

Thermo- and Photosensitive Flower Micelle of Poly(*N*-isopropylacrylamide) with Azobenzene Moieties Regularly Inserted in the Main Chain

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1. Polymer Synthesis

Materials. All chemicals were purchased from Aldrich unless otherwise stated. Prior to use, tetrahydrofuran (THF, 99%) was refluxed with sodium and a small amount of benzophenone and distilled; dichloromethane (DCM, 99%) was refluxed with CaH₂ and distilled; triethylamine (TEA) (≥99%) was refluxed with *p*-toluenesulfonyl chloride (Fluka, ≥99%) and distilled. Potassium carbonate (K₂CO₃, 99%), potassium iodide (KI, 99%), 6-chlorohexanol (96%), 4-nitrophenol (≥99%), oxalyl chloride (2.0 M in methylene chloride) and ethanol (95%) were used without purification. Azobisisobutyronitrile (AIBN, 98%) was recrystallized from methanol and *N*-isopropylacrylamide (NIPAM, 97%) was recrystallized from hexane. 4,4'-Dihydroxyazobenzene and *S,S'*-bis(α,α' -dimethyl- α'' -acetic acid)-trithiocarbonate were synthesized according to reported methods.^{10,11}

Synthesis of 4,4'-Dihydroxyhexyloxyazobenzene (2 in Scheme 1). 4,4'-Dihydroxyazobenzene (23.4 mmol, 5.0 g), 6-chlorohexanol (56.2 mmol, 7.7 g), K₂CO₃ (56.2 mmol, 7.8 g), ethanol (250 mL) and trace of KI were added into a 500 mL one-necked flask. The mixture was refluxed at 85 °C for 36 h under stirring. After evaporating ethanol, the residue was poured into water (1 L, pH=12). The yellow precipitate was washed with copious water and further recrystallized from methanol to give a yellow crystal (6.6 g with 68% yield). ¹H-NMR (300 MHz, δ ppm, DMSO-*d*₆): 7.82 (d, 4H, *o*-ArH to -N=N-), 7.11 (d, 4H, *o*-ArH to OCH₂(CH₂)₄CH₂OH), 4.40 (t, 2H, OCH₂(CH₂)₄CH₂OH), 4.09 (t, 4H, OCH₂(CH₂)₄CH₂OH), 3.75 (m, 4H, OCH₂(CH₂)₄CH₂OH), 1.30-1.86 (m, 16H, OCH₂(CH₂)₄CH₂OH).

Synthesis of Azobenzene-Containing Multifunctional Chain Transfer Agent (3). The polytrithiocarbonate RAFT agent was prepared by step-growth polymerization of **1** with **2** (Scheme 1). A typical preparation process is as follows. In the presence of argon, oxalyl chloride (9.0 mL, 18 mmol) was added dropwise to *S,S'*-bis(α,α' -dimethyl- α'' -acetic acid)-trithiocarbonate (BDATC) (0.54 g, 1.94 mmol). At the end of addition, the reaction mixture was heated to 60 °C for 3 h, resulting in the formation of a bright yellow solution. The excess oxalyl chloride was removed completely under reduced pressure to obtain a yellow solid (**1** in Scheme 1). Afterward, a THF solution of **1** (1.94 mmol) was added dropwise to 10.0 mL of THF solution of **2** (0.75 g, 1.8 mmol) containing 0.6 mL of TEA as catalyst. After the reaction mixture was stirred for 36 h at room temperature, the THF solution was concentrated and then precipitated into hexane to obtain the polytrithiocarbonate RAFT agent as a dark yellow solid (1.06 g with 85% yield). ¹H-NMR (300 MHz, δ ppm, CDCl₃): 7.80 (q, 4H, *o*-ArH to -N=N-), 6.97 (q, 4H, *o*-ArH to -OCH₂(CH₂)₄CH₂O-), 4.0-4.3 (m, 8H, -OCH₂(CH₂)₄CH₂O-), 1.98 (m, 12H, -C(CH₃)₂S(C=S)S C(CH₃)₂-), 1.40-1.80 (m, 16H, -OCH₂(CH₂)₄CH₂O-). M_n=4600, PDI=1.60, according to size exclusion chromatography (SEC) measurements using polystyrene (PS) standards. The estimated average number of trithiocarbonate groups (and thus the number of azobenzene moieties) in the macro-CTA is about 7. Also, in order to have azobenzene moieties in the main chain while growing PNIPAM chains using RAFT, an excess of **1** was used for the condensation reaction with **2**, which, statistically, should make the macro-CTA bear two trithiocarbonate end groups.

