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Synthesis and Photoinduced Phase Transitions of Poly(*N*-isopropylacrylamide) Derivative Functionalized with Terminal Azobenzene Units

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ABSTRACT: We have used an azobenzene derivative substituted with a 2-chloropropionyl group as an initiator for the atom transfer radical polymerization of *N*-isopropylacrylamide. The resulting polymers, which possessed azobenzene moieties at one of their termini, had molecular weights of 1.7−12.0 kDa. Aqueous solutions of these polymers displayed low critical solution temperatures that alternated reversibly in response to *E*-to-*Z* photoisomerization cycles of the terminal azobenzene moieties. The difference between the transition temperatures after exposure to UV and visible irradiation increased linearly up to a value of over 10 °C upon decreasing the molecular weight of the polymer.

Introduction

Poly(*N*-isopropylacrylamide) (polyNIPAM) is a well-known thermoresponsive polymer that changes its appearance in water from a clear solution to a turbid suspension at a relatively low critical solution temperature (LCST) of ca. 32 °C.[1] This sharp thermoresponse results from coil-to-globule transitions of single chains. This useful property can be exploited in many new applications, such as adsorption/desorption sheets for cell cultures,[2] drug delivery,[3] tunable optical devices,[4] and chromatographic separation.[5] Photofunctional polymers attract much interest for their application in optical and mechanical devices because of their ready accessibility. Polymeric systems that combine thermoresponsive polyNIPAM with photoresponsive units have been reported.[6] For example, a random copolymer of NIPAM and a small amount of photoisomerizable azobenzene acrylamide derivatives has been demonstrated to undergo photoinduced alternation of its cloud point in aqueous solution.[6a] In such polymers, the polar *Z* form of the azobenzene unit has increased aqueous solubility in comparison with its relatively nonpolar *E* form; the balance between polar and nonpolar moieties has a great impact over the transition temperture.[6a,c−f] We reported that structural optimization of the azobenzene unit in such a copolymer is an effective means to controlling the cloud point shift;[6g] indeed, the photoinduced shift was observed in the polymers with wide copolymerization ratio. Upon increasing the number of azobenzene units, the photoinduced shift increased up to a certain value but decreased thereafter with accompanied by expanding temperature range of the transition (i.e., the transition is no longer sharp). These phenomena might be due to inhomogeneity in the copolymer. The synthesized polymers exhibited polydispersity; in addition, when we prepared them through copolymerization, they exhibited a variety in the number and position of their photofunctional units. Such low uniformity can lead to a decrease in the sharpness of the photoresponsive nature. Ideally, we would like to obtain polymeric systems in which the isomerization of a single photoresponsive unit would exert a physical response. For example, in the highly sensitive ocular system expressed in vertebrate photoreceptor cells, photoisomerization of a single retinal molecule from the 11-cis conformation to the all-trans isomer induces a change in the higher-order structure of the macromolecule contacting that rhodopsin unit.[7] The increased sensitivity of this “one-to-one” system results from molecules of uniform size being located in specific positional relationships. In this paper, we report the atom transfer radical polymerization (ATRP)-based synthesis of a polyNIPAM derivative possessing a single photoresponsive azobenzene unit at one of its termini and the cloud point shift in its water solution response upon exposure to light. Recently, ATRP has been utilized widely to synthesize block copolymers, star polymers, and controlled molecular weight polymers.[8] ATRP, which occurs with slow chain propagation, can result in lower polydispersity relative to that obtained from conventional free radical polymerization and, thus, can lead to more-uniform molecular weights. Another benefit is that a simple alkyl chloride can be used to initiate the polymerization. The ease of synthesis of the initiator can be exploited as a means to functionalize the terminus of the resulting polymer. For example, we can use thermally and chemically stable initiators having complicated structures (e.g., photoresponsive residues) for ATRP to provide polymers with functionalized chain ends.

