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A cyanine dye based supramolecular photosensitizer enabling visible-light-driven organic reaction in water

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We report the aggregation-induced photosensitizing activity of a cyanine dye in water and the mechanism. In addition, using the supramolecular assembly, visible-light-driven photooxidation of hydrophobic aromatic compounds in water was successfully performed.

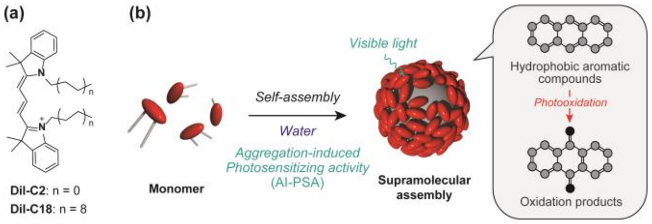

Figure 1. (a) Chemical structures of **DiI-C2** and **DiI-C18**. (b) Schematic representation of aggregation-induced photosensitizing activity (AI-PSA) of **DiI-C18**. The supramolecular photosensitizer promotes visible-light-driven transformation of hydrophobic aromatic compounds in aqueous media.

Light and water are inexpensive, non-hazardous, environmentally safe, and readily available. Natural photosynthesis, one of the most important chemical processes in the world, utilizes solar energy in aqueous environments to perform organic transformations.[1] Inspired by this, photocatalytic reactions in water have great potential for solar energy utilization, energy consumption saving, and green chemical processes.[2] The development of photocatalysts and photosensitizers enabling the transformation of hydrophobic organic compounds in aqueous media can definitely contribute to efficient solar energy conversion.[3]

Molecular photocatalysts and photosensitizers have been widely developed as powerful tools in organic synthesis over the last decade.[4] However, the development of photocatalysts and photosensitizers enabling organic reactions of hydrophobic molecules in water is still in an early stage.[5] The main obstacle of organic reactions in aqueous media is the low water solubility and dispersibility of organic substrates. To overcome this obstacle, micelles have been used to provide the effective dispersion of hydrophobic molecules in water and allow organic transformations.[6] On this subject, König and co-workers reported the light-driven activation of stable C-Cl bonds of alkyl chlorides for C-C bond formation in aqueous solution.[7] Goez and co-workers comprehensively studied photo-redox processes involving the generation of hydrated electrons as reductants using Ru complexes supported by micellar compartmentalization.[8] These hybrid systems consisting of photocatalysts and micelles clearly demonstrate the potential for photocatalytic organic reactions in water. However, these systems include multiple chemical species and employ rare metal complexes such as Ir and Ru. Simple light-driven reaction systems composed of metal-free materials in water provide many advantages such as environmental safety, easy purification, and cost saving. Development of metal-free photocatalysts and photosensitizers, enabling organic reactions in water generate a novel approach for environment friendly solar energy utilization. However, to our best knowledge, there has been no reports on metal-free supramolecular photocatalysts or photosensitizers with hydrophobic field for dispersion of water-insoluble molecules. For the development of such photocatalysts, we have explored a molecular design strategy.

Herein, we describe an amphiphilic carbocyanine dye bearing two octadecyl alkyl chains (1,1'-dioctadodecyl-3,3',3'-

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tetramethyl-indocarbo-cyanine percolate (**DiI-C18**))[9] catalyzes the visible-light-driven oxidation of hydrophobic aromatics in water through the self-assembly (Figure 1). The result that monomeric carbocyanine dye has no photosensitizing activity proves that its photosensitizing activity is due to the formation of supramolecular aggregates by **DiI-C18** molecules. **DiI-C18** supramolecular photosensitizer (SPS) can transform hydrophobic aromatic compounds with significant conversion yields in aqueous media. A mechanistic study of the aggregation-induced photosensitizing activity (AI-PSA) has clarified that the charge-separated (CS) state of **DiI-C18** supramolecular assembly is formed after photoirradiation and involves the photosensitizing reactions. These results indicate the potential of supramolecular assemblies composed of organic dyes as metal-free photosensitizers enabling organic reaction in water.

