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Synthesis of Thermoresponsive Shell Cross-Linked Micelles via Living Cationic Polymerization and UV Irradiation

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ABSTRACT: A series of well-defined thermoresponsive poly(2-ethoxyethyl vinyl ether)-*block*-poly(2-hydroxyethyl vinyl ether) (PEOVE-*b*-PHOVE) block copolymers have been synthesized via sequential living cationic polymerization, containing methacryloyl groups derived from 2-(vinyloxy)ethyl methacrylate (VEM) in the PHOVE segment, PEOVE-*b*-P(HOVE/VEM). The ratio of EOVE/HOVE in the block copolymers was fixed at 1:2. The obtained PEOVE-*b*-P(HOVE/VEM) dissolved molecularly in aqueous solution, when below the lower critical solution temperature (LCST) of PEOVE. Upon heating above LCST of PEOVE, spherical micellization occurred, comprising of PEOVE cores and PHOVE shells. This was confirmed by dynamic light scattering (DLS) and ^{1}H NMR spectroscopy at various temperatures. The methacryloyl groups in the block copolymer are located around the surface of the PHOVE shells as a random copolymer of HOVE and VEM. The micelles were cross-linked by UV (254 nm) irradiation in water to obtain shell cross-linked (SCL) micelles. The SCL micelles were characterized by ^{1}H NMR spectroscopy, DLS, and atomic force microscopy. The micellar core was reversibly hydrated or dehydrated, depending on the solution temperature. The size of SCL micelles was controlled by molecular weight, with longer lengths leading to increased size of the SCL micelles, as expected. These SCL micelles served as nanoreactors for the synthesis of gold or silver nanoparticles prepared by in situ chemical reduction of Au(III) or Ag(I), respectively. The gold- or silver-loaded SCL micelles exhibited colloid stability, and the nanosized SCL micelle image containing the Au(0) was observed by transmittance electron microscopy.

Introduction

Micellar assemblies are of great fundamental interest and industrial importance. In particular, shell cross-linked (SCL) micelles are covalently stabilized supramolecular structures that combine some of the desirable properties of micelles, microgels, nanoparticles, and dendrimers.[1−12] The SCL micelle settled one fundamental problem with block copolymer micelles, which is spontaneous dissociation of micelle below critical micelle concentration (CMC). Wooley et al. reported the first paper on SCL micelles in 1996, where the SCL micelles were prepared from diblock copolymer based on both a hydrophobic polystyrene and a hydrophilic 4-(chloromethyl)styrene-quaternized poly(4-vinylpyridine).[1] Armes et al. successively reported the first example of stimuli-responsive SCL micelles with tunable core hydrophilicity, using an aqueous solution of poly[2-(dimethylamino)ethyl methacrylate]-*block*-poly-[2-(*N*-morpholino)ethyl methacrylate] (PDMA-*b*-PMEMA) reacted with a bis-functional cross-linker.[4] Following these two pioneering works, many examples for synthesis of SCL micelles have been reported from well-defined block copolymers using a variety of cross-linking techniques such as amidation,[6,7] quaternization,[4] Michael addition,[8] polyelectrolyte complexation,[9] UV-irradiation,[10] metal-catalyzed,[11] and click chemistry.[12] Furthermore, various functional applications such as targeted drug delivery, sequestration of metabolites, entrapment of environment pollutants, templates for the carbon nanoparticles, hybrid form using biomineralization, intelligent emulsifiers, and many other have been reported and reviewed.[2,3,5]

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The synthesis of well-defined block copolymers generally requires living polymerization technique. Recent progress in living polymerization has led to the design and synthesis of novel well-defined block copolymers and their applications. We have also developed living cationic polymerization such as metal-free methods[13,14] and the combination copolymerization[15] and have demonstrated the synthesis of hydrogel microspheres using UV-irradiation.[16] However, there have been no reports on SCL micelles prepared by living cationic polymerization until now.

In cationic polymerizable monomers, there is an interesting vinyl ether with a methacryloyl moiety, 2-(vinyloxy)ethyl methacrylate (VEM). It is impossible to polymerize the methacryloyl moieties by cationic polymerization, and cationically obtained poly(VEM) retained the metacryloyl groups intact.[16,17] The remaining methacryloyl moieties can be reacted with each other on exposure to UV (254 nm), which is used for facile and rapid cross-linking. There is no need for the preparation of any reaction sites on a polymer after polymerization and no need for the addition of any small molecule cross-linkers. Thus, cationic polymerization method using VEM is promising for SCL micelle formation.

On the other hand, poly(2-ethoxyethyl vinyl ether)-*block*-poly-(2-hydroxyethyl vinyl ether) (PEOVE-*b*-PHOVE) formed macrolattice of spherical micelles above LCST of PEOVE in relatively concentrated aqueous solution, as reported previously.[18] For 17 wt % of $EOVE_{200}$-*b*-$HOVE_{400}$ in D_2O, the size of the core and the aggregation number of diblock chains were 180−200 Å and 633 by SANS, respectively.[18,19] The thermoresponsive behavior is highly sensitive, reversible, and simple because of one-step transition between dissolved state and micelle. The block copolymer, PEOVE-*b*-PHOVE, is a good candidate for the first SCL

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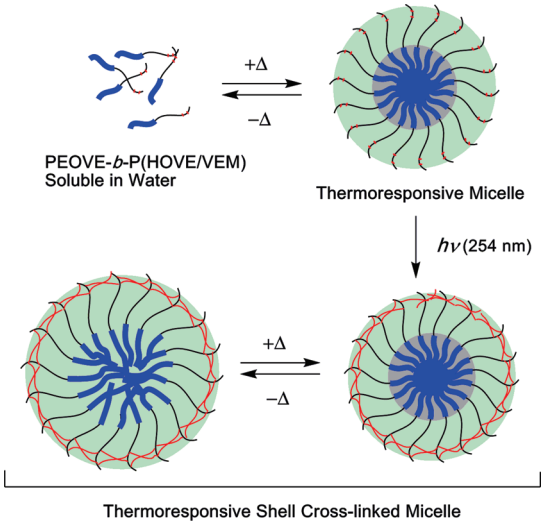
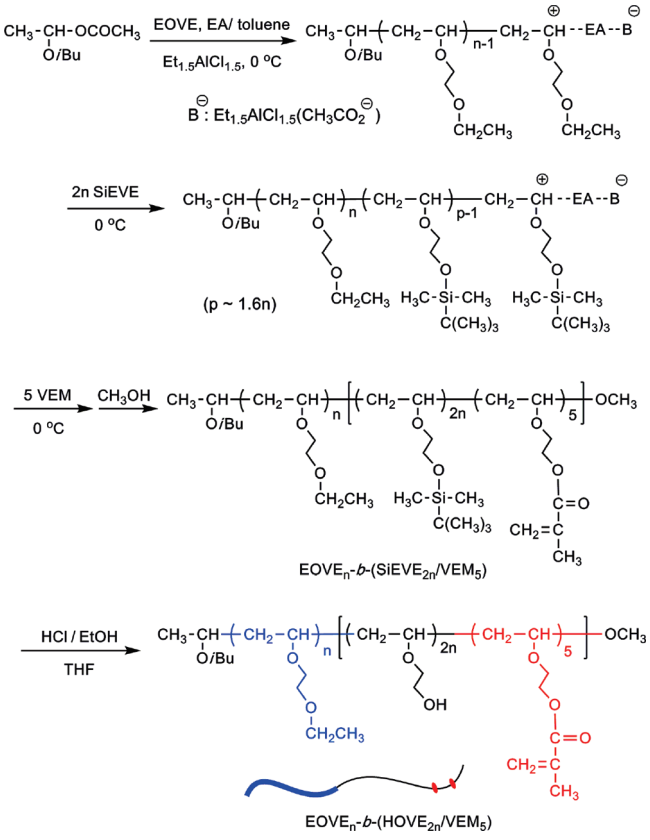


