Photoresponsive Vesicles

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Photocontrolled Reversible Supramolecular Assemblies of an Azobenzene-Containing Surfactant with α-Cyclodextrin**

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Amphiphilic surfactants can self-organize into molecular assemblies, such as micelles and vesicles, which have been widely used as capsules for drug delivery[1] and microreactors for nanoparticle preparation.[2] Covalently attached functional groups on surfactants that are responsive to external stimuli—for example, pH,[3] temperature,[4] redox state,[5] light,[6] and even carbon dioxide and argon[7]—can control the assembly and disassembly of these amphiphilic surfactants. Different from the self-organization of surfactants induced by a hydrophobic effect, most supramolecules are formed on the basis of host–guest interaction, and some of them can also be fine-tuned by external stimuli.[8] The understanding and control of noncovalent interactions in those supramolecular assemblies may open a way for the design of advanced materials and devices.[9] As an example, the two isomers of azobenzene, the *trans* and *cis* forms, can be reversibly switched to each other upon photoirradiation. Driven by hydrophobic and van der Waals interactions, *trans*-azobenzene can be well-recognized by α-cyclodextrin (α-CD), a type of cyclodextrin with six glucose units.[10] However, when *trans*-azobenzene is transformed to *cis*-azobenzene, α-CD cannot include the bulky *cis* form any more because of the mismatch between the host and guest. Therefore, the host–guest assembly and disassembly between azobenzene and α-CD by external photostimuli can act as a driving force to build up molecular shuttles, motors, and machines.[11]

Herein, we attempted to make use of photocontrolled inclusion and exclusion reaction of an azobenzene-containing surfactant with α-CD for fabricating a supramolecular system that can undergo reversible assembly and disassembly (see Figure 1). It is anticipated that this research will provide a model system that combines photochemistry and host–guest chemistry for a stimulus-responsive vesicle.

To realize the photocontrolled assembly and disassembly, we designed and synthesized the surfactant 1-[10-(4-phenylazophenoxy)decyl]pyridinium bromide (termed AzoC10),

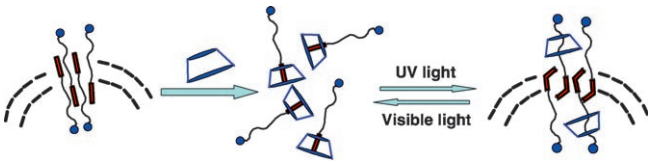

Figure 1. Illustration of the photocontrolled reversible assembly and disassembly of AzoC10; red bar: azobenzene moiety, blue spot: pyridinium group.

which was fully characterized by ^{1}H NMR spectroscopy and electrospray ionization mass spectrometry (ESI-MS). As expected, the azobenzene part at the tail of the hydrophobic alkyl chain of AzoC10 can be photoisomerized. As shown in Figure 2, upon irradiation with UV light at 365 nm the

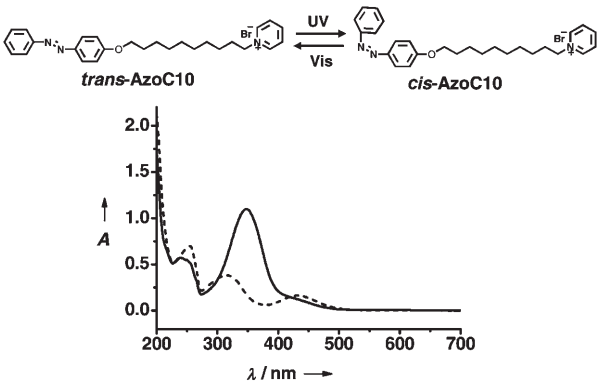

Figure 2. Reversible photoisomerization of AzoC10 upon irradiation with UV and visible light, respectively. UV/Vis spectra before (——) and after (-----) irradiation of AzoC10 ($c = 7 \times 10^{-5}$ M) with UV light of 365 nm.

absorption band at around 347 nm decreases remarkably, and concomitantly the band at around 430 nm increases slightly. The absorption bands at 347 and 430 nm are ascribed to π–π* and n–π* transitions, respectively. The change of the absorption bands induced by UV irradiation is indicative of the photoisomerization of AzoC10 from the *trans* to the *cis* state. When irradiated by visible light at 450 nm, the π–π* absorption increases again with a slight decrease in the n–π* absorption, which indicates that the photoisomerization of AzoC10 undergoes a change from the *cis* to the *trans* state.

We wondered whether AzoC10 could be associated with α-CD and how strong the association was. To answer these questions, we measured the association constant of AzoC10 with α-CD by detecting the UV absorption of AzoC10 at the same concentration while increasing the concentration of α-

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Supporting information for this article (synthesis of AzoC10, association constant for AzoC10–α-CD, measurement of the critical aggregate concentration, photoisomerization rates, and ESI-MS and XRD data) is available on the WWW under http://www.angewandte.org or from the author.