Synthesis of PNIPAM with Regularly Inserted Azobenzene Moieties in the Main Chain. A typical RAFT polymerization of NIPAM using the polytrithiocarbonate RAFT agent is as follows. **3** (82.8 mg, 0.018 mmol), AIBN (0.3 mg, 0.0018 mmol), NIPAM (1.5 g, 0.013 mol) and 4.0 mL THF were added into a 10-mL flask with a stirring bar. The solution was deoxygenated by bubbling argon for 30 min and then placed into an oil bath preheated to 70 °C. The polymerization was allowed to proceed for 2 h with the mixture under stirring. The polymer was collected after two precipitations of a THF solution in diethyl ether. This reaction gave rise to a sample of multi-azo-PNIPAM with M_n (NMR) \sim 31600 g/mol (using SEC-based M_n of **3**). $^1\text{H-NMR}$ (300 MHz, δ ppm, CDCl_3): 7.80 (broad, 4H, *o*-ArH to $-\text{N}=\text{N}-$), 6.97 (broad, 4H, *o*-ArH to $-\text{OCH}_2(\text{CH}_2)_4\text{CH}_2\text{O}-$), 6.90-5.70 (broad, 1H, NH in PNIPAM), 4.30-3.90 (broad, 9H, $-\text{C}(\text{CH}_3)_2\text{S}(\text{C}=\text{S})\text{SC}(\text{CH}_3)_2\text{COOCH}_2(\text{CH}_2)_4\text{CH}_2\text{O}-$ and CH_3CHCH_3 in PNIPAM), 2.30-1.20 (broad, 31H, $-\text{C}(\text{CH}_3)_2\text{S}(\text{C}=\text{S})\text{SC}(\text{CH}_3)_2\text{COOCH}_2(\text{CH}_2)_4\text{CH}_2\text{O}-$ and aliphatic main chain), 1.13 (s, 6H, CH_3CHCH_3 in PNIPAM).

2. Characterisations

Unless otherwise stated, all polymer solutions were prepared in deionised water at the concentration of 10 mg/mL; in cold water at 10 °C, all samples of multi-azo-PNIPAM were well dissolved. The cloud point measurements were conducted by taking UV-vis spectra with a spectrophotometer (Varian 50 Bio) while heating the solution (4 mL) in a cuvette held in a thermostat sample holder (Varian SPVF). The change in solution transmittance at 700 nm, which is far from absorption of azobenzene, was recorded as a function of temperature. The solution was heated stepwise with an interval of 2 °C and held at each temperature for 5 min for thermal equilibrium before the spectral taking. For the measurements with azobenzene in the *cis* form, the polymer solution was exposed to UV light at 10 °C for the *trans-cis* isomerization, the UV beam being generated from a spot-curing system (Novacure) with a UV filter (354 nm, \sim 50 mW/cm²). After the photostationary state rich in *cis* azobenzene was obtained, the cloud point measurements were carried out. The same spot-curing system was also used to produce visible light with a visible filter (440 nm, \sim 5 mW/cm²) for the reverse *cis-trans* isomerization of azobenzene.

While a Bruker 300 MHz spectrometer (AC 300) was used to record ^1H NMR spectra for general sample characterizations, variable-temperature ^1H NMR spectra of multi-azo-PNIPAM dissolved in D_2O were recorded on a Varian 600 MHz spectrometer (INOVA system). For these measurements, the polymer concentration was 5 mg/mL. Other experimental conditions were the same as in the cloud point measurements, i. e. solution temperature raised stepwise by 2 °C with the solution held at a given temperature for 5 min before taking the spectrum. Dynamic light scattering (DLS) measurements were carried out on a Brookhaven goniometer (BI-200) equipped with a highly sensitive avalanche photodiode detector (Brookhaven, BI-APD), a digital correlator (Brookhaven, TurboCorr) that calculates the photon intensity autocorrelation function $g^2(t)$, a helium-neon laser (wavelength $\lambda=632.8$ nm), and a thermostat sample holder. Volume-weighted hydrodynamic diameters (D_H) of the flower micelles were obtained by CONTIN analysis. Changes in scattering intensity were measured at 90°. D_H reported in the paper is the average value from more than 10 measurements. Flower micelles in the dry state were also examined by using a Hitachi H-7500 transmission electron microscope (TEM) operating at 60 KV. Samples were prepared by casting a polymer solution at a chosen