Figure 1. Reaction scheme for the synthesis of SCL micelles using PEOVE-*b*-P(HOVE/VEM) in water.

Scheme 1. Synthesis of PEOVE-*b*-P(HOVE/VEM) by Living Cationic Polymerization



micelle with tunable hydrophilic core prepared by living cationic polymerization.

Herein, we introduce an approach to synthesis of thermoresponsive shell cross-linked micelles via living cationic polymerization and UV irradiation. The formation of the SCL micelle comprising of PEOVE-*b*-P(HOVE/VEM) is depicted in Figure 1 as a schematic illustration. The block copolymers are based on PEOVE-*b*-PHOVE with methacryloyl groups derived from VEM in the PHOVE segment. The reaction scheme for the synthesis of PEOVE-*b*-P(HOVE/VEM) is shown in Scheme 1. The resulting SCL micellar core was reversibly hydrated or dehydrated, depending on the solution temperature, because an aqueous PEOVE solution undergoes LCST-type phase separation around 20 °C.[18,20] The effect of varying the molecular weight of the SCL micelles and the applications of the SCL micelles as stable nanoreactors of gold or silver were also investigated.

Experimental Section

Materials. 2-(*tert*-Butyldimethylsilyloxy)ethyl vinyl ether (SiEVE) was prepared from 2-hydroxyethyl vinyl ether (HOVE, Maruzen Petrochemical) as reported previously.[18] VEM was prepared from 2-chloroethyl vinyl ether as reported previously.[16] EOVE (donated by Maruzen Petrochemical) were washed with aqueous alkaline solution and then with water. These monomers were distilled twice over calcium hydride and were stored in a brown ampule under dry nitrogen. $Et_{1.5}AlCl_{1.5}$ (Aldrich; 1.82 M solution in toluene) was used as commercially supplied. Toluene was washed by the usual methods. The toluene and ethyl acetate were distilled over calcium hydride just before use. Cationogen (1-isobutoxyethyl acetate, IBEA) was prepared from isobutyl vinyl ether and acetic acid and was distilled over calcium hydride under reduced pressure.

Block Copolymerization Procedures. Polymerization was carried out at 0 °C under a dry nitrogen atmosphere in a glass tube equipped with a three-way stopcock baked at 250 °C for 10 min before use. The reaction was initiated by the addition of 200 mM $Et_{1.5}AlCl_{1.5}$ solution in toluene (1.0 mL) into a mixture of toluene (6.73−5.94 mL), EOVE (0.27−1.06 mL), ethyl acetate (EA, 1.0 mL), and 40 mM IBEA in hexane (1.0 mL) at 0 °C by a dry medical syringe (total conditions: $[EOVE]_0$ = 0.2−0.8 M, [ethyl acetate] = 1.0 M, $[IBEA]_0$ = 4.0 mM, $[Et_{1.5}AlCl_{1.5}]_0$ = 20 mM). After EOVE was polymerized, the second monomer SiEVE (1.08−4.30 mL, EOVE/SiEVE = 1/2 molar ratio) was added at 0 °C. The polymerization was monitored by ^{1}H NMR spectroscopy and by gravimetry using the batch method; the 80% conversion was determined using the both methods. At the time, next monomer 10% (v/v) toluene solution of VEM at 5.0 for VEM/IBEA molar ratio (0.031 mL) was added at 0 °C. After a certain period, the polymerization was quenched with prechilled methanol containing a small amount of aqueous ammonia solution (0.1 wt %). The quenched reaction mixture was diluted with dichloromethane and then washed with water to remove the initiator residues. The product polymer was recovered from the organic layer by evaporation of the solvents under reduced pressure and vacuum-dried overnight. The conversion of a monomer was determined by gravimetry. (All the monomer conversions were ~100%.) Desilylation of the product block copolymer was carried out in tetrahydrofuran at 0 °C by adding hydrochloric acid in ethanol solution: $[\text{block copolymer}]_0 = 2.1 \times 10^{-2}$ g/mL, $[HCl]_0$ = 0.3 M. The mixture was stirred at 0 °C for 1 h and then for an additional 3 h after a small amount of EtOH was added into it to change transparent solution. The mixture were neutralized, filtered off, and purified by reprecipitation into hexane. The product block copolymers were dialyzed against pure water in fridge for 3 days using a cellulose tube (SPECRTA/POR, corresponding to a cutoff molecular weight of 3500).

Polymer Characterization. Molecular weight distributions (MWDs) were assessed by size exclusion chromatography (SEC) in tetrahydrofuran (THF) at 38 °C using two polystyrene gel columns [TSK gel G-MH_{HR}-M × 2 (exclusion limit: 4×10^6 (polystyrene, PSt)); 7.8 mm i.d.×300 mm each; flow rate 1.0 mL/min] connected to a Tosoh CCPS dual pump and a RI-8011 refractive detector. The number-average molecular weight (M_n) and M_w/M_n were calculated from SEC curves on the basis of a polystyrene (PSt) calibration. ^{1}H NMR spectra for structure such as composition of block copolymers were recorded on a JEOL JNM-EX500 spectrometer (500 MHz).

Preparation of SCL Micelles. SCL micelles obtained from block copolymers were prepared at 1.0×10^{-3} g/mL dissolved in water (Mill-Q water). After the aqueous solution was degassed

in a quartz test tube, the solution was heated to 40 °C, and then the aqueous micellar solution was subjected to UV (254 nm) irradiation using a mercury lamp (120 W, Eikosha) for 40 min. For a SCL micelle formation, the approximate disappearance of the methacryl double bonds was confirmed by means of the same NMR spectrometer as that for the measurement of block copolymer composition.

