Dual Stimuli-Responsive Microgels Based on Photolabile Crosslinker: Temperature Sensitivity and Light-Induced Degradation

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ABSTRACT: The synthesis and characterization of a new photocleavable crosslinker is presented here. Dual stimuli-responsive P(VCL-*co*-NHMA) microgels were prepared by precipitation polymerization of vinylcaprolactam (VCL) with *N*-hydroxymethyl acrylamide (NHMA) and the new crosslinker. The microgels had distinct temperature sensitivity as observed in the case of PVCL-based particles and their volume phase transition temperature (VPTT) shifted to higher temperature with increasing NHMA content. Photolytic degradation experiments were investigated by irradiation with UV light, which led to microgel disintegration caused by cleavage of the photolabile crosslinking points. The degradation behavior of the microgels was conducted with respect to degradation rates by means of the relative turbidity changes. Hence, the microgels could totally degrade into short linear polymers by UV light, thus representing a great potential as new light and temperature dual responsive nanoscale materials. © 2014 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2014**, *52*, 1676–1685

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INTRODUCTION The research of polymer-based microgels has gained increasing attention since the discovery of microgels as a unique class of polymeric nanoscale materials. Microgels possess more flexible and outstanding properties, such as fluid-like transport performance, superior colloid stability, and possible control of particle size.^{1,2} Especially, stimuli-responsive microgels represent complex multifunctional systems, which are able to change the physicochemical properties of the network-forming polymers upon application of external triggers, which mainly include temperature,^{3,4} pH,^{5–8} light,⁹ redox,¹⁰ and so on. Microgels can be applied in numerous fields such as sensors,¹¹ optics, colloidal crystals,¹² and biomedical fields including drug delivery systems^{13–15} and biotechnology.¹⁶

Light presents an outstanding position among the different stimuli as it can be applied in a very precise manner by selecting suitable wavelength, polarization direction, and intensity in a noncontact approach, respectively.^{17,18} In addition, light offers the possibility to change the polymer properties in confined spaces and time scales. The utilization of a broad variety of chromophores, such as aniline,¹⁹ azobenzene,²⁰ spiropyran,²¹ and *o*-nitrobenzyl derivatives has in general been realized for advantages in triggering release applications.^{22,23} Among those, *o*-nitrobenzyl (*o*-NB) alcohol

derivatives have attracted extensive attention in the synthetic organic chemistry area.²⁴ An *o*-nitrobenzyl ester changes into a corresponding *o*-nitrosobenzaldehyde or *o*-nitrosobenzophenone upon irradiation with UV light based on the photoisomerization mechanism, simultaneously releasing a free carboxylic acid.^{25,26} Linkers and protecting groups based on *o*-NB chemistry can usually be cleaved when exposed to 300–365 nm light, with time varying from several hours at a low intensity to a few minutes when applying light of high intensities.¹⁶

Even though *o*-NB derivatives have been investigated in polymer science since 1977,^{27,28} it has not been realized until very recently that studies appeared to take full advantage of this photo responsive group in polymer and material science applications. For example, *o*-NB-based crosslinkers have been used in the crosslinking of hydrophilic poly(ethylene glycol) chains, making hydrogels which are commonly used as scaffolds in tissue engineering and drug delivery.²⁴ Turro and coworkers reported an example of model crosslinked networks based on *o*-NB linkers in 2007.²⁹ Recently, dual stimuli-responsive P(HEMA-*co*-MAA) microgels were prepared by D. Klinger and K. Landfester with *o*-NB-based photolabile crosslinker, and the microgels performed pH-dependent swelling and light-induced degradation behavior,

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SCHEME 1 Schematic representation of the preparation and the dual stimuli-responsive characters of the photodegradable PVCLbased microgels. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

which enabled the efficient loading and subsequent release of myoglobin as a model protein. $^{\rm 30}$

Temperature-sensitive microgels have gained extensive attention for their potential chemical and biomedical applications.³¹⁻³⁵ As a thermally sensitive polymer, the closely lower critical solution temperature (LCST) of poly(*N*-vinylcaprolactam) (PVCL) to body temperature bestowed it widely attention for both scientific studies and technological applications.^{36,37} PVCL microgel has been proved to be an excellent drug carrier because of the swelling and shrinking of a polymeric gel network.³⁸⁻⁴⁰ Few studies related to temperature and light dual stimuli microgels have been publicly reported though Liu's group reported a thermo- and lightregulated formation and disintegration double hydrophilic block copolymer micelle.⁴¹

