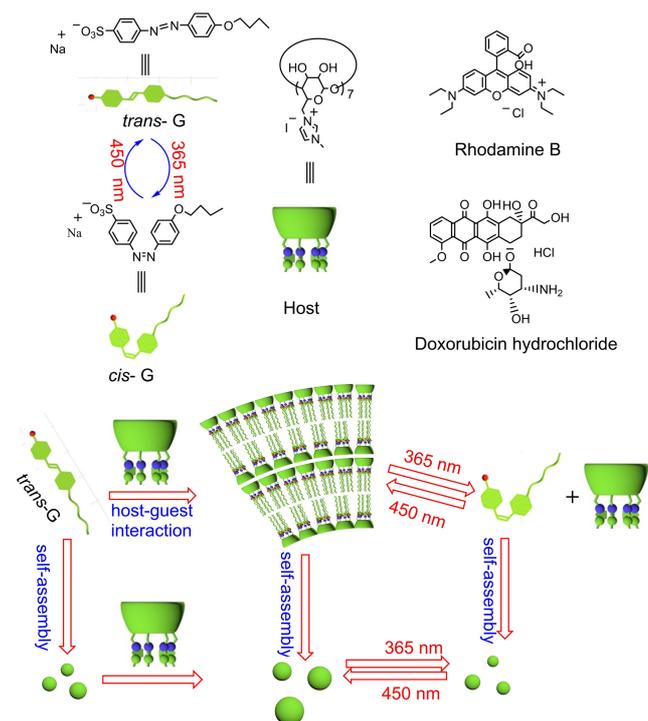
particles of about 181 nm in diameter. The resulting large nanoparticles can shrink into small nanoparticles with an average diameter of about 90 nm but recover to the original level by alternating UV and visible light radiation. Due to its photo-triggered growth/shrinkage behavior, the nanoparticles can efficiently up-load/release dyes and drug substrates in a controlled manner.

Introduction

In the past few decades, scientists have been committed to driving the supramolecular self-assembly through a variety of weak non-covalent interactions to construct a series of special functional architectures.^[1,2] Controllable supramolecular pre-organization has played an important role in these sophisticated constructions^[3] due to their ease of preparation and good practical application in functional materials and biochemistry.^[4,5] Compared with other conventional assemblies, supramolecular amphiphiles are responsive to external stimuli such as temperature, pH, light irradiation, redox, enzymes and electricity.^[6,7] So far, there are several typical macrocyclic molecules, such as cyclodextrin,^[6b,8] sulfonatocalixarene,^[9] cucurbiturils^[10] and pillararene,^[11] for the preparation of supramolecular amphiphiles.

Recently, Liu et al.^[6a] reported the effect of head/tail groups on molecular induced aggregation of polycationic cyclodextrin towards anionic surfactants. Yu et al.^[12a] reported the construction of a photo-responsive supra-amphiphile based on a tetracationic cyclobis(paraquat-p-phenylene) host and an azobenzene-containing guest in water. Zhang et al.^[12b] reported the photocontrolled reversible supramolecular assemblies of an azobenzene-containing surfactant with α -cyclodextrin. Huang et al.^[12c] reported the pillar[6]arene-based photoresponsive host-guest complexation. Wang et al.^[12d] reported the dual

photo- and pH-responsive supramolecular nanocarriers based on water-soluble pillar[6]arene and different azobenzene derivatives for intracellular anticancer drug delivery. In this work, we wish to report the construction and photo-induced assembly/disassembly of nanoparticle based on cationic β -cyclodextrin (H)^[6b] and anionic azobenzene-containing surfactant (G)^[13] (Scheme 1). Although the employed compounds



Scheme 1. Chemical structures of the compounds H, *trans*-G, *cis*-G, DOX and RhB with a cartoon representation of reversible formation of the photo-responsive self-assembly and disassembly.

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(host and guest) are prepared according to the reported methods, the strategy of combining the molecular-induced aggregation and the photo-induced assembly/disassembly in the construction of nanoparticles should be novel. The assembly and disassembly behaviors of nanoparticle in aqueous solution were investigated by UV-Vis, fluorescence, zeta-potential, dynamic light scattering (DLS) and high-resolution transmission electron microscopy (TEM). It is noteworthy that this nanoparticle not only can shrink under UV irradiation but also reversibly resumes its original morphology after further exposure to visible light and can be effectively loaded/released dye and drug substrates by the light-controlled assembly/disassembly. Therefore, this nanoparticle system has the reasonable potential applications in drug delivery system. For example, it can load the drug and released the loaded material under the light irradiation.