Determination of Critical Micelle Solution Concentration (CMC) and Temperature (CMT). To a 10 mL of aqueous block copolymer solution at desired polymer concentration, 5.0 μL of 2,6-diphenyl-1,3,5-hexatriene (DPH) in THF ($[DPH]_0 = 10$ mM) was added. The solution was incubated for at least 30 min in the dark at the desired temperature before UV/vis absorption measurements. The absorbance at 356 nm was recorded from 5 and 80 °C at a rate of 1.0 °C/min on heating by means of a JASCO V-550 UV/vis spectrometer equipped with a Peltier-type thermostatic cell holder ETC-505.

Synthesis of Gold- and Silver-Nanoparticles Using SCL Micelles as Nanoreactors. For gold-loaded nanoparticles, an aqueous SCL micellar solution (0.01 wt %) was mixed with an aqueous solution of $HAuCl_4$ at 0.2 for $HAuCl_4$/EOVE molar ratio. After stirring for 30 min, an aqueous solution of excess $NaBH_4$ was added to the aqueous $HAuCl_4$/SCL micelle solution. The solution immediately turned from light yellow to wine red, indicating the formation of colloidal gold. For silver-loaded nanoparticles, $AgNO_3$ aqueous solution was used at the 0.2 for $AgNO_3$/EOVE molar ratio instead for $HAuCl_4$. The aqueous $AgNO_3$/SCL micelle solution was transparent and colorless. After adding an aqueous solution of excess $NaBH_4$, the solution turned from colorless to light yellow, indicating the formation of colloidal silver. The formation of these metallic nanoparticles was monitored by observing changes in the absorption spectra using the same UV/vis spectrometer as that for the measurement of CMC and CMT.

Characterization for SCL Micelles (DLS, AFM, and TEM). Dynamic light scattering (DLS) studies were performed on a DLS-7000 (Photal, Otsuka Electronics) at various temperatures. Intensity-average hydrodynamic diameter (D_h) of both non-cross-linked and SCL micelles in water were determined by cumulants analysis of the experimental correlation function. The light source was a He−Ne laser (10 mW, λ = 632.8 nm), and correlation function and the apparent (z-average) diffusion coefficient (D_{app}) for each solution was obtained as described in our previous paper[16] and the other.[21]

Samples for atomic force microscopy (AFM) imaging were prepared by depositing a drop of sample (5 μL, 0.5 wt % concentration) onto freshly cleaved mica at 40 °C and allowed to dry in air at the same temperature. AFM imaging were performed using a SII SPA300 (Seiko Instruments) under ambient conditions. The AFM image was taken with the DFM mode operating by SPI-3800N.

Transmission electron microscopy (TEM) measurements for gold-loaded SCL micelles were performed with a JEOL JEM-2000FX at an acceleration voltage of 200 kV. To prepare the TEM samples, a small drop of the sample solution was deposited onto a carbon-coated copper electron microscopy grid and dried under ambient temperature and atmospheric pressure.

Results and Discussion

Synthesis of PEOVE-*b*-P(SiEVE/VEM) by Living Cationic Polymerization. For aqueous PEOVE-*b*-PHOVE solutions, thermoresponsive micellization comprising PEOVE cores and PHOVE shells occurs above LCST of poly(EOVE). Since $EOVE_{200}$-*b*-$HOVE_{400}$ is allowed to form spherical micelles, the target ratio of EOVE/HOVE in the block copolymers was fixed at 1:2 in order to investigate the relationship between molecular weight and SCL micellar size without shape factors. The target length of VEM units was fixed at pentamer because of enough length for cross-linking by UV (254 nm) irradiation according to preliminarily investigation.[22] If VEM units were located at the outer side of the block copolymer as a PVEM block, the resulting assemblies could be formed either flowerlike micelles with both PEOVE and PVEM cores or open associations because of both hydrophobic PEOVE and PVEM. Therefore, VEM was located as a random sequence of HOVE and VEM around the surface of the PHOVE shells, PEOVE-*b*-P(HOVE/VEM). In other words, $EOVE_n$-*b*-$HOVE_{1.6n}$-*b*-($HOVE_{0.4n}$-*r*-VEM_5) (n = 50−200) was designed according to the synthetic route in Scheme 1. Since the HOVE is protected using a *tert*-butyldimethylsilyloxy group, the first target is PEOVE-*b*-P(SiEVE/VEM).

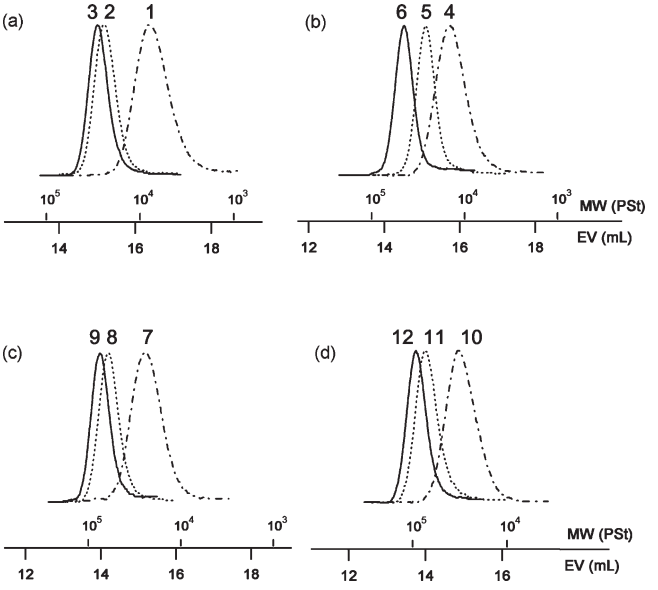


Figure 2. Molecular weight distribution curves for PEOVE-*b*-P(SiEVE/VEM) (3, 6, 9, and 12), their corresponding PEOVE (1, 4, 7, and 10) and PEOVE-*b*-PSiEVE (2, 5, 8, and 11) obtained with IBEA/$Et_{1.5}AlCl_{1.5}$ in toluene in the presence of ethyl acetate at 0 °C ($[IBEA]_0$ = 4.0 mM; $[Et_{1.5}AlCl_{1.5}]_0$ = 20 mM, [ethyl acetate] = 1.0 M, EOVE/SiEVE molar ratio = 1/2, $[VEM]_0$ = 20 mM): (a) $[EOVE]_0$ = 0.2, (b) 0.4, (c) 0.6, and (d) 0.8 M.

