ABC or ACB Triblock Copolymers? Changing the RAFT Group Position in Diblock Copolymer Macro-RAFT Agents leads to different PISA Behaviors in RAFT Dispersion Polymerization

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EXPERIMENTAL SECTION

Materials.

Monomethoxy poly(ethylene glycol) (mPEG$_{45}$, 2000 g/mol, Sigma-Aldrich), dicyclohexylcarbodiimide (DCC, Aladdin), 4-dimethylaminopyridine (DMAP, Aladdin), hydroquinone (Aladdin), *N,N*-dimethylacetamide (DMA, Aladdin), and 1,3,5- trioxacyclohexane (Aladdin) were used as received. 2,2-Azobisisobutyronitrile (AIBN, Aladdin) was recrystallized from ethanol prior to storage under refrigeration at 4 °C. Styrene (St, Aladdin) was purified by passing through a basic alumina oxide (Aladdin) column prior to storage at 4 °C. 3-(Benzylthiocarbonothioylthio)propanoic acid (BTPA) and 4-(*n*-butylsulfanylthiocarbonyl)sulfanyl methylbenzoic acid (BTSMA) were synthesized according to published procedures. [1,2]

Characterization.

Transmission Electron Microscopy (TEM). The obtained dispersions were diluted 100-fold with methanol/water. A drop of the solution was placed on a copper grid for 3 min and then blotted with filter paper to remove excess solution. Transmission electron microscopy (TEM) observations were carried out on a Hitachi 7700 instrument operated at 100 kV.

Size Exclusion Chromatography (SEC). The molar mass and polydispersity of polymers were measured by SEC at 35 ºC using a Waters 1515 SEC instrument with tetrahydrofuran (THF) as the mobile phase and Waters Styragel HR1, HR4 columns. The flow rate of THF was 1.0 mL/ min. Linear polystyrene polymers with narrow molar mass distributions were used as standards to calibrate the apparatus.

¹H NMR Spectroscopy. ¹H NMR spectra were recorded in CDCl₃ using a Bruker Avance III 400 MHz NMR spectrometer at a temperature of 25 ℃.

Ultraviolet visible photometer. UV-Visible spectra were recorded with a 1.0 cm quartz cuvette using a UV 2450 spectrometer.

Dynamic Light Scattering. Intensity-average hydrodynamic diameters of the dispersions (0.1% v/v) were obtained using a Brookhaven nanoparticle size-zeta potential analyzer.

Synthesis of mPEG₄₅-BTPA. A solution of BTPA (3.81 g, 14 mmol) in 40 mL of anhydrous dichloromethane (DCM) was introduced in a dry flask under nitrogen atmosphere containing mPEG₄₅ (20.0 g, 10 mmol). Then a solution of DCC (2.89 g, 14 mmol) and DMAP (0.43 g, 3.5 mmol) in 10 mL of anhydrous DCM was added dropwise to the reaction mixture at 0 °C. The esterification reaction proceeded under stirring at room temperature for 24 h. After 24 h of the reaction, additional DCC (2.07 g, 10 mmol) was added in the reaction mixture. The reaction was conducted for another 24 h. The polymer was then collected by precipitation of the reaction mixture in *n*-hexane, and then was further purified by silica column chromatography (CH₂Cl₂:CH₃OH = 25:1, v/v). Finally, the sample dried at 35 ℃ under vacuum to obtain a yellow powder.

Synthesis of mPEG₄₅-BTSMA. A solution of BTSMA (4.20 g, 14 mmol) in 40 mL of anhydrous DCM was introduced in a dry flask under nitrogen atmosphere containing mPEG₄₅ (20.0 g, 10 mmol). Then a solution of DCC (2.89 g, 14 mmol) and DMAP (0.43 g, 3.5 mmol) in 10 mL of anhydrous DCM was added dropwise to the reaction mixture at 0 °C. The esterification reaction proceeded under stirring

at room temperature for 24 h. After 24 h of the reaction, additional DCC (2.06 g, 10 mmol) was added in the reaction mixture. The reaction was conducted for another 24 h. The polymer was then collected by precipitation of the reaction mixture in *n*-hexane, and was further purified by silica column chromatography (CH$_2$Cl$_2$:CH$_3$OH = 25:1, v/v). Finally, the sample was dried at 35 °C under vacuum to obtain a yellow powder.

Synthesis of the mPEG$_{45}$-BTPA-PDMA$_{20}$. DMA (9.02 g, 90.8 mmol), mPEG$_{45}$-BTPA (10.23 g, 4.5 mmol), AIBN (0.2485 g ,1.51 mmol), 1,4-dioxane (18.30 g), and 1,3,5-trioxacyclohexane (0.82 g, 9.08 mmol) were weighted into a 50 mL round bottom flask and purged with nitrogen for 30 min. The flask was then immersed into a preheated oil bath at 70 °C for 4 h (Monomer conversion = 100% as judged by ^{1}H NMR). The polymerization was then quenched by immersion in ice water and exposure to air. The product was precipitated by adding excess hexane and washed several times with additional hexane. The precipitated product was then dried at 35 °C under vacuum overnight. mPEG$_{45}$-BTPA-PDMA$_{3.9}$ was synthesized in a similar protocol.

