

Photochemical Formation of a Core-crosslinked Micelle using an Anthracene-containing Amphiphilic Copolymer

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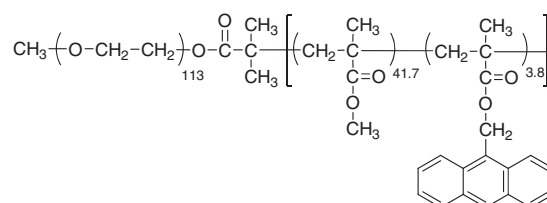
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In order to develop photoresponsive polymeric micellar systems, an amphiphilic block copolymer consisting of anthracene moieties was successfully prepared by atom transfer radical polymerization. In an aqueous solution, the photodimerization of the anthracene moieties occurred in the micellar core upon irradiation ($\lambda > 360$ nm), keeping the mean diameter constant. The photodimerization caused the interpolymer reaction to form a core-crosslinked micelle.



Scheme 1. Structure of PEG₁₁₃-*b*-P(MMA_{41.7}-AM_{3.8}).

Stimulus-responsive micelles, whose functions such as formation, collapse, and shrinking behavior are triggered by various external factors, have attracted considerable interest in industry and academia because of their potential use as sensors, nanoreactors, and encapsulation-releasing boosters.¹ Photoirradiation is a fairly versatile stimulus for controlling micelle aggregation behavior because the irradiation process does not require any contact with the target systems or additives like acid and base.^{2,3} Another advantage of irradiation is the ability to control irradiation area and power to induce a response from the system.

Some functional molecules are known to exhibit photoactive behavior, including cleavage, isomerization, dimerization, and coupling. Amphiphilic copolymers containing cinnamoyl, coumarin, or thymine photoactive moieties, which are responsive to photoirradiation at ca. 300 nm, have been prepared to form crosslinked micelles in an aqueous solution.^{2,4} However, when the photoresponsive system is applied to biomedical applications, the ultraviolet irradiation can lead to serious damage to the body and to substrate, which arises from high-energy, low-wavelength UV light. Therefore, the photocontrolled architectures need to be responsive to visible or near-infrared light irradiation.² We believe that one promising approach to solve this wavelength problem is to use π -extended molecules which exhibit photoactivity. Anthracene derivatives are photoactive molecules that display absorption bands with a large molar absorption coefficient of ca. 10^4 , assigned to π - π^* transitions. They can be dimerized via [4,4]-cycloaddition by photoirradiation at 300–400 nm.⁵ The resulting photodimers undergo dissociation upon irradiation or heating. Here, we report the photochemical formation of crosslinked micelles in water through the photodimerization of anthracene units tethered to an amphiphilic copolymer as a photosensitive micellar system.

PEG₁₁₃-*b*-P(MMA_{41.7}-AM_{3.8}) is an amphiphilic block copolymer composed of poly(ethylene glycol) monomethyl ether (PEG), methyl methacrylate (MMA), and 9-anthrylmethyl

methacrylate⁶ units (AM) (Scheme 1). The copolymer is expected to form micellar aggregates in an aqueous solution through self-assembly.

At first, a copolymer, PEG₁₁₃-AM_{36.9} (absent MMA units) was prepared, but insoluble in water, resulting in difficulty in studying the copolymer. Thus, we introduced MMA as a comonomer to the copolymer, changing AM contents.

The copolymer, PEG₁₁₃-*b*-P(MMA_{41.7}-AM_{3.8}), was prepared from MMA, AM, and a PEG-based macroinitiator⁷ through a modified procedure of atom transfer radical polymerization (ATRP) from previous reports.^{7,8} ¹H NMR analysis revealed MMA and AM units in the copolymer were 41.7 and 3.8, respectively.⁹ Furthermore, the concentration of 0.5 g L⁻¹ copolymer solution in CHCl₃ corresponds to AM unit concentration of 0.028 mM compared with 9-anthrylmethyl acetate¹⁰ in CHCl₃. The copolymer dissolved in water (10 g L⁻¹), presumably due to low AM units of 3.8. The apparent critical micelle concentration (cmc) of the copolymer in water was estimated using Nile red as a fluorescence probe¹¹ to be 0.036 g L⁻¹, meaning that the interpolymer micellar aggregation occurred above the concentration.

Photoirradiation at $\lambda > 360$ nm of the aqueous solution (10 g L⁻¹) was conducted after bubbling argon gas to avoid reactions between anthracene moieties and oxygen.¹² Portions of the aqueous solution were taken before irradiation and at predetermined irradiation times, and diluted to 0.5 g L⁻¹ with water for UV-vis measurements. Before irradiation, the absorption maxima corresponding to π - π^* transitions of the anthracene moieties in water were observed at 388, 368, 350, and 334 nm (Figure 1). Upon irradiation, the absorption peak intensities decreased. This decrease is due to the photodimerization of the anthracene moieties, as reported previously.¹³ An isosbestic point was observed at 311 nm in the early stages. The peak intensities were 69, 48, 30, and 21% of the initial intensity after 270, 540, 900, and 1200 min of irradiation, respectively, for the peak at 388 nm. The photodimerization degree of the