The sequential block copolymerization of EOVE, SiEVE, and VEM was examined with IBEA/$Et_{1.5}AlCl_{1.5}$ in toluene in the presence of ethyl acetate. The first-stage polymerization of EOVE proceeded smoothly without induction phase to reach almost complete conversion in 3.0, 3.7, 4.0, and 4.2 h for n = 50, 100, 150, and 200, respectively. The second monomer, SiEVE (neat), was then fed into the polymerization mixture at the same temperature. After SiEVE addition, the second polymerization began immediately and reached 80% conversion determined by ^{1}H NMR spectroscopy in 27, 27.4, 28, and 29 h for n = 50, 100, 150, and 200, respectively. VEM at 5.0 for VEM/IBEA molar ratio was finally added to the reaction mixture as a 10% (v/v) of toluene solution. The third-stage polymerization also proceeded smoothly to quantitative yield at 24 h for all polymerization. Figure 2 shows these SEC chromatograms during the syntheses of PEOVE-*b*-P(SiEVE/VEM). The broken line of the chromatogram shows the SEC trace of the PEOVE homopolymer just before the addition of SiEVE; the polymerization of the SiEVE was almost complete at this point (>98% conversion). The dotted line shows that of the $EOVE_n$-*b*-$SiEVE_{1.6n}$ diblock copolymer just before the addition of VEM; the polymerization of the SiEVE was 80% conversion at this point. The full line shows that of final PEOVE-*b*-P(SiEVE/VEM) block copolymers. At all stages, the M_n was shifted toward high molecular weight region after monomer

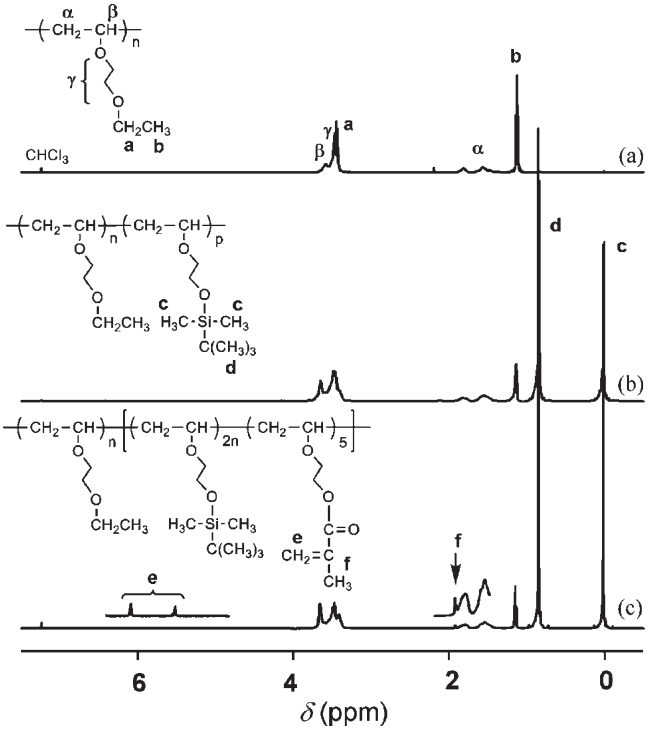


Figure 3. ^{1}H NMR spectra of (a) PEOVE (entry 10), (b) PEOVE-*b*-PSiEVE (entry 11), and (c) PEOVE-*b*-P(SiEVE/VEM) (entry 12) in $CDCl_3$ at 25 °C (n = 200).

addition, and all the resulting polymers have quite narrow MWDs.

Figure 3 depicts the ^{1}H NMR spectra recorded for the polymers at all stage for synthesis of PEOVE-*b*-P(SiEVE/VEM) (entries 10, 11, and 12). Composition of the final block copolymers was determined from the ^{1}H NMR spectroscopy before desilylation and was calculated from the peak intensity of the methyl protons of EOVE at 1.2 ppm (peak b), SiEVE at 0.1 and 0.9 ppm (peak c and d), and the methacryloyl moieties of VEM at 5.6 and 6.1 ppm (peak e) and 2.0 ppm (peak f) as shown in Figure 3. These peaks existence suggested that only vinyl ether-type polymerization occurred without the both polymerization of methacryloyl moieties and deprotection of the silyloxy pendants under those conditions as shown in Figure 3a−c. The observed compositions as shown in Table 1 were in good agreement with the monomer feed ratios in the target compositions, $EOVE_n$-*b*-($HOVE_{2n}$/VEM_5) (n = 50, 100, 150, and 200). In addition to the composition, the M_n and M_w/M_n values of the product copolymers, including their related polymers at all stages, are summarized in Table 1. SEC chromatograms and the compositions indicated that successful block copolymerizations were carried out under our conditions.

Desilylation of the PEOVE-*b*-P(SiEVE/VEM) was carried out with the addition of an aqueous HCl−EtOH in THF at 0 °C. Quantitative desilylation was confirmed by the disappearance of the methyl protons in silyloxy moieties with retaining the methacryloyl group of VEM in D_2O at 10 °C, as shown in Figure 4a. At 10 °C, all peaks are appeared at a high resolution regardless of composition. These results indicate that all desilylated products dissolved molecularly in water at 10 °C. The PEOVE-*b*-P(HOVE/VEM)s after desilylation are described as entries 3′, 6′, 9′, and 12′, which are corresponding to entries 3, 6, 9, and 12 of PEOVE-*b*-P(SiEVE/VEM) before desilylation.

Thermoresponsive Micellization in Water. The successful micellization was also confirmed by ^{1}H NMR spectroscopy

Table 1. Molecular Parameters of PEOVE, PEOVE-*b*-PSiEVE, and PEOVE-*b*-P(SiEVE/VEM) in This Study[a]

entry[b]	polymer structure[c]	M_n[d]	M_w/M_n[d]
1	$EOVE_{50}$	6000	1.18
2	$EOVE_{50}$-*b*-$SiEVE_{80}$	23 000	1.08
3	$EOVE_{50}$-*b*-($SiEVE_{99}$-VEM_5)	26 000	1.08
4	$EOVE_{100}$	12 000	1.13
5	$EOVE_{100}$-*b*-$SiEVE_{162}$	32 000	1.06
6	$EOVE_{100}$-*b*-($SiEVE_{192}$-VEM_4)	40 000	1.07
7	$EOVE_{150}$	18 000	1.13
8	$EOVE_{150}$-*b*-$SiEVE_{229}$	50 000	1.06
9	$EOVE_{150}$-*b*-($SiEVE_{288}$-VEM_4)	61 000	1.06
10	$EOVE_{200}$	24 000	1.13
11	$EOVE_{200}$-*b*-$SiEVE_{325}$	59 000	1.06
12	$EOVE_{200}$-*b*-($SiEVE_{401}$-VEM_5)	77 000	1.06

[a] Polymerization conditions: see Figure 2. [b] Entry no. corresponds to no. in Figure 2. [c] Determined by ^{1}H NMR spectroscopy in $CDCl_3$ on the basis of degree of polymerization (DP) of EOVE block. The DP of EOVE block was calculated from the feed molar ratio of monomer and IBEA. [d] Determined by SEC using polystyrene calibration standards.

