# Multiple Micellization and Dissociation Transitions of Thermo- and Light-Sensitive Poly(ethylene oxide)-*b*-poly(ethoxytri(ethylene glycol) acrylate-*co*-*o*-nitrobenzyl acrylate) in Water

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ABSTRACT: This article reports on the synthesis of thermo- and light-sensitive hydrophilic block copolymers, poly(ethylene oxide)-*b*-poly(ethoxytri(ethylene glycol) acrylate-*co*-*o*-nitrobenzyl acrylate), and the study of their micellization/dissociation transitions in water in response to temperature changes and UV irradiation. The block copolymers with controlled molecular weights and narrow polydispersities were synthesized by atom transfer radical polymerization of a mixture of ethoxytri(ethylene glycol) acrylate and *o*-nitrobenzyl acrylate with a molar ratio of 100:10 from a PEO macroinitiator. Dynamic light scattering and fluorescence spectroscopy studies showed that these copolymers were molecularly dissolved in water at lower temperatures and self-assembled into micelles with the thermosensitive block associating into the core and the PEO block forming the corona when the temperature was above the lower critical solution temperature (LCST) of the thermosensitive block. Upon UV irradiation, the *o*-nitrobenzyl group was cleaved and the LCST of the thermosensitive block was increased, causing the dissociation of micelles into unimers and the release of encapsulated fluorescent dye Nile Red into water. Further increasing the temperature induced the formation of micelles again and the re-encapsulation of Nile Red. The thermo-induced formation and dissociation of micelles were reversible.

## Introduction

Environmentally responsive micelles or vesicles formed from the self-assembly of stimuli-sensitive block copolymers or low-mass amphiphiles in solution have received growing interest in recent years.[1–3] These micellar aggregates can spontaneously dissociate into the molecularly dissolved unimers or undergo morphology changes upon application of external stimuli.[1–49] Thus, they are particularly suitable for controlled encapsulation and triggered release of substances and have potential applications in targeted drug delivery, cosmetics, etc.[1] A common principle for destabilizing micelles or vesicles involves the modification of the polarity or hydrophobicity/hydrophilicity balance of the core-forming component by the use of an environmental trigger. When the core-forming component becomes soluble in the medium, the driving force for the formation of micellar aggregates is eliminated, causing the micelles or vesicles to disassemble. Depending on the response mechanism, dissociation of micellar aggregates can be reversible or irreversible.[1–3] In some applications, the reversible dissociation and micellization can be advantageous or are desired because the re-formation of micellar aggregates enables the re-encapsulation of the released substance.[35,36]

Various chemical and physical stimuli including pH,[1–16] specific molecules,[1,17–19] redox,[1,20–27] light,[28–36] and temperature[37–49] have been employed to induce the disassembly or morphology changes of micellar aggregates. Light is an especially attractive external stimulus because the triggered release of encapsulated substances can be controlled at a specific time and location.[28–36] For example, Jiang et al. synthesized photoresponsive poly(ethylene oxide)-*b*-poly(pyrenyl methacrylate) (PEO-*b*-poly(pyrenyl methacrylate)) and PEO-*b*-poly(*o*-nitrobenzyl methacrylate) and prepared the micelles by addition of water into their THF solutions.[31,32] Upon UV irradiation, the pyrenyl or *o*-nitrobenzyl group was cleaved, converting the core-forming hydrophobic block into hydrophilic. Consequently, the micelles dissociated into the unimers. Goodwin et al. used IR light to trigger the release of Nile Red from the micelles of a low-mass nonionic surfactant that contained a photoresponsive 2-diazo-1,2-naphthoquinone (DNQ) group.[33] Light irradiation of DNQs induced Wolff rearrangement, resulting in a drastic increase in water solubility and thus the dissociation of micelles. Jiang et al. reported the assembly and disassembly of vesicles formed by a light-responsive PEO-terminated malachite green derivative.[35] Very recently, Lee et al. synthesized a diblock copolymer of ethylene glycol and a spiropyran-containing methacrylate.[36] The block copolymer micellar aggregates were disrupted by UV irradiation and regenerated by exposure to visible light.

Temperature is another attractive environmental trigger.[37–52] The behaviors of hydrophilic block copolymers with one or more blocks exhibiting thermosensitive properties in water are intriguing.[37–49] These block copolymers undergo reversible micellization and dissociation in response to temperature changes. It should be emphasized here that one advantage of the preparation of micelles from doubly hydrophilic diblock copolymers is the elimination of the use of organic solvents. It is known that the lower critical solution temperature (LCST) of a thermosensitive polymer can be modified by incorporation of a different monomer.[1–3,52–59] Hennink et al. recently developed a series of diblock copolymers composed of PEO and thermosensitive polymers that contained lactate side chains.[1,54–57] Hydrolysis of lactate groups caused an increase of the LCST of the thermosensitive block. When the polymer became soluble in water, dissociation of micelles occurred, and the encapsulated molecules were released.

In this article, we report on the synthesis of thermo- and light-sensitive hydrophilic block copolymers, PEO-*b*-poly(ethoxytri(ethylene glycol) acrylate-*co*-*o*-nitrobenzyl acrylate) (PEO-*b*-P(TEGEA-*co*-NBA), Scheme 1), by atom transfer radical polymerization (ATRP) and the study of their micellization and dissociation transitions in water in response to temperature changes and UV irradiation. PTEGEA is a thermosensitive water-soluble polymer. Above the LCST of the thermosensitive block (LCST$_1$), the copolymers self-assemble into micelles in water. Upon UV irradiation, the hydrophobic *o*-nitrobenzyl group is cleaved,[32] and the LCST of the thermosensitive block

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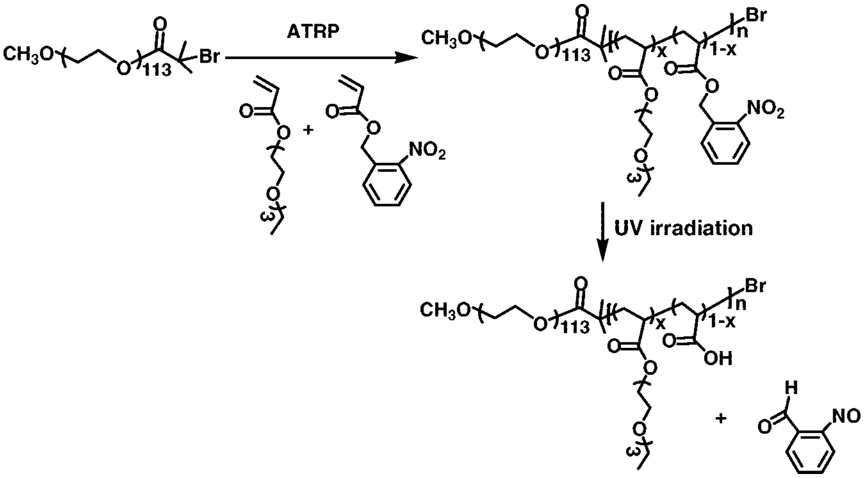
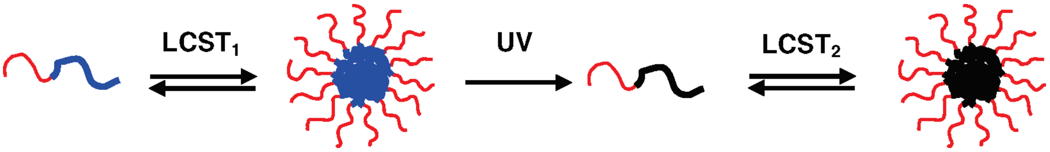
**Scheme 1. Synthesis of Thermo- and Light-Sensitive Poly(ethylene oxide)-*b*-poly(ethoxytri(ethylene glycol) acrylate-*co*-*o*-nitrobenzyl acrylate) and Cleavage of *o*-Nitrobenzyl Group by UV Irradiation**



**Scheme 2. Multiple Micellization and Dissociation Transitions of Thermo- and Light-Sensitive Poly(ethylene oxide)-*b*-poly(ethoxytri(ethylene glycol) acrylate-*co*-*o*-nitrobenzyl acrylate) in Water in Response to Temperature Changes and UV Irradiation**



increases, causing the dissociation of micelles into unimers (Scheme 2). Further increasing the temperature to above the LCST of the new thermosensitive block (LCST$_2$) induces the formation of micelles again. The temperature-induced micellization is reversible. As a demonstration, we show in this work that Nile Red can be encapsulated by micelles when $T >$ LCST$_1$, released into $H_2O$ upon UV irradiation, and re-encapsulated when $T >$ LCST$_2$.

## Results and Discussion

By introducing a short oligo(ethylene glycol) group onto the polymer backbone as a pendant from each repeat unit, a class of new thermosensitive water-soluble polymers, including poly(vinyl ether)s,[37–40] polymethacrylates,[60–64] polystyrenics,[44,65–67] polyacrylates,[44,66] and dendritic polymers,[68] has been developed recently. The cloud point can be easily tuned by varying the type of polymer backbone, the length, and end group of oligo(ethylene glycol) pendant as well as the chain end group.[37–40,60–68] In this article, we report on the synthesis of thermo- and light-responsive block copolymers, PEO-*b*-P(TEGEA-*co*-NBA), and their micellization/dissociation behavior in water in response to temperature changes and UV irradiation. We first synthesized a homopolymer of TEGEA and a random copolymer of TEGEA and NBA (P(TEGEA-*co*-NBA)) by ATRP. Their thermosensitive properties were studied, and the effect of photocleavage of *o*-nitrobenzyl group on the cloud point of the random copolymer in water was investigated. For comparison with PEO-*b*-P(TEGEA-*co*-NBA), a thermosensitive diblock copolymer PEO-*b*-PTEGEA was prepared, and its temperature-induced micellization/dissociation transitions in water were studied.