Results and Discussion

UV-Vis, dynamic light scattering (DLS) and transmission electron microscopy (TEM) were carried out to investigate the assembly behavior and photo-switching property of host-guest system in aqueous solution. The azobenzene-containing surfactant G having a hydrophilic sulfonate head and a hydrophobic alkyl tail can self-aggregate in the aqueous solution. By observing the dependence of the optical transmittance at 560 nm on the concentration of transformer of azobenzene guest (*trans*-G) in the absence and presence of H, the critical aggregation concentration (CAC) was measured as $0.128 \text{ mmol/L}^{-1}$ without H (Figure S1a), but this value greatly decreased to $6.1 \times 10^{-3} \text{ mmol/L}^{-1}$ (Figure 1a.), owing to the H-induced aggregation of *trans*-G.^[14] The preferable mixing ratio between the polycationic H and the anionic G was also measured. By gradually adding H to the solution of *trans*-G at a fixed concentration of $0.021 \text{ mmol/L}^{-1}$, the optical transmittance of resulting mixture at 560 nm decreased rapidly and then gradually increased thereafter to a quasi-plateau, and a minimum was reached at concentration of H at $0.003 \text{ mmol/L}^{-1}$ (Figure 1b.), referring to a H/*trans*-G ratio of 1:7, i.e. a imidazolium cation/sulfonate anion ratio of 1:1.

The rapid decrease of optical transmittance, along with the obvious Tyndall effect (Figure S2), jointly indicated the formation of large aggregates between H and *trans*-G. Then further addition of an excess amount of H resulted in the disassembly of aggregates and the formation of a simple inclusion complex, accompanied by the decrease of turbidity.^[12] Control experiments showed that the optical transmittance of *trans*-G at 560 nm showed no appreciable changes in the experimental concentration range in the absence of H, indicating that no self-aggregation happened at these concentrations of G. Moreover, the H/*trans*-G assembly was found very stable at room temperature, giving no appreciable changes of optical transmittance or turbidity or Tyndall effect after at least 6 h (Figure S1d, S2a). In the control experiment, *cis*-G could not form the supramolecular assembly with H under the same condition (Figure S1b, S1c).

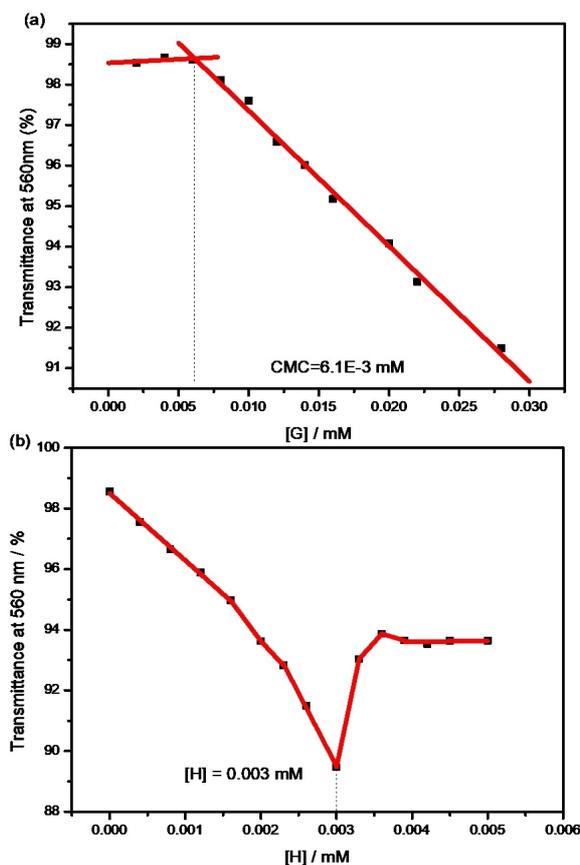


Figure 1. (a) Dependence of optical transmittance of *trans*-G at 560 nm at different concentrations in the presence of H (0.02 mM) at 25 °C. (b) Dependence of the optical transmittance of *trans*-G (0.021 mM) at 560 nm with the increasing concentration of H at 25 °C. (H refer to cationic β -cyclodextrin, G refer to anionic azobenzene-containing surfactant)