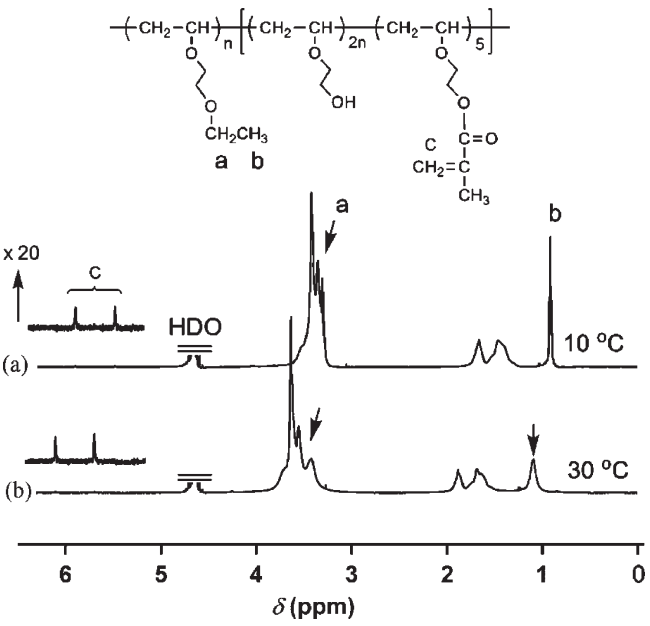


Figure 4. ^{1}H NMR spectra in D_2O of 1.0 wt % PEOVE-*b*-P(HOVE/VEM) (entry 12′, n = 200) obtained after desilylation of entry 12 at 10 °C (a) and at 30 °C (b).

at different temperatures. Figure 4b shows the ^{1}H NMR spectra of recorded for entry 12′ at 30 °C. At 10 °C, the representative signals for each block are present, indicating the block copolymers are fully solvated. While at 30 °C, the signals due to the PEOVE block at 1.1 ppm (peak b) and 3.4 ppm (peak a) are significantly broadened and slightly shifted toward downfield against HDO, indicating the formation of micelles comprised of PEOVE cores. While the signals due to the HOVE block and VEM at 5.6 and 6.1 ppm (peak c) maintained its sharpness. This is indicative of solvation of HOVE and VEM chains in the shell at 30 °C. This micelle formation was observed for all block copolymers (entries 3′, 6′, 9′, and 12′). The resulting micelle was reversibly formed or deformed, depending on the solution temperature, because an aqueous PEOVE solution undergoes LCST-type phase separation around 20 °C.[18,20]

To determine of an optimize condition for shell crosslinking, the critical micelle concentration (CMC) and critical micelle temperature (CMT) of PEOVE-*b*-P(HOVE/VEM) were determined employing a dye solubilization method.[18] For the measurements of CMC, the concentration of the sample

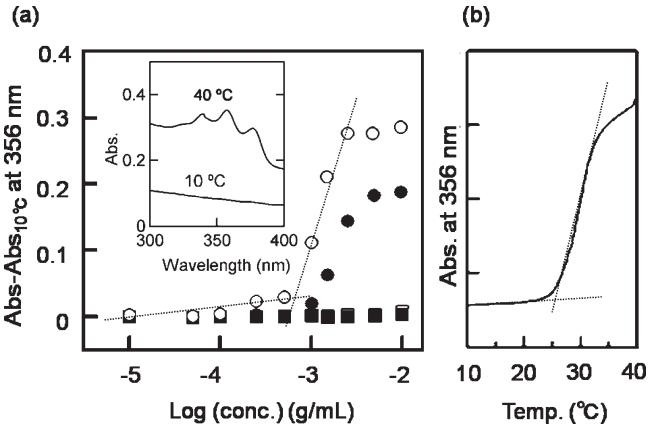


Figure 5. Determination of (a) CMC and (b) CMT of PEOVE-*b*-P(HOVE/VEM) (entry 3′) in aqueous solution by dye solubilization methods. (a) Difference absorption intensity at 356 nm between 10 °C and the monitored temperature (Abs − $Abs_{10\,°C}$), as a function of logarithm concentration at 40 (○), 30 (●), 23 (□), and 20 °C (■). Inset: UV/vis absorption spectra of DPH (5 μM) in a 5.0×10^{-3} g/mL of PEOVE-*b*-P(HOVE/VEM) aqueous solution at 10 and 40 °C. (b) Absorption intensity at 356 nm for DPH (5 μM) in a 5.0×10^{-3} g/mL PEOVE-*b*-P(HOVE/VEM) aqueous solution as a function of temperature. Heating rate: 1.0 °C/min.

Table 2. CMC and CMT of PEOVE-*b*-P(HOVE/VEM)

	CMC at 40 °C		CMT	
entry[a]	(g/L)	(μM)[b]	1.0×10^{-3} g/mL[c] (°C)	5.0×10^{-3} g/mL[c] (°C)
3′	0.74	48.0	28.2	26.1
6′	0.93	31.8	25.8	23.6
9′	0.55	12.6	23.7	20.8
12′	0.54	9.1	21.3	21.0

[a] Entries 3′, 6′, 9′, and 12′ correspond to desilylated 3, 6, 9, and 12, respectively. [b] Caluculated by the actual molecular weight of PEOVE-*b*-P(HOVE/VEM) using the polymer structure in Table 1. [c] Aqueous PEOVE-*b*-P(HOVE/VEM) concentration.