**Synthesis of Monomers and Polymers.** TEGEA and NBA were synthesized by the reactions of acryloyl chloride with tri(ethylene glycol) monoethyl ether and *o*-nitrobenzyl alcohol, respectively, in the presence of triethylamine. The two monomers were thoroughly purified by vacuum distillation and/or silica gel column chromatography. Their molecular structures were confirmed by $^1$H NMR, $^{13}$C NMR, and mass spectroscopy analysis. The macroinitiator, PEO with one end functionalized with an ATRP initiator (PEO-Br), was prepared according to a literature procedure.[69] Prior to the reaction of poly(ethylene glycol) monomethyl ether (PEO-OH) with excess 2-bromoisobutyryl bromide, the trace amount of water in PEO-OH was removed by azeotropic distillation with dry toluene. The macroinitiator was purified by precipitation in diethyl ether, dissolution in water, and extraction with methylene chloride. After drying in high vacuum, it was used for the synthesis of block copolymers.

A homopolymer of TEGEA with $M_{n,GPC}$ of 14 500 g/mol and PDI of 1.16 was prepared by ATRP of TEGEA in anisole at 90 °C using ethyl 2-bromoisobutyrate (EBiB) as initiator and CuBr/*N*,*N*,*N*′,*N*′,*N*″-pentamethyldiethylenetriamine (PMDETA) as catalyst. The DP, calculated from the monomer conversion and the monomer-to-initiator ratio, was 74. Similarly, a random copolymer of TEGEA and NBA, P(TEGEA-*co*-NBA), with $M_{n,GPC}$ of 13 900 g/mol and PDI of 1.13 was prepared by ATRP of a mixture of TEGEA and NBA with a molar ratio of 100:10. The composition of the random copolymer was determined from its $^1$H NMR spectrum using the peaks located at 5.44 ppm ($-CH_2-$ of the benzyl group in NBA unit) and 4.15 ppm ($-CH_2OOC-$ of TEGEA unit). The molar ratio of TEGEA and NBA was 100:13, close to the feed composition. Block copolymers, PEO-*b*-PTEGEA and PEO-*b*-P(TEGEA-*co*-NBA), were synthesized from macroinitiator PEO-Br by ATRP of either pure TEGEA or a mixture of TEGEA and NBA with a molar ratio of 100:10 at 90 °C using CuBr/PMDETA as catalyst. The polymers were purified by repetitive precipitation in hexanes (for PEO-*b*-PTEGEA) or in a mixture of hexanes and diethyl ether (v/v, 60:40, for PEO-*b*-P(TEGEA-*co*-NBA)). Figure 1 shows the GPC curves of macroinitiator PEO-Br and one sample of PEO-*b*-P(TEGEA-*co*-NBA). The peak completely shifted to the high molecular weight side and remained narrow, indicating that the

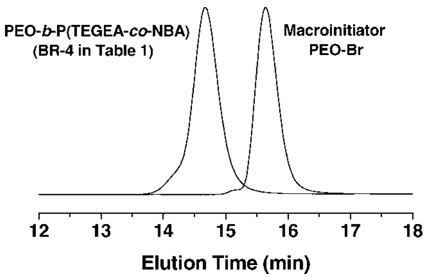


**Figure 1.** Gel permeation chromatography curves of macroinitiator PEO-Br and PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4** in Table 1, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07).

**Table 1. Characterization Data for PTEGEA, P(TEGEA-*co*-NBA), PEO-*b*-PTEGEA, and Two Samples of PEO-*b*-P(TEGEA-*co*-NBA) Used in the Present Work**

| no. | polymer | $M_{n,GPC}$ (g/mol)[a] | PDI[b] | $n_{EO}$:$n_{TEGEA}$:$n_{NBA}$[c] |
|---|---|---|---|---|
| H-**1** | PTEGEA | 14 500 | 1.16 | 0:74[d]:0 |
| R-**2** | P(TEGEA-*co*-NBA) | 13 900 | 1.13 | 0:66:9[d,e] |
| B-**3** | PEO-*b*-PTEGEA | 21 400 | 1.07 | 113:92:0 |
| BR-**4** | PEO-*b*-P(TEGEA-*co*-NBA) | 18 300 | 1.07 | 113:70:9 |
| BR-**5** | PEO-*b*-P(TEGEA-*co*-NBA) | 24 700 | 1.11 | 113:109:14 |

[a] The number-average molecular weight ($M_{n,GPC}$) was determined by gel permeation chromatography using polystyrene calibration. [b] The polydispersity index (PDI) was determined by gel permeation chromatography using polystyrene calibration. [c] $n_{EO}$, $n_{TEGEA}$, and $n_{NBA}$ are the numbers of EO (in the PEO block), TEGEA, and NBA units in the polymers, respectively. The values of $n_{TEGEA}$ and $n_{NBA}$ in the block copolymers were determined from $^1$H NMR spectra. [d] The degrees of polymerization (DPs) of PTEGEA and P(TEGEA-*co*-NBA) were calculated from the monomer conversion and the monomer-to-initiator ratio. [e] The DP of P(TEGEA-*co*-NBA) was 75. The molar ratio of TEGEA and NBA in the random copolymer was determined from the $^1$H NMR spectrum.

block copolymerization was a well-controlled process. The DP of TEGEA units in the PEO-*b*-PTEGEA and the numbers of TEGEA and NBA units in the two samples of PEO-*b*-P(TEGEA-*co*-NBA) were determined from $^1$H NMR spectra. The molar ratio of TEGEA to NBA units in PEO-*b*-P(TEGEA-*co*-NBA)s was 100:13, essentially identical to the composition of P(TEGEA-*co*-NBA). The characterization data for the polymers used in the present work are summarized in Table 1. The PDIs of all these polymers, determined by GPC using polystyrene calibration, were ≤1.16.

**Thermosensitive Properties of PTEGEA and P(TEGEA-*co*-NBA).** The cloud points of PTEGEA (H-**1**) and P(TEGEA-*co*-NBA) (R-**2**) in water were determined by turbidimetry. Figure 2 shows the optical transmittances of 0.2 wt % aqueous solutions of H-**1** and R-**2** at wavelength of 550 nm as a function of temperature in both heating and cooling processes. For PTEGEA, the solution turned cloudy at ~35 °C during the course of increasing temperature. The transparent-to-cloudy transition was relatively sharp, and the transition zone was ~4 °C. If 50% of the transmittance change is used for the determination of cloud point (CP), the CP of H-**1** in water is 36 °C. The CP of P(TEGEA-*co*-NBA) in a 0.2 wt % aqueous solution was 18.5 °C; therefore, the incorporation of 13 mol % of hydrophobic monomer NBA with respect to TEGEA into the polymer chain decreased the CP by 17.5 °C. From Figure 2, one can also find that there was essentially no hysteresis for H-**1** and R-**2** between heating and cooling. The thermo-induced LCST transitions of both polymers were reversible. Note that Lutz et al. also observed that there was no hysteresis between heating and cooling in the LCST transitions of copolymers of 2-(2-methoxyethoxy)ethyl methacrylate and oligo(ethylene glycol) methacrylate in water.[63,64]

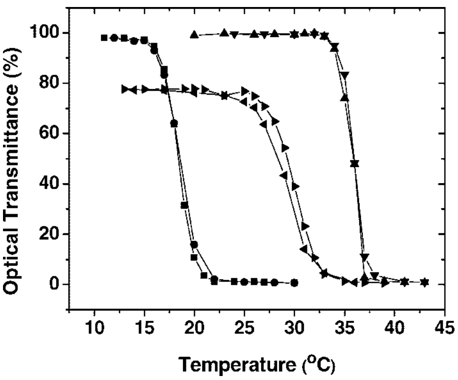


**Figure 2.** Optical transmittances at wavelength of 550 nm of an aqueous solution of PTEGEA (H-**1**, $M_{n,GPC}$ = 14 500 g/mol, PDI = 1.16, 0.2 wt %, heating (▲), cooling (▼)) and an aqueous solution of P(TEGEA-*co*-NBA) (R-**2**, $M_{n,GPC}$ = 13 900 g/mol, PDI = 1.13, 0.2 wt %) before (heating (■), cooling (●)) and after irradiation with 365 nm UV light at 13 °C for 485 min (heating (right-pointing ▲), cooling (left-pointing ▲)) as a function of temperature. The transmittances were recorded with a UV–vis spectrometer.

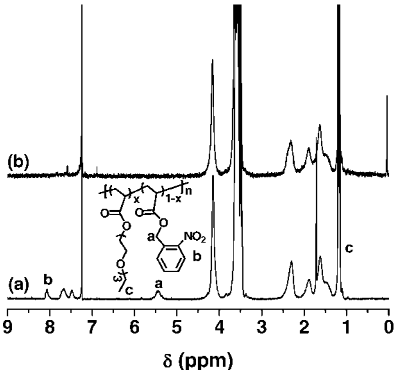


**Figure 3.** $^1$H NMR spectra of (a) P(TEGEA-*co*-NBA) (R-**2**, $M_{n,GPC}$ = 13 900 g/mol, PDI = 1.13) and (b) the polymer obtained from the 0.2 wt % aqueous solution of R-**2** after irradiation with 365 nm UV light at 13 °C for 485 min. CDCl$_3$ was used as the solvent.