Results and Discussion

The synthesis of a polyNIPAM derivative through the ATRP method has been reported when using 2-chloropropionic ethyl ester as the initiator.[9] In this study, we polymerized NIPAM from a new initiator, **Az-Cl**, under similar conditions. We used NMR spectroscopy to monitor the kinetics of this polymerization process. Figure 1 displays the dependence of the degree of polymerization (PD) on the polymerization time at a NIPAM-to-initiator feed ratio of 100:1. For these measurements, samples were extracted with a syringe from the reaction mixture during each polymerization and concentrated prior to NMR spectroscopic analysis. The methine protons of the isopropyl groups appeared separately as a single broad peak at 4.0 ppm for polyNIPAM and as an octet at 4.2 ppm for NIPAM (SFigure 1). Aromatic protons characteristic of the azobenzene moiety appeared at 7.1 and 7.9 ppm. We determined the PDs from the

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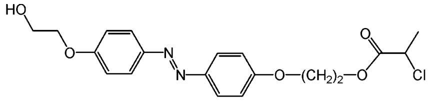

Az-Cl

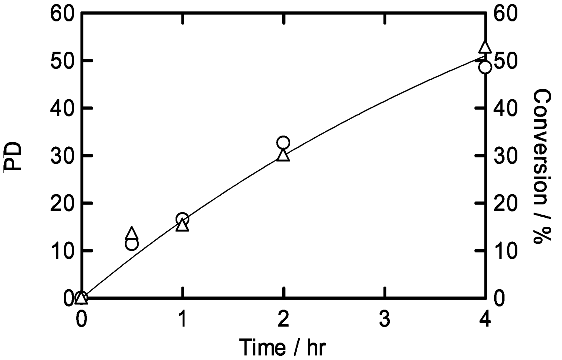

Figure 1. Plots of the degree of polymerizaton (PD; circles) and conversion (triangles) as a function of the reaction time for the polymerization initiated from 1.0 mol % (to NIPAM) of **Az-Cl**. Values were estimated from peak areas in NMR spectra. The solid line represents results of curve fitting to first-order kinetics.

Table 1. Polymerization

	time[a]/h	NIPAM/Az	yield/%	PD[b]	M_w[c] (PDI[d])
p-1	4	25	46.4	14	1690 (1.05)
p-2	4	50	50.0	31	3940 (1.07)
p-3	4	100	50.4	67	7670 (1.06)
p-4	8	100	95.1	93	12000 (1.08)

[a] Polymerization time. [b] Polymerization degree. [c] Weight-average molecular weight estimated from MALDI-TOF MS spectra. [d] Polydispersion index.

ratios of the peak areas of the signals for the methine protons of the polyNIPAM units (4.0 ppm) to those of the aromatic protons of the azobenzene units (7.9 ppm); we estimated the conversions from the area ratio of the polyNIPAM units (4.0 ppm) to the total peak area of the polyNIPAM and NIPAM units (4.2 ppm). The calculated conversions and PDs coincided and both increased upon increasing the reaction time. These plots fitted well to first-order kinetics (solid line), indicating that the polymerization proceeded stoichiometrically. We used the same reaction conditions to preparation of polymers shown below, but at various monomer-to-initiator feed ratios, and applied both column chromatography and reprecipitation as purification methods.[10] Table 1 indicates that the resulting polymers had different molecular weights depending on the feed ratio. We estimated the molecular weights (M_w in Table 1) from MALDI-TOF mass spectra (SFigure 2); a distance between neighboring signals of m/z 113 corresponded to a difference of a single NIPAM unit. Considering that the molecular weight of NIPAM unit is 113 g/mol, we converted the average molecular weight determined from a series of peaks to average degrees of polymerization [(M_w/PDI-357)/113] of 11.1 for **p-1**, 29.4 for **p-2**, and 60.9 for **p-3**; these values match to values of PD estimated from the NMR spectra (PD in Table 1). The polydispersity index (PDI, represented by M_w/M_n) of each polymer was below 1.1. These results suggest that our polymerization conditions provided a controlled ATRP process. Strangely, the signals in the MALDI-TOF mass spectra matched values expected for the $[\text{Az-Cl} + n(\text{NIPAM}) - \text{Cl}]^+$ ions; i.e., the chloride residues disappeared from all of the polymers. If a chloride ion was eliminated from a polymer terminus during polymerization, the propagation reaction would stop. We observed, however, that prolonged polymerization gave rise to the higher-molecular-weight polymer **p-4** in a higher yield than that of **p-3**, yet still resulted in a low PDI (<1.1). These findings indicate that the terminal chlorine atom remained in place during polymerization; it is possible that the chlorine atom was eliminated during the purification process or during ionization in the mass spectrometer. The yields were almost 50% for the polymers prepared during a 4 h reaction (**p-1**, **p-2**, and **p-3**). The perspective molecular weights expected from these yields should be half of the feed; because the measured values of PD are larger than the perspective molecular weights, it is likely that higher molecular weight polymers were recovered selectively after performing the reprecipitation process.