On the basis of these considerations, we designed and synthesized a symmetrical photolabile crosslinker ((((ethane-1,2-diylbis (oxy))bis(ethane-2,1-diyl))bis(oxy))bis(5-methoxy-2-nitro-4,1phenylene))bis(ethane-1,1-diyl)bis(2-methylacrylate) (DMANB) through a convenient route. The cleavage behavior of the new crosslinker was investigated by means of 365-nm UV light irradiation. Then, the photocleavable crosslinker was used to build up dual stimuli-responsive P(VCL-*co*-NHMA) microgels. The obtained microgels could be completely disintegrated upon irradiation due to the light-cleavable crosslinking points. Meanwhile, the microgels were stable in physiological condition and the volume phase transition temperature (VPTT) could be adjusted by changing the amount of hydrophilic co-monomer *N*-hydroxymethyl acrylamide (NHMA) (Scheme 1).

EXPERIMENTAL

Materials and Chemicals

Acetovanilone (99%) and 1,2-bis(2-chloroethoxy) ethane (99%) were purchased from J&K Scientific. *N*-Vinylcaprolactam (VCL) was obtained from Fluka. NHMA was purchased from Aladdin Internet Reagent Database. Tetramethyl ethylene diamine (TMEDA) was purchased from TCI Tokyo Chemical Industry. Potassium persulfate (KPS), sodium dodecyl sulfate (SDS), and sodium bicarbonate (NaHCO₃) were purchased from Shanghai Chemical Reagents Company. All chemicals were of analytical grade or better and used without further purification except as mentioned above.

Characterization

¹H nuclear magnetic resonance (¹H NMR) (500 MHz) spectra were obtained using a Bruker spectrometer. Ultraviolet visible (UV-vis) spectra were measured using a Perkin-Elmer Lambda 35 spectrophotometer. Hydrodynamic diameter and light-scattering intensity of the microgels were obtained by a Malvern Zetasizer (Nano-ZS90) at scattering angle of 90°. Transmission electron microscopy (TEM) images were determined on a Hitachi H-600 transmission electron microscope, and the microgels were negative stained with 1% phosphotungstic acid for TEM measurement. Fourier transform infrared (FTIR) spectra were measured on a Nicolet Nexus-6700 FTIR spectroscopy.

The average molecular weight and molecular weight distribution (M_w/M_n) of the degradable polymer linear chains

SCHEME 2 Synthesis of photolabile crosslinker DMANB.

were estimated by gel permeation chromatography (GPC) measurements, which were carried out on a HP Angilent series 1100 Chromatograph equipped with a G1310A pump, a G1362A refractive index detector, and a G1315A diode-array detector. Poly(ethylene oxide) (PEO) standard samples were used for calibration, and the measurement condition is 0.1 M NaNO₃ aqueous solution at 40 °C with an elution rate of 0.5 mL/min.

Synthesis of Photolabile Crosslinker 1,1'-((((Ethane-1,2-diylbis(oxy))bis(ethane-2,1-

diyl))bis(oxy))bis(3-methoxy-4,1-phenylene))diethanone (3) To a solution of acetovanilone **1** (4.0 g, 23.8 mmol) in 50 mL of DMF, potassium carbonate (5.5 g, 39.8 mmol) and 1,2bis(2-chloroethoxy) ethane **2** (1.9 g, 10.0 mmol) were added (Scheme 2). The reaction mixture was heated to 120 °C and kept for 12 h under nitrogen atmosphere. The resulting solution was poured into 200 mL water and extracted with 200 mL ethyl acetate. Then, the ethyl acetate layer was washed with Na₂CO₃ (5%), and then brine. The ethyl acetate layer was dried with Na₂SO₄, filtered, and removed under reduced pressure. The product was recrystallized with ethyl acetate and hexane to give compound **3** as a pale white solid (3.0 g, 67% yield).

¹H NMR (CDCl₃): δ = 7.56 (d, 2H), 7.54 (s, 2H), 6.93 (d, 2H), 4.26 (t, 4H), 3.95 (t, 4H), 3.93 (s, 6H), 3.78 (s, 4H), 2.58 (s, 6H).