**Photocleavage of *o*-Nitrobenzyl Group of NBA in P(TEGEA-*co*-NBA) and the Cloud Point of the Obtained Polymer in Water.** *o*-Nitrobenzyl has been widely used as a protective group;[32,70–73] it can be cleaved by long wavelength UV irradiation. To study the photocleavage of *o*-nitrobenzyl group in the random copolymer, a 0.2 wt % aqueous solution of R-**2** was irradiated with 365 nm UV light from a Spectroline ENF-240C hand-held UV lamp at 13 °C, which was below the CP of R-**2**. Initially, the solution was colorless. With the increase of irradiation time, the solution gradually turned slightly yellow. To determine the time that was needed to achieve the maximum degree of cleavage of *o*-nitrobenzyl groups, we used UV–vis spectrometry to monitor the photolysis reaction.[74] The absorbances in the wavelength range of 330−550 nm increased rapidly in the first 180 min and then leveled off with further increasing the irradiation time. To confirm that the *o*-nitrobenzyl group was cleaved, $^1$H NMR spectroscopy was employed. Figure 3 shows the $^1$H NMR spectra of R-**2** and the polymer obtained from the 0.2 wt % aqueous solution of R-**2** after UV irradiation for 485 min. Clearly, the aromatic peaks and the peak located at 5.44 ppm, which were from the NBA unit, disappeared. By comparing the two $^1$H NMR spectra, one can also find that the peaks from the TEGEA units did not undergo any changes, indicating that the TEGEA units were stable under UV irradiation.

Figure 2 shows the optical transmittance of a 0.2 wt % aqueous solution of R-**2** after UV irradiation for 485 min (i.e., the aqueous solution of P(TEGEA-*co*-acrylic acid) (P(TEGEA-

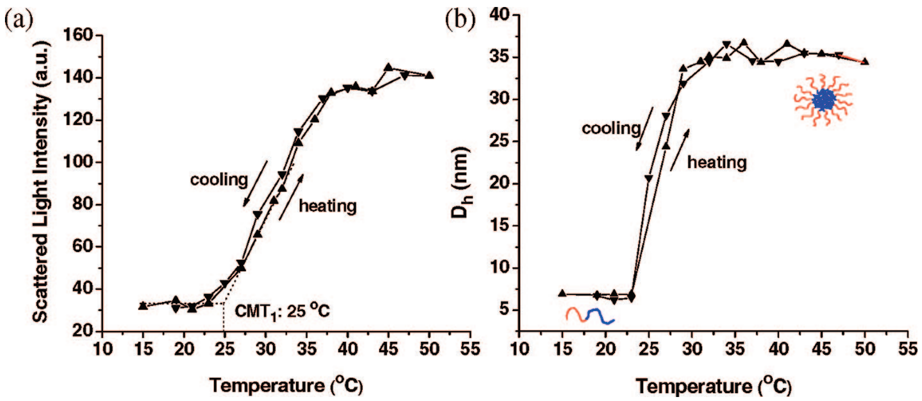


**Figure 4.** Intensity of scattered light at a scattering angle of 90° (a) and the hydrodynamic diameter (b) as a function of temperature ((▲) heating, (▼) cooling) in a dynamic light scattering study of a 0.2 wt % aqueous solution of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC} = 18\,300$ g/mol, PDI = 1.07). In (b), at 25 and 27 °C, two size distributions, one attributed to the unimers and one to the micelles, were observed,[74] and the reported hydrodynamic diameters for these temperatures were the average values over two hydrodynamic size distributions (the sizes of micelles at these temperatures were similar to that of micelles at higher temperatures[74]).

*co*-AA))) as a function of temperature in both heating and cooling processes. The slightly lower transmittances (~78%) of the polymer solution below the LCST transition were due to the absorbance of the colored product formed from the photocleavage reaction. The CP, determined from the heating curve at 50% of the transmittance change, was 30 °C, which was only 11.5 °C higher than that of P(TEGEA-*co*-NBA). Since the AA units in P(TEGEA-*co*-AA) are hydrophilic, a CP higher than that of PTEGEA (36 °C) was expected.[75] However, the observed CP of P(TEGEA-*co*-AA) was 6 °C lower. We found that the pH of a 0.2 wt % copolymer solution after UV irradiation was ~4.2 (note that deionized water was used to prepare the polymer solution). It is known that pH can affect the cloud point of an acid-containing thermosensitive polymer in water.[75,76] Calculations show that only a few percent of AA units in the P(TEGEA-*co*-AA) are needed to be ionized to produce a pH of ~4.2. The remaining un-ionized AA units are likely to form hydrogen bonds with neighboring TEGEA units, which would depress the CP. Another possible reason is the presence of an organic compound, *o*-nitrosobenzaldehyde, generated from the photocleavage reaction in the solution. Organic additives are known to affect the cloud points of thermosensitive polymers in water.[52] A further study is needed and underway.

**Reversible Micellization of Block Copolymers in Water in Response to Temperature Changes.** Two samples of PEO-*b*-P(TEGEA-*co*-NBA) with different molecular weights but essentially the same compositions for the thermosensitive blocks (BR-**4** and BR-**5**) were used for demonstration of thermo- and light-induced multiple micellization and dissociation transitions in water. We first studied their reversible micellization in response to temperature changes by dynamic light scattering (DLS) and fluorescence spectroscopy (FS). For comparison, PEO-*b*-PTEGEA (B-**3**) was also investigated. Figure 4 shows the intensity of scattered light at scattering angle of 90° and the hydrodynamic size as a function of temperature for a 0.2 wt % aqueous solution of BR-**4**. When the temperature was ≤23 °C, the intensity of scattered light was very low and the hydrodynamic size was <7 nm, indicating that the block copolymer was molecularly dissolved in water. With the increase of temperature, the scattered light intensity gradually increased, and two size distributions, one attributed to the unimers and one to the micelles, were observed at 27 °C with an average hydrodynamic size of 24.4 nm, suggesting that the thermosensitive block was undergoing a hydration-to-dehydration transition.[74] The critical micellization temperature (CMT$_1$), determined from the plot of the intensity of scattered light vs temperature (Figure 4a), was 25 °C, which was 6.5 °C higher than the CP of P(TEGEA-*co*-NBA) with the same composition. It is known that the LCST transition temperature is slightly higher when a thermosensitive polymer is attached to a hydrophilic block.[1–3]

When the temperature reached 29 °C, only micelles were observed. With further increasing the temperature, the average size of micelles remained at ~35 nm, but the intensity of scattered light continued to increase. A similar phenomenon was observed by Zhou and Chu in the study of thermo-induced micellization of poloxamer 188 (PEO-*b*-PPO-*b*-PEO) in water and was considered to result from the decreased micellar hydration and the increased aggregation number at higher temperatures.[77] The polydispersity of micelles at 50 °C was 0.048, indicating that the micelles were uniform in size (Figure 5a). Moreover, we found that the value of $\Gamma/q^2$ was nearly independent of scattering angle (Figure 5b), suggesting that the micelles were spherical.[5] This thermo-induced micellization was reversible. Decreasing the temperature caused the micelles to dissociate into the unimers (Figure 4).

The thermo-induced reversible micellization behaviors of BR-**5** and B-**3** were also investigated by DLS,[74] and the results are summarized in Table 2. The CMT$_1$ of BR-**5** at the same concentration (0.2 wt %) was 21 °C, 4 °C lower than that of BR-**4**, which is reasonable because the molecular weight of the thermosensitive block in BR-**5** is higher than that in BR-**4**. For B-**3**, the CMT was found at 39 °C, which was 3 °C higher than the CP of PTEGEA. For all three block copolymers, the stabilized micelles had similar hydrodynamic sizes (~35 nm), narrow polydispersities, and spherical shapes (as suggested by the independence of $\Gamma/q^2$ on scattering angle).

The thermo-induced reversible formation and dissociation of micelles of BR-**4**, BR-**5**, and B-**3** in water were further studied by FS. Nile Red was used as the hydrophobic fluorescence probe because its fluorescence is negligible in water but is known to increase substantially in a hydrophobic environment such as the core of micelles.[7,8,32] Furthermore, its absorption $\lambda_{max}$ is at 553 nm, far from the interfering absorptions of the block copolymers. Figure 6 shows the fluorescence emission spectra of Nile Red in a 0.2 wt % aqueous solution of BR-**4** at various temperatures in the heating process. The noticeable fluorescence intensity at lower temperatures (<18 °C) might be due to the enhanced solubilization of Nile Red by the polymer in water. A similar observation was reported by Jiang et al.[32] When the temperature was increased to above 20 °C, the fluorescence emission intensity increased significantly, indicating that the molecularly dissolved polymer chains began to associate into micelles and the dye molecules were sequestered into the core. The maximum

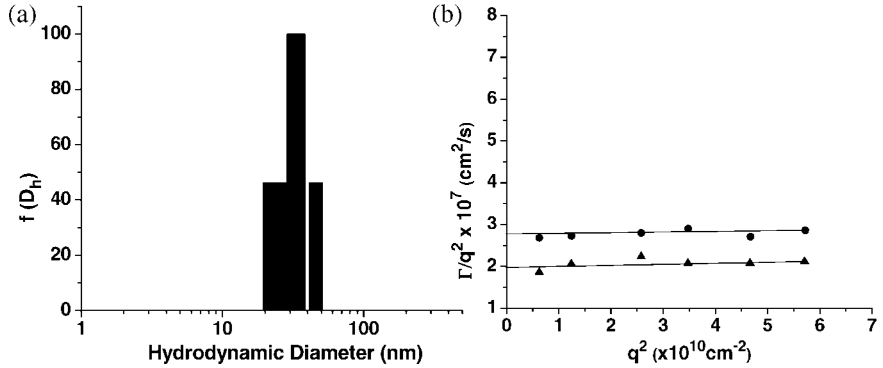


**Figure 5.** (a) Hydrodynamic diameter ($D_h$) distribution of micelles of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07) at 50 °C and (b) plot of $\Gamma/q^2$ of micelles of BR-**4** (●) and the corresponding PEO-*b*-P(TEGEA-*co*-AA) (▲) vs $q^2$ at 50 °C. The polydispersity of micelles of BR-**4** at 50 °C was 0.048. PEO-*b*-P(TEGEA-*co*-AA) was obtained by UV irradiation of a 0.2 wt % aqueous solution of BR-**4** at 32 °C for 480 min.