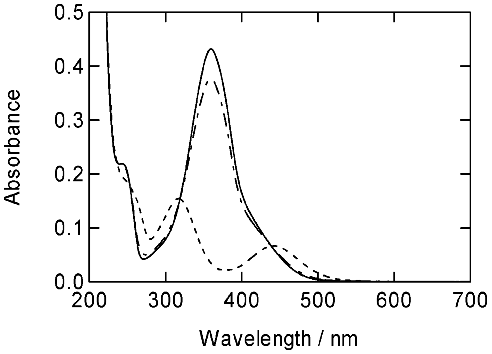

Figure 2. Absorption spectra of **p-4** in water before (solid line) and after exposure to UV (dashed line) and visible light (dashed-dotted line).

Each of the polymers was soluble in cold water. Figure 2 displays UV−vis spectra of an aqueous solution of **p-4**. The spectrum obtained prior to exposing the solution to light corresponded to that of the thermally stable *E* isomer of azobenzene, which differed from that obtained from an organic solution with respect to the positions of the central wavelengths of the n−π* and π−π* transitions. The absorption band of the n−π* transition appeared at ca. 400 nm as a shoulder of the large π−π* absorption band (360 nm). These signals overlapped in water as a result of a polar solvent effect that caused a blue shift of the n−π* transition and a red shift of the π−π* transition. The spectrum of the polymer solution became equivalent to that of a typical *Z* isomer after exposure to UV irradiation. The two absorption bands of the π−π* (317 nm) and n−π* (443 nm) transitions were clearly separated. The isomerization ratio after exposure to the UV irradiation (365 nm), calculated using the Fisher method,[11] was 96%. Exposure to visible light (488 nm) resulted in a change in spectral shape back to that of the *E* isomer, but with absorption intensities slightly lower than they had been originally. The calculated isomerization ratio was 13%, i.e., an 87% recovery of the *E* isomer.

We monitored the change in transmittance of light (600 nm) upon increasing the temperature of the various (irradiated and nonirradiated) solutions of polymer; each system exhibited its onset of precipitation (i.e., its cloud point, which is almost equal to the LCST) at a different temperature, as indicated in Figure 3. The measured value of the cloud point of the sample that had not been exposed to light was lower than the LCST of conventional polyNIPAM (32 °C). The cloud point after UV irradiation was higher than that observed prior to irradiation. Irradiation with visible light induced a shift back to a lower-temperature cloud point, one that was close to the transition temperature prior to irradiation. Increasing the azobenzene content led to a decrease in the cloud point of the polymer solution both before and after irradiation with visible light, relative to that of conventional polyNIPAM, but it did not significantly affect the cloud point after UV irradiation. This

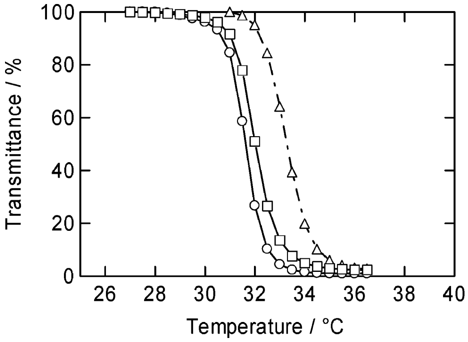

Figure 3. Temperature dependence of the transmittance of 600 nm light through a 0.2 wt % solution of **p-4** in water measured before (circle) and after irradiation at 365 nm (triangle) and 436 nm (rectangle).

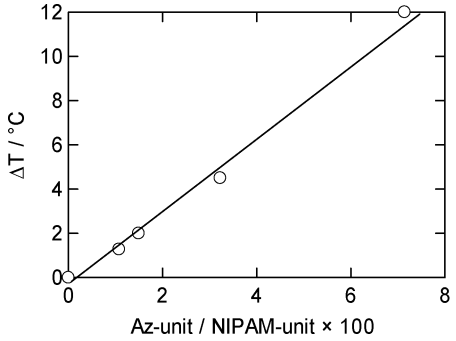

Figure 4. Cloud point shifts (ΔT) of polymer solutions—between samples irradiated with UV light and those irradiated with visible light—plotted as a function of the ratio of azobenzene units.