solution was adjusted ranging from 0.01 to 1.0×10^{-5} g/mL with DPH (5 μM). The absorbance of DPH in a solution of PEOVE-*b*-P(HOVE/VEM) was monitored by UV/vis spectrometry. DPH is a hydrophobic dye, which has characteristic absorbance at 356 nm. As block copolymers formed micelles, the DPH was preferred to partition into the core of micelles, thus increasing the absorbance. The different absorption intensity between 10 °C and the monitored temperature (Abs-$Abs_{10\,°C}$) at 356 nm was plotted against logarithmic concentration, and the crossing point of the extrapolated two straight lines was defined as the CMC as shown in Figure 5a. Figure 5b shows the plot of absorption intensity at 356 nm as a function of temperature to determine CMT as well as CMC. The CMC and CMT values of PEOVE-*b*-P(HOVE/VEM) are summarized in Table 2. The CMTs are in good agreement with the LCSTs of PEOVE. Furthermore, the CMC and CMT depend on the molecular weight. As molecular weight is increased from entry 3′ to entry 12′, the CMC at 40 °C decreased from 48.0 to 9.1 μM and the CMT decreased from 28.2 to 21.3 °C in 1.0×10^{-3} g/mL of aqueous polymer solution. The CMC and CMT of PEOVE-*b*-P(HOVE/VEM) are closed to that of PEOVE-*b*-PHOVE in water.[18] On the basis of these results, shell cross-linking by UV irradiation was, thus, carried out above CMC and CMT and at high dilution to avoid undesirable intermicellar cross-linking, which inevitably results in micelle fusion. In practice, insoluble gel was partly prepared at high concentration (~10% solid). On the other hand, below CMC and CMT, no SCL micelles were obtained.

Synthesis of SCL Micelles by UV irradiation. Shell cross-linking micelles can be prepared by UV irradiation (254 nm).

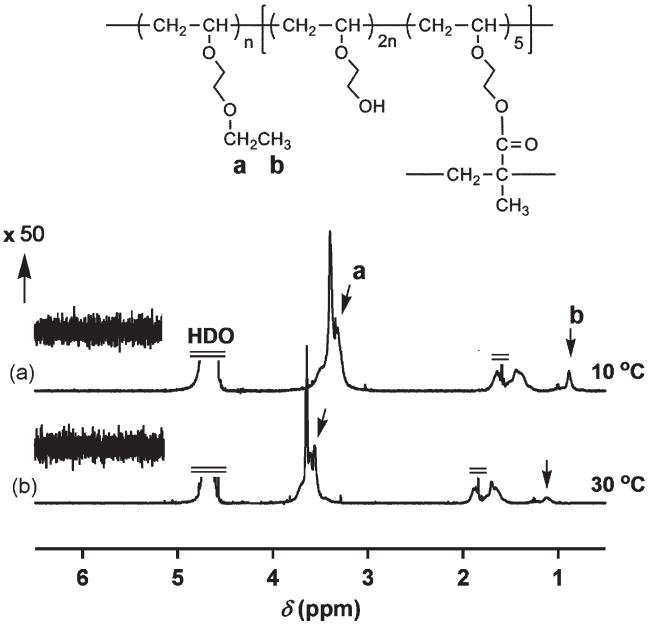


Figure 6. ^{1}H NMR spectra in H_2O/D_2O of 0.5 wt % SCL micelle prepared from entry 12′ (n = 200) at 10 °C (a) and at 30 °C (b).

The UV-induced cross-linking is facile under mild conditions because of aqueous solution, no addition of any small molecule cross-linkers, and no purification after cross-linking. The UV-induced cross-linking reaction was performed at 40 °C using 1.0×10^{-3} g/mL of synthesized PEOVE-P(HOVE/VEM)s in water. The concentration is over CMC and the temperature is set over CMT, as shown in Table 2. The reaction reaches 100% conversion after 40 min, which confirmed by the approximate disappeared of $CH_2=$ of a methacryloyl group (around 5.5−6.5 ppm) and remained another peaks by means of ^{1}H NMR spectroscopy in H_2O/D_2O at 30 °C, as shown in Figure 6b. At 10 °C, the signal due to PEOVE (signals a and b in Figure 6) changed to be slightly sharp, indicating the now-hydrophilic PEOVE core. The results indicate that thermoresponsibility was maintained even after cross-linking. In addition, the formed micelles were stable in water over a month because no precipitation was observed after cross-linking. Thus, the cross-linking chemistry hardly leads to reduced hydrophilicity of the cross-linking chains due to random copolymerization of HOVE and VEM.

Figure 7 shows the DLS size distributions for the non-cross-linked micelle formed by entry 12′ at 40 °C and the SCL micelle at 10 and at 40 °C. On the basis of these results, Table 3 summarizes DLS studies of the non-cross-linked micelles and the SCL micelles obtained from a series of PEOVE-*b*-P(HOVE/VEM) with different molecular weight but approximately constant EOVE/HOVE molar ratio and VEM length. At 10 °C, PEOVE-*b*-P(HOVE/VEM)s were molecularly dissolved in water, and DLS confirmed very weak light scattering in all cases. As expected, at 40 °C, which is the same temperature as that in shell cross-linking, adjusting the temperature to above the CMT produced much more intense light scattering due to formation of micelles. As molecular weight of PEOVE-*b*-P(HOVE/VEM) was increased from entry 3′ to entry 12′, the intensity average diameter (D_h) of the non-cross-linked micelle increased from 47 to 83 nm. For SCL micelles, similar phenomena were observed compared to the non-cross-linked micelles. As the molecular weight of corresponding PEOVE-*b*-P(HOVE/VEM) was increased from entry 3′ to entry 12′, the SCL micelles size

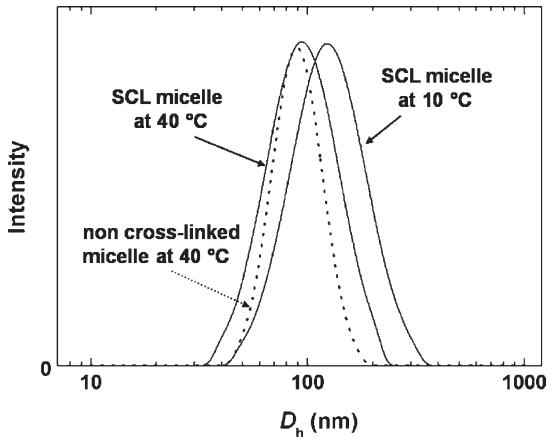


Figure 7. DLS size distributions for the non-cross-linked micelle formed by entry 12′ at 40 °C (···) and the SCL micelle (—) at 10 and at 40 °C.

