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Supporting information to

Facile Access to Thermoresponsive Filomicelles with Tuneable Cores

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Experimental Section

Materials

Ethanethiol (97%), carbon disulfide (>99.9%), p-toluenesulfonyl chloride (>99%), sodium dodecyl sulfate (SDS, >99%), and dimethyl sulfoxide (>99.9%, anhydrous) were purchased from Sigma-Aldrich and used as received. Potassium hydroxide (pellet, AR grade) was obtained from ChemSupply and used as received. Di(ethylene glycol) methyl ether methacrylate (DEGMA, 95%, Sigma-Aldrich), *N*-(2-hydroxypropyl)methacrylamide (HPMA, Polysciences), styrene (>99%, Sigma-Aldrich), methyl methacrylate (MMA, >99%, Sigma-Aldrich), benzyl methacrylate (BzMA, 96%, Sigma-Aldrich), ethyl methacrylate (EMA, 99%, Sigma-Aldrich), propyl methacrylate (PMA, 97%, Sigma-Aldrich), and butyl methacrylate (BMA, 99%, Sigma-Aldrich) were passed through a column of basic alumina (activity I) to remove inhibitor prior to use. 4,4'-Azobis(4-cyanopentanoic acid) (ACPA, 98%, Alfa Aesar) and azobisisobutyronitrile (AIBN) were recrystallized twice in methanol prior to use. MilliQ water (resistivity > 18.2 MΩcm^{-1}) was generated using a Millipore MilliQ Academic Water Purification System. All other chemicals and solvents used were of at least analytical grade.

Synthesis of chain transfer agent (CTA), 4-cyano-4-(ethylthiocarbonothioylthio)pentanoic acid (ECT). The synthesis of ECT was carried out as previously described.[1]

Synthesis of macromolecular chain transfer agent (macro-CTA), P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$.[2] The polymerization was carried out in a 50 mL vial equipped with a magnetic stir bar. DEGMA (3.50 g, 1.86 x 10^{-2} mol), HPMA (1.33 g, 9.3 x 10^{-3} mol), ECT (122 mg, 4.65 x 10^{-4} mol), and ACPA (11 mg, 3.72 x 10^{-5} mol) were dissolved in DMSO (20 mL, anhydrous). The vial was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 60 min at room temperature (23 °C). After polymerizing for 7 h at 70 °C, the reaction was quenched by cooling to 0 °C (by immersing the vial in an ice bath) and exposing the solution to air. A 50 µL aliquot of the solution was sampled to determine conversion by ^{1}H NMR. The solution was then

dialyzed against acetone (1 L) for 1 h using a dialysis membrane with molecular weight cut-off of 3.5 kDa, principally to reduce the amount of DMSO. The polymer was recovered by precipitating into a large excess of a diethyl ether / petroleum ether mixture (2:1 v/v), after which the precipitated polymer was isolated by centrifugation and redissolved in acetone. This purification process was repeated three times. The product was dried under high vacuum for 24 h to give a sticky yellow solid (2.81 g, yield 57%).

Kinetic investigation of the RAFT-mediated emulsion polymerization of benzyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA. Macro-CTA (120 mg, 1.76 x 10^{-5} mol), and SDS (2.0 mg, 7.0 x 10^{-6} mol) were dissolved in MilliQ water (4 mL) in a Schlenk tube. The tube was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 30 min at ambient temperature, and then heated to 60 °C for 10 min to form a latex under a nitrogen atmosphere. AIBN (1 mg, 6.1 x 10^{-6} mol) was dissolved in benzyl methacrylate (0.5 mL) in a 1.5-mL vial. The vial was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 10 min at room temperature. After 40 min of deoxygenating and heating at 60 °C, a portion of the deoxygenated benzyl methacrylate (200 μL) was added into the Schlenk tube using a gas-tight syringe to start the polymerization. Approximately 0.1 mL of the emulsion was sampled periodically during the polymerization using a gas-tight syringe. These samples were used to evaluate conversion (by ^{1}H NMR), and molecular weight (by SEC) as a function of reaction time. After 3.5 h stirring at 60 °C and 700 rpm, the emulsion polymerization was stopped by exposing the latex to air at 60 °C.

Formation of poly(benzyl methacrylate) nanoparticles with different morphologies from hot latexes after the RAFT-mediated emulsion polymerization and exposing the latex to air at 60 °C. 0.5 mL aliquots of hot latex from the Schlenk tube were transferred to 1.5-mL vials each having a different amount of benzyl methacrylate (i.e., 10 μL, 20 μL, 40 μL μL). These vials were sealed,

vortexed for 2 seconds, and then slowly cooled to room temperature (23 °C) over 24 h by leaving these vials to sit on the bench.

RAFT-mediated emulsion polymerization of methacrylate monomers in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA. Macro-CTA (60 mg, 8.80 x 10^{-6} mol), and SDS (1.0 mg, 3.5 x 10^{-6} mol) were dissolved in MilliQ water (2 mL) in a Schlenk tube. The tube was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 30 min at ambient temperature, and then heated to 60 °C for 10 min to form a latex under a nitrogen atmosphere. AIBN (1 mg, 6.1 x 10^{-6} mol) was dissolved in the chosen methacrylate monomers (0.5 mL) in a 1.5-mL vial. The vial was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 10 min at room temperature prior to use. After 40 min, a portion of the deoxygenated methacrylate monomers (100 μL) was added into the Schlenk tube using a gas-tight syringe to start the polymerization. After the chosen reaction time for the particular methacrylate (see Table 1), the emulsion polymerization was stopped by exposing the latex to air at 60 °C.

Formation of methacrylate filomicelles from hot latexes after the RAFT-mediated emulsion polymerization and exposing the latex to air at 60 °C. 1 mL aliquots of hot latex from the Schlenk tubes were transferred to 1.5-mL vials each having a 40 μL of the same methacrylate monomer used for the polymerization. These vials were sealed, vortexed for 2 seconds, and then slowly cooled to room temperature (23 °C) over 24 h by leaving these vials to sit on the bench. All samples were then dialyzed again MilliQ water for 3 days (4 x 500 mL).

RAFT-mediated emulsion polymerization of styrene in water at 70 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA. Macro-CTA (60 mg, 8.80 x 10^{-6} mol), and SDS (1.0 mg, 3.5 x 10^{-6} mol) were dissolved in MilliQ water (2 mL) in a Schlenk tube. The tube was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 25 min at ambient temperature, and then heated to 70 °C for 5 min to form a latex under a nitrogen atmosphere. AIBN

(1 mg, 6.1 x 10^{-6} mol) was dissolved in styrene (0.3 mL) in a 1.5-mL vial. The vial was sealed with a rubber septum and the solution was deoxygenated by sparging with nitrogen for 10 min at room temperature prior to use. After 30 min of deoxygenating and heating at 60 °C, a portion of the deoxygenated styrene (60 μL, 5.2 x 10^{-4} mol) was added into the Schlenk tube using a gas-tight syringe to start the polymerization. After 4 h stirring at 70 °C and 700 rpm, the emulsion polymerization was stopped by exposing the latex to air at 70 °C. Aliquots were taken to evaluate conversion (by gravimetric analysis), and molecular weight (by SEC).