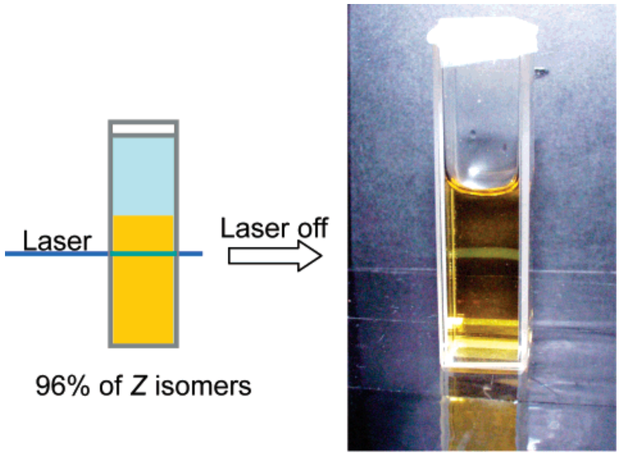

Figure 5. Photograph of a **p-1** solution irradiated with UV light and then irradiated with an Ar ion laser beam at room temperature.

finding suggests that the *E* isomers of azobenzene units at polymer termini function as hydrophobic units, with the *Z* isomers having hydrophilicity similar to that of NIPAM units. In fact, cloud point shifts of polyNIPAMs away from 32 °C as a result of end-group effects have been reported: less-polar terminal groups decrease the polymer solubility and cloud point, while polar terminal groups increase the cloud point; these effects are most pronounced in low-molecular-weight polymers.[12] Figure 4 displays a plot of the difference between the temperatures for the 50% transition changes after UV and visible light irradiation ($\Delta T_{c-50\%}$) as a function of the ratio of azobenzene units. This temperature difference increased linearly upon increasing the ratio of azobenzene units, which is a stark contrast to the transition behavior we observed from our previous copolymers.[6g] For the corresponding copolymer solutions, we observed the largest value of cloud point shift between the differently irradiated samples at an azobenzene content of 1.5%; increasing the azobenzene content above 2% caused a decrease in ΔT_c. Other groups have also reported such a dependence of the ΔT_c on the azobenzene content. In one case, the azobenzene concentration range over which a photoinduced cloud point change occurred was quite narrow;[6a] in another, for a copolymer of NIPAM and hydroxyethylacryamide partially substituted with azobenzene derivatives, the value of ΔT_c increased upon increasing the azobenzene content, but no values of ΔT_c were described for polymers having an azobenzene content above 3.1 mol %.[6e] Our largest ΔT_c (>10 °C) as a response to exposure to light is unsurpassed by any previously reported NIPAM-based polymer. We believe that the presence of just one azobenzene unit at a single terminus of each polymer results in the controlled T_c shift; i.e., large photoinduced shifts (>10 °C) are possible, with a linear dependence on the azobenzene content.

We have demonstrated that photoisomerization of a single terminal unit of a polymer can trigger a phase transition of whole polymer chains—in this case, end-functionalized polyNIPAM derivatives exhibiting narrow polydispersity that had been prepared using the ATRP method. The cloud point shifts of these polymer solutions after exposure to UV and visible light reached up to values higher than 10 °C. Their sharp transitions allowed rapid transformation from clear solutions to turbid states along the laser beamline (40-50 mJ), as indicated in Figure 5. This linear scattering body was formed after irradiation for 1 s. We expect that such high accessibility to localized areas in space could lead to the creation of new optical devices such as movable screens for volume scan-type three-dimensional displays or optical shutters.

Experimental Section

General. The cloud points of 0.2 wt % polymer solutions in water heated at a rate of 1 °C/min and the absorption spectra were measured using a Hewlett-Packard UV−vis spectrophotometer (Agilent 8453) equipped with a Mettler FP90 unit. The sample solution was placed in a handmade flat quartz cell having an optical length of 1 mm. Irradiation was conducted using an Ushio ultrahigh-pressure mercury arc through a combination of Optima color filters (WB360 and ZWB2) for 365 nm light (for UV irradiation) and using an Ion Laser Technology argon ion laser (5500ASL) for 488 nm light (for vis irradiation). Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) was conducted using an Applied Biosystems Voyager-DE pro instrument operated in reflector mode; samples were prepared through deposition of methanol solutions of the polymers and α-cyano-4-hydoroxycinnamic acid. ^{1}H NMR spectra were measured on Varian Gemini 300 with sample dissolved in $CDCl_3$ or DMSO-d_6.