**Table 2. Critical Micellization Temperatures, Critical Micelle Concentrations, and Micelle Characteristics of Three Block Copolymers**

| no. | CMT$_{1\text{-DLS}}$[a] (°C) | micelle size[b] | PD[c] | CMT$_{1\text{-FS}}$[d] (°C) | CMC (mg/mL)[e] |
|---|---|---|---|---|---|
| B-3 | 39 | 35.4 nm (50 °C) | 0.044 (50 °C) | 39 | 0.33 (45 °C) |
| BR-4 | 25 | 34.4 nm (50 °C) | 0.048 (50 °C) | 23 | 0.064 (32 °C) |
| BR-5 | 21 | 33.9 nm (30 °C) | 0.030 (30 °C) | 20 | 0.025 (30 °C) |

[a] The critical micellization temperature (CMT$_{1\text{-DLS}}$) was determined by dynamic light scattering study of a 0.2 wt % aqueous polymer solution. [b] The average size of micelles at a specific temperature was obtained by the use of the CONTIN method. [c] The polydispersity (PD) of micelles at a specific temperature. [d] The CMT$_{1\text{-FS}}$ determined by fluorescence spectroscopy (FS) analysis of a 0.2 wt % aqueous polymer solution. [e] Critical micelle concentration (CMC) at a specific temperature determined by FS.

peak underwent a blue shift with the increase of temperature, from 621 nm at 14 °C to 615 nm at 50 °C, which further supported that the dye molecules moved from a hydrophilic to a hydrophobic environment.[7,8,32] The CMT$_1$, determined from the plot of maximum fluorescence intensity vs temperature, was 23 °C, close to that obtained from DLS study (25 °C). When the temperature decreased to 16 °C, the fluorescence emission intensity gradually decreased,[74] implying that the micelles dissociated into the unimers and the dye was released into water. Thus, consistent with DLS study, the thermo-induced micellization was reversible.

Since the micelles of BR-**4** were well developed at 32 °C from both DLS and FS studies, we determined the critical micelle concentration (CMC) of this block copolymer at this temperature. A series of aqueous solutions of BR-**4** with different concentrations that were loaded with the same amounts of Nile Red were made. After equilibration for >3 h, the fluorescence emission spectra were recorded at 32 °C and are shown in Figure 6b. From the plot of maximum emission intensity vs the logarithm of copolymer concentration, the CMC of this polymer at 32 °C was determined to be 0.064 mg/mL. With the increase of polymer concentration above the CMC, the maximum peak also underwent a blue shift from 625.5 nm at concentration of 0.0104 mg/mL to 617 nm at concentration of 0.407 mg/mL, consistent with the formation of micelles.

Similarly, we studied the temperature-induced reversible micellization of BR-**5** and B-**3** at concentration of 0.2 wt % by FS and determined the CMTs,[74] which were found to be 20 and 39 °C, respectively (Table 2). While the CMT of B-**3** determined from FS was identical to that from DLS, the values of CMT$_1$ for BR-**4** and -**5** were slightly lower than those obtained by DLS. The CMC was 0.33 mg/mL for B-**3** at 45 °C and 0.025 mg/mL for BR-**5** at 30 °C (Table 2). The CMC of B-**3** at 45 °C was much higher than those of BR-**4** and BR-**5**, which can be attributed to that the thermo-sensitive random copolymer block P(TEGEA-*co*-NBA) is more hydrophobic than PTEGEA, making the association of copolymer molecules occur at a lower concentration. The slightly lower CMC of BR-**5** compared with that of BR-**4** is likely due to the longer thermosensitive block in BR-**5**.

**UV-Irradiation-Induced Dissociation of Micelles of PEO-*b*-P(TEGEA-*co*-NBA).** The study of the photocleavage of *o*-nitrobenzyl group in the random copolymer P(TEGEA-*co*-NBA) showed that the cloud point increased by 11.5 °C. The CMT of BR-**4** at concentration of 0.2 wt % was 25 °C (CMT$_{1\text{-DLS}}$). If the photocleavage of *o*-nitrobenzyl in BR-**4** increases the CMT by the same magnitude as for the random copolymer, the CMT of the new block copolymer (CMT$_2$) would be 36.5 °C. Considering that well-defined spherical micelles of BR-**4** were observed at 32 °C from DLS, UV irradiation at this temperature is expected to induce the dissociation of micelles. Because at 32 °C the *o*-nitrobenzyl groups were located in the core of micelles, the irradiation time that was needed to achieve a maximum degree of cleavage might be different from that for P(TEGEA-*co*-NBA) below the LCST. Therefore, we used UV–vis spectrometry to monitor the photocleavage reaction. A 0.2 wt % aqueous micellar solution of BR-**4** was irradiated with 365 nm UV light at 32 °C, and the UV–vis spectra at various times were recorded.[74] It appeared that there was no further change in the absorbances from 330 to 650 nm after 183 min. The polymer after UV irradiation for 400 min was isolated, and the $^1$H NMR spectroscopy analysis showed that the aromatic peaks and the peak at 5.44 ppm, which were from NBA, were no longer present in the spectrum. To ensure that the photocleavage of *o*-nitrobenzyl groups in the micelle core reached the maximum degree, we irradiated the micellar solutions for 480 min in the following DLS and FS studies.

DLS study provided direct evidence for the UV-irradiation-induced dissociation of micelles of BR-**4** at 32 °C. The 0.2 wt % aqueous solution of BR-**4** used in the DLS study shown in Figure 4 was irradiated with 365 nm UV light at 32 °C for 480 min. The intensity of scattered light at scattering angle of 90° decreased to the level for the solution of BR-**4** below 22 °C before UV irradiation (Figure 7a). Meanwhile, the hydrodynamic diameter decreased to <7 nm (Figure 7b). These confirmed that the micelles were disrupted by the UV irradiation. When the solution temperature was increased from 32 °C to above 36 °C, the intensity of scattered light increased significantly. Two size distributions were observed in the range 36–42 °C: one attributed to the unimers and one to the micelles. With further increasing the temperature, the micelle size was found to be stabilized at ~41 nm, slightly larger than that of the micelles of BR-**4** (~35 nm). This might be the result of more water being retained in the core due to the hydrophilic carboxylic acid groups. The

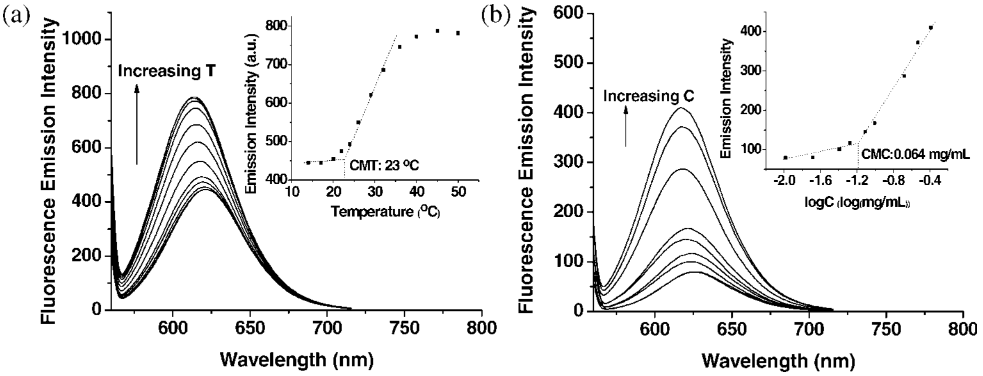


**Figure 6.** Fluorescence spectra of Nile Red (a) in a 0.2 wt % aqueous solution of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07) at various temperatures during the heating process and (b) in a series of aqueous solutions of BR-**4** with different concentrations at 32 °C. The inset in (a) is the plot of maximum fluorescence intensity vs temperature, from which the critical micellization temperature ($CMT_I$) was determined. The inset in (b) is the plot of maximum fluorescence intensity vs polymer concentration at 32 °C, from which the critical micelle concentration (CMC) was determined.

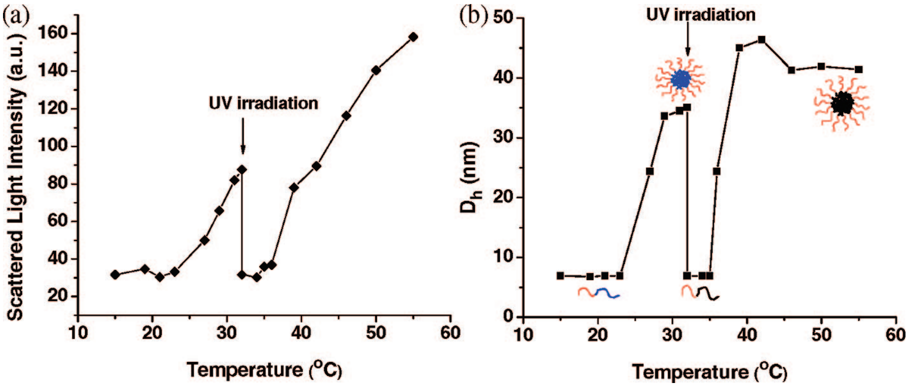


**Figure 7.** Intensity of scattered light at scattering angle of 90° (a) and hydrodynamic diameter (b) as a function of temperature in a dynamic light scattering study of multiple micellization and dissociation transitions of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07, 0.2 wt % aqueous solution—the same solution used in Figure 4) in response to temperature changes and UV irradiation. The data points from 15 to 32 °C before UV irradiation were from the heating process in Figure 4. At 32 °C, the polymer solution was irradiated with 365 nm UV light for 480 min. The collection of light scattering data was resumed thereafter. In (b), at 27, 36, 39, and 42 °C, two size distributions, one attributed to the unimers and one to the micellar aggregates, were observed, and the reported hydrodynamic diameters at these temperatures were the average values over two hydrodynamic size distributions.

intensity of scattered light continued to increase with the increase of temperature, similar to the observations for the micelles of BR-**4**, BR-**5**, and B-**3**. The polydispersity of micelles at 50 °C was 0.062.[74] The nearly independence of $\Gamma/q^2$ on scattering angle at 50 °C suggested that the micelles were spherical (Figure 5b).