Formation of styrene filomicelles from hot latex after RAFT-mediated emulsion polymerization and exposing the latex to air at 70 °C. A 1 mL aliquot of hot latex from the Schlenk tube was transferred to a 1.5-mL vial containing 40 μL of toluene. The vial was sealed, vortexed for 2 seconds, and then slowly cooled to room temperature (23 °C) over 24 h by leaving the vial sit on the bench. The latex was then dialyzed again MilliQ water for 3 days (4 x 500 mL).

Characterization Techniques

^{1}H Nuclear Magnetic Resonance (NMR). All NMR spectra were recorded on a Bruker Advance III 400 MHz spectrometer using an external lock and referenced to the residual non-deuterated solvent.

Size Exclusion Chromatography (SEC). SEC analyses of polymer samples were performed using a Shimadzu modular system comprising a DGU-12A degasser, an SIL-20AD automatic injector, a 5.0 μm bead-size guard column (50 × 7.8 mm) followed by three KF-805L columns (300 × 8 mm, bead size: 10 μm, pore size maximum: 5000 Å), an SPD-20A ultraviolet detector, and an RID-10A differential refractive-index detector. The temperature of the columns was maintained at 40 °C using a CTO-20A oven. The eluent was tetrahydrofuran and the flow rate was kept at 0.8 mL/min using an LC-20AD pump. A molecular weight calibration curve was produced using commercial narrow molecular weight distribution polystyrene standards with molecular weights ranging from

500 to 2 x 10^6 g mol^{-1}. Polymer solutions at approx. 2 mg mL^{-1} were prepared and filtered through 0.45 μm filters prior to injection.

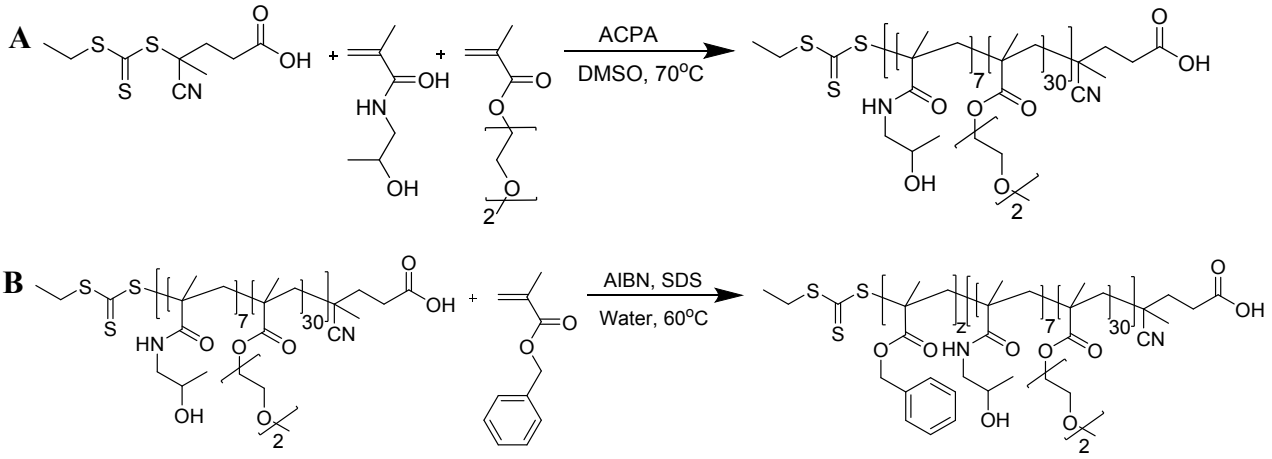
Dynamic Light Scattering (DLS). Cloud point temperature (T_{cp}) was identified by a sudden change in particle size using DLS.[3] Dynamic light scattering measurements were performed using a Malvern Zetasizer Nano Series running DLS software and operating a 4 mW He-Ne laser at 633 nm. Analysis was performed at an angle of 173° and a constant temperature of 25 °C. The sample refractive index (RI) was set at 1.59 for polystyrene. The dispersant viscosity and RI were set to 0.89 $Ns.m^{-2}$ and 1.33, respectively. 10 mg of macro-CTA was dissolved in cold MilliQ-water (1 mL) by vortexing for 10 min. The measurement was carried out by slowly increasing the temperature from 15°C to 60 °C using the standard operating procedures function of the DLS software. The sample was incubated for 5 min at each temperature prior to measurement.

Transmission Electron Microscopy (TEM). TEM images were recorded using a Tecnai F20 or Tecnai F30 transmission electron microscope at an accelerating voltage of 200 kV at ambient temperature. A typical TEM grid preparation was conducted as follow: a 2 μL aliquot of a 0.1 wt% solution was dropped onto a Formvar-film copper grid (GSCu100F-50, Proscitech), after which the sample was allowed to dry under air overnight. For samoples requiring negative staining, another 2 μL aliquot of uranyl formate solution (2 % in MilliQ water) was dropped onto the dried sample on the Formvar-film copper grid. The staining solution was allowed to dry overnight before characterization.

Differential Scanning Calorimetry (DSC). DSC measurements were performed on a PerkinElmer DSC8500 instrument at a heating rate of 50 °C min^{-1} under nitrogen atmosphere.[4] A typical measurement was conducted by the following method: Initially, approx. 10 mg of sample was sealed in an aluminum pan by compression molding, after which the sample was inserted into the sample holder of the calorimeter and subjected to two heating/cooling cycles. Glass transition temperature (T_g) was determined by identifying the inflection point in final DSC heating curve using the PerkinElmer Pyris software.[5]

Supporting Schemes, Tables and Figures

Scheme S1. (A) Synthesis of P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ macro-CTA. (B) RAFT-mediated emulsion polymerization of benzyl methacrylate in water.