1,1'-((((Ethane-1,2-diylbis(oxy))bis(ethane-2,1diyl))bis(oxy))bis(5-methoxy-2-nitro-4,1phenylene))diethanone (4)

To a solution of **3** (2.2 g, 5 mmol) in 20 mL of acetic anhydride, nitric acid (2 mL) was added dropwise at 0 °C. Then, the solution was heated to room temperature and stirred for 2 h. The precipitate was obtained by filtration and washed with methanol for three times to give compound **4** as a light yellow solid (1.9 g, 70% yield).

¹H NMR (CDCl₃): δ = 7.70 (s, 2H), 6.73 (s, 2H), 4.27 (t, 4H), 3.94 (s, 6H), 3.92 (t, 4H), 3.74 (s, 4H), 2.48 (s, 6H).

1,1'-((((Ethane-1,2-diylbis(oxy))bis(ethane-2,1diyl))bis(oxy))bis(5-methoxy-2-nitro-4,1phenylene))diethanol (5)

To a solution of **4** (536 mg, 1 mmol) in 50 mL of THF, NaBH₄ (84 mg, 2.2 mmol) was added at room temperature and allowed to stir at the same temperature. The reaction progress was monitored by thin-layer chromatography. After completion of the reaction (3 h), the reaction mixture was quenched with aqueous solution of saturated NH₄Cl. THF was evaporated under reduced pressure and the crude mixture was purified by silica gel column chromatography to give compound **5** as a yellow solid (450 mg, 83% yield).

¹H NMR (CDCl₃): δ = 7.61 (s, 2H), 7.28 (s, 2H), 5.53 (m, 2H), 4.23 (t, 4H), 3.95 (s, 6H), 3.91 (t, 4H), 3.75 (s, 4H), 1.53 (d, 6H).

TABLE 1	Synthetic	Details	for	P(VCL-a	co-NHMA)	Microgels
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Sample	VCL (mg)	NHMA (mg)	DMANB (mg)	<i>D</i> _h ^c (nm)	PI ^d
P(VCL- <i>co</i> -NHMA-1 ^a)	198	2	10	531	0.02
P(VCL- <i>co</i> -NHMA-3)	194	6	10	589	0.05
P(VCL- <i>co</i> -NHMA-5)	190	10	10	712	0.10
P(VCL- <i>co</i> -NHMA-5–2.5 ^b)	190	10	5	686	0.06
P(VCL- <i>co</i> -NHMA-5–7.5)	190	10	15	862	0.06

^a Weight ratio of NHMA in respect to sum of NHMA and VCL.

^b Weight ratio of crosslinker DMANB in respect to monomer and 5 wt % DMANB were used if not labeled specifically.

((((Ethane-1,2-diylbis(oxy))bis(ethane-2,1diyl))bis(oxy))bis(5-methoxy-2-nitro-4,1phenylene))bis(ethane-1,1-diyl)bis(2-methylacrylate)

To a solution of compound **5** (270 mg, 0.5 mmol) in 25 mL DCM, triethylamine (500 μ L) was added into the mixture at ice bath temperature. To this, methacryloyl chloride (200 μ L) in dichloromethane (25 mL) was added dropwise and stirred for 12 h at room temperature. The reaction mixture was quenched with water, extracted with dichloromethane, and the combined organic extracts were dried over Na₂SO₄ and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography to give the crosslinker DMANB as yellow oil (300 mg, 89% yield).

¹H NMR (DMSO- d_6): $\delta = 7.67$ (s, 2H), 7.02 (s, 2H), 6.52 (q, 2H), 6.18 (s, 2H), 5.62 (s, 2H), 4.23 (t, 4H), 3.95 (s, 6H), 3.91 (t, 4H), 3.74 (s, 4H), 1.95 (s, 6H), 1.66 (d, 6H).

Preparation of DMANB-Crosslinked P(VCL-co-NHMA) Microgels by Precipitation Polymerization