Interestingly, the photo-induced isomerization of azobenzene moiety in G could lead to the reversible and recyclable growth/shrinkage movement of H/G assembly. As shown in Figure 2, the absorption band of H/*trans*-G assembly at ca. 351 nm distinctly decreased, accompanied by the increase of absorption band at ca. 431 nm, when the solution of H/*trans*-G was irradiated at 365 nm irradiation for 30 min. Because the absorption bands located at 351 nm and 431 nm were assigned to the π - π^* transitions and n - π^* transitions of azobenzene chromophore respectively,^[15] these absorption changes indicated the photo-induced isomerization of *trans*-G moiety in the H/*trans*-G assembly. Then, when further irradiating the resultant H + *cis*-G mixture with visible light (450 nm) for 40 min, the absorption bands at 351 nm and 431 nm nearly recovered to the original level, indicating that the H + *cis*-G mixture reverted to the H/*trans*-G assembly again. The H/*trans*-G \rightarrow H + *cis*-G and H + *cis*-G \rightarrow H/*trans*-G transformation ratios were calculated as 90% and 96%, respectively. TEM images (Figure 2) and DLS (Figure S2) showed that, without H, *trans*-G formed the relatively small nanoparticles with an average diameter about 93 nm at a relatively high concentration owing to the self-aggregation of amphiphilic *trans*-G, which would convert to

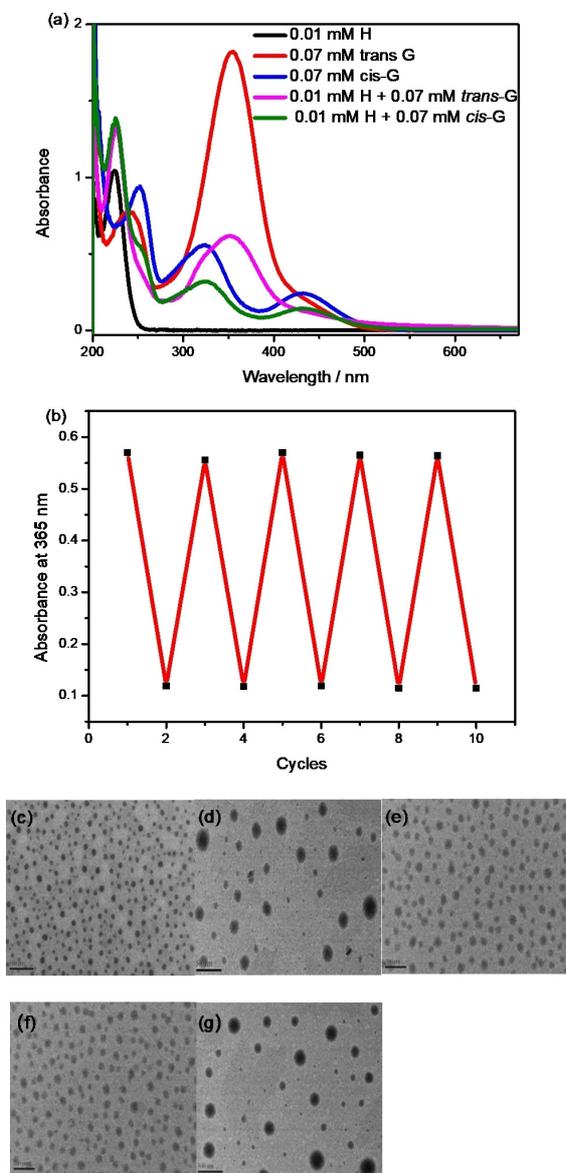


Figure 2. (a) UV-Vis spectra of H (0.02 mM), *trans*-G (0.14 mM) and H/*trans*-G (1:7) before and after irradiation with UV light at 365 nm. (b) Absorbance of H/*trans*-G at 365 (0.02 mM [H], 0.14 mM [G]) by alternating irradiation with UV and visible light for multi-cycle. TEM images: (c) The aggregates of *trans*-G (0.14 mM). (d) The aggregates of H (0.02 mM) and *trans*-G (0.14 mM). (e) After irradiation with UV light at 365 nm for 30 min of (c). (f) After irradiation with UV light at 365 nm for 30 min of (d). (g) After irradiation with visible light at 450 nm for 1 h of (f).