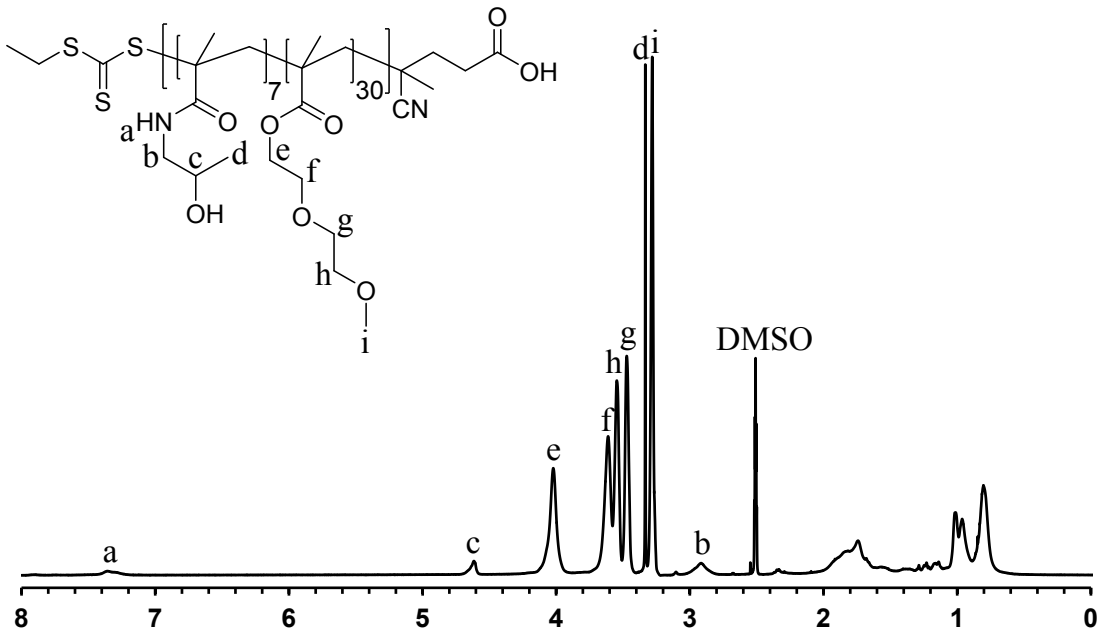


Figure S1. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ macro-CTA in DMSO-d$_6$.

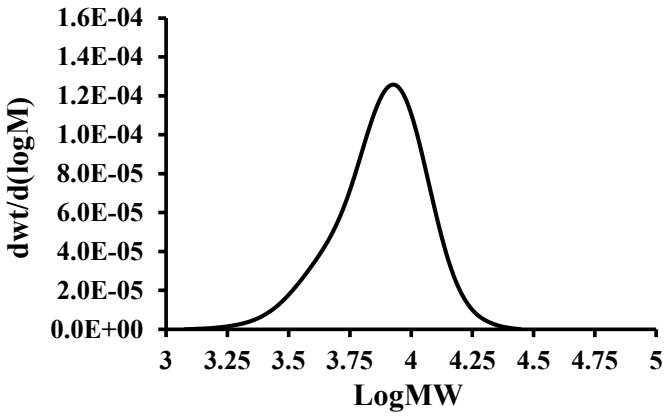


Figure S2. SEC of P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ macro-CTA.

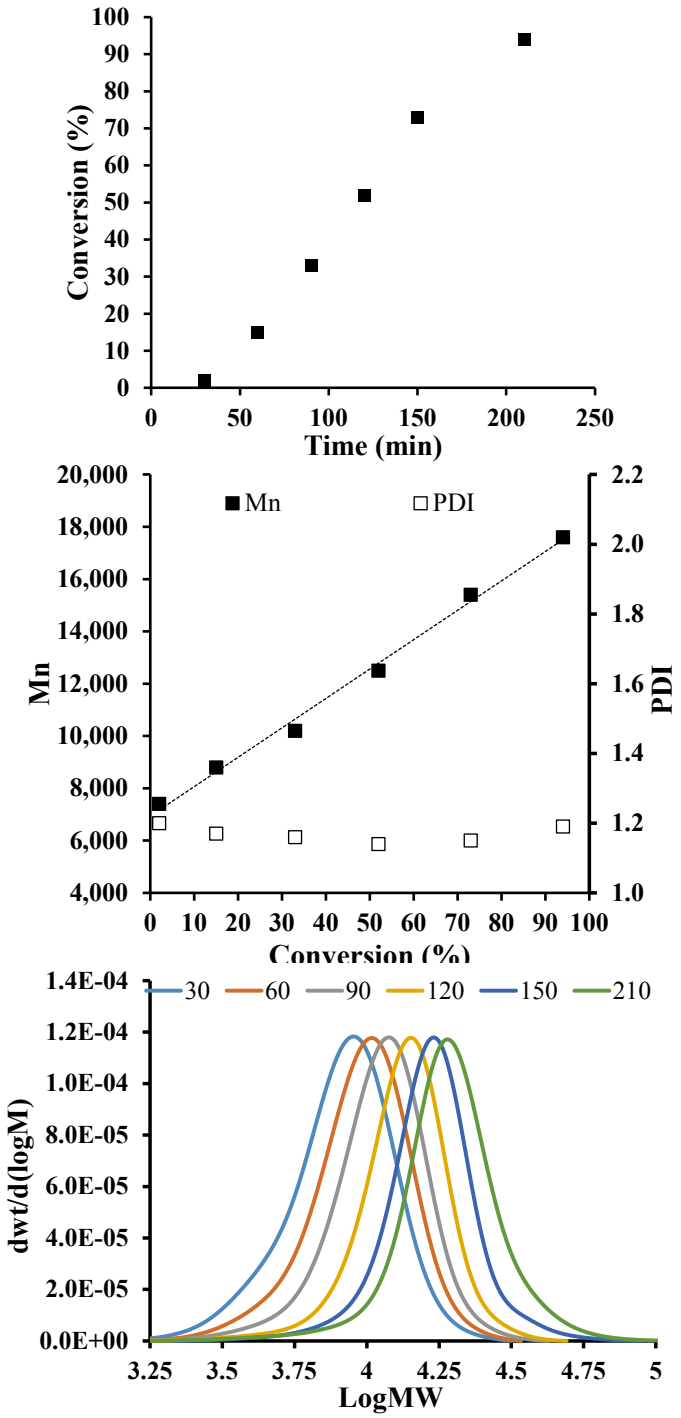


Figure S3. (A) Conversion vs time, (B) number-average molecular weight and dispersity vs conversion, and (C) molecular weight distributions (MWDs) for the RAFT-mediated emulsion polymerization of benzyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as Macro-CTA and AIBN as initiator.