We recently reported that amphiphilic rhodamines with a single alkyl chain showed AI-PSA and provided SPSs in water.[10] Although the detailed mechanism and the generality of AI-PSA is still unclear, it could be caused by the promotion of triplet excited state generation and/or intermolecular charge separation upon self-assembly. These phenomena are considered a general mechanism for various organic dyes; therefore, we expected that AI-PSA would be an advantageous approach for photocatalyst and photosensitizer development. In this study, the carbocyanine dye **DiI-C18** was employed to develop an SPS for the transformation of hydrophobic molecules in aqueous media (Figure 1a). Cyanine dyes have excellent light absorption properties and tenable absorption wavelengths from ultraviolet to near infrared regions by expanding π-conjugation (*i.e.* the number of double bonds). **DiI-C18** is a gemini-type amphiphilic molecule composed of a carbocyanine unit and double alkyl chains. The long and flexible double alkyl chains and gemini-type molecular shape are expected to give rise to a hydrophobic compartment suitable for the incorporation of organic molecules and their transformation in aqueous medium (Figure 1b). For comparison, a hydrophilic carbocyanine dye with short ethyl chains (1,1'-Diethyl-3,3,3',3'-tetramethyl-indocarbo-cyanine: **DiI-C2**) was also employed to evaluate the self-assembly effect of **DiI-C18** (Figure 1a).

The photophysical properties of monomeric **DiI-C2** and **DiI-C18** were first evaluated by UV-vis absorption and photoluminescence (PL) spectra in dimethyl sulfoxide (DMSO) to confirm whether **DiI-C2** and **DiI-C18** are a suitable pair for evaluating the effect of **DiI-C18** self-assembly on photosensitizing activity. The UV-vis spectral shapes of **DiI-C2** and **DiI-C18** corresponded well with each other (Figure S1a), and these compounds exhibited similar absorption maxima at 553 and 555 nm for **DiI-C2** and **DiI-C18**, respectively. **DiI-C2** and **DiI-C18** also exhibited similar PL spectra with emission peaks at 571 and 574 nm, respectively (Figure S1b). These results indicate that the electronic states of **DiI-C2** and **DiI-C18** are quite similar despite the difference in the alkyl chain length, and the **DiI-C2**/**DiI-C18** pair is suitable for evaluating the effect of self-assembly on the photosensitizing properties of the carbocyanine dye.

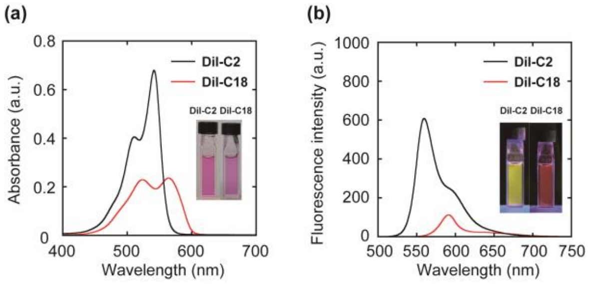

Figure 2. (a) UV-vis absorption and (b) photoluminescence spectra of **DiI-C2** and **DiI-C18** in aqueous buffer solution. (a,b) Experimental conditions: [**DiI-C2**] = [**DiI-C18**] = 5.0 μM, rt, 1.0 mM phosphate buffer (pH 7.4), excitation wavelength: 450 nm. Insets: Optical photos of **DiI-C2** and **DiI-C18** in water under (a) daylight and (b) UV light (365 nm).

We subsequently evaluated the self-assembly properties of **DiI-C18** and **DiI-C2** by UV-vis and PL spectra in an aqueous buffer solution (1.0 mM phosphate buffer, pH 7.4) (Figure 2a,b). The UV-vis spectrum of **DiI-C2** in the aqueous buffer solution displayed a shape similar to that in DMSO, with a blue-shifted absorption maximum (λ_{abs} = 553 nm (DMSO), 541 nm (water)) (Figure 2a). **DiI-C18** exhibited a broad spectrum with split peaks at 524 and 564 nm, which can be assigned to the aggregation states of **DiI-C18**. The broadening of the absorption band with split peaks would be derived from disordered structure composed of **DiI-C18** H-type dimer.[11] The PL spectrum of **DiI-C2** (Figure 2b) in aqueous buffer solution also exhibited an emission spectrum similar to that in DMSO (λ_{em} = 571 nm (DMSO), 560 nm (water)), whereas, **DiI-C18** showed weaker emission with a significant red shift (λ_{em} = 592 nm). The quantum yields of **DiI-C2** and **DiI-C18** were 0.023 and 0.007, respectively, in the aqueous buffer solution. The lower quantum yield of **DiI-C18** could be due to aggregation-causing quenching. Dynamic light scattering (DLS) measurements and transmission electron microscopy (TEM) observations of **DiI-C18** in aqueous solution were also performed to clarify the details of the supramolecular assemblies. DLS measurements indicated the presence of **DiI-C18** aggregates with an average diameter of 48 nm (Figure S2a). TEM revealed the spherical shape of the supramolecular assemblies of **DiI-C18** (Figure 2b). These results clearly show that **DiI-C18** forms a supramolecular assembly in the aqueous buffer solution, whereas **DiI-C2** is present as a monomer.