CD. According to the modified Benesi–Hildebrand equation, the association constant $K_{azo/\alpha\text{-CD}}$ for the 1:1 inclusion complex of α-CD with *trans*-AzoC10 is $2.82\times10^4\ \text{M}^{-1}$. As shown in Figure 3, the absorption of *trans*-AzoC10 at 346 nm is

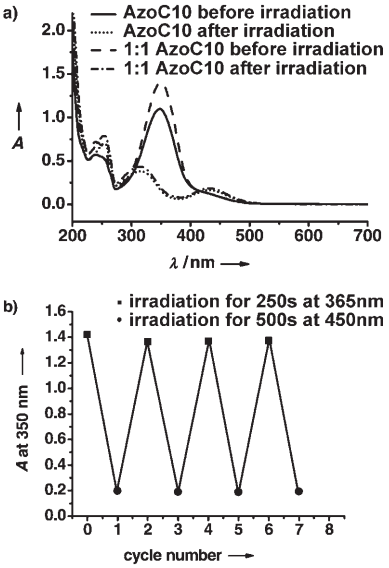

Figure 3. a) Photoisomerization spectra of AzoC10 in the presence of α-CD (1:1 molar ratio) before and after UV irradiation. b) Changes of AzoC10–CD inclusion (absorbance at 350 nm) upon alternating irradiation with UV and visible light. The concentration of AzoC10 is 7×10^{-5} M.

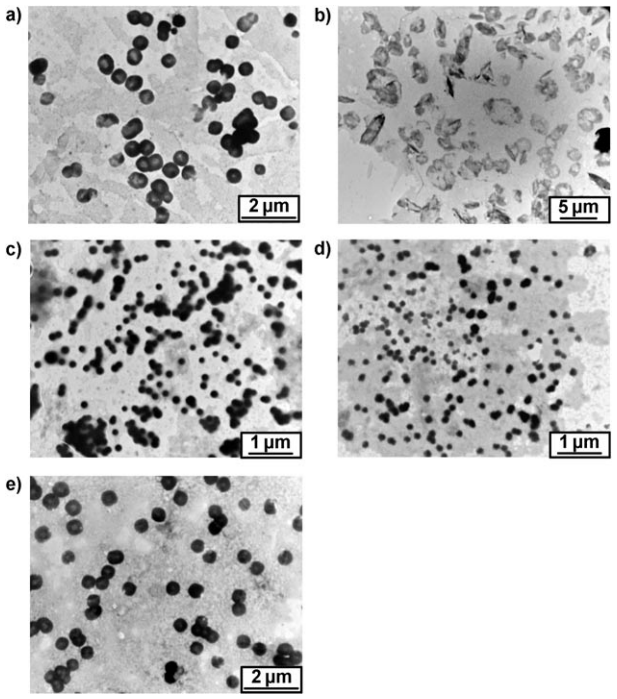

Figure 4. TEM images of a) AzoC10 and b) AzoC10 mixed with α-CD (1:1 molar ratio); c) after irradiation at 365 nm for 500 s; d) after irradiation at 450 nm for 2500 s, then further irradiation at 365 nm for 500 s; e) *cis*-rich AzoC10 mixed with α-CD (1:1 molar ratio). The concentration of AzoC10 is 7×10^{-5} M, which is larger than the critical aggregate concentration (CAC) of *trans*-AzoC10 (3.5×10^{-5} M) and *cis*-AzoC10 (3.9×10^{-5} M).

enhanced after association with α-CD. The molar extinction coefficients of *trans*-AzoC10 in the absence and presence of α-CD are 6.95×10^3 and $1.07\times10^4\ \text{M}^{-1}\text{cm}^{-1}$, respectively. Therefore, the enhanced absorption should be caused by the enhanced molar extinction coefficient after association. In other words, the enhanced absorption suggests that *trans*-AzoC10 forms an inclusion complex with α-CD.

The inclusion complex of AzoC10 with α-CD can undergo *trans–cis* photoisomerization reversibly. As shown in Figure 3a, upon irradiation by UV light at 365 nm the absorption of *trans*-AzoC10 decreases dramatically, and concomitantly an absorption peak attributable to *cis*-AzoC10 appears. Interestingly, the absorption of *cis*-AzoC10 in the presence of α-CD is almost the same as that of pure *cis*-AzoC10, which suggests that the *cis*-azobenzene moiety of AzoC10 hardly interacts with α-CD. On alternating irradiation of the solution with UV and visible light, this reversible photoisomerization process can be recycled many times (see Figure 3b).