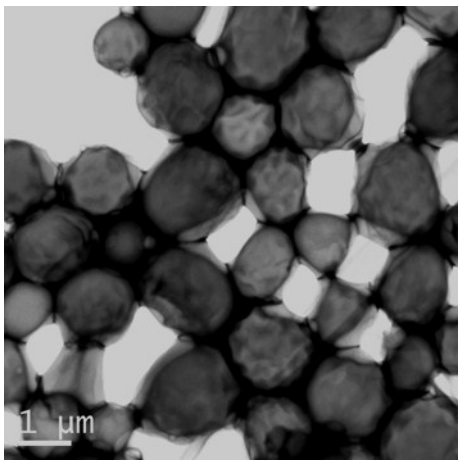
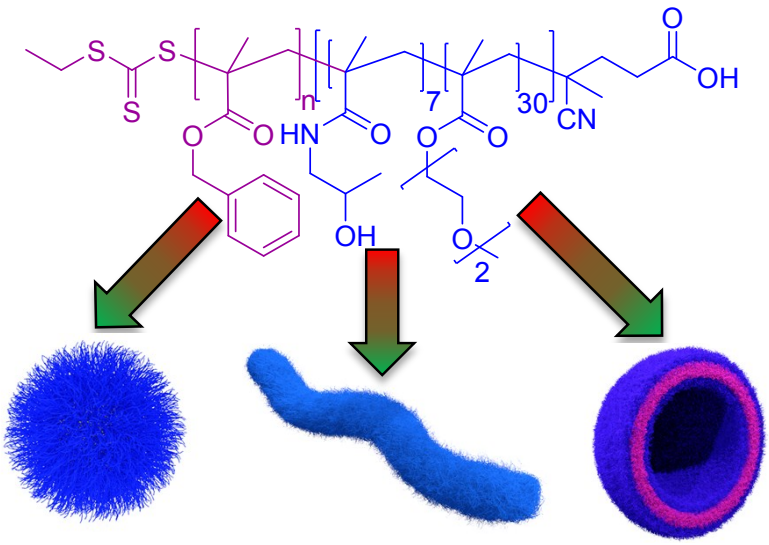
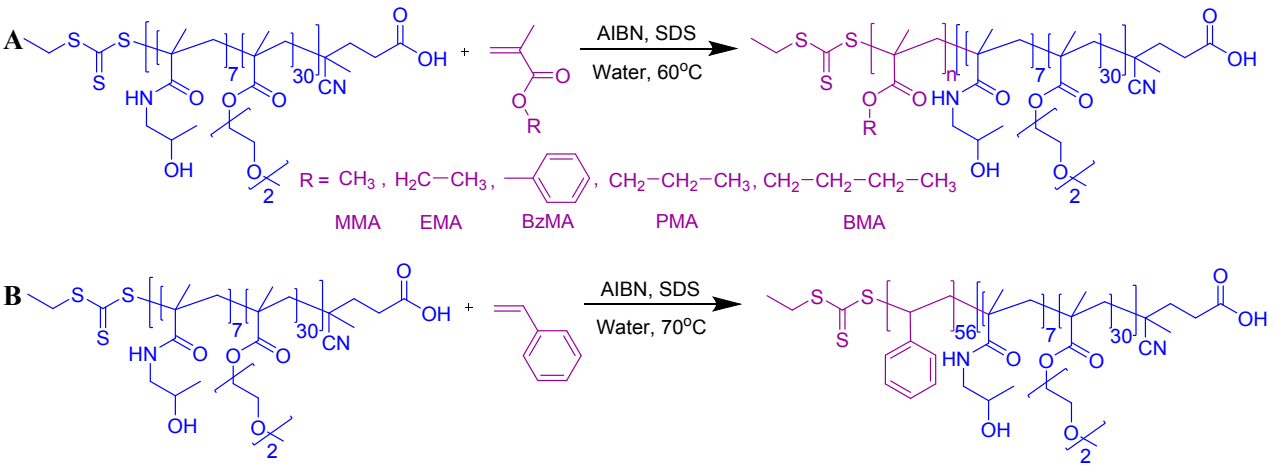


Figure S4. Representative TEM images of the latex of benzyl methacrylate copolymer at 60 °C after 3.5 h of polymerization and dried on the Formvar-film copper grid at 60 °C.

Scheme S2. A 3D cartoon represents PBzMA nanoaggregates with different morphologies in water via temperature-induced morphological transformation (TIMT).





Scheme S3. (A) RAFT-mediated emulsion polymerization of methacrylate monomers in water. (B) RAFT-mediated emulsion polymerization of styrene in water.

Table S1. Summary of thermoresponsive diblock copolymers synthesized via RAFT-mediated emulsion polymerization in water using AIBN as initiator and P($DEGMA_{30}$-co-$HPMA_7$)-$SC(=S)SC_2H_5$ as macro-CTA.

Copolymer	Monomer	[M]:[Macro-CTA]:[I]	Time (h)	Temp. (°C)	Conv.[a]	SEC[b]		^{1}H NMR		DSC
						M_n (g/mol)	$Đ$	DP[c] (n)	M_n[d] (g/mol)	T_g[e] (°C)
P1	MMA	106:1:0.1	3.0	60	96	13,500	1.21	99	17,321	101
P2	STY	59:1:0.2	4.0	70	92	14,700	1.17	56	10,128	95
P3	EMA	91:1:0.1	3.0	60	94	16,100	1.19	85	14,565	61
P4	BzMA	67:1:0.1	3.5	60	96	17,700	1.19	61	10,897	51
P5	PMA	80:1:0.1	3.5	60	91	15,100	1.16	75	12,777	31
P6	BMA	71:1:0.1	4.5	60	93	16,200	1.22	68	11,664	14

[a] Conversions were determined by gravimetric analysis. [b] SEC data measured in THF solution using PSTY standards for calibration. [c] Degree of polymerization of styrene was calculated by comparing the ^{1}H NMR intensity of 90 protons of -O-CH_3 of the DEGMA component (I_j) to the protons of phenyl rings (I_S) using the following equation: $n_{STY} = I_S / I_j * 90 / 5$. Degree of polymerization of MMA was calculated by comparing the ^{1}H NMR intensity of 90 protons of -O-CH_3 of the DEGMA component (I_i) to the protons of -C(=O)-O-CH_3 of methacrylate blocks (I_t) using the following equation: $n = I_t / I_i * 90 / 3$. Degree of polymerization (DP) of EMA, BzMA, PMA, and BMA were calculated by comparing the ^{1}H NMR intensity of 90 protons of -O-CH_3 of the DEGMA component (I_i) to the protons of -C(=O)-O-CH_2- of methacrylate blocks (I_j) using the following equation: $n = I_j / I_i * 90 / 2$. [d] M_n were calculated using the following equation: $M_n = n \times M_{monomer} + 6087$. [e] Glass transition temperatures (T_g) were determined by identifying the inflection points in final DSC heating curves using Pyris software.

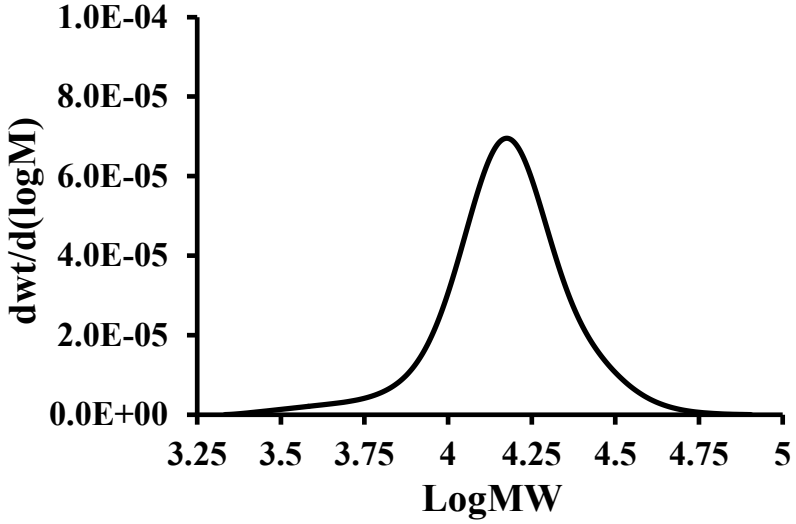


Figure S5. SEC traces for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(MMA$_{99}$)-SC(=S)SC$_2$H$_5$ prepared by the RAFT-mediated emulsion polymerization of methyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA and AIBN as initiator.