The photosensitizing activity of the **DiI-C18** supramolecular assemblies in the aqueous buffer solution was evaluated using 1,1',3,3,3',3'-hexamethylindotricarbocyanine iodide (**HITCI**) (Figure S3a).[12] The UV-vis spectra of **DiI-C2/HITCI** and **DiI-C18/HITCI** mixtures were recorded after photoirradiation (irradiation wavelength: 520 nm; 300 W, Xe lamp, FWHM: 10 nm). In the case of **DiI-C2**, the absorption band at approximately 735 nm derived from **HITCI** showed almost no change (Figure S3b). On the other hand, the **HITCI** absorption band rapidly decreased within 30 sec using **DiI-C18** (Figure S3c). After 60 sec photoirradiation, the residual ratios of **HITCI** were estimated as

0.98 and 0.01 for **DiI-C2** and **DiI-C18**, respectively. These results indicate the AI-PSA of **DiI-C18** in aqueous buffer solution. The **HITCI** degradation rate by **DiI-C18** was clearly decreased under deoxidizing conditions (Figure S4), suggesting that the reactive oxygen species (ROS) generated by **DiI-C18** SPS oxidated **HITCI**.

We subsequently examined the photooxidation of hydrophobic aromatic molecules using **DiI-C18** SPS in water. Anthracene was selected as a model compound for photooxidation in water (Scheme S1). Before the reaction, the effect of **DiI-C18** SPS on anthracene in water was examined. The UV-vis spectrum of **DiI-C18** was red-shifted in the presence of anthracene (Figure S5b), indicating the interaction (i.e. encapsulation) between **DiI-C18** SPS and anthracene. Contrarily, the UV-vis spectrum of **DiI-C2** showed no change after the addition of anthracene (Figure S5a). In aqueous solutions, hydrophilic **DiI-C2** had almost no interaction with anthracene. Additionally, the PL spectra of anthracene supported the encapsulation of the polyaromatic compound into **DiI-C18** SPS. The normalized PL spectra of **DiI-C2**/anthracene and **DiI-C18**/anthracene mixtures are shown in Figure S5c. The PL intensity ratio (I_{402}/I_{419}) of anthracene with or without **DiI-C2** was virtually unchanged (anthracene: 1.0, anthracene with **DiI-C2**: 1.0).[13] On the contrary, the intensity ratio of anthracene changed significantly after adding **DiI-C18**: the value was 1.3, indicating that anthracene molecules existed in different environments.

High-performance liquid chromatography (HPLC) was used to monitor the photooxidation reactions of aromatic compounds in water (Figure S6). The retention time of anthracene was 19 min under these conditions. After 20 min of photoirradiation (520 nm, Xe lamp, 300 W) of the **DiI-C18**/anthracene mixture, the anthracene peak almost disappeared, and a new peak assigned to 9,10-anthraquinone appeared (retention time: 10 min) (Figure S6b, Table 1). The conversion yield determined using HPLC was 97 %. **DiI-C2** did not promote visible-light-driven anthracene oxidation under the same conditions (Figure S6a).We attempted the visible-light-driven oxidation of 9,10-dimethyanthracene (**DMA**) and 9,10-diphenylanthracene (**DPA**), which are more hydrophobic than anthracene (Figure S7). **DiI-C18** successfully oxidized **DMA** and **DPA** (Figure S8, Table 1), whereas **DiI-C2** did not. **DMA** and **DPA** are also considered to be oxidized and give the endoperoxides. The endoperoxides are unstable, therefore the product characterizations were difficult. In addition, **DiI-C18** successfully proceeded photooxidation of 1-naphthol and 2-naphthol, although **DiI-C2** cannot perform the photooxidations (Table 1, Figure S9).