Table 3. DLS Size for Non-Cross-Linked and SCL Micelles from PEOVE-*b*-P(HOVE/VEM)

	non-cross-linked micelle (nm)	SCL micelle[a] (nm)	
entry	40 °C	40 °C	10 °C
3′	47	46	58
6′	78	72	87
9′	79	78	99
12′	83	82	105

[a] SCL micelles were prepared by UV irradiation for 40 min at 1.0×10^{-3} g/mL non-cross-linked micelles of PEOVE-*b*-P(HOVE/VEM) in water at 40 °C.

was increased from 46 to 82 nm at 40 °C and from 58 to 105 nm at 10 °C. At 40 °C, the sizes of both SCL micelles and non-cross-linked micelles are almost the same values, which suggested that shell-cross-linking had little effects on an average micellar size at this temperature using PEOVE-*b*-P(HOVE/VEM). However, a slightly broader size distribution was obtained, judging from Figure 7. This may be due to the shape distortion of SCL micelles at 40 °C as explained in Figure 8, while SCL micellar size at 10 °C is one of the evidences of successful SCL micelle formation. If shell cross-linking had been unsuccessful, no micelles could exist at 10 °C since the PEOVE block is hydrophilic at this temperature and micelle dissociation would occur. Furthermore, the small increase in SCL micelle diameter on cooling the solution to 10 °C suggests a little swelling as a result of the ingress of water into the hydrophilic PEOVE core at 10 °C. This is also indicated by ^{1}H NMR results in Figure 6a. The same phenomena were obtained by the first thermoresponsive SCL micelles of PDMA-*b*-PMEMA.[4]

Figure 8 shows the dependence of the apparent diffusion coefficient (D_{app}) on detection angles (q) for SCL micelles (prepared from entries 6′ and 12′) at 10 and 40 °C. For spherical particles, the diffusion coefficient should be independent of the scattering vector, or detection angle, because of the undetectable rotational motion.[21] The analysis of the correlation function at 40 °C for SCL micelle prepared from entry 6′ showed that the average values of D_{app} had a small angular dependence. It may be due to slight distortion by decrease in degree of freedom which is induced by both hydrophobized PEOVE segments in a core at 40 °C and shell cross-linking. However, the plots at 10 °C showed that the D_{app} values were independent of the scattering vectors, regardless of the molecular weight. It suggests that the resulting SCL micelle virtually have a spherical shape as well as non-cross-linked micelles, as expected at the beginning.

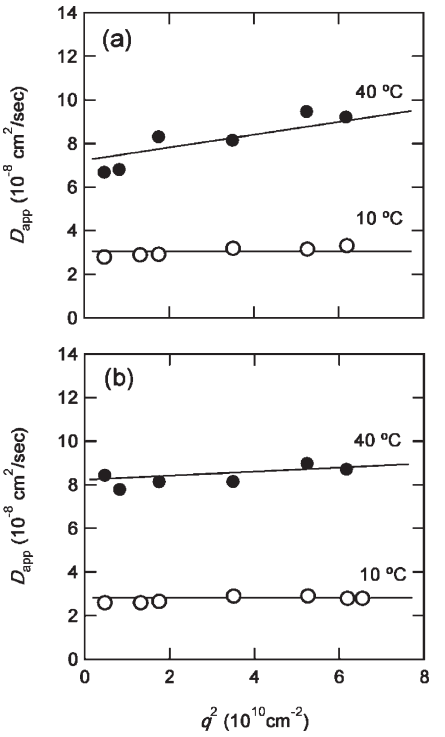


Figure 8. Apparent diffusion coefficient (D_{app}) at 10 °C (○) and 40 °C (●) as a function of scattering vector (q) for SCL micelles prepared from (a) entry 6′ and (b) 12′.

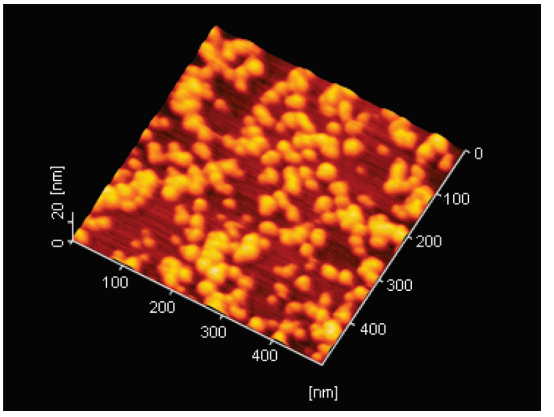


Figure 9. Tapping-mode AFM image (height image) of SCL micelles prepared from entry 12′. Samples were prepared by drop deposition onto freshly cleaved mica at 40 °C and allowed to dry in air at the same temperature.

Figure 9 shows a typical AFM image of the SCL micelles prepared from entry 12′, dropped from a 1.0 wt % aqueous solution on a mica. In the case of non-cross-linked polymer micelles of PEOVE-*b*-PHOVE, it is hard to obtain clear AFM images due to quite a low glass transition temperature. In fact, upon adsorption onto a mica, the micelle assembly was destroyed even after drying carefully at 40 °C, similar to poly(isoprene-*b*-acrylic acid).[2] In contrast, the SCL micelles become robust and imaging by AFM confirms the stabilization as shown in Figure 9. It can be seen that many particles were formed with an average height of 2.8 nm determined by the section analysis, significantly less than the micelles diameter. The average size is 41 nm, smaller than the value derived from DLS. All of these indicate some flattening of the loose SCL micelles[2] on the AFM substrate and then shrinking under the dry condition.

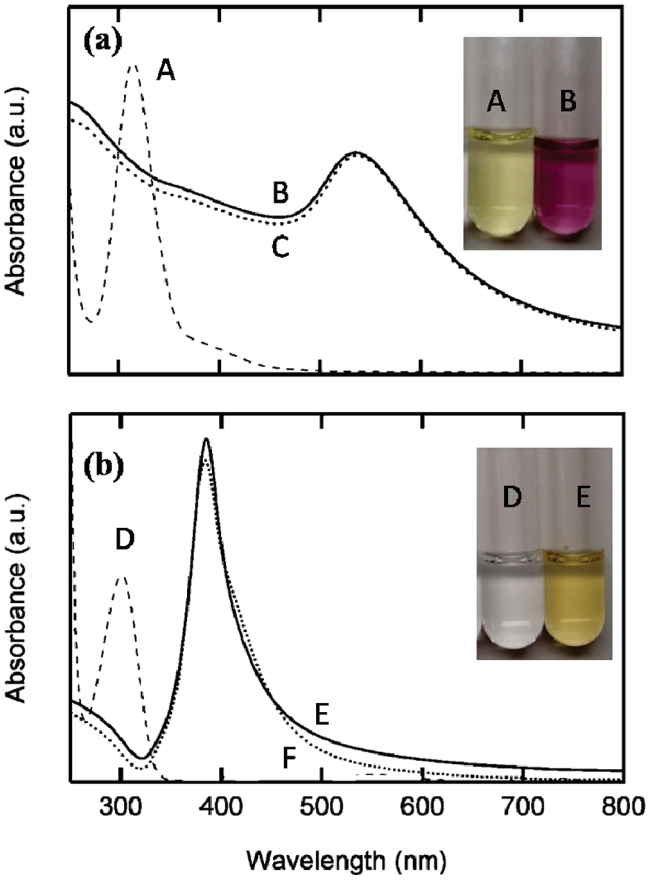


Figure 10. UV/vis spectra of SCL micells prepared from entry 12′ in aqueous solution after (a) gold loading and (b) silver loading, followed by reduction at 10 °C. (a) (A, ---) after loaded of $HAuCl_4$ at $HAuCl_4$/EOVE molar ratio of 0.2; (B, —) at 10 °C after reduction with $NaBH_4$ at the same $HAuCl_4$/EOVE molar ratio; (C, ···) at 40 °C after rising temperature of (B). (b) (D, ---) after loaded of $AgNO_3$ at $AgNO_3$/EOVE molar ratio of 0.2; (E, —) at 10 °C after reduction with $NaBH_4$ at the same $AgNO_3$/EOVE molar ratio; (F, ···) at 40 °C after rising temperature of (E).