Crosslinked P(VCL-co-NHMA) microgels were synthesized by a redox-initiated, aqueous precipitation polymerization approach.⁴² Microgels were prepared by first mixing VCL, NHMA, water (20.0 g, 1.1 mol), and 5 wt % of the crosslinker DMANB dissolving in 1 mL DMSO. In the synthesis of the family of P(VCL-co-NHMA) microgels, 1 wt % of the sum of VCL and NHMA but different mass ratios of VCL to NHMA (VCL/NHMA: 99/1, 97/3, 95/5) were used (Table 1). Hereafter, the mixture was added to a 50-mL glass flask containing 10.0 mg (5 wt % to monomers) SDS, 10.0 mg (5 wt %) NaHCO₃, then the contents of the vial were heated to 50 $^{\circ}$ C and kept under nitrogen atmosphere. After mechanical stirring of 200 rpm for 1 h, the initiator, KPS (10.0 mg) in 1 mL water was added to the mixture, followed by 10 μ L of the activator TMEDA. The polymerization reaction, while shielded from light, was conducted under nitrogen condition for 6 h. After the polymerization, the obtained microgels were dialyzed for a week via a dialysis bag (molecular weight cutoff 14,000) to remove the excess surfactant and the unreacted reagents and impurities.

Thermosensitivity Studies of Crosslinked P(VCL-co-NHMA) Microgels

The microgels were dispersed in phosphate buffer of pH 7.4 and the thermosensitivity of the microgels was determined

 $^{\rm c}$ The hydrodynamic diameter ($D_h)$ was determined in water at 25 $^{\circ}\text{C}$ by DLS.

 $^{\rm d}$ PI, polydispersity index of the particle size, PI = $<\!\!\mu_2\!\!>\!\!/\Gamma^2\!.^{43}$

by DLS measurement. By monitoring the hydrodynamic diameters of the particles as a function of NHMA content with changing temperature from 25 to 60 °C, different VPTT of the family of P(VCL-*co*-NHMA) were obtained. The stabilization time between each measurement was 300 s.

Photocleavable Studies of DMANB

A quartz cuvette containing a solution of the crosslinker DMANB in DMSO (c = 0.01% w/v) for UV-vis measurements and in DMSO- d_6 for ¹H NMR was placed under a UV lamp ($\lambda = 365$ nm, I = 90 mW/cm²) and the measurements were performed, respectively, after the sample being irradiated for fixed time intervals.

Photodegradation of DMANB-Crosslinked Microgels in Water

Samples of 0.125% (w/v) microgels in water were placed in a quartz cuvette and irradiated with 365-nm UV light. Samples were prepared and turbidity measurements were conducted by using a Malvern Zetasizer. After every measurement, the irradiated sample was retained by returning the withdrawn samples to the cuvette. The turbidity was determined by calculating the ratio of the scattering intensity at 90° of the irradiated samples relative to the nonirradiated sample. Particle size distributions of the irradiated particle dispersions were obtained by DLS in water.

RESULTS AND DISCUSSION

A novel dual stimuli-responsive P(VCL-*co*-NHMA) microgel was synthesized by redox-initiated precipitation polymerization with a new photolabile crosslinker DMANB. The synthesized crosslinker structure was determined by ¹H NMR and its photolabile behavior was analyzed by ¹H NMR and UV-vis measurement with the irradiation by 365-nm UV light. The existence of VCL led to the temperature-sensitivity of the microgels and the microgels exhibited higher VPTT with the increasing content of the co-monomer NHMA. Light sensitivity of the microgels was achieved by the utilization of the new photolabile crosslinker. Irradiation of the microgels by UV light resulted in the degradation of the particle structure. This dual stimuli-responsive property was designed to enable the thermosensitivity microgels degrade under the

FIGURE 1 ¹H NMR (DMSO- d_6) spectrum of crosslinker DMANB.

irradiation of 365-nm UV light, which had potential use in the biochemistry field.

Synthesis of Crosslinker DMANB

To obtain the photodegradable microgel, we designed and synthesized a symmetrical photodegradable crosslinker DMANB (Scheme 2). Here, a methoxy-nitrobenzyl ether derivative was selected as the photodegradable part because of its well-established chemistry and great utilization in numerous biological applications. Also, a triethylene glycol spacer was introduced to the nitrobenzyl unit in order to improve its solubility in water. The key photodegradable crosslinker DMANB was obtained in four steps as shown in Scheme 2 which was shorter than the routes of former crosslinkers^{9,30,44} and compound **3**, **4**, **5**, DMANB have not been reported. First, the phenolic hydroxyl group of starting acetovanilone **1** was treated with 1,2-bis(2-chloroethoxy) ethane 2 to form 3. Acetic anhydride was a selective solution for the nitration because the product 4 would precipitate from acetic anhydride to avoid the byproduct. The nitroacetovanillone derivative 4 was reduced by NaBH₄ and then followed by methacrylation of terminal hydroxyl groups to yield the crosslinker DMANB.⁹

¹H NMR spectrum of DMANB was shown in Figure 1. The peaks of *a*, *b*, and *c* were assigned to the protons of methacrylic acid ester. The peaks of *f* and *g* were assigned to the protons of benzene ring and the peaks of *i*, *j*, and *k* were assigned to the protons of triethylene glycol spacer.