As reported, the aggregation of some surfactants, such as cetyltrimethylammonium bromide, can be disrupted upon addition of the cyclodextrin, due to formation of an inclusion complex of hydrophobic alkyl chains with water-soluble cyclodextrin.[12] We wondered how the presence of α-CD and photoirradiation could affect the aggregation of AzoC10. To address this question, we performed transmission electron microscopy (TEM) measurements. First, as indicated by Figure 4a, the pure AzoC10 can form vesicle-like aggregates in aqueous solution. Second, when α-CD is added to an aqueous solution of AzoC10 to a molar ratio of 1:1, the vesicle-like aggregates disassemble (see Figure 4b). One plausible reason is that the inclusion of the azobenzene group of AzoC10 by α-CD renders this amphiphilic AzoC10 hydrophilic. As a result, vesicle-like aggregates disassemble. Third, when the above system is irradiated by UV light at 365 nm, we found interestingly that the vesicle-like aggregates form again (see Figure 4c). As discussed before, α-CD may leave the azobenzene group when AzoC10 is photoisomerized to the *cis* state, because α-CD cannot include the *cis*-azobenzene of AzoC10. This means that AzoC10 in the presence of α-CD becomes amphiphilic once again after UV irradiation. Therefore, the self-organization of AzoC10 in the *cis* form leads to the formation of a vesicle-like structure. Moreover, the aggregates (Figure 4c) are disassembled by further irradiation at 450 nm, and are largely recovered on subsequent UV irradiation at 365 nm (Figure 4d).

Notably, there is some difference between Figure 4a and c in terms of the size and shape of the vesicle-like aggregates. There are several reasons that may cause the difference. 1) Figure 4c shows the vesicle-like aggregates formed by *cis*-AzoC10 in the presence of α-CD, which should be different from the aggregates formed by *trans*-AzoC10 (Figure 4a). To clarify this issue, we used UV light to irradiate the solution of *trans*-AzoC10 for a sufficient time and then added α-CD to the solution. In this way, most of the AzoC10 was photoisomerized into the *cis* form, thus rendering it hardly able to interact with α-CD. However, on comparing Figure 4e and a,

we find that after this treatment *cis*-AzoC10 forms similar aggregates to those of *trans*-AzoC10, which indicates that the photoisomerization of the azobenzene group has no significant influence on the size and shape of the vesicle-like aggregates of AzoC10 in the present situation. 2) Although α-CD prefers to bind with the azobenzene moiety of AzoC10, it can interact with the alkyl chain of AzoC10 as well.[13] Upon UV irradiation, the weak interaction between α-CD and *cis*-azobenzene may drive some of the α-CD to slide onto the alkyl chain, and thus the self-organization of AzoC10 complexed with α-CD could form different vesicle-like aggregates.

The influence of α-CD on the aggregation behavior of AzoC10 is supported by the different kinetic behavior of photoisomerization under various conditions. Usually, the photoisomerization of the azobenzene group proceeds in first order in solution; the initial *trans–cis* photoisomerization rate constants (k_t) are shown in Table 1. On increasing the concentration of AzoC10, the value of k_t decreases remarkably. Note that the isomerization rate of AzoC10, with a concentration lower than the CAC, decreases upon addition of α-CD (1:1), but increases when AzoC10 is mixed with α-CD above the CAC. The most likely reason could be as follows. At a concentration lower than the CAC, AzoC10 is freely dispersed in the bulk solution, and hence there is enough space for AzoC10 to undergo *trans–cis* conversion; the added α-CD molecules will incorporate AzoC10 in their cavities, thereby restricting the *trans–cis* isomerization of AzoC10 to some extent. The situation is different for AzoC10 aggregating at a concentration above the CAC. In that case, the azobenzene group does not have enough space for the *trans–cis* conversion, which results in weakening of the photoisomerization. On the other hand, the space for the photoisomerization of azobenzene in the presence of α-CD may be larger than that in the vesicle aggregates. Therefore, we can draw the conclusion that the added α-CD increases the initial isomerization rate of AzoC10 at a concentration above the CAC, thus indicating that α-CD destroys the aggregates of AzoC10, which also agrees well with the previous TEM observations.

Table 1: Photoisomerization rate constants of AzoC10 at different concentrations in the absence or presence of α-CD (1:1).

c(AzoC10) [M]	k_t [s^{-1}]	k_c [s^{-1}]
10^{-5}	0.1723	0.0286
10^{-5} (CD)	0.1003	–
3.5×10^{-5}	0.0237	0.0130
7×10^{-5} (CD)	0.0126	0.0059
7×10^{-5}	0.0055	0.0052

Interestingly, α-CD has little effect on the *cis–trans* isomerization of AzoC10 when above its CAC. The *cis–trans* photoisomerization rate constant (k_c) of AzoC10 associated with α-CD after UV irradiation stays almost the same as that of AzoC10 itself. This result is different from the *trans–cis* behavior of AzoC10, whose k_t value increases upon association with α-CD, which suggests that the *cis*-azobenzene groups of AzoC10 in the presence of α-CD can still form aggregates like *cis*-AzoC10 alone.