Metallic Nanoparticles Using SCL Micelles as Nanoreactors. There has been a great deal of interest in metallic nanoparticles. Among them, polymer-coated metallic nanoparticles exhibit increased colloid stability, enhanced protection against oxidation, and much higher catalytic activity. Armes et al. synthesized the gold nanoparticles using methacrylate-based SCL micelles with diethylamino moieties in a core,[23] while a poly(ethylene oxide)-based polymer[24] and a star poly(vinyl ether) with an oxyethylene pendant[25] have been used as stabilizers for gold and silver nanoparticles. On the basis of these reports, we used the resulting SCL micelle as a scaffold for gold or silver nanoparticles prepared by in situ chemical reduction of either $HAu(III)Cl_4$ or $Ag(I)NO_3$. In situ chemical reduction of either Au(III) or Ag(I) with $NaBH_4$ leads to elemental metallic nanoparticles confined within the SCL micelles, which acts as a nanoreactor. The reduction of both from Au(III) to Au(0) and from Ag(I) to Ag(0) can be followed by UV/vis absorption spectroscopy. Figure 10 shows UV/vis absorption spectra of each metal-loaded SCL micelles at 10 °C obtained before and after $NaBH_4$ reduction. Few temperature effects on the wavelength of maximum absorption after reduction were observed between 10 and 40 °C. For gold nanoparticles in Figure 10a, $HAuCl_4$ with precursor SCL micelles were light yellow, and an absorption band was observed 313 nm. After $NaBH_4$ reduction, the solution turned with wine red as shown in photograph of Figure 10a. The absorption band was observed 535 nm, attributed to the surface plasmon resonance characteristic of the metallic gold nanoparticles. For silver nanoparticles in Figure 10b, an absorption band of $AgNO_3$ with precursor SCL micelles was observed 303 nm. After $NaBH_4$ reduction, the solution turned with light yellow, and the absorption band was observed 386 nm due to surface plasmon resonance of small metallic silver particles.[26] These samples are stable for a several days; no changes in the visible absorption spectra were observed, suggesting colloidal stability for these metal-loaded SCL micelles.

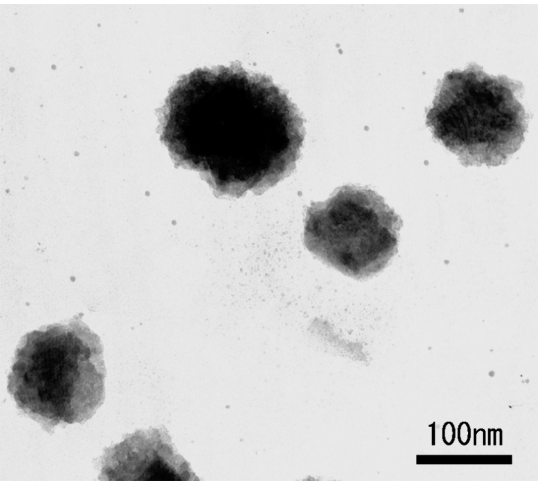


Figure 11. Typical TEM image of gold nanoparticles in water supported by SCL micelles prepared from entry 12′ at 10 °C. The sample corresponds to (B) in Figure 10a.

By using the gold-loaded SCL micelles, TEM image can be easily obtained without staining. Figure 11 shows a typical TEM image of gold-loaded SCL micelles at 10 °C obtained after $NaBH_4$ reduction. There are many gold nanoparticles inside each SCL micelle. This image indicates that poly(EOVE) segment is still located in a core of each SCL micelle at 10 °C, which is below LCST of poly(EOVE) segment, as shown in the reaction scheme in Figure 1. Approximately spherical micelles with an average diameter of 103 nm are observed by TEM, which is in good agreement with the D_h by DLS of 105 nm of the SCL micelle at 10 °C. Furthermore, around SCL micelles, there are small isolated gold nanoparticles. This indicates that SCL micelles are decorated with many small gold nanoparticles, and a stable SCL micelle can be used as a scaffold for gold nanoparticles.

Conclusion

In summary, we have demonstrated a synthesis of novel thermoresponsive shell cross-linked micelles from well-defined vinyl ether-type block copolymers, PEOVE-*b*-P(HOVE/VEM), using living cationic polymerization and UV irradiation which induced the cross-linking reaction that does not require the addition of an external cross-linking agent. For PEOVE-*b*-P(HOVE/VEM), the ratio of EOVE/HOVE in the block copolymers was fixed at 1:2. The methacryloyl groups in the block copolymer are located around the surface of the PHOVE shells as a random copolymer of HOVE and VEM. The block copolymers had narrow molecular weight distributions, determined by SEC of the PEOVE-*b*-P(SiEVE/VEM) before desilylation. The resulting PEOVE-*b*-P(HOVE/VEM) was dissolved molecularly in aqueous solution at 10 °C, which is below LCST of PEOVE. Upon heating above LCST of PEOVE, spherical micellization comprising PEOVE cores and PHOVE shells occurred. The micelles were cross-linked by UV (254 nm) irradiation in high diluted aqueous solution over CMC and CMT to obtain SCL micelles. The SCL

micellar core was reversibly hydrated or dehydrated, depending on the solution temperature. The size of SCL micelles was controlled by molecular weight from 46 to 82 nm at 40 °C, with longer length leading to increased size of the SCL micelles. Furthermore, the small increase in SCL micelle diameter on cooling the solution to 10 °C was observed due to the ingress of water into the hydrophilic PEOVE core. These SCL micelles served as nanoreactors for the synthesis of gold or silver nanoparticles prepared by in situ chemical reduction of Au(III) or Ag(I), respectively. The gold-loaded SCL micelles exhibited colloid stability and the nanosized SCL image containing the Au(0) was observed by TEM. The diameter was in good agreement with the D_h by DLS.

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