Accelerated Recombination of Lophyl Radicals with Self-Assembled Amphiphilic Lophine Dimer

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Abstract: This report focuses on acceleration of the recombination of lophyl radicals with a lophine dimer derivative by forming molecular assemblies. A newly synthesized cationic amphiphilic lophine dimer formed molecular assemblies with a diameter of ~220 nm in an aqueous medium. When the molecular assemblies were formed, the rate of recombination of lophyl radicals, produced by ultraviolet light irradiation, was accelerated 50,000-fold compared to that in an organic solvent. The rate enhancement is likely derived from the short diffusion distance of the lophyl radicals in the molecular assemblies. These results revealed that accumulation of the lophine dimers via self-assembly remarkably accelerated the recombination of lophyl radicals. This novel photoisomerization system could rapidly control the interfacial properties or morphologies of molecular assemblies when used for applications, such as efficient delivery of drugs or active components.

Key words: photoisomerization, surfactant, molecular assembly, lophine dimer, radical

1 Introduction

Photochromic compounds, such as azobenzene, spiropyran, and diarylethene, and their derivatives reversibly vary their colors when they isomerize upon irradiation with light of specific wavelengths. Photoswitching of optical properties has been applied to molecular memories¹ and logic gates². Furthermore, photo-switchable morphologies and the polarity of amphiphilic photochromic compounds have been exploited to control interfacial properties and to form molecular assemblies upon light irradiation^{3, 4}. For example, in prior studies, we demonstrated the controlled release of oily substances^{5, 6} and solution viscosity⁷ upon varying the micelle structures formed by an azobenzene-type cationic surfactant. These systems can be applied in the controlled release of drugs and active components. Raghavan and Zakin also achieved solution viscosity control using photoresponsive surfactants and demonstrated efficient heat transfer upon photoswitching of micellar structures^{8, 9}. Photoresponsive surfactants have promising application in personal care products, medicines, and mechanical devices. However, photoresponsive surfactants currently require several tens of minutes or hours to complete the switching process. Acceleration of photoisomer-

ization enables the rapid response and switching of properties at an arbitrary time. Although there are some reports on the kinetics of photoresponsive surfactants¹⁰⁻¹², acceleration of controlled systems has not been investigated thus far.

The lophine dimer cleaves into two lophyl radicals and presents a strong color upon ultraviolet (UV) irradiation, and these radical species recombine thermally to form the initial dimer, as shown in Fig. 1a¹³. This colorization is ultrafast, which proceeds on a femtosecond time scale¹⁴. However, because free diffusion of the produced radical species in solution reduces the collision frequency for recombination, the decolorization is slow. Abe and co-workers accomplished rapid photoisomerization of the lophine dimer using a synthetic approach. To inhibit diffusion of lophyl radicals, two lophine moieties were covalently bound through a linker, such as naphthalene^{15, 16} and [2.2] cyclophane¹⁷ moieties. Strehmel and co-workers reported accelerated recombination of lophyl radicals in ionic liquid (IL) media¹⁸⁻²⁰. They considered the rate enhancement results from confinement of lophyl radicals in a microscopic domain formed by IL molecules. However, we achieved enhanced recombination using a simple solubilization tech-

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Fig. 1 (a) Photoisomerization of the lophine dimers and the chemical structures. (b) Schematic images of previous²¹⁾ and this micellar systems toward acceleration of the photoisomerization.

nique. When a lipophilic lophine dimer was solubilized in a micellar solution, the produced lophyl radicals were confined inside the nanospace that was formed by the micelles, which enhanced the recombination (Fig. 1b)²¹⁾. Based on this result, we assume that the recombination is further accelerated in molecular assemblies composed of only lophine dimer derivatives because distance between the radical species is extremely short (Fig. 1b). In this study, we synthesized a novel amphiphilic lophine dimer and examined the interfacial properties and self-assembly via surface tension measurements and dynamic light scattering (DLS). Recombination of the lophyl radicals forming the molecular assembly was examined by UV-vis absorption spectroscopy.