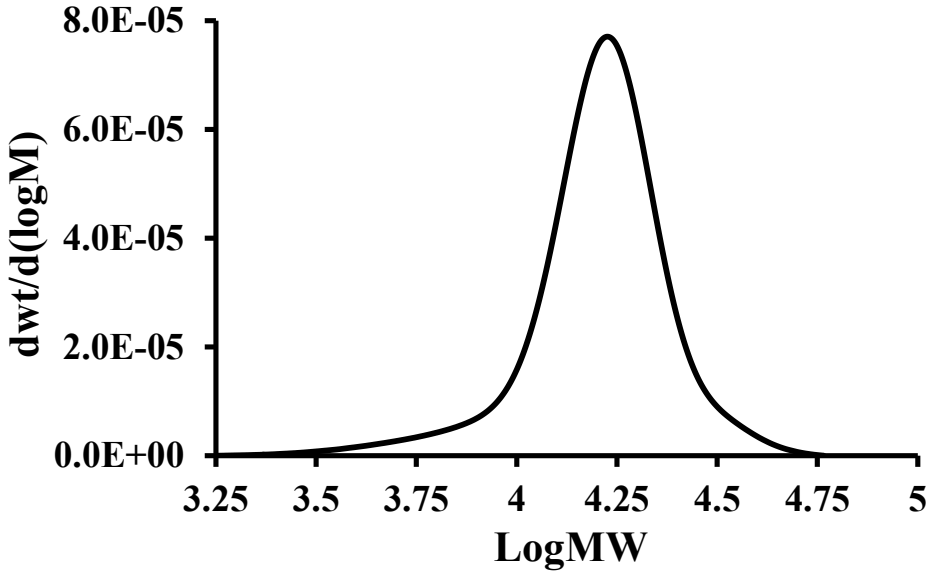


Figure S6. SEC traces for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(STY$_{56}$)-SC(=S)SC$_2$H$_5$ prepared by the RAFT-mediated emulsion polymerization of styrene in water at 70 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA and AIBN as initiator.

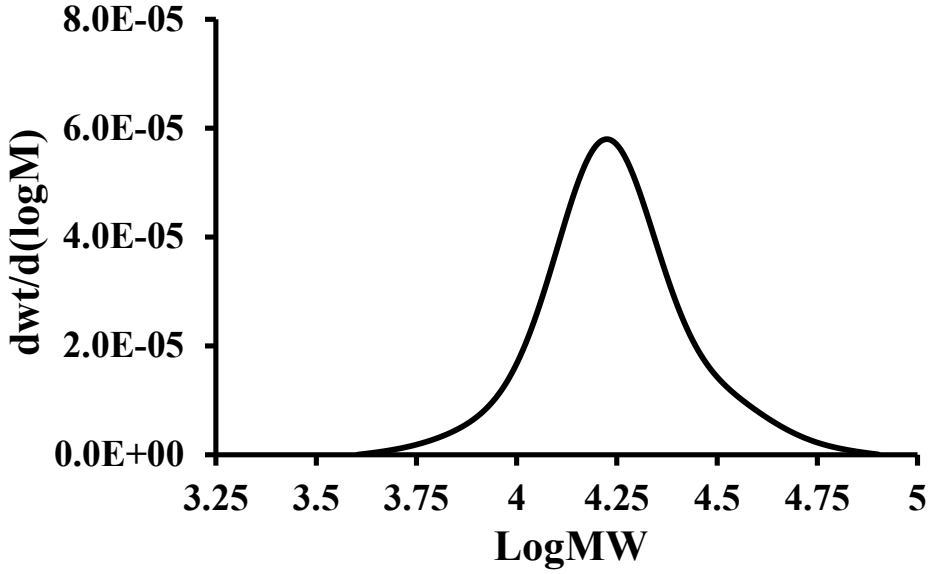


Figure S7. SEC traces for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(EMA$_{85}$)-SC(=S)SC$_2$H$_5$ prepared by the RAFT-mediated emulsion polymerization of ethyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA and AIBN as initiator.

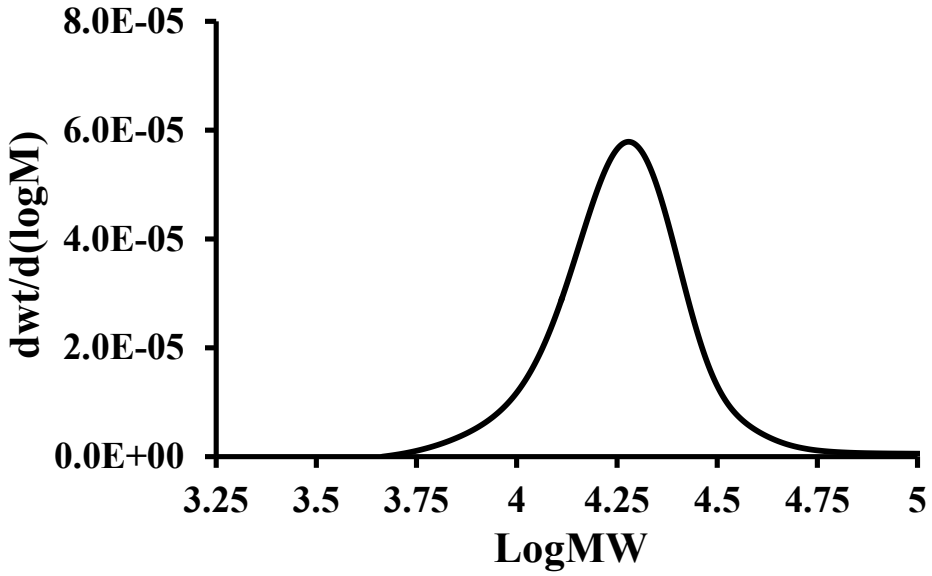


Figure S8. SEC traces for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(BzMA$_{61}$)-SC(=S)SC$_2$H$_5$ prepared by the RAFT-mediated emulsion polymerization of benzyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA and AIBN as initiator.

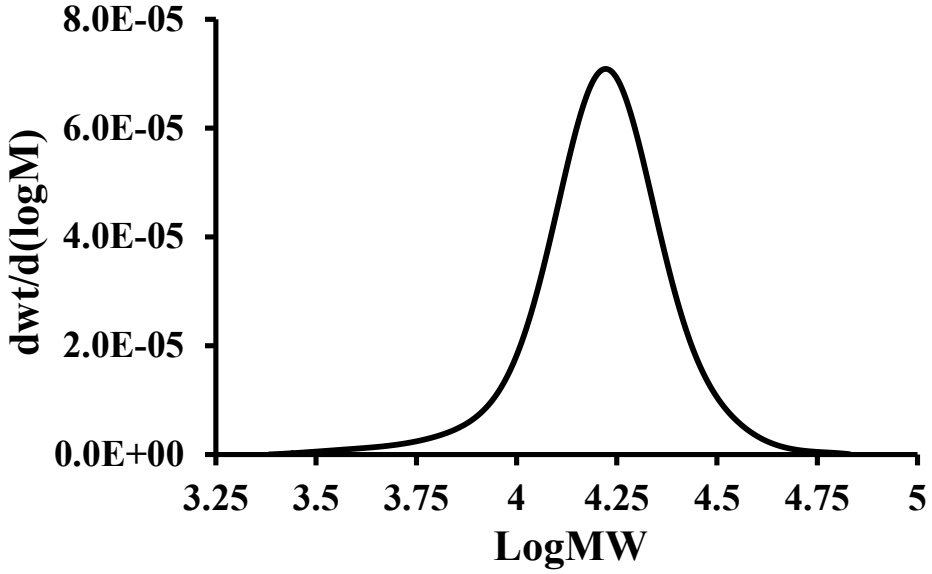


Figure S9. SEC traces for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(PMA$_{75}$)-SC(=S)SC$_2$H$_5$ prepared by the RAFT-mediated emulsion polymerization of propyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA and AIBN as initiator.