After UV irradiation of the inclusion complex of AzoC10 and α-CD, we mentioned that α-CD is likely to move from the azobenzene group to the hydrophobic alkyl chain of AzoC10. If this is true, then α-CD can also move back from the alkyl chain to the azobenzene group under irradiation by visible light. Therefore, the movement of α-CD is like that of a molecular shuttle, which can influence the aggregation of AzoC10 in aqueous solution. To confirm this speculation, we used ^{1}H NMR spectroscopy to provide evidence about the interaction of α-CD and AzoC10 under different conditions. The concentration of AzoC10 in D_2O chosen was 2.5×10^{-4} M, at which the NMR signals of AzoC10 can be collected adequately. As shown in Figure 5, in the aryl region only protons of the hydrophilic pyridine group of AzoC10 are readily detected by NMR measurements, and no proton of the azobenzene group is clearly observed. This fact suggests the formation of AzoC10 aggregates on the basis of a hydrophobic effect.[14] However, the signals of the azobenzene group of AzoC10 appear in the presence of α-CD (1:1 molar ratio), which indicates that α-CD can associate the azobenzene group of AzoC10 and induce the disassembly of the aggregates. Further irradiation at 365 nm for sufficient time ensures that azobenzene converts into the *cis* form in a photostationary state. As indicated by Figure 5c, α-CD has almost no interaction with the azobenzene group in this case. Upon UV irradiation, if all α-CD molecules migrate back into the bulk after disassembly of α-CD with AzoC10, then AzoC10 may aggregate again and in that case the NMR spectrum should be similar to that shown in Figure 5a. However, the proton signals of azobenzene (see Figure 5c) are not screened again, which suggests that upon UV irradiation, some of the α-CD moves onto the alkyl chain of AzoC10. Upon irradiation at 450 nm for a sufficient time, the proton signals of Figure 5d are similar to those of Figure 5b, which indicates that α-CD can move back and interact with the azobenzene group of AzoC10 once again, thus behaving like a molecular shuttle.

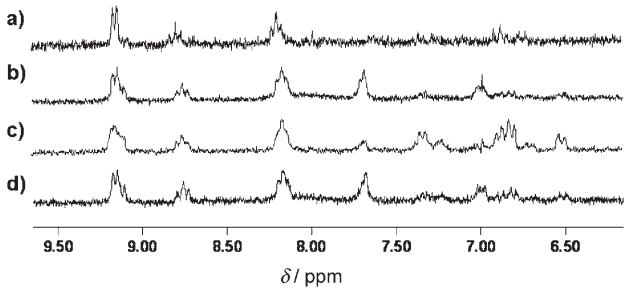

Figure 5. ^{1}H NMR spectra of a) AzoC10, b) AzoC10 in the presence of α-CD (1:1 molar ratio), and c) after irradiation at 365 nm for 500 s, then d) irradiation at 450 nm for 2700 s. The concentration of AzoC10 is 2.5×10^{-4} M. The solvent is D_2O; $\delta(H_2O) = 4.79$ ppm.

The above discussion is further supported by ESI-MS data. Before UV irradiation, there is a peak with m/z 1387.79, which corresponds to the 1:1 inclusion complex of AzoC10

(minus the bromine anion) and α-CD. After irradiation at 365 nm, a peak with *m*/*z* 1387.82 still exists, which suggests that *cis*-AzoC10 can also form a 1:1 inclusion complex with α-CD. As α-CD does not interact with the *cis*-azobenzene group, it must form an inclusion complex with the alkyl chain of AzoC10 under these conditions. In other words, ESI-MS data provide further evidence to support the speculation that some α-CD shifts from the azobenzene group to the alkyl chain of AzoC10 upon UV irradiation.

We have confirmed the formation of vesicle-like aggregates that can be reversibly controlled by external photostimuli. However, there is one unclear point as to whether the vesicle aggregates have a bilayer structure. To answer this question, we employed X-ray diffraction (XRD) to provide information about the layered structure. To do so, we fabricated a cast film from a solution of AzoC10 with a concentration of 7×10^{-5} M. XRD shows a Bragg peak at $2\theta \approx 3°$, which corresponds to a *d* spacing of 29.7 Å. Considering that AzoC10 is about 26 Å in length, we may draw the conclusion that AzoC10 molecules are well interdigitated in the vesicle-like aggregates. It is hoped that such a line of research may provide a way to fabricate smart responsive and reversible materials.

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