Photolysis of Crosslinker DMANB in Solution

The crosslinker consists of a central *o*-nitrobenzylic group, the respective molecular attachment of the radically photolabile chromophore resulted in two mainly photoproducts as shown in Figure 2(a). A radical mechanism including a rearrangement and bond cleavage following by the intramolecular benzylic hydrogen abstraction by a nitro oxygen group

was put forward to explain the photoreaction.⁹ The photolabile crosslinker degraded into a molecule containing two ketone moieties and two carboxylic acid groups under UV light.

Time-dependent ¹H NMR spectra and UV-vis measurements of the crosslinker solution in DMSO were performed to investigate the photolytic performance of the new photolabile crosslinker (Fig. 2). As was shown in Figure 2(a), the peaks of *b* and *c* were assigned to the protons of double bonds of methacrylic acid ester and the peak of d was assigned to the proton of methine of phenethyl alcohol. Along with the irradiation with 365-nm UV light, the peaks of *b*, *c*, and *d* decreased at the same ratio, which indicated the generation of ketone moieties, and meantime the peaks of *b*' and *c*' increased, which were assigned to the protons of opened methacrylic acid. The peaks of *b*, *c*, and *d* vanished

FIGURE 2 Irradiation of the new photolabile crosslinker DMANB in DMSO for an intensity of 90 mW/cm² at 365-nm UV light: time dependent (a) ¹H NMR spectra; (b) UV-vis spectra. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 3 Evolution of the conversion of VCL.

in 6 min and b' and c' got maximum values at the same time, which indicated the end of the reaction.

In Figure 2(b), irradiation with 365-nm UV light resulted in a red shift of the absorption maximum at 350 nm and the reduction of the absorbance at 305 nm. Two new absorption bands at 270 and 380 nm arose under irradiation as shown in Figure 2(b). The spectra changed slowly after 240 s, which meant the crosslinker almost photolysis totally under 365-nm UV light. These light-induced changes of the spectra toward well-defined isosbestic points over the complete irradiation time scale points, which indicated a successful cleavage of the chromophore in sympathy with the research of D. Klinger and K. Landfester.⁴⁵

Preparation of DMANB-Crosslinked P(VCL-co-NHMA) Microgels

DMANB-crosslinked P(VCL-*co*-NHMA) microgels were prepared by precipitation polymerization, which is a most common technique for the preparation of thermosensitive microgels.⁴⁶ With regard to the preparation of polymeric microgels, the precipitation polymerization technique is a simple one-pot preparation method. In the process of precipitation polymerization, the growing polymer chains collapse when they reach a critical length with the phase-separation from the continuous medium above its LCST to form particle nuclei.⁴ The sulfate groups from initiator incorporated into polymer chains to stabilize the larger polymer colloid, which is the result of the nuclei further aggregate. The resulting microgel aqueous dispersion is a swelling network at room temperature and could be stable by the formation of hydrogen bonds between water molecules and polymer segments.

In this work, a dual-stimuli responsive PVCL-based network was prepared with VCL, NHMA, and the new photolabile crosslinker DMANB by precipitation polymerization (Scheme 1 and Table 1). KPS acted as initiator, and NaHCO₃ was used as buffer to avoid the hydrolysis of VCL.⁴⁷ The incorporation of co-monomer NHMA controlled the VPTT of the copolymer with changing the mass of NHMA. In order to compare the

swelling and degradation property of the microgels, 5 wt % of crosslinker was added generally. After being dialyzed for a week via a dialysis bag to remove the excess surfactant, the unreacted reagents and impurities, the mean hydrodynamic diameters of microgels were obtained by DLS measurements.