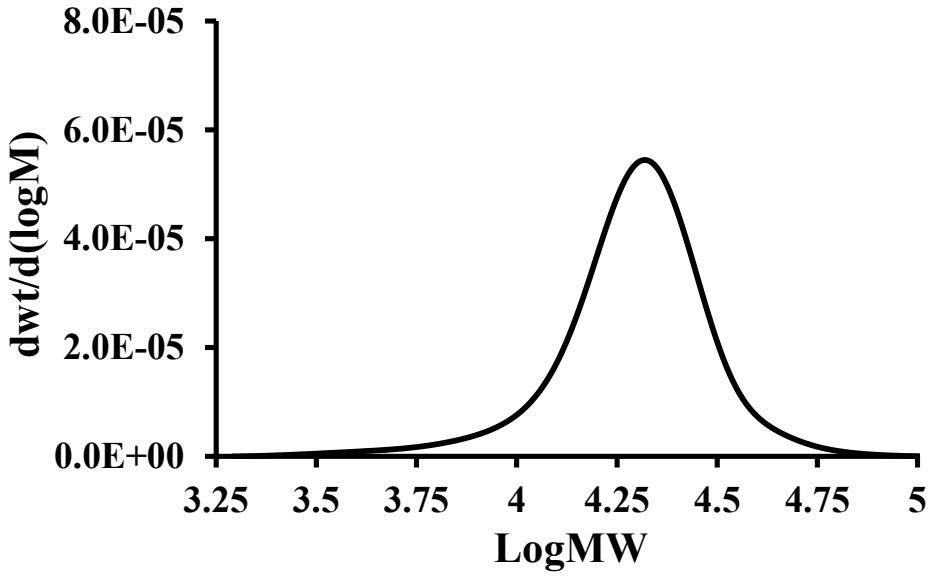


Figure S10. SEC traces for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(BMA$_{68}$)-SC(=S)SC$_2$H$_5$ prepared by the RAFT-mediated emulsion polymerization of butyl methacrylate in water at 60 °C using P(DEGMA$_{30}$-co-HPMA$_7$)-SC(=S)SC$_2$H$_5$ as macro-CTA and AIBN as initiator.

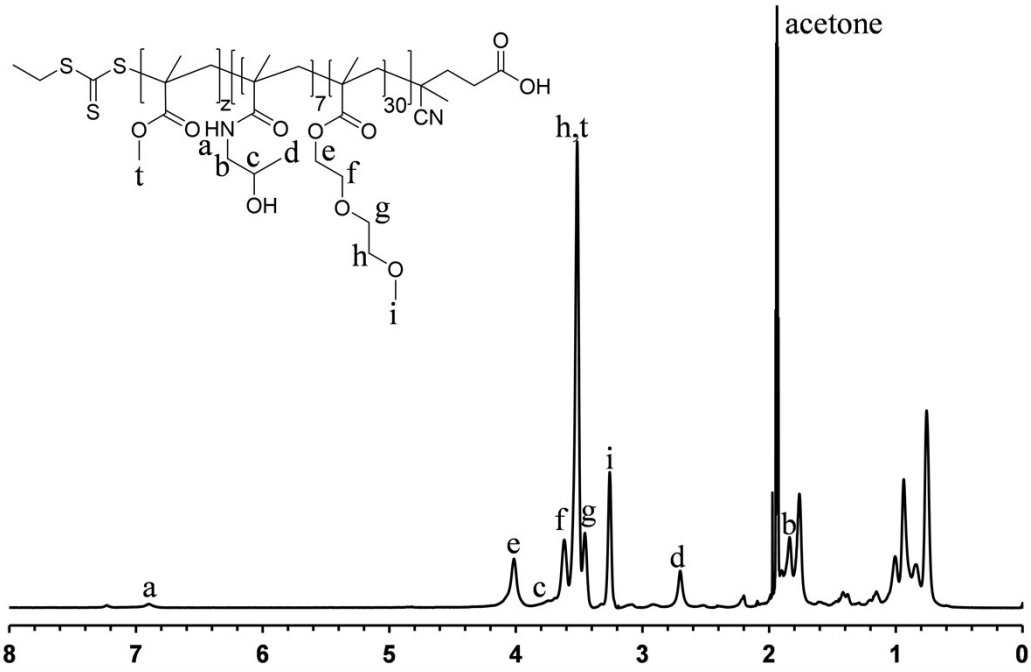


Figure S11. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_{7}$)-b-(MMA$_{99}$)-SC(=S)SC$_2$H$_5$ in acetone-d$_6$.

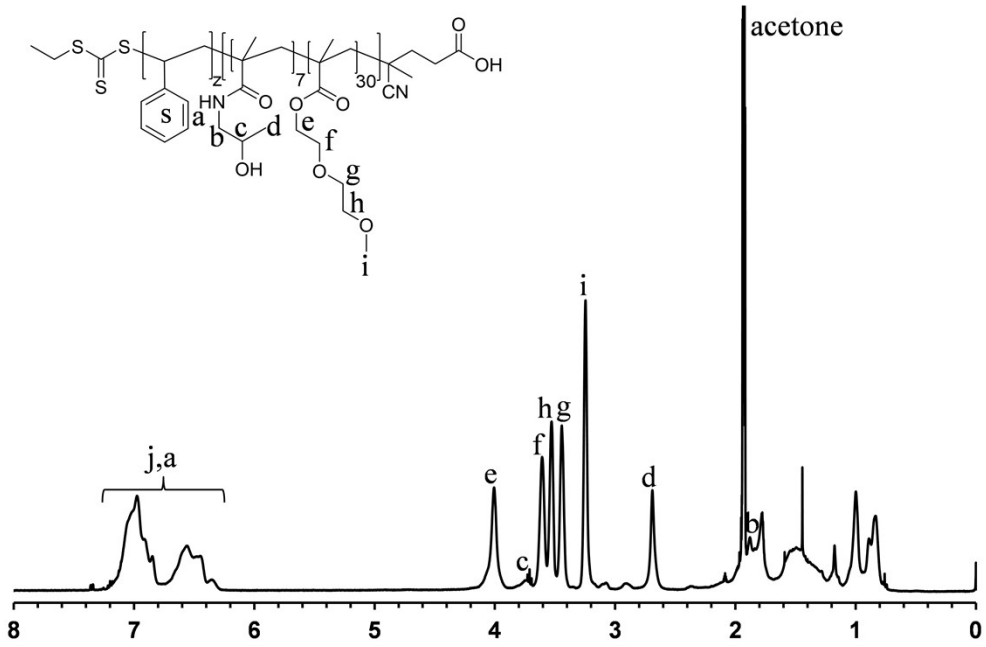


Figure S12. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_{7}$)-b-(STY$_{56}$)-SC(=S)SC$_2$H$_5$ in acetone-d$_6$.