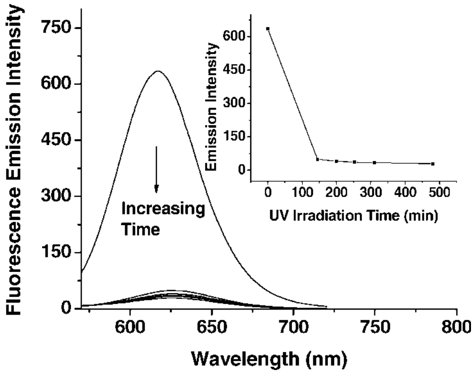


**Figure 8.** Fluorescence spectra of Nile Red in a 0.2 wt % aqueous solution of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07) after exposure to 365 nm UV light at 32 °C for 0, 145, 199, 253, 311, and 480 min. The inset is the plot of maximum fluorescence emission intensity vs UV irradiation time. The wavelengths of the maximum peak were 617 nm (0 min), 625 nm (145 min), 626 nm (199 min), 625 nm (253 min), 628.5 nm (311 min), and 625 nm (480 min).

The UV-induced dissociation of micelles of BR-**4** was further studied by FS. Figure 8 shows the fluorescence emission spectra of Nile Red in a 0.2 wt % aqueous micellar solution of BR-**4** at 32 °C after UV irradiation for various times. In only 140 min, the fluorescence intensity at the maximum peak decreased dramatically. Further increasing the irradiation time did not change the emission intensity significantly. The maximum peak underwent a red shift from 617 nm at 0 min to 625 nm at 480 min, which indicated that the dye molecules were transferred from a hydrophobic to a hydrophilic environment. Note that the maximum fluorescence intensity after UV irradiation for 140 min was much lower than that of Nile Red in the solution of BR-**4** below the CMT before UV irradiation (Figure 6a), which is likely due to the photobleaching. To confirm it, we performed a control experiment. A 0.2 wt % aqueous micellar solution of B-**3** loaded with Nile Red was irradiated at 45 °C with 365 nm UV light for 500 min. Figure 9 shows the fluorescence emission spectra at various irradiation times. No change was observed at 58 min. With increasing the irradiation time, the fluorescence intensity decreased but at a slower pace compared with that in Figure 8. We decreased the temperature to 15 °C and then gradually increased it and recorded the fluorescence spectra of the photobleached Nile Red dye. The CMT was found at 38 °C (Figure 9b), essentially identical to that of B-**3** before UV irradiation, indicating that the photobleaching did not affect the

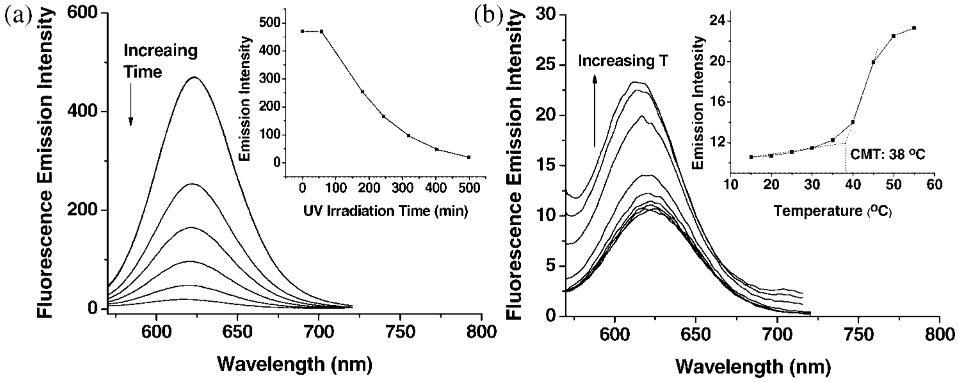


**Figure 9.** Fluorescence spectra of (a) Nile Red in a 0.2 wt % aqueous solution of PEO-*b*-PTEGEA (B-**3**, $M_{n,GPC}$ = 21 400 g/mol, PDI = 1.07) after exposure to 365 nm UV irradiation for 0, 58, 180, 244, 319, 403, and 500 min and (b) photobleached Nile Red in the UV-irradiated solution of B-**3** at various temperatures during the heating process. The inset in (a) is the plot of maximum fluorescence emission intensity vs UV irradiation time. The inset in (b) is the plot of maximum fluorescence intensity vs temperature, from which the CMT was determined.

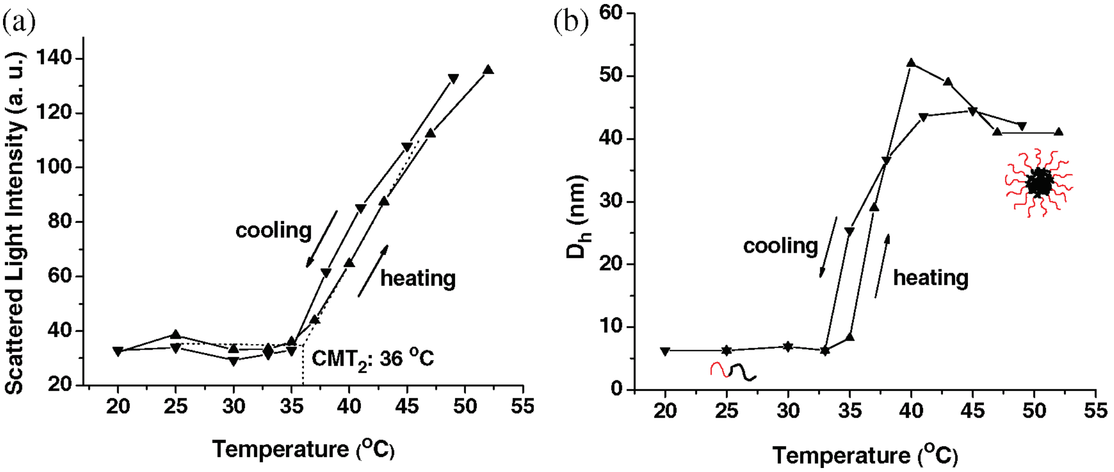


**Figure 10.** Intensity of scattered light at scattering angle of 90° (a) and hydrodynamic diameter (b) as a function of temperature ((▲) heating, (▼) cooling) in a dynamic light scattering study of thermo-induced reversible formation and dissociation of micelles of PEO-*b*-P(TEGEA-*co*-AA), which was obtained in situ by UV irradiation of a 0.2 wt % aqueous solution of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07) for 480 min. In (b), at 37, 40, and 43 °C in the heating process and at 38 and 35 °C in the cooling process, two size distributions, one attributed to the unimers and one to the micellar aggregates, were observed, and the reported hydrodynamic diameters at these temperatures were the average values over two hydrodynamic size distributions.

determination of CMT, though the emission intensity was much lower.

The UV irradiation-induced dissociation of micelles of BR-**5** was conducted at 30 °C.[74] After 480 min, the intensity of scattered light at scattering angle of 90° decreased to the level for the polymer solution below the CMT$_1$ before UV irradiation, and the hydrodynamic size decreased to <7 nm, indicating that the micelles dissociated into the unimers. Further increasing temperature induced the formation of micelles again, similar to the observation for thermo- and light-induced micellization and dissociation of BR-**4**.

**Temperature-Induced Reversible Formation and Dissociation of Micelles of PEO-*b*-P(TEGEA-*co*-AA).** As for the micellization of BR-**4**, the thermo-induced formation of micelles of PEO-*b*-P(TEGEA-*co*-AA) was reversible. Figure 10 shows the DLS data for the cooling-induced dissociation of micelles and the heating-induced micellization. In the heating process, when the temperature was above 35 °C, the intensity of scattered light at scattering angle of 90° began to increase. The CMT$_2$ was found at 36 °C. At temperatures >43 °C only micelles were observed, and the hydrodynamic size became stabilized at ~41 nm with further increasing the temperature.

The thermo-induced reversible formation and dissociation of micelles of PEO-*b*-P(TEGEA-*co*-AA) was then studied by FS. The 0.2 wt % aqueous micellar solution of BR-**4** loaded with Nile Red was irradiated at 32 °C for 480 min (Figure 7) and then cooled to 16 °C. Figure 11a shows the fluorescence spectra of photobleached Nile Red in this solution at various temperatures in the heating process. Above 40 °C, the fluorescence emission intensity began to increase. The maximum peak shifted from 625.5 nm at 16 °C to 618 nm at 51 °C, suggesting that the dye molecules were re-encapsulated in the hydrophobic core of the micelles. The control experiment with PEO-*b*-PTEGEA showed that the UV-induced photobleaching did not affect the determination of CMT. However, the CMT$_2$ determined from FS analysis was 41 °C (Figure 11a), 5 °C higher than that from DLS. Since the core contained hydrophilic carboxylic acid groups and the fluorescence intensity of Nile Red is sensitive to the polarity of the environment, a higher temperature might be required for the fluorescence emission intensity of the dye to begin to increase. The micellization was reversible. Decreasing the temperature resulted in the dissociation of micelles and the decrease of fluorescence emission intensity.[74] The maximum peak underwent a red shift from 619 nm at 48 °C to 625 nm at 25 °C, which indicated that Nile Red was released into water.