2 Experimental

2.1 Materials

The solvents and reagents were purchased from Tokyo Chemical Industry Co. Ltd. (Tokyo, Japan) or Wako Pure Chemical Co. (Osaka, Japan) and were used without further purification. All reaction mixtures and fractions eluted by column chromatography were monitored using thin layer chromatography (TLC) plates (Merck, Kieselgel 60 F254). The developed TLC plates were observed under UV light at 254 and 365 nm. Flash column chromatography over a silica gel (Wakosil C-200, 64–201 μm) was used for all separations. Pure water and dimethyl sulfoxide (DMSO), which were degassed by argon, were used to prepare the N-C₆-LPD solutions.

2.2 Measurements

¹H-NMR spectra were measured at 298 K from a

DMSO-*d*₆ solution of the samples using a JEOL model JNM-AL500 (500 MHz) spectrometer with Si(CH₃)₄ as the internal standard. Chemical shifts (δ) and coupling constants (*J*) are reported in parts per million (ppm) and Hertz (Hz), respectively. ESI-MS spectra were measured using a JASCO model JMS-T100CS instrument. Melting points were recorded using a Bibbly Stuart Scientific SMP3 instrument. Dynamic light scattering (DLS) was conducted using a NICOMP 380ZLS (Particle Sizing Systems). An argon laser (514.5 nm) was used as the light source. UV-vis absorption spectra were measured using an Agilent 8453 or Jasco V-670 UV/vis spectrophotometer with a quartz cuvette (1.0 cm path length).

2.3 Synthesis of the amphiphilic lophine dimer

The synthesis of N-C₆-LPD was performed using the route shown in Scheme 1.

2.3.1 Synthesis of compound 2

A mixture of **1**, benzil (0.406 g, 1.93 mmol), ammonium acetate (1.49 g, 19.3 mmol), and acetic acid (15 mL) was heated at 125 °C for 1 h. After the reaction, cold water and aqueous sodium hydroxide solution were added to neutralize the solution. Ethyl acetate was added to the solution, and the organic phase was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate; then, the solvent was removed under reduced pressure. The crude product was subjected to column chromatography (SiO₂, chloroform/ethyl acetate = 15/1 v/v), yielding the product as a colorless solid (70%). ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 8.00 (d, *J* = 8.8 Hz, 2H), 7.53–7.21 (m, 10H), 7.03 (d, *J* = 8.8 Hz, 2H), 4.02 (t, *J* = 6.3 Hz, 2H), 3.55 (t, *J* = 6.7 Hz, 2H), 1.85–1.73 (m, 4H), 1.48–1.45 (m, 4H) ppm. ESI-MS: *m/z* = 475.2 [M + H]⁺, 497.1 [M + Na]⁺, 971.3 [2M + Na]⁺. Mp: 153.8 °C.

Scheme 1 Synthesis of N-C₆-LPD.

2.3.2 Synthesis of compound 3

A mixture of **2** (0.208 g, 0.44 mmol) in dichloromethane (23 mL), potassium ferricyanide (0.574 g, 1.74 mmol), and 3 M NaOH aqueous solution (4.5 mL) was stirred at room temperature under dark conditions for 24 h. The reaction mixture was washed twice with water and an aqueous solution of sodium hydrogen carbonate solution. The isolated organic phase was dried using anhydrous sodium sulfate; then, the solvent was removed under reduced pressure. The crude product was subjected to recycling preparative high-performance liquid chromatography (LC-9210NEXT, Japan Analytical Industry Co., Ltd.) with chloroform as the eluent, yielding the product as a colorless solid (50%). ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 8.32 (d, *J* = 8.6 Hz, 2H), 7.75 (d, *J* = 7.5 Hz, 2H), 7.52–6.73 (m, 22H), 6.58–6.51 (m, 2H), 4.15 (t, *J* = 5.6 Hz, 2H), 3.92–3.82 (m, 2H), 3.59–3.34 (m, 4H), 1.88–1.61 (m, 8H), 1.51–1.40 (m, 8H) ppm. ESI-MS: *m/z* = 971.2 [M + Na]⁺. Mp: 118.6 °C.