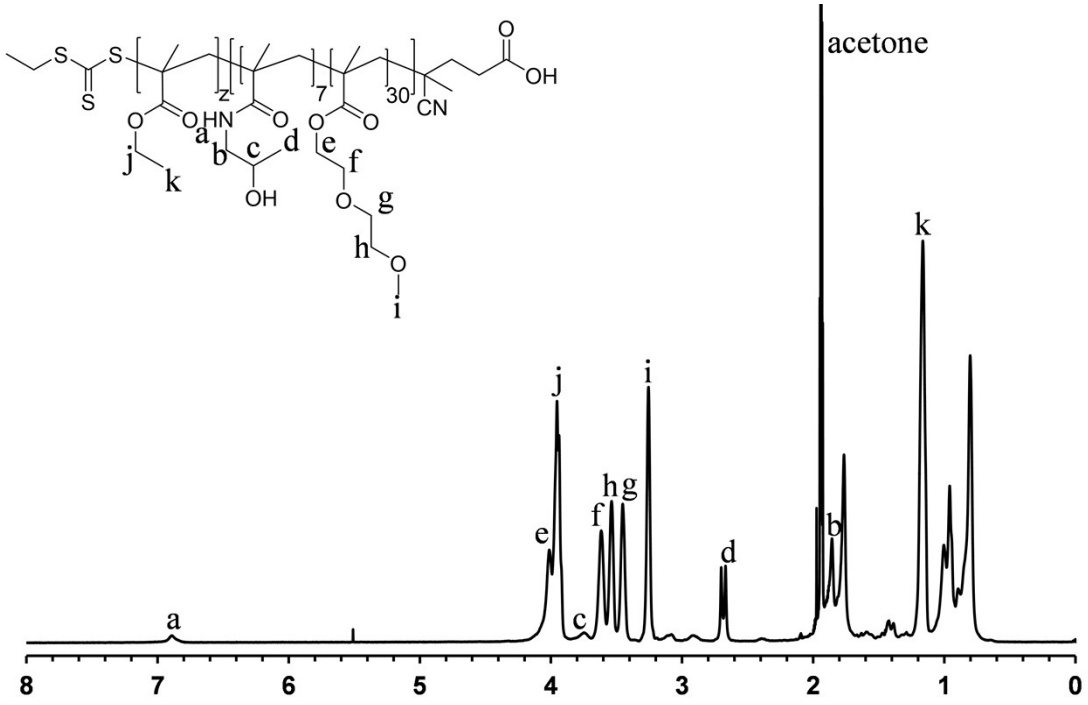


Figure S13. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_{7}$)-b-(EMA$_{85}$)-SC(=S)SC$_2$H$_5$ in acetone-d$_6$.

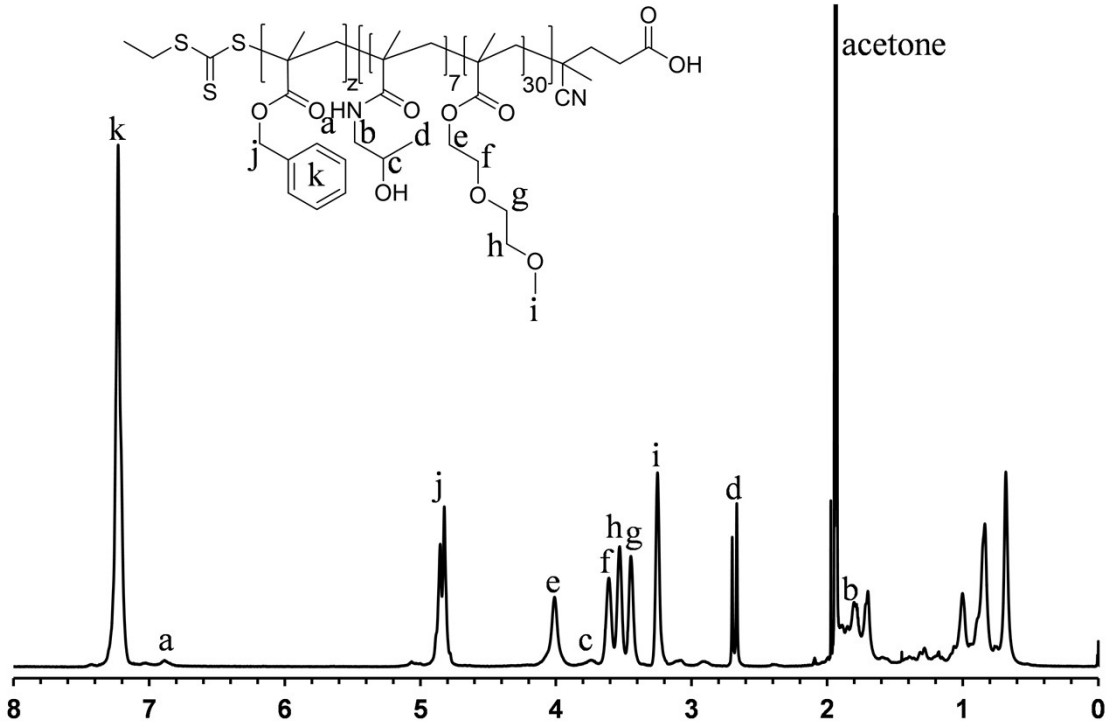


Figure S14. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(BzMA$_{61}$)-SC(=S)SC$_2$H$_5$ in acetone-d$_6$.