Because of the photobleaching, the fluorescence emission intensity in Figure 11a was very low even at $T$ > 50 °C. To better demonstrate the re-encapsulation of Nile Red by the micelles of PEO-*b*-P(TEGEA-*co*-AA) at temperatures higher than CMT$_2$, we transferred the polymer solution into a vial that

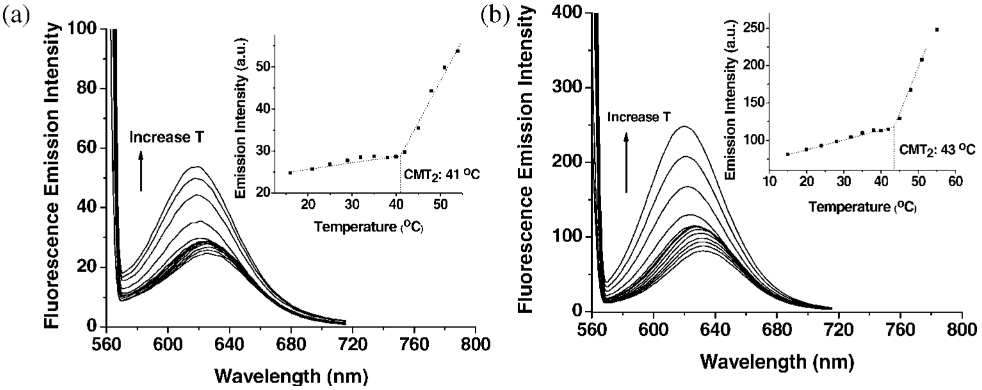


**Figure 11.** Fluorescence spectra of (a) photobleached Nile Red and (b) photobleached dye plus reloaded fresh Nile Red in an aqueous solution of PEO-*b*-P(TEGEA-*co*-AA) at various temperatures in the heating process. The aqueous solution of PEO-*b*-P(TEGEA-*co*-AA) was obtained in situ by UV irradiation of a 0.2 wt % aqueous solution of PEO-*b*-P(TEGEA-*co*-NBA) (BR-**4**, $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07) at 32 °C for 480 min. The insets are the plots of maximum fluorescence emission intensity vs temperature, which are used to determine the $CMT_2$.

**Table 3. Critical Micellization Temperatures and Micelle Characteristics of PEO-*b*-P(TEGEA-*co*-AA) Obtained from BR-4 and -5 by UV Irradiation**

| PEO-*b*-P (TEGEA-*co*-AA) | $CMT_{2\text{-DLS}}$[a] (°C) | micelle size[b] | PD[c] | $CMT_{2\text{-FS}}$[d] (°C) |
|---|---|---|---|---|
| obtained from BR-**4** | 36 | 41.9 nm (50 °C) | 0.062 (50 °C) | 41 |
| obtained from BR-**5** | 34 | 45.6 nm (50 °C) | 0.013 (50 °C) | 39 |

[a] The critical micellization temperature of PEO-*b*-P(TEGEA-*co*-AA) ($CMT_{2\text{-DLS}}$) was determined by dynamic light scattering (DLS). [b] The size of micelles was obtained by the use of the CONTIN method. [c] The polydispersity (PD) of micelles at a specific temperature. [d] The critical micellization temperature ($CMT_{2\text{-FS}}$) was determined by fluorescence spectroscopy (FS).

contained fresh Nile Red. Figure 11b shows the fluorescence spectra of the reloaded Nile Red plus the photobleached dye at various temperatures in the heating process. The emission intensity of the dye was much higher at 20 °C than that of the photobleached dye (Figure 11a) and increased substantially with the increase of temperature to 55 °C. The $CMT_2$ determined from this plot was 43 °C, slightly higher than that determined from Figure 11a. Moreover, the maximum peak shifted from 633 nm at 15 °C to 620 nm at 55 °C, implying that the dye molecules were encapsulated in the micelle core. Lowering the temperature caused the fluorescence emission intensity to decrease with the release of dye into water.[74]

The PEO-*b*-P(TEGEA-*co*-AA) obtained from the photocleavage of BR-**5** was also investigated.[74] DLS study showed that the $CMT_2$ was 34 °C. The size of micelles at 50 °C was 45.6 nm, which was about 10 nm larger than that of micelles of BR-**5** at 30 °C before UV irradiation. The micelles were spherical as implied by the nearly independence of $\Gamma/q^2$ on $q^2$ at 50 °C. These observations were similar to the results obtained from BR-**4**. The $CMT_2$, determined by FS, was 39 °C, which was 5 °C higher than that from DLS. Regardless of what technique was used for the determination of CMT, the $CMT_2$ of the higher molecular weight block copolymer was lower, which is reasonable because higher molecular weight thermosensitive water-soluble polymers tend to undergo the hydration-to-dehydration transition at a lower temperature.[67] Table 3 summarizes the values of $CMT_2$ and micelle characteristics for the two samples after UV irradiation.[74]

## Conclusion

In summary, we demonstrated thermo- and light-induced multiple formation and dissociation of micelles of PEO-*b*-P(TEGEA-*co*-NBA). Well-defined block copolymers that contained photosensitive NBA units in the thermosensitive blocks were synthesized by ATRP of a mixture of TEGEA and NBA with a molar ratio of 100:10 from macroinitiator PEO-Br. DLS and FS studies showed that the block copolymers underwent reversible micellization of micelles in response to temperature changes. The micelles had hydrodynamic sizes of ~35 nm, narrow polydispersities, and spherical shapes. The CMCs were found to be much lower than that of PEO-*b*-PTEGEA. Upon UV irradiation, the *o*-nitrobenzyl groups were cleaved, and the LCST of the thermosensitive block was increased by ≥11 °C, triggering the dissociation of micelles into unimers and the release of encapsulated molecules into water at appropriate temperatures. With further increasing the temperature above the LCST of the new thermosensitive block, micellization occurred again, and the released Nile Red was re-encapsulated by the micelles. Since *o*-nitrobenzyl group can be cleaved via two-photon absorption of near-IR light,[32] these thermo- and light-sensitive block copolymers might be of interest for targeted drug delivery.

## Experimental Section

**Materials.** Tri(ethylene glycol) monoethyl ether (technical grade) and poly(ethylene glycol) monomethyl ether (PEO-OH, MW = 5000 g/mol) were purchased from Aldrich and used as received. 2-Nitrobenzyl alcohol (98%), triethylamine (99%), acetone (HPLC grade), and Nile Red (99%) were obtained from Acros and used without further purification. Acryloyl chloride (96%, Alfa Aesar) was used as received. Dichloromethane and anisole (99%, Acros) were distilled from calcium hydride and stored in solvent storage flasks prior to use. Toluene was distilled from sodium and benzophenone and used immediately. *N,N,N′,N′,N″*-Pentamethyldiethylenetriamine (PMDETA, Aldrich) and ethyl 2-bromoisobutyrate (EBiB, Aldrich) were distilled over calcium hydride under reduced pressure. CuBr (98%, Aldrich) was purified according to the procedure described in the literature[78] and was stored in a desiccator. All other chemicals were purchased from either Aldrich or Fisher and used without purification.

**General Characterization.** Gel permeation chromatography (GPC) was carried out at room temperature using PL-GPC 20 (an integrated GPC system from Polymer Laboratories, Inc.) with a refractive index detector, one PLgel 5 μm guard column (50 × 7.5 mm), and two PLgel 5 μm mixed-C columns (each 300 × 7.5 mm, linear range of molecular weight from 200 to 2 000 000 according to Polymer Laboratories). The data were processed using Cirrus GPC/SEC software (Polymer Laboratories). THF was used as the carrier solvent at a flow rate of 1.0 mL/min. Standard monodisperse polystyrenes (Polymer Laboratories) were used for calibration. The $^1H$ (300 MHz) and $^{13}C$ (75 MHz) spectra were recorded on a Varian Mercury 300 NMR spectrometer, and the residual solvent proton signal was used as the internal standard. Mass spectroscopy was performed at the Mass Spectrometry Center of the Department of Chemistry at the University of Tennessee at Knoxville using a PE

Sciex QSTAR XL triple quadrupole time-of-flight (QTOF) mass spectrometer (Concord, Ontario, Canada) with an electrospray ionization source. The cloud points of thermosensitive polymers in water were measured by turbidimetry. The optical transmittances of aqueous polymer solutions at various temperatures were recorded at wavelength of 550 nm with a UV–vis spectrometer (Biomate 5 from Thermospectronic). The sample cell was thermostatted with an external water bath of a Fisher Scientific Isotemp refrigerated circulator. At each temperature, the solutions were equilibrated for 5 min.

**Preparation of Aqueous Polymer Solutions for Dynamic Light Scattering and Fluorescence Spectroscopy Studies.** The polymers were dried under vacuum at 40 °C for >3 h. An aqueous solution of a polymer with a desired concentration was prepared either by direct addition of water into the small vial that contained the weighed polymer or by dilution of a polymer solution with a known concentration. The polymer solutions were sonicated in an ultrasonic ice/water bath for 5 min to ensure complete dissolution. The polymer solutions that contained Nile Red for fluorescence spectroscopy studies were made by the following procedure. 10 $\mu$L of a stock solution of Nile Red in acetone (concentration: 0.042 mg/mL) was added into an empty vial via a microsyringe, which was then placed in vacuum for >3 h to remove the solvent. A calculated amount of a stock aqueous polymer solution (1.0 wt %) was added into the vial, and a certain amount of deionized water was added to bring the total weight of the solution to 2.00 g. The nominal concentration of Nile Red was $6.6 \times 10^{-7}$ M. The solution was allowed to equilibrate at a specific temperature for >3 h before the fluorescence spectroscopy study.