Table 1. Photocatalytic oxidation of hydrophobic aromatic compounds in an aqueous buffer solution by **DiI-C2** and **DiI-C18**.

Entry	Substrate	Conversion yield (%)	
		DiI-C2	**DiI-C18**
1	Anthracene	< 1	97
2	**DMA**	15	97
3	**DPA**	< 1	60
4	1-Napthol	< 1	87
5	2-Napthol	< 1	87

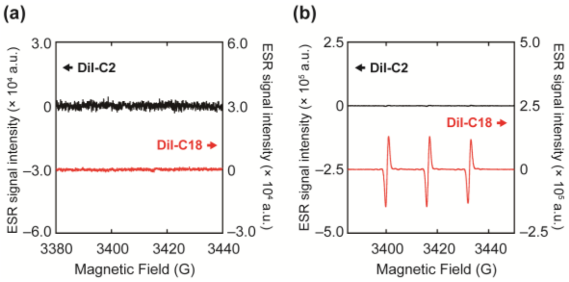

Figure 3. ESR signals of (a) **4-OH-TEMPO** and (b) **CP$^\bullet$** in **DiI-C2** or **DiI-C18** and **4-OH-TEMP** or **CPH** mixtures after photoirradiation, respectively. Black and red lines indicate ESR signals in the mixtures with **DiI-C2** and **DiI-C18**, respectively. Experimental conditions: [**4-OH-TEMP**] = 100 mM, [**CPH**] = 25 mM, [**DiI-C2**] = [**DiI-C18**] = 50 µM, 1.0 mM phosphate buffer (pH 7.4), rt, Photoirradiation: 520 nm (Xe lamp, 300 W), 1 min.

The photooxidation reactions involved molecular oxygen and were catalyzed by ROS. The mechanism of ROS generation is classified in two types: electron- and energy transfer processes,[14] which generate superoxide ($O_2^{\bullet-}$) and singlet oxygen ($^1O_2$) from ground state oxygen, respectively. Electron spin resonance (ESR) spectra were measured to examine $^1O_2$ generation using a spin-trapping reagent, 4-hydroxy-2,2,6,6-tetramethylpiperidine (**4-OH-TEMP**). **4-OH-TEMP** reacts with $^1O_2$ to generate an ESR-detectable 4-hydroxy-2,2,6,6-tetramethylpiperidine 1-oxyl (**4-OH-TEMPO**) radical (Figure S10a). Figure 3a displays the ESR spectra of **DiI-C2/4-OH-TEMP** and **DiI-C18/4-OH-TEMP** mixtures after 3 min of photoirradiation, which showed no ESR signals, suggesting that $^1O_2$ was not generated after photoirradiation. Subsequently, we examined a spin-trapping reagent, 1-hydroxy-3-carboxy-2,2,5,5-tetramethylpyrrolidine (**CPH**), for $O_2^{\bullet-}$ detection (Figure S10b). The intense triplet ESR signal of the CP radical (**CP$^\bullet$**) was observed in the **DiI-C18/CPH** mixture after photoirradiation (Figure 3b). These results suggest that the supramolecular assembly formation of **DiI-C18** promotes electron transfer to molecular oxygen, and the CS state is generated. To observe the **DiI-C18** CS state directly, the ESR spectrum of the photo-irradiated **DiI-C18** at 173 K was measured. The ESR spectrum showed a clear signal corresponding to the **DiI-C18** radical at 3420 G (Figure S11).[15] These results imply the generation of the CS state in **DiI-C18** SPS, and that the photochemical reactions proceeded via oxygen radicals, mainly $O_2^{\bullet-}$. From these results, we hypothesized reaction mechanism of anthracene photooxidation is shown in Figure S12.[16]

Nanosecond laser flash photolysis was also performed to elucidate the mechanistic details of **DiI-C18** AI-PSA. The nanosecond transient absorption (ns-TA) spectra of **DiI-C2** and **DiI-C18** were measured after laser excitation at 532 nm in a deaerated aqueous buffer solution (Figure S13). In the case of **DiI-C2**, a TA band at 570 nm with a relatively long lifetime ($t_{1/2}$ = 0.82 µs) was observed (Figure S14b), which could be assigned to triplet states or the cis isomer of **DiI-C2**.[17] Under oxygen-