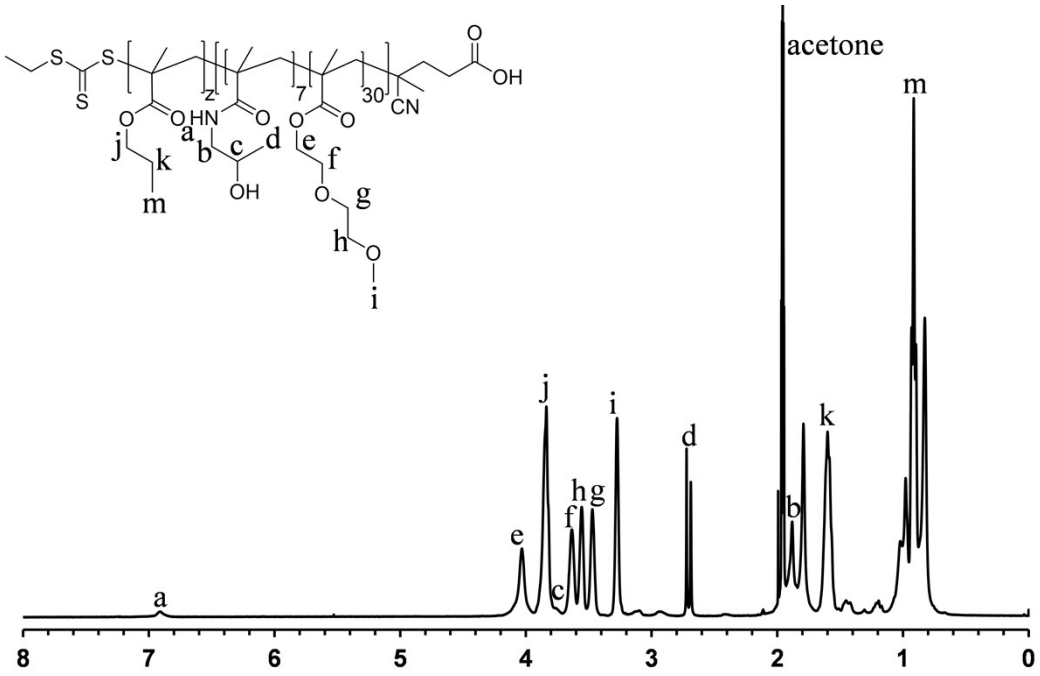


Figure S15. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_7$)-b-(PMA$_{75}$)-SC(=S)SC$_2$H$_5$ in acetone-d$_6$.

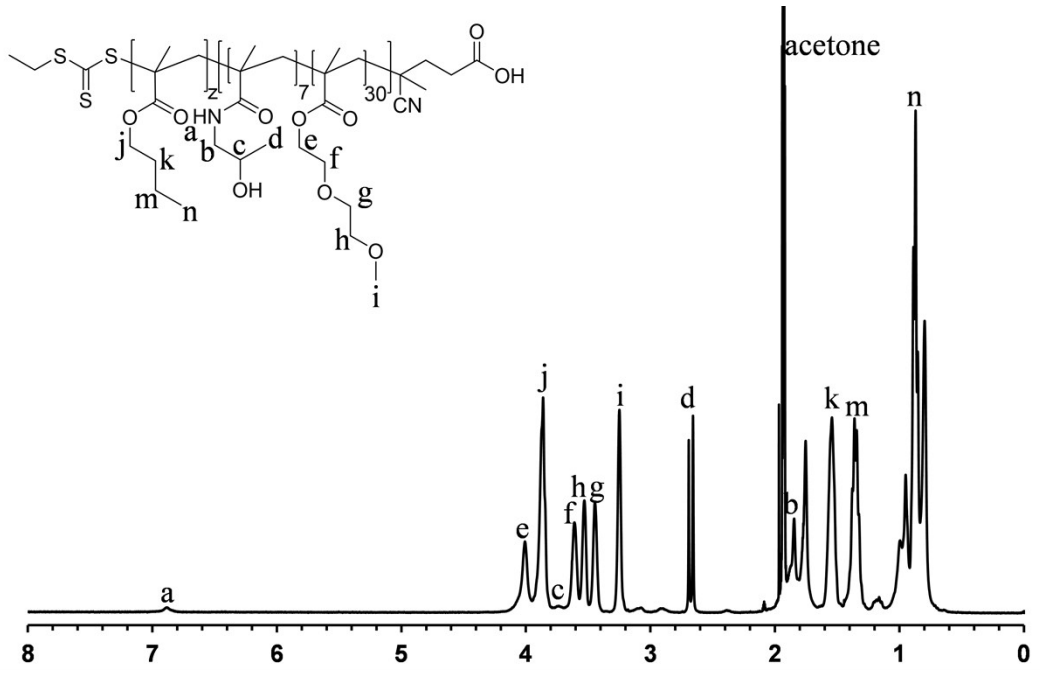


Figure S16. ^{1}H NMR spectrum for P(DEGMA$_{30}$-co-HPMA$_{7}$)-b-(BMA$_{68}$)-SC(=S)SC$_2$H$_5$ in acetone-d$_6$.

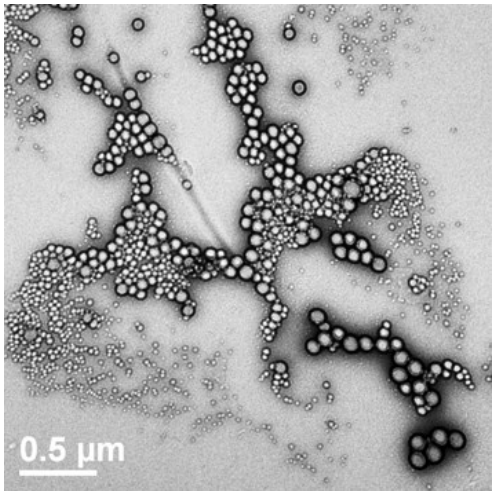


Figure S17. Representative TEM images of the latexes of P6 formed in water after: emulsion polymerization, subsequent addition of 40 µL/mL of butyl methacrylate, then cooling to room temperature (23 °C) overnight. Sample was negatively stained with uranyl formate solution (2 % in MilliQ water).

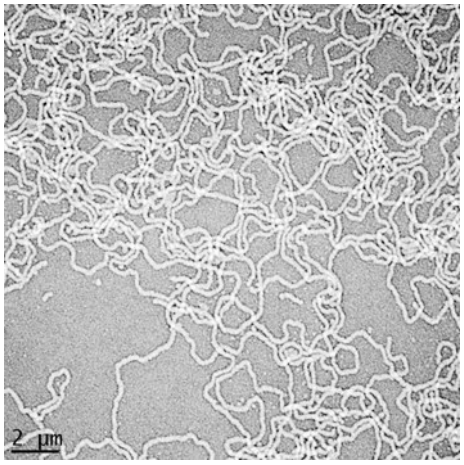


Figure S18. Representative TEM images of the latexes of P5 formed in water after: emulsion polymerization, subsequent addition of 40 µL/mL of propyl methacrylate, then cooling to room temperature (23 °C) overnight, dialysis against MilliQ water for 72 h, heating to 50 °C for 1 min,

and finally cooling to room temperature. Sample was negatively stained with uranyl formate solution (2 % in MilliQ water).

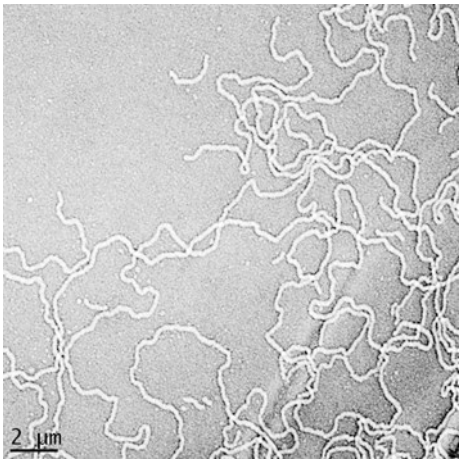


Figure S19. Representative TEM images of the latexes of P5 formed in water after: emulsion polymerization, subsequent addition of 40 µL/mL of propyl methacrylate, then cooling to room temperature (23 °C) overnight, dialysis against MilliQ water for 72 h, and finally dialysis against PBS buffer for 72 h. Sample was then stored for a week before negatively staining with uranyl formate solution (2 % in MilliQ water) for TEM characterization.

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