nanoparticles with an average diameter about 90 nm due to the transformation of *trans*-G self-aggregates to *cis*-G ones. From the DLS of H/*trans*-G (Figure S2c) with an arithmetic average diameter of 181 nm, a part of nanoparticles concentrated in the vicinity of 100 nm, and another part of nanoparticles concentrated in the vicinity of 300 nm. This is well consistent with the TEM that showed two discrete populations (ca. 90 nm and ca. 300 nm). The population with ca. 90 nm could be *trans*-G nanoparticle, but the population with ca. 300 nm should be owing to the formation of large assembly

between H and *trans*-G. With irradiating the H/*trans*-G solution with UV light (365 nm), the large nanoparticles of H/*trans*-G converted to small nanoparticles with an average diameter about 90 nm, which was quite similar to that of *cis*-G self-aggregate. When further irradiating this solution with visible light (450 nm), the arithmetic average diameter of nanoparticles recovered to about 181 nm, along with the reappearance of large nanoparticles with an average diameter of ca. 300 nm. Therefore, we deduced a possible assembly/disassembly mechanism as illustrated in Scheme 1. Therein, one H and several *trans*-G could form a complex. Then, various complexes integrated together to form the bilayer aggregates that subsequently bended to spherical nanostructures. The resulting spherical nanostructures were simultaneously stabilized by several non-covalent interactions including electrostatic and π - π interactions.

Because there was no critical evidence to prove that inside of such spheres was hollow or solid, thus we classified them as a kind of nanoparticle. Furthermore, the UV light-induced *trans*-G \rightarrow *cis*-G isomerization led to the disassembly of nanoparticles as well as the shrinking of nanoparticles, because *cis*-G could not assemble with H. However, large H/*trans*-G nanoparticles could recover via a visible light-induced *cis*-G/*trans*-G isomerization. Interestingly, UV-vis spectra, DLS and TEM experiments jointly confirmed that the shrink and recovery of nanoparticles could repeat by the photo-irradiation under different wavelengths for several cycles, indicating the good reversibility and repetitiveness of shrinkage nanoparticles.

Zeta potential of H/*trans*-G assembly was measured to be ca. 0 V (Figure S2d), indicating that the outside surface of nanoparticles should be the neutral β -cyclodextrin cavities. Therefore, it is reasonable to expect that the H/*trans*-G assembly can load the model substrate within numerous β -cyclodextrin cavities. In order to investigate the photo-sensitive upload/release behavior of H/*trans*-G assembly, RhB was selected as a model substrate (Scheme 1). A normal curve diagram of RhB and free with RhB-loaded H/G nanoparticles were obtained by UV/Vis spectra (Figure S3). The fluorescence spectra showed that the fluorescence intensity of RhB slightly decreased in the presence of H or *trans*-G, but greatly decreased in the presence of H/*trans*-G assembly (Figure S4). Moreover, the zeta potential of H/*trans*-G assembly increased to +3.22 mV (Figure S4b) in the presence of RhB. These phenomena jointly indicated that RhB was uploaded to the H/*trans*-G assembly, and the encapsulation efficiency and loading efficiency of H/*trans*-G assembly towards RhB were calculated as 22% and 8.2%, respectively.

Significantly, without UV light, the RhB-loaded H/*trans*-G assembly showed the good stability (Figure 3). However, when exposed to UV light (365 nm), the obvious release of RhB was observed by fluorescence test, and the cumulative release ratio could reach ca. 81% within 2 h. In addition to RhB, the H/*trans*-G assembly also showed the satisfactory uploading and photo-induced releasing behavior to aniline, a neutral model substrate, and doxorubicin (DOX), an anti-cancer drug. The releases of aniline and DOX were investigated by fluorescence and UV-vis spectroscopy, respectively (Table 1, Figure 4a–4b). The ratios