Materials. All reagents, unless otherwise noted, were purchased from Wako Chemicals and used without further purification. Anhydrous dichloromethane and anhydrous dimethyformamide (DMF) were obtained in organic synthesis grade; all others were of special grade (>99.5%). NIPAM was purified twice by recrystallization from methanol. Tris[2-(dimethylamino)ethyl]amine was synthesized using a procedure described in the literature.[13]

4,4′-Dihydroxyethoxyazobenzene. 4,4′-Dihydroxyazobenzene was synthesized from 4-nitrophenol.[14] A mixture of 4,4′-dihydroxyazobenzene (0.77 g), ethylene carbonate (0.64 g), potassium carbonate (1.0 g), and DMF (5 mL) was stirred at 90 °C for 12 h. The mixture was poured into water, and the precipitate was filtered off, dissolved in THF, and filtered. The THF solution was concentrated, and the residue recrystallized from methanol to yield yellow crystals (0.77 g); mp 204−205 °C. ^{1}H NMR (DMSO-d_6, δ): 3.75 (dt, 4H, $J = 4.7$, 5.5 Hz, CH_2CH_2OCO), 4.09 (t, 4H, $J = 4.7$ Hz, CH_2CH_2OH), 4.92 (t, 2H, $J = 5.5$ Hz, OH), 7.11 (d, 4H, $J = 9.0$ Hz, ArH), 7.83 (d, 4H, $J = 9.0$ Hz, ArH).

Azobenzene Initiators. 2-Chloropropionyl chloride purchased from Tokyo Chemical Industry (0.589 g) was added slowly to a solution of 4,4′-bis(hydroxyethoxy)azobenzene (0.70 g) and triethylamine (0.47 g) in DMF (20 mL). After stirring for 4 h, the solution was diluted with dichloromethane and the insoluble matter removed by filtration. The solution was concentrated the residue purified through silica gel column chromatography (EtOAc/CH_2Cl_2, 1:3) to yield 4-(2-hydroxyethoxy)-4′-(2-(2-chloropropionyloxy)ethoxy)azobenzene (**Az-Cl**, 0.20 g) and 4,4′-bis(2-(2-chloropropionyloxy)ethoxy)azobenzene (**1**, 0.50 g). **Az-Cl**: mp 130−131 °C. ^1H NMR ($CDCl_3$, δ): 1.71 (d, 3H, $J = 7.0$ Hz, CH_3), 2.06 (broad s, 1H, OH), 4.01 (broad t, 2H, $J = 4.5$ Hz, CH_2OH), 4.17 (t, 2H, $J = 4.5$ Hz, CH_2CH_2OH), 4.29 (t, 2H, $J = 4.7$ Hz, CH_2CH_2OCO), 4.45 (q, 1H, $J = 7.0$ Hz, $CHClCH_3$), 4.56 (t, 2H, $J = 4.7$ Hz, CH_2OCO), 7.00 (d, 2H, $J = 8.9$ Hz, ArH), 7.03 (d, 2H, $J = 8.9$ Hz, ArH), 7.88 (d, 4H, $J = 8.9$ Hz, ArH). **1**: ^1H NMR ($CDCl_3$, δ): 1.72 (d, 6H, $J = 6.9$ Hz, CH_3), 4.29 (t, 4H, $J = 4.7$ Hz, CH_2CH_2OCO), 4.46 (q, 2H, $J = 6.9$ Hz, $CHClCH_3$), 4.57 (t, 4H, $J = 4.7$ Hz, CH_2OCO), 7.01 (d, 4H, $J = 9.0$ Hz, ArH), 7.87 (d, 4H, $J = 9.0$ Hz, ArH).

PolyNIPAM. Typical procedure: **Az-Cl** (24.4 mg) and NIPAM (0.34 g) were dissolved in DMF (0.75 mL). The solution was purged thoroughly with argon and maintained at 20 °C. Tris[2-(dimethylamino)ethyl]amine (16.5 μL) was injected into degassed suspension of copper chloride (6.0 mg) in DMF or water (0.19 mL). After the suspension had become a homogeneous solution, it was added to the monomer solution under an argon atmosphere. The solutions were stirred for 4 h at 20 °C. The reaction mixture was subjected to column chromatography (Al_2O_3; THF) to remove the copper complex. The solution of the polymeric material was concentrated, and then the viscous mixture was poured into diethyl ether. The precipitate was separated out by filtration. This purification procedure was repeated at least twice for each polymer. The purity was checked using thin layer chromatography, which indicated the absence of any monomeric fractions.

Supporting Information Available: ^1H NMR spectra of sample from reaction mixture after polymerization (SFigure 1), MALDI-TOF MS of **p-1**−**p-4** (SFigure 2), and plot of transmittance vs temperature of **p-1** in water (SFigure 3). This material is available free of charge via the Internet at http://pubs.acs.org.

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