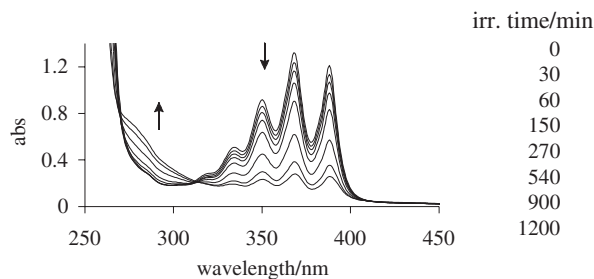


Figure 1. Changes in UV-vis spectra of the copolymer upon irradiation. The irradiated samples were diluted with water (0.5 g L^{-1}).

anthracene moieties was estimated to be approximately 31, 52, 70, and 79% from the change in intensity because the polymer main chain and anthracene dimers do not absorb light. Long irradiation times (i.e., 1200 min) may induce side reactions to some degree, as suggested by the deviation of the isosbestic point in the UV-vis spectra. The dissociation of the anthracene dimer was not observed in the UV-vis spectra when the aqueous solution photolyzed for 1200 min was heated at 80°C for 20 h, consistent with the formation of a stable core-crosslinked micelle. After irradiation, an apparent cmc for the photoproduct disappeared under the measured concentrations ($>0.0012 \text{ g L}^{-1}$), suggesting crosslinking reaction of the amphiphilic copolymer occurred to form a nanogel-like crosslinked aggregate.

Size exclusion chromatography (SEC) and ^1H NMR measurements were also performed for the copolymer and the corresponding photoproducts after the sample was recovered from the aqueous solution by freeze-drying. The SEC profiles of the copolymer before irradiation were found to show a unimodal distribution, and number- (M_n) and weight-average molecular weight (M_w) values calibrated using PEG standards were 7690 and 9300, respectively. In addition, the polydispersity index (M_w/M_n) was relatively small (1.21) similar to previous trends for ATRP.^{7,8} As irradiation started, the fraction corresponding to higher molecular weights appeared at early elution times (Figure 2). The photoproduct obtained through irradiation for 1200 min exhibited SEC peaks around 6 and 10–12 min of elution. The first fraction corresponds to high M_n of more than 18.9×10^4 . The increase in M_n values was clearly caused by interpolymer crosslinking through the dimerization of anthracene moieties. The volume (V) ratio at 5–10 and 10–12 min was roughly estimated (Figure 2, right). The ratio increased with irradiation time, indicating V_{5-10} was formed with consumption of V_{10-12} . The remaining fraction at 10–12 min is presumably due to intrapolymer photodimerization or low crosslinking degree of the polymer. This would arise from low AM unit of 3.8 and/or photodimerization degree of 79% in Figure 1. In the ^1H NMR spectra of the photoproduct, a broad signal appeared at 6.7 ppm, while the signal attributed to the AM methylene protons (6.1 ppm) disappeared.⁹ These results are identical to photodimerization behaviors reported previously.¹³

The copolymer did not form a gel in water upon irradiation. Before irradiation, dynamic light scattering measurements of the aqueous solution (0.5 g L^{-1}) showed a unimodal distribution and the hydrodynamic mean diameter was estimated to be $27.8 (\pm 6.0) \text{ nm}$. This indicates that the copolymer formed core-corona micellar aggregation in water. After 270, 540, and

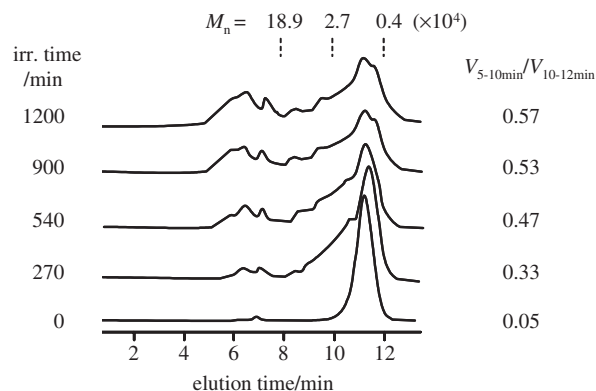


Figure 2. SEC profiles of the samples before and after irradiation.

1200 min of irradiation, the size distribution of the micellar aggregates had diameters of $24.2 (\pm 5.6)$, $23.5 (\pm 7.1)$, and $24.9 (\pm 7.8) \text{ nm}$, respectively.⁹ These results indicate that the photo-crosslinking of the polymer-tethered anthracene moieties occurred in the hydrophobic micellar core without intermicellar crosslinking.

In conclusion, a novel amphiphilic block copolymer with anthracene moieties was prepared by ATRP. Upon irradiation of the aqueous copolymer solutions, the photodimerization of the anthracene moieties occurred without gelation, keeping the mean diameter constant. The photodimerization caused interpolymer crosslinking in the micellar core, increasing the M_n values. This photochemically formed crosslinked micelle would be used to develop encapsulation-releasing systems that are responsive to long-wavelength irradiation.

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