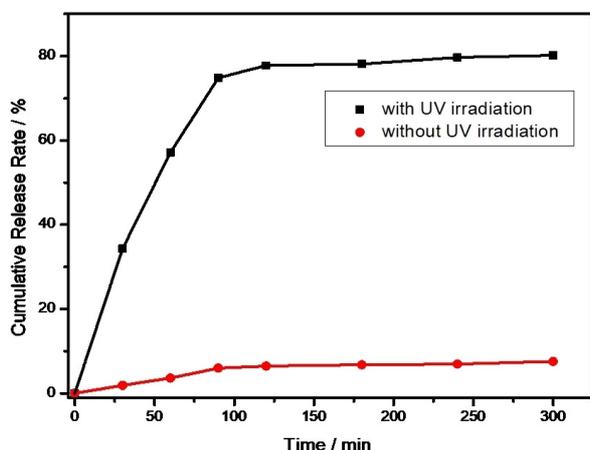


Figure 3. Photo-induced release of RhB from H/*trans*-G assembly ([G] = 0.14 mM, [H] = 0.02 mM, RhB = 3 mg).

Substrate	Encapsulation efficiency	Release ratio
aniline	36.3%	81% (within 5 h)
DOX	31.5%	77% (within 5 h)

of fluorescence (or UV absorbance) intensity at different time points to total fluorescence (or UV absorbance) intensity were measured to calculate the release rate of aniline (or DOX). The encapsulation efficiency and photo-induced release ratio of H/*trans*-G assembly towards aniline and DOX were listed in Table 1.

Conclusions

In conclusion, we have successfully constructed a photo-controlled water-soluble supramolecular nanoparticle using polycationic cyclodextrins and anionic azobenzene derivatives as the structural units. The diameter of resultant nanoparticles could shrink 2 times, i.e. volume shrinking 8 times, under UV light irradiation, but recover upon further exposure to visible light. This nanoparticle could be used as a light-triggered controllable release carrier for dyes and drugs, which is reasonable prospect for potential applications in drug delivery system.

Supporting Information Summary:

General experimental materials, methods and characterizations were attached in the Supporting information.

Acknowledgements

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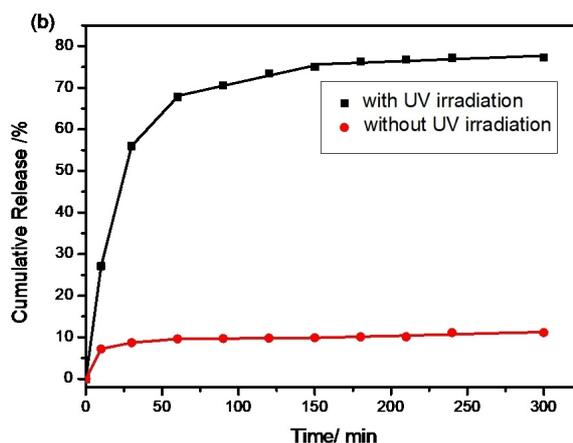
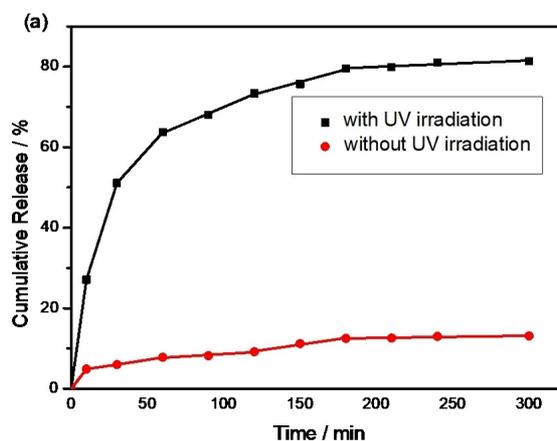


Figure 4. (a) Photo-induced release of Aniline from H/*trans*-G assembly ([G] = 0.14 mM, [H] = 0.02 mM, Aniline = 5 mg). (b) photo-induced release of DOX from H/*trans*-G assembly ([G] = 0.14 mM, [H] = 0.02 mM, DOX = 4 mg).

Conflict of Interest

The authors declare no conflict of interest.

Keywords: azobenzene · assembly · cyclodextrin · disassembly · photo-induced

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