temperature on a carbon-coated copper grid pre-heated to the same temperature; followed by drying at the temperature before cooling to room temperature for the observation. Fluorescence emission spectra of Nile Red loaded in flower micelles were recorded on a Varian Cary Eclipse spectrometer. Encapsulation of the hydrophobic dye by the micelles was obtained by adding 25 μL of a THF solution of Nile Red (0.5 mg/mL) into 4mL of a polymer solution at room temperature, which was followed by more than 6 h of stirring to evaporate THF. Finally, size exclusion chromatograph (SEC) measurements were performed on a Waters system equipped with a refractive index detector (RI 410) and a photodiode array detector (PDA 996). THF was used as the eluent at an elution rate of 1 mL/min, while polystyrene (PS) standards were used for calibration.

3. ^1H NMR, UV-vis and Fluorescence Spectroscopic Results

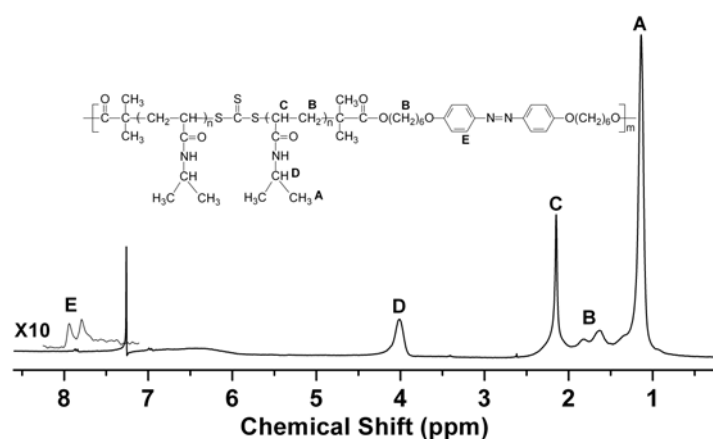


Figure S1 shows the ^1H NMR spectrum of P2 in CDCl_3 . The amount of PNIPAM with respect to azobenzene moieties could be determined by comparing the integrals of peak D at $\delta=3.98\text{-}4.20$ ppm and peak E at $\delta=7.80$ ppm. Combining with $M_n \sim 4600$ g/mol for the azobenzene-containing CTA (from SEC), the NMR analysis yielded $M_n \sim 44300$ g/mol for P2. Similar analysis gave rise to $M_n \sim 31600$ g/mol for P1.

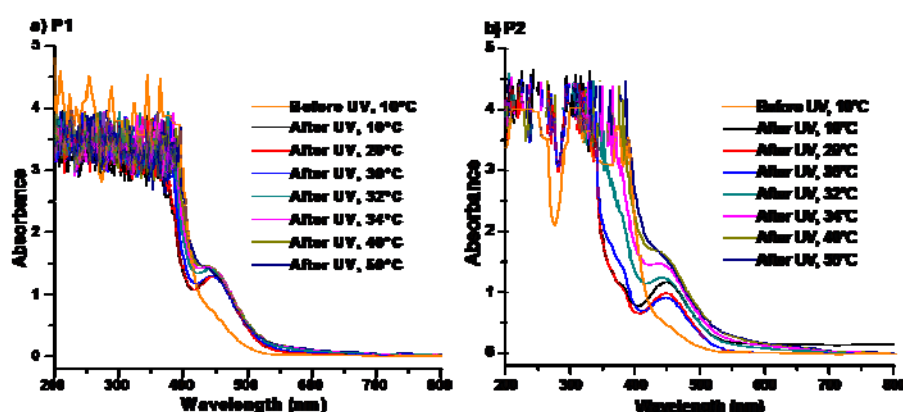


Figure S2 shows variable-temperature UV-vis spectra of the P1 and P2 solutions. In both cases, the absorption band of cis-azobenzene around 450 nm largely remained after the process of stepwise heating (2°C interval), thermal equilibrium (5 min) and measurement.