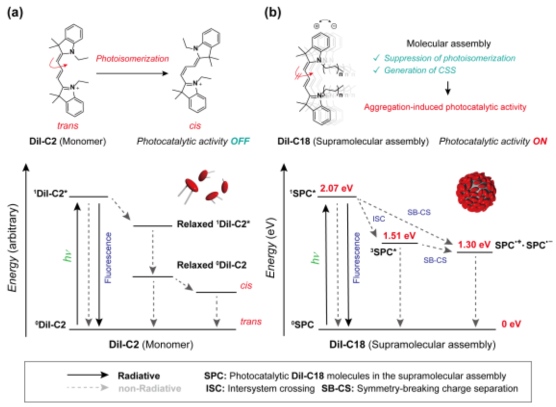

Figure 4. Plausible decay processes and energy diagrams of (a) **DiI-C2** and (b) **DiI-C18** SPC after photoirradiation.

saturated conditions, the transient signal decay profile did not change ($t_{1/2}$ = 0.81 µs) compared to that under deaerated argon atmosphere. The transient species would not be oxygen-interactive species (*i.e.* triplet state). From these results, we assigned the transient signal at 570 nm to the cis isomer of **DiI-C2**.[18] Although **DiI-C2** has significant excited oxidation potential (E_{ox}* = –2.55 V vs SHE, Table S1), its excited state would be consumed by photoisomerization (Figure 4a) and showed a low quantum yield (Φ_f = 0.023). In contrast, **DiI-C18** showed no transient absorption band at 570 nm (Figure S14d). The photoisomerization was suppressed by steric hindrance in aggregation state or changes in the energy diagram. Instead of photoisomerization, **DiI-C18** exhibited a new TA band around 430 nm ($t_{1/2}$ = 66 µs), which was not observed in **DiI-C2** (Figure S14a,c). The lifetime of this transient species is long enough for chemical reaction, and the species is considered a CS state involved in the photoreaction. The change in absorption at 430 nm decreased significantly under oxygen atmosphere, which supports the electron transfer to molecular oxygen. The energy levels of the triplet and CS states of the **DiI-C18** supramolecular assembly were estimated by spectroscopic and electrochemical analyses. The phosphorescence spectrum of **DiI-C18** at 77 K is shown in Figure S15. It was possible to identify the 0–0 band of the phosphorescence at 822 nm, and the energy level of the triplet state was calculated to be 1.51 eV. The energy level of the CS state was determined by electrochemical analysis (Figure S16, Table S1) to be 1.30 eV. The energy level of the CS state was lower than that of the triplet state in the **DiI-C18** assembly. The energy diagram and plausible mechanism of the **DiI-C18** SPS are shown in Figure 4b. **DiI-C18** forms the S1 state after photoirradiation and is converted into the CS state through symmetry-breaking charge separation (SB-CS) process directly or *via* a triplet state.[19] On the other hand, monomeric **DiI-C2** mainly loses the absorbed energy through isomerization processes (Figure 4a). The isomerization process is suppressed in the aggregation state, and the triplet state smoothly changes to the CS state in the **DiI-C18** supramolecular assembly. The low quantum yield (Φ_f = 0.007) of **DiI-C18** supports the process and the estimated excited oxidation potential (E_{ox}* = –2.43 V vs SHE, Table S1) is enough for the organic reactions. This is a plausible mechanism of the AI-PSA for **DiI-C18**.

In summary, we demonstrated that the supramolecular assembly of simple amphiphilic dye **DiI-C18** functioned as a photosensitizer in water. The mechanism of the AI-PSA was revealed using spectroscopic and electrochemical techniques. Owing to the AI-PSA and formation of a hydrophobic compartment in **DiI-C18** aggregates, hydrophobic aromatics were dispersed and efficiently oxidized by visible light in water. This study demonstrates that supramolecular assemblies of amphiphilic organic dyes have potential as photosensitizer or photocatalyst working in water for organic transformations, and provides a novel approach for the design of organic photocatalysts and photosensitizers.

Conflicts of interest

There are no conflicts to declare.

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