To investigate the conversion of the monomers with the new crosslinker DMANB, P(VCL-*co*-NHMA-5) microgels were prepared in deuterium oxide and the products at different reaction time were analyzed by ¹H NMR.¹⁰ Figure 3 showed the conversion of main monomer VCL, which indicated most VCL had been polymerized into polymers in 3 h. In spite of the good conversion of VCL, the new crosslinker performed slower conversion rate comparing with methylene biacryla-mide⁴⁸ and *N*,*N*-bis(acryloyl) cystamine (BAC)¹⁰ on account of the inhibition and retardation effects of *o*-NB-based cross-linker DMANB on the free radical polymerization. Size distributions of P(VCL-*co*-NHMA) with different NHMA content measuring by DLS were shown in Figure 4(a) which

FIGURE 4 (a) Size distribution of P(VCL-*co*-NHMA) microgels with different NHMA content measuring by DLS at 25 °C. (b) Typical TEM image of P(VCL-*co*-NHMA-1). The dark ring in the TEM image was obtained by stained phosphotungstic acid to enhance the polymer contrast. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 5 FTIR spectra of NHMA, P(VCL-*co*-NHMA-5) and the crosslinker DMANB (from up to down). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary. com.]

indicated that all microgels had good size distribution (PI \leq 0.10) and the hydrodynamic diameter increased from 531 to 712 nm with increasing the mass of NHMA in the recipe from 1 to 5 wt % (Table 1). The microgels were more swollen with more hydrophilic NHMA incorporated into the polymer network, leading to larger size.⁴⁹ With the increasing mass content of NHMA, the growing polymer chains became more hydrophilic and were unable to complete efficient chain collapse, which resulted in the decrease of the particle nucleic number, leading to a larger size.⁵⁰ When the weight ratio of NHMA in respect to sum of monomer was fixed at 5 wt %, with the feeding amounts of DMANB crosslinker from 2.5 to 7.5 wt %, the hydrodynamic diameter of the asprepared microgels increased from 686 to 862 nm which resulted that P(VCL-co-NHMA) microgels with high crosslinker density were usually higher in the consideration of their total size.51

Figure 4(b) showed the TEM image of P(VCL-*co*-NHMA-1), which exhibited uniform and regular spherical morphology. The size of the microgel observed in TEM was about 300 nm. DLS measurements yielded the hydrodynamic diameters of the swollen microgels showed an obvious increase compared to the values obtained from TEM measurement. We reckoned that the microgels could be swollen in an aqueous solution during the DLS measurement while they collapsed in dry state in a TEM testing.^{51,52}

The FTIR measurement was used to confirm the structure of P(VCL-*co*-NHMA) microgels. The FTIR spectra were shown in Figure 5. The peaks appearing at 1634/cm caused by amide I band and 1480/cm of C-N belonged to the characteristic peaks of PVCL.¹⁶ The bands at 2930, 2856, and 1443/cm were attributed to stretching and bending vibrations of C-H groups. The spectrum of P(VCL-*co*-NHMA-5) performed higher intensity peaks at 2930 and 2856/cm with respect to the pure crosslinker DMANB on account of abundant -CH₂ groups in PVCL.⁵³ The peak appearing at 1541/cm in the

spectrum of P(VCL-*co*-NHMA-5) was attributed to the typical bending vibration of amide from PNHMA,⁵⁴ which indicated that NHMA had been copolymerized into the microgels successfully via the crosslinker DMANB. In the spectrum of P(VCL-*co*-NHMA-5), the peak at 1718/cm was caused by the stretching vibration of C=0 belonged to crosslinker DMANB,⁵⁵ which demonstrated that the crosslinker had been successfully introduced into the microgels.

Thermosensitivity of the Microgels

The prepared microgels were designed to exhibit a temperature-sensitivity behavior on the basis of VCL monomer. With the aim to investigate the described behavior, the DLS measurements were used as shown in Figure 6 under a heating process. As expected, the DLS results showed a decreasing hydrodynamic diameters with an increase in temperature, which corresponded to a sharp volume phase transition as observed in PVCL-based crosslinked particles.⁵⁶ The hydrodynamic diameter of P(VCL-co-NHMA-1) microgels decreased from 550 nm at 25 °C to 437 nm at 55 °C. By comparing the temperature-sensitivity behavior of the three microgels, it was noteworthy that the microgels owned higher VPTT with the increasing NHMA content. The VPTT of the P(VCL-co-NHMA-1) microgels was 41 °C, while that of P(VCL-co-NHMA-3) and P(VCL-co-NHMA-5) microgels shifted to 44 and 48 °C, respectively. These results indicated that hydrophilic co-monomer NHMA was able to control a shift to the higher temperature for VPTT of microgels.