2.3.3 Synthesis of N-C₆-LPD

A mixture of **3** (0.063 g, 0.067 mmol), acetone (2.8 mL), and aqueous 4.3 M trimethylamine solution (0.160 g, 0.69 mmol) was stirred at room temperature under dark conditions for 24 h. Under reduced pressure, the solvents and unreacted trimethylamine were removed, and the product was obtained as a yellow solid. ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 8.36–7.99 (m, 2H), 7.75 (d, *J* = 5.0 Hz, 2H), 7.65–6.49 (m, 24H), 4.19–4.06 (m, 2H), 4.01–3.79 (m, 2H), 3.30–3.22 (m, 4H), 1.87–1.63 (m, 8H), 1.58–1.27 (m, 8H) ppm. ESI-MS: *m/z* = 453.2 [M–2Br]²⁺, 987.5 [M–Br]⁺. Mp: 158.1 °C.

2.4 Static surface tension measurements

The surface tension of the aqueous N-C₆-LPD solution was measured by a Drop Master 700 (Kyowa Interface Science Co. Ltd.) using the pendant drop method. All mea-

surements were conducted at 25 °C.

2.5 Ultraviolet (UV) light irradiation

UV light irradiation was conducted using a 200-W Hg–Xe Lamp (SUPERCUR UVF-203S, San-Ei Electronic). The irradiation wavelength (260–390 nm) was achieved using a color filter (U340, HOYA). Light at a constant intensity (30 mW/cm²) was irradiated into a cuvette that contained the solution.

3 Results and Discussion

The cationic amphiphilic lophine dimer (N-C₆-LPD) was synthesized by **Scheme 1**. Quaternary ammonium moieties were introduced at the end of the hexyl groups of the lipophilic lophine dimer (C₆-LPD), which we previously reported²¹⁾ (**Fig. 1a**). The interfacial properties and self-assembly of N-C₆-LPD were examined. **Figure 2a** shows the static surface tension of aqueous solutions of N-C₆-LPD as a function of their concentrations. The surface tension decreased with increasing surfactant concentration and remained constant above a certain concentration. The critical aggregation concentration (cac) of N-C₆-LPD was 0.51 mM, and the surface tension measured at cac (γ_{cac}) was 44.6 mN/m. Dynamic light scattering (DLS) measurements were performed on an aqueous N-C₆-LPD solution at 5.0 mM above the cac to determine the size of the formed molecular assembly (**Fig. 2b**). The result showed that the average particle diameter of the molecular assemblies was ~220 nm, suggesting that N-C₆-LPD forms large molecular assemblies, such as vesicles. From these results, upon self-assembly of the amphiphilic lophine dimers, the lophine dimer moieties were successfully accumulated in the supramolecular nanospace formed by the molecular assembly,

Fig. 2 (a) Static surface tension of aqueous $\text{N-C}_6\text{-LPD}$ solutions measured at various surfactant concentrations. (b) Dynamic light scattering measurement of 5.0 mM aqueous $\text{N-C}_6\text{-LPD}$ solution.

Fig. 3 Variations in color (a) and UV-vis absorption spectra of 5.0 mM aqueous (b) or 5.0×10^{-2} mM DMSO (c) solutions of $\text{N-C}_6\text{-LPD}$ before and after UV light irradiation. Reversible changes in the absorbance of the 5.0 mM aqueous $\text{N-C}_6\text{-LPD}$ solution at 620 nm before and after UV light irradiation (d) and the zoomed plots around the light irradiation (e).

which enhances their photoisomerization.