**Dynamic Light Scattering.** Dynamic light scattering (DLS) measurements were conducted with a Brookhaven Instruments BI-200SM goniometer equipped with a PCI BI-9000AT digital correlator, a temperature controller, and a solid-state laser (model 25-LHP-928-249, $\lambda = 633$ nm) at a scattering angle of 90°. The copolymer solutions were filtered into borosilicate glass tubes with an inner diameter of 7.5 mm by the use of Millipore Teflon filters (0.2 $\mu$m pore size). The glass tubes were then sealed with a PE stopper. At each temperature, the solutions were equilibrated for 15 min prior to data recording. The second-order correlation function of the scattered light intensity, $g^{(2)}(t)$, was analyzed by the CONTIN method. $g^{(2)}(t)$ can be expressed by the following equation

$$g^{(2)}(t) = A(1 + \beta|g^{(1)}(t)|^2) \tag{1}$$

where $A$ is the baseline, $\beta$ is the coherence factor determined by the geometry of the detection, and $g^{(1)}(t)$ is the normalized electric field correlation function. Generally, $g^{(1)}(t)$ is expressed by the distribution function $G(\Gamma)$ as

$$|g^{(1)}(t)| = \int G(\Gamma) \exp(-\Gamma t)\, d\Gamma \tag{2}$$

For a translational diffusion mode, $\Gamma$ can be used to determine the diffusion coefficient $D$ through $\Gamma = Dq^2$, where $q$ is the scattering vector. The hydrodynamic diameter $D_h$ is related to the diffusion coefficient $D$ by the Stokes–Einstein equation

$$D = k_B T/(3\pi\eta D_h) \tag{3}$$

where $k_B$ is the Boltzmann constant, $T$ is the absolute temperature, and $\eta$ is the viscosity of the solvent.

**Fluorescence Spectroscopy.** Fluorescence emission spectra were recorded from Perkin-Elmer LS 55 fluorescence spectrometer equipped with a 20 kW xenon discharge lamp. The excitation wavelength was 550 nm, and the fluorescence emission spectra were recorded from 560 to 720 nm. The slit width was 10 nm. The sample cell was thermostatted with an external water bath of a Fisher Scientific Isotemp refrigerated circulator. At each temperature, the sample was equilibrated for 10 min.

(1) Determination of critical micellization temperature (CMT). The fluorescence emission spectra of Nile Red in a 0.2 wt % aqueous polymer solution at various temperatures were recorded. At each temperature, the solution was equilibrated for 10 min. The maximum fluorescence intensities were plotted against temperatures for the determination of CMT.

(2) Determination of critical micelle concentration (CMC). A series of aqueous polymer solutions with different concentrations that were loaded with the same amounts of Nile Red were made. The fluorescence emission spectra of Nile Red in these solutions at a specific temperature were recorded. The maximum fluorescence intensities were then plotted against the logarithm of polymer concentrations for the determination of CMC.

(3) Reloading of Nile Red into the polymer solution after UV irradiation for 480 min and the determination of CMT. 10 $\mu$L of a stock solution of Nile Red in acetone (concentration: 0.042 mg/mL) was added into an empty vial via a microsyringe, which was then placed in high vacuum for >3 h to remove the solvent. The 0.2 wt % aqueous solution of BR-**4** that was irradiated with 365 nm UV light for 480 min was transferred into the vial. The solution was allowed to equilibrate at 32 °C for >3 h. The fluorescence emission spectra were then recorded at various temperatures for the determination of CMT.

**Synthesis of Ethoxytri(ethylene glycol) Acrylate (TEGEA).** A solution of tri(ethylene glycol) monoethyl ether (40.8 g, 0.229 mol) and triethylamine (21.6 g, 0.214 mol) in dichloromethane (50 mL) was stirred under nitrogen atmosphere in a 250 mL three-necked flask in an ice/water bath. A solution of acryloyl chloride (16.1 g, 0.178 mol) in dichloromethane (20 mL) was added dropwise into the flask from an additional funnel. The reaction mixture was warmed to room temperature and stirred overnight. The precipitate was filtered off, and the filtrate was washed sequentially with an aqueous solution of sodium bicarbonate (50 mL), water (50 mL), and a saturated aqueous solution of NaCl. The organic layer was separated and dried over anhydrous sodium sulfate. The crude product was purified by silica gel column chromatography with ethyl acetate as eluent. The product was further purified by vacuum distillation (90 °C/30 mTorr) with addition of a small amount of hydroquinone as inhibitor. The monomer was then dissolved in dichloromethane (150 mL) and washed with 0.1 M aqueous solution of NaOH until the aqueous layer became colorless. The organic layer was subsequently washed with water to neutral and dried over anhydrous sodium sulfate. The product was obtained as a colorless liquid (25.5 g, yield: 62%). $^1$H NMR ($CDCl_3$): $\delta$ (ppm) 6.37 (dd, 1H, $\mathit{CH}H{=}CH-$), 6.10 (dd, $CHH{=}\mathit{CH}-$), 5.78 (dd, $CH\mathit{H}{=}CH-$), 4.25 (t, 2H, $-COO\mathit{CH_2}-$), 3.70–3.50 (m, 10H, $-\mathit{CH_2}O-$), 3.46 (q, 2H, $-O\mathit{CH_2}CH_3$), 1.14 (t, 3H, $-OCH_2\mathit{CH_3}$). $^{13}$C NMR ($CDCl_3$): $\delta$ (ppm) 166.04 ($-\mathit{C}OOCH_2-$), 130.93 ($\mathit{C}H_2{=}CH-$), 128.14 ($CH_2{=}\mathit{C}H-$), 70.58, 70.49, 70.46, 69.69, 68.97 ($-\mathit{C}H_2O-$), 66.51 ($-O\mathit{C}H_2CH_3$), 63.58 ($-COO\mathit{C}H_2-$), 15.05 ($-OCH_2\mathit{C}H_3$). MS (ES): 255.0 ([M + Na$^+$]).

**Synthesis of *o*-Nitrobenzyl Acrylate (NBA).** 2-Nitrobenzyl alcohol (2.56 g, 16.7 mmol) and triethylamine (2.59 g, 25.6 mmol) were dissolved in dichloromethane (30 mL) in a 100 mL flask, which was then placed in an ice/water bath. A solution of acryloyl chloride (2.02 g, 22.3 mmol) in $CH_2Cl_2$ (10 mL) was added dropwise into the flask under $N_2$ from an additional funnel over a period of 10 min. After 24 h, the reaction mixture was poured into a separatory funnel and sequentially washed with an aqueous solution of $NaHCO_3$ (30 mL), $H_2O$ (30 mL), and a saturated aqueous solution of NaCl (40 mL). The organic layer was separated and dried over anhydrous $Na_2SO_4$ overnight. The solvent was removed by a rotavapor, and the crude product was purified by silica gel column chromatography with ethyl acetate and hexanes (v/v, 1:4) as eluent. The pure product was obtained as a light yellow liquid (3.16 g, yield: 92%). $^1$H NMR ($CDCl_3$): $\delta$ (ppm) 8.09 (d, 1H, aromatic), 7.66–7.44 (m, 3H, aromatic), 6.47 (dd, 1H, $\mathit{CH}H{=}CH-$), 6.19 (dd, 1H, $CHH{=}\mathit{CH}-$), 5.90 (dd, 1H, $CH\mathit{H}{=}CH-$), 5.58 (s, 2H, $-\mathit{CH_2}O-$). $^{13}$C NMR ($CDCl_3$): $\delta$ (ppm) 165.38 ($-\mathit{C}OO-$), 147.07, 133.73, 132.09, 128.81, 127.70, 125.01 (aromatic), 131.84 ($CH_2{=}\mathit{C}H-$), 128.72 ($\mathit{C}H_2{=}CH-$), 62.88 ($-COO\mathit{C}H_2-$); MS (ES): 229.9 ([M + Na$^+$]).

**Synthesis of PEO Macroinitiator PEO-Br.** Poly(ethylene glycol) monomethyl ether (PEO-OH, MW = 5000 g/mol, 13.0 g, 2.60 mmol) was added into a 500 mL three-necked flask. The trace amount of water was removed by azeotropic distillation with toluene (40 mL) under reduced pressure. The polymer was then dissolved in toluene (250 mL), followed by addition of triethylamine (1.05 g, 10.4 mmol). The flask was placed in an ice/water bath. 2-Bromoisobutyryl bromide (1.45 g, 6.31 mmol) was added dropwise into the flask through an additional funnel. After being stirred at room temperature for 24 h, the solution was treated with charcoal, which was subsequently removed by filtration. The solvent was removed by the use of a rotavapor, and the concentrated solution was precipitated in diethyl ether (100 mL). The crude product was dried under vacuum, redissolved in water, and then extracted with dichloromethane. The organic extracts were combined and dried over anhydrous sodium sulfate. The pure product was obtained after the solvent was removed in vacuum. $^1$H NMR ($CDCl_3$): $\delta$ (ppm) 4.28 (t, 2H, $-CH_2CH_2OC{=}O-$), 3.90–3.36 (m, $-CH_2O-$), 3.34 (s, 3H, $-OCH_3$), 1.90 (s, 6H, $-CBr(CH_3)_2$).

**Synthesis of PTEGEA by ATRP.** A typical procedure for the synthesis of PTEGEA by ATRP using ethyl 2-bromoisobutyrate (EBiB) as initiator is described below. CuBr (6.3 mg, 0.044 mmol), TEGEA (2.50 g, 10.8 mmol), anisole (1.27 g), PMDETA (6.8 mg, 0.039 mmol), and EBiB (9.3 mg, 0.048 mmol) were added into a two-necked flask. The mixture was stirred under $N_2$ atmosphere and degassed by three freeze–pump–thaw cycles. A sample was taken for $^1$H NMR spectroscopy analysis and the flask was immediately placed in a 90 °C oil bath. After the polymerization proceeded for 210 min, a sample was taken for $^1$H NMR spectroscopy analysis of monomer conversion. The reaction mixture was opened to air, diluted with THF, and passed through a neutral $Al_2O_3$ column with THF as eluent to remove the catalyst. The obtained polymer solution was concentrated and precipitated in hexanes (100 mL). The polymer was then dissolved in THF (3 mL) and precipitated again in hexanes. A colorless polymer was obtained. GPC analysis results (polystyrene standards): $M_{n,GPC} =$ 14 500 g/mol, polydispersity index (PDI) = 1.16. The degree of polymerization (DP) of the polymer was calculated from the monomer conversion and the monomer-to-initiator ratio. The integral values of the peak located at 4.25 ppm (from $-CH_2OOC-$ of monomer) and the peak at 4.15 ppm (from $-CH_2OOC-$ of polymer) were used for the calculation of monomer conversion. The calculated DP was 74.