Photodegradation of DMANB-Crosslinked P(VCL-co-NHMA) Microgels

Photodegradation of the P(VCL-*co*-NHMA-5) microgels (c = 0.125% w/v) was investigated by irradiating particles by 365-nm UV light. The light-induced degradation behavior was determined by turbidity of the samples. Turbidity was characterized as the relative scattering intensity at 90° by DLS measurements. The degradation of cleavable

FIGURE 6 Effect of NHMA content on the temperature dependence of the hydrodynamic diameter of the P(VCL-*co*-NHMA) microgels in phosphate buffer of pH 7.4. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 7 Investigations on the light-induced P(VCL-*co*-NHMA-5) microgels degradation with 365-nm UV light: (a) The relative turbidity for different light intensities at 25 °C; (b) The degradation behavior of collapsed state for an intensity of 270 mW/cm² at 60 °C; (c) The size changes of the microgels at an intensity of 270 mW/cm² at 25 °C; (d) GPC measurement [the embedded photograph was the comparison of undegraded microgels (left) and degraded microgels (right)]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

crosslinking points led to a loosening of the network structure which resulted in the decreased turbidity, because a more swollen gel particle was measured by a reduced contrast in the refractive indices between solvent and particles.⁹

Figure 7(a) showed the resulting turbidity curve of P(VCL-co-NHMA-5) microgels with UV light of the wavelength of 365 nm, and all the three different intensities could lead to a complete degradation of the microgels in different time at 25 °C. An intensity of 90 mW/cm² did result in a decay of the turbidity down to a constant level of zero in about 90 min. In contrast, increasing the UV light intensity up to 180 and 270 mW/cm² resulted in a faster degradation for microgels while 50 min for 180 mW/cm² and 15 min for 270 mW/cm², respectively. In general, it is possible to control the degradation rate via changing the light intensity and irradiation time used. After the irradiation of 365-nm UV light at the three different intensities for a certain time, the turbid dispersion turned into the corresponding transparent solution as shown in Figure 7(d). The imbedded photograph right in Figure 7(d) was made by irradiating microgels at 270 mW/cm² for

15 min. In consideration of the temperature sensitivity of the microgels, photodegradation behavior of the collapsed P(VCLco-NHMA-5) microgels (c = 0.125% w/v) was also investigated by irradiating particles by 365-nm UV light at 60 °C. It was interesting that it performed a faster degradation rate in 480 s at collapsed state for completely degradation at 270 mW/cm² than 900 s at swollen state as shown in Figure 7(b).

To better demonstrate the photodegradable property of DMANB crosslinked P(VCL-co-NHMA) microgels, the microgels were tested with 365-nm UV light at an intensity of 270 mW/ cm² and the particle size and size distribution of the microgels were measured by DLS at different time intervals. As shown in Figure 7(c), the microgels had the mean size of 698 nm before degradation and swelled to 752 nm within 60 s due to the decreased crosslinking density by the rupture of some crosslinking points. After degradation of 660 s, only a peak of 4 nm was observed which could demonstrate the microgels completely degrade into short linear polymers. For a further analysis of the molecular weight of the degraded polymer chains under the irradiation of UV light, GPC

measurement was used. The degraded polymer was filtered through a 0.45- μ m filter before its injection to GPC to avoid Mw influence from other polymer chains. In Figure 7(d), the GPC trace showed that the degraded polymer had a low molecular weight (M_w , 1990 g/mol) and narrow molecular weight distribution $(M_w/M_{n\nu} 1.1)$ which indicated the crosslinking points in the microgels were cleaved under irradiation of UV light leading to the formation of short linear polymers.

CONCLUSIONS

A novel photodegradable dual stimuli-responsive P(VCL-co-NHMA) microgel was prepared by redox-initiated precipitation polymerization of VCL and hydrophilic co-monomer NHMA with a new photolabile crosslinker DMANB. The crosslinker was synthesized in a facile route and it performed a good photolabile behavior. The obtained microgels presented uniform spherical shape and narrow size distribution (PI < 0.1). These microgels exhibited higher VPTT with increasing NHMA content. UV light irradiation caused cleavage of the DMANB crosslinking points leading to microgel disintegration. The microgels could totally degrade into short linear polymers by UV light and increasing light intensity resulted in a faster degradation. By changing light properties, we could control the degradation rate of microgels, which may indicate the potential application in some fields.

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