The photoisomerization of $\text{N-C}_6\text{-LPD}$ that formed the molecular assemblies was examined. As shown in Fig. 3a and in the movie in the Supporting Information, 5.0 mM of aqueous $\text{N-C}_6\text{-LPD}$ solution was pale yellow, and the color immediately changed to green-blue after UV light irradiation

(260–390 nm). When the irradiation stopped, the color of the solution also immediately recovered to the original color. This showed that photoisomerization of $\text{N-C}_6\text{-LPD}$ proceeds even when it forms molecular assemblies in an aqueous medium. However, in DMSO when a molecular assembly did not form, recovery of the color change required

Fig. 4 Plots of $1/A$ vs. t of 5.0 mM aqueous $N-C_6$ -LPD solution, and 5.0 mM $N-C_6$ -LPD DMSO solution. A is the absorbance at 620 nm. The inset shows the plots in the range of 0 and 0.006 min.

over 1 day after removal the UV irradiation, while the color of the solution varied from colorless to blue upon irradiation. These results show that $N-C_6$ -LPD forms molecular assemblies in an aqueous medium that exhibit rapid photochromism.

The photoisomerization was characterized by using UV-vis absorption spectroscopy. For $N-C_6$ -LPD solutions, UV light irradiation led to the appearance of a new absorption band at 460 nm and 620 nm originating from the lophyl radical (Figs. 3b and 3c). Figure 3d shows the time course of the absorbance at 620 nm in the absence and presence of UV light irradiation. The absorbance immediately increased upon light irradiation and reached a photostationary state (Fig. 3e). When the irradiation stopped, the absorbance immediately recovered to the initial level. Furthermore, repeatability of the photoisomerization of the amphiphilic lophine dimer was observed. These spectroscopic changes correspond to the aforementioned naked-eye observations (Fig. 3a).

Figure 4 shows plots of $1/A$ vs. t , where A is the absorption of the lophyl radical at time t . The linearity of these plots shows that the recombination follows a second-order reaction rate. The apparent reaction rate, k' , was determined from the slope of the plots because the initial concentrations of the produced lophyl radicals could not be determined. For the aqueous $N-C_6$ -LPD solution, the apparent rate constant was $6.1 \times 10^3 \text{ min}^{-1}$, which is over 50,000-fold larger than the one for that in DMSO solution (0.11 min^{-1}). Compared to the lipophilic lophine dimer (C_6 -LPD) solubilized in micelles, the recombination accelerated ~ 500 fold²¹. The time constants were 1.64×10^{-4} , 9.1 min (aqueous or DMSO solutions of $N-C_6$ -LPD), and 9.1

$\times 10^{-2}$ min (C_6 -LPD in aqueous CTAB solution), respectively, and reflected significant recombination reaction enhancements. We assumed that this remarkable rate enhancement was achieved by accumulation of the lophine dimers upon self-assembly, which reduced the distance between the radical species and enhanced the frequency of radical recombination (Fig. 1b). These results suggest that both confinement and concentration of the lophine dimer molecules in a molecular assembly contributes to efficient recombination.

4 Conclusions

A cationic amphiphilic lophine dimer ($N-C_6$ -LPD) was newly synthesized. $N-C_6$ -LPD formed molecular assemblies that have a diameter of ~ 220 nm in aqueous medium. UV light irradiation cleaved $N-C_6$ -LPD into lophyl radicals, and the radical species recovered to their initial form when the irradiation stopped. When $N-C_6$ -LPD formed molecular assemblies, the rate of recombination of lophyl radicals accelerated 50,000-fold compared to that in an organic solvent. Formation of the molecular assemblies by the amphiphilic lophine dimer decreased the distance between the lophyl radicals, which lead to a recombination enhancement. These results show that accumulation of the lophine dimers significantly accelerated the recombination of the lophyl radicals. We are currently investigating the rapid control of interfacial properties and morphologies of molecular assemblies with photoirradiation for promising applications, such as efficient controlled release of drugs and active components.

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6 Supporting information

This material is available free of charge via the Internet at <http://dx.doi.org/10.5650/jos.ess19010>.

The movie of the color changes in the aqueous $N-C_6$ -LPD solution upon photoirradiation is available.

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