**Synthesis of Random Copolymer of TEGEA and NBA by ATRP.** A typical procedure for the synthesis of P(TEGEA-*co*-NBA) by ATRP using EBiB as initiator is described below. CuBr (7.5 mg, 0.052 mmol), TEGEA (2.06 g, 8.88 mmol), NBA (0.182 g, 0.88 mmol), EBiB (8.9 mg, 0.046 mmol), anisole (0.91 g), and PMDETA (8.3 mg, 0.048 mmol) were added into a 25 mL two-necked flask. The mixture was stirred under $N_2$ atmosphere and degassed by three freeze–pump–thaw cycles. A sample was taken for $^1$H NMR spectroscopy analysis, and the flask was immediately placed in a 90 °C oil bath. After the polymerization proceeded for 305 min, a sample was taken for analysis of monomer conversion, and the reaction mixture was then diluted with THF. The catalyst was removed by passing the reaction mixture through a neutral $Al_2O_3$ column with THF as eluent. The obtained polymer solution was concentrated and precipitated in a mixture of hexanes and diethyl ether (v/v = 80:20, 100 mL). The polymer was then dissolved in THF (3 mL) and precipitated again in the mixture of hexanes and diethyl ether (v/v = 80:20, 100 mL). A nearly colorless polymer was obtained. GPC analysis results (polystyrene standards): $M_{n,GPC}$ = 13 900 g/mol, polydispersity index (PDI) = 1.13. The DP of the polymer was determined from the monomer conversion and the monomer-to-initiator ratio. The peaks located in the range of 4.0–4.6 ppm, which were from $-CH_2OOC-$ of monomer TEGEA and the TEGEA units in the polymer, were used as internal standard. The conversion was calculated from the integral values of the peaks from 6.0 to 5.7 ppm ($CHH{=}CH-$ from both NBA and TEGEA monomers) at $t = 0$ and 305 min. The DP was 75. The molar ratio of TEGEA and NBA units in the copolymer was calculated from the integral values of the peaks at 4.15 ($-CH_2OC{=}O-$ of the TEGEA unit in the copolymer) and 5.44 ppm ($-CH_2OC{=}O-$ of the NBA unit in the copolymer). The obtained value was 100:13.

**Synthesis of Diblock Copolymer PEO-*b*-PTEGEA by ATRP from Macroinitiator PEO-Br.** A typical procedure for the synthesis of PEO-*b*-PTEGEA by ATRP using macroinitiator PEO-Br is described below. CuBr (11.1 mg, 0.077 mmol), TEGEA (2.06 g, 8.88 mmol), PEO-Br (0.28 g, 0.054 mmol), anisole (0.90 g), and PMDETA (9.8 mg, 0.057 mmol) were added into a two-necked flask. The mixture was stirred under nitrogen atmosphere and degassed by three freeze–pump–thaw cycles. The flask was then placed in a 90 °C oil bath. The polymerization was stopped after 193 min. The reaction mixture was diluted with THF and passed through a neutral $Al_2O_3$ column with THF as eluent to remove the catalyst. The obtained polymer solution was concentrated and precipitated in hexanes (100 mL). The solvent was discarded, and THF (3 mL) was added to dissolve the polymer. The polymer was precipitated again in hexanes (100 mL). A colorless polymer was obtained. GPC analysis results (polystyrene standards): $M_{n,GPC} =$ 21 400 g/mol, PDI = 1.07. The DP of PTEGEA in the diblock copolymer was calculated from the NMR spectrum using the integral values of the peak from 4.0 to 4.5 ppm ($-CH_2OOC-$ of TEGEA unit) and the peaks from 3.2 to 3.9 ppm ($-OCH_2-$ from PEO and PTEGEA). The DP of PEO was 113. The calculated DP of PTEGEA was 92.

**Synthesis of Block Copolymer PEO-*b*-P(TEGEA-*co*-NBA) by ATRP Using Macroinitiator PEO-Br as Initiator.** A typical procedure for the synthesis of PEO-*b*-P(TEGEA-*co*-NBA) is described below. CuBr (7.1 mg, 0.049 mmol), TEGEA (2.14 g, 9.22 mmol), PEO-Br (0.23 g, 0.045 mmol), NBA (0.186 g, 0.90 mmol), anisole (1.17 g), and PMDETA (9.9 mg, 0.057 mmol) were added into a 25 mL two-necked flask. After the mixture was degassed by three freeze–pump–thaw cycles, the flask was placed in a 90 °C oil bath. The polymerization was allowed to proceed for 172 min. The mixture was diluted with THF and passed through a neutral $Al_2O_3$ column with THF as eluent to remove the catalyst. The obtained polymer solution was concentrated and precipitated in a mixture of hexanes and diethyl ether (v/v = 60:40). The polymer was redissolved in THF and precipitated again in the mixture of hexanes and diethyl ether (v/v = 60:40). This purification process was repeated one more time. The polymer was then dried in high vacuum and obtained as a partially solidified liquid. GPC analysis results (polystyrene standards): $M_{n,GPC}$ = 18 300 g/mol, PDI = 1.07. The composition of the block copolymer was determined from the NMR spectrum. The number of TEGEA units in the block copolymer was calculated using the integral values of the peak from 4.0 to 4.5 ppm ($-CH_2OCO-$ of TEGEA unit) and the peaks from 3.2 to 4.0 ppm ($-OCH_2-$ from the PEO block and TEGEA unit). The obtained number of TEGEA units was 70. The number of NBA units was calculated from the integral values of the peak from 5.2 to 5.7 ppm ($-CH_2OOC-$ of NBA unit) and the peaks from 3.2 to 4.0 ppm ($-OCH_2-$ in the PEO block and TEGEA unit). The obtained number of NBA units was 9.

**Photocleavage of *o*-Nitrobenzyl Group.** The long wavelength (365 nm) UV light from a Spectroline ENF-240C hand-held UV lamp equipped with one 4 W long wavelength tube filtered at 365 nm and one short wavelength tube filtered at 254 nm was used for photocleavage of *o*-nitrobenzyl group. The typical intensity of the 365 nm UV light from this lamp is 300 $\mu$W/cm$^2$ at a distance of 15 cm. The vials or cuvettes or glass tubes that contained polymer solutions were placed in a water bath with a preset temperature and were irradiated with 365 nm UV light at a distance of ~2 cm. UV–vis spectrometry was used to monitor the photocleavage reaction by recording the UV–vis spectra at various irradiation times at a specific temperature.

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**Supporting Information Available:** UV–vis spectra of a 0.2 wt % aqueous solution of R-**2** after UV irradiation at 13 °C for various times; hydrodynamic diameter distribution function of BR-**4** in a 0.2 wt % aqueous solution at 27 °C in the cooling process; dynamic DLS study of multiple micellization and dissociation transitions of BR-**5** in water in response to temperature changes and UV irradiation; hydrodynamic diameter distribution function of BR-**5** in a 0.2 wt % aqueous solution at 30 °C in the heating process and plot of $\Gamma/q^2$ of micelles of BR-**5** at 30 °C vs $q^2$; DLS study of thermo-induced formation and dissociation of micelles of B-**3** in a 0.2 wt % aqueous solution; hydrodynamic diameter distribution function of micelles of B-**3** at 50 °C and plot of $\Gamma/q^2$ of micelles of B-**3** vs $q^2$ at 50 °C; fluorescence spectra of Nile Red in a 0.2 wt % aqueous solution of BR-**4** at different temperatures during the cooling process; fluorescence spectra of Nile Red in a 0.2 wt % aqueous solution of B-**3** at various temperatures during the heating process and in a series of aqueous solutions of B-**3** with different concentrations at 45 °C; fluorescence spectra of Nile Red in a 0.2 wt % aqueous solution of BR-**5** at various temperatures during the heating and cooling processes and in a series of aqueous solutions of BR-**5** with different concentrations at 30 °C; UV–vis spectra of an aqueous solution of BR-**4** with a concentration of 0.2 wt % after UV irradiation for various times at 32 °C; $^1$H NMR spectra of BR-**4** and the corresponding polymer obtained after UV irradiation at 32 °C for 400 min; hydrodynamic diameter distribution function of micelles of PEO-*b*-P(TEGEA-*co*-AA) obtained from BR-**4** at 50 °C; fluorescence spectra of photobleached Nile Red in the aqueous solution of PEO-*b*-P(TEGEA-*co*-AA) obtained from BR-**4** at various temperatures in the cooling process; fluorescence spectra of Nile Red (photobleached dye plus reloaded fresh Nile Red dye) in the aqueous solution of PEO-*b*-P(TEGEA-*co*-AA) obtained from BR-**4** at various temperatures in the cooling process; hydrodynamic diameter distribution function of PEO-*b*-P(TEGEA-*co*-AA) obtained from photocleavage of BR-**5** in the heating process and plot of $\Gamma/q^2$ of micelles of PEO-*b*-P(TEGEA-*co*-AA) vs $q^2$ at 50 °C; fluorescence spectra of photobleached Nile Red in the aqueous solution of PEO-*b*-P(TEGEA-*co*-AA) obtained from BR-**5** at various temperatures in the heating and cooling process. This material is available free of charge via the Internet at http://pubs.acs.org.

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