Synthesis of the mPEG$_{45}$-PDMA$_{21}$-BTSMA. DMA (4.57 g, 46 mmol), mPEG$_{45}$-BTSMA (5.00 g, 2.19 mmol), AIBN (0.1196 g ,0.73 mmol), 1,4-dioxane (9.12 g), and 1,3,5-trioxacyclohexane (0.42 g, 4.6 mmol) were weighted into a 50 mL round bottom flask and purged with nitrogen for 30 min. The flask was then immersed into a preheated oil bath at 70 °C for 4 h (Monomer conversion = 99.5% as judged by ^{1}H NMR). The polymerization was then quenched by immersion in ice water and exposure to air. The product was precipitated by adding excess hexane and washed several times with additional hexane. The

precipitated product was then dried at 35 °C under vacuum overnight.

RAFT dispersion polymerization of Styrene mediated by mPEG$_{45}$-BTPA-PDMA$_{20}$. In a typical experiment (target DP = 300): Styrene (3.00 g, 28.8 mmol), mPEG$_{45}$-BTPA-PDMA$_{20}$ (0.41 g, 0.096 mmol), 1,3,5-trioxacyclohexane (0.26 g, 2.9 mmol), AIBN (0.0053 g, 0.032 mmol), and methanol/water (9.6 g/2.4 g, 80/20, w/w) were weighed into a 25 mL round bottom flask. The reaction mixture was purged with nitrogen for 30 min, sealed, and immersed into a 70 °C pre-heated oil bath. The polymerization was conducted for 24 h under magnetic stirring and quenched by immersing into an ice-water bath.

RAFT dispersion polymerization of styrene mediated by mPEG$_{45}$-PDMA$_{21}$-BTSMA. In a typical experiment (target DP = 300): Styrene (2.00 g, 19.2 mmol), mPEG$_{45}$-PDMA$_{21}$-BTSMA (0.2787 g, 0.064mmol), 1,3,5-trioxacyclohexane (0.1734 g, 1.92 mmol), AIBN (0.0035 g, 0.021 mmol), and methanol/water (6.4 g/1.6 g, 80/20, w/w) were weighed into a 25 mL round bottom flask. The reaction mixture was purged with nitrogen for 30 min, sealed, and immersed into a 70 °C pre-heated oil bath. The polymerization was conducted for 24 h under magnetic stirring and quenched by immersing into an ice-water bath.

Kinetic study of RAFT dispersion polymerization using mPEG$_{45}$-BTPA-PDMA$_{20}$. In a typical experiment (target DP = 300): Styrene (2.50 g, 24.0 mmol), mPEG$_{45}$-BTPA –PDMA$_{20}$ (0.34 g, 0.08 mmol), 1,3,5-trioxacyclohexane (0.22g, 2.4 mmol), AIBN (0.0044 g, 0.027 mmol), and methanol/water (6.0 g/1.5 g, 80/20, w/w) were weighed into a 25 mL round bottom flask. The reaction mixture was purged with nitrogen for 30 min, sealed, and immersed into a 70 °C pre-heated oil bath. Samples were extracted using

syringes under nitrogen at different times and quenched by immersing into an ice-water bath. The obtained samples were characterized by ^{1}H NMR, TEM, and THF GPC.

Kinetic study of RAFT dispersion polymerization using mPEG$_{45}$-PDMA$_{21}$-BTSMA. In a typical experiment (target DP = 300): Styrene (2.50 g, 24.0 mmol), mPEG$_{45}$-PDMA$_{21}$-BTSMA (0.35 g, 0.08 mmol), 1,3,5-trioxacyclohexane (0.2167g, 2.4 mmol), AIBN (0.0044 g, 0.027 mmol), and methanol/water (6.0 g/1.5 g, 80/20, w/w) were weighed into a 25 mL round bottom flask. The reaction mixture was purged with nitrogen for 30 min, sealed, and immersed into a 70 °C pre-heated oil bath. Samples were extracted using syringes under nitrogen at different times and quenched by immersing into an ice-water bath. The obtained samples were characterized by ^{1}H NMR, TEM, and THF GPC.

RAFT solution polymerization of Styrene using mPEG$_{45}$-BTPA-PDMA$_{20}$. St (1.50 g, 14.4 mmol), mPEG$_{45}$-BTPA-PDMA$_{20}$ (0.20 g, 0.048 mmol), 1,3,5-trioxacyclohexane (0.13 g, 1.44 mmol), AIBN (0.0026 g, 0.016 mmol), and toluene (3.50 g) were weighted in to a 10 mL round bottom flask. The reaction mixture was purged with nitrogen for 30 min and sealed. The flask was then immersed into a preheated oil bath at 70 °C for 96 h (Monomer conversion = 46.7% as judged by ^{1}H NMR). The sample was then characterized by THF GPC.

RAFT solution polymerization of Styrene using mPEG$_{45}$-PDMA$_{21}$-BTSMA. St (1.50 g, 14.4 mmol), mPEG$_{45}$-PDMA$_{21}$-BTSMA (0.21 g, 0.048 mmol), 1,3,5-trioxacyclohexane (0.13 g, 1.44 mmol), AIBN (0.0026 g, 0.016 mmol), and toluene (3.50 g) were weighted in to a 10 mL round bottom flask. The reaction mixture was purged with nitrogen for 30 min and sealed. The flask was then immersed into a

preheated oil bath at 70 °C for 96 h (Monomer conversion = 46.5% as judged by ^{1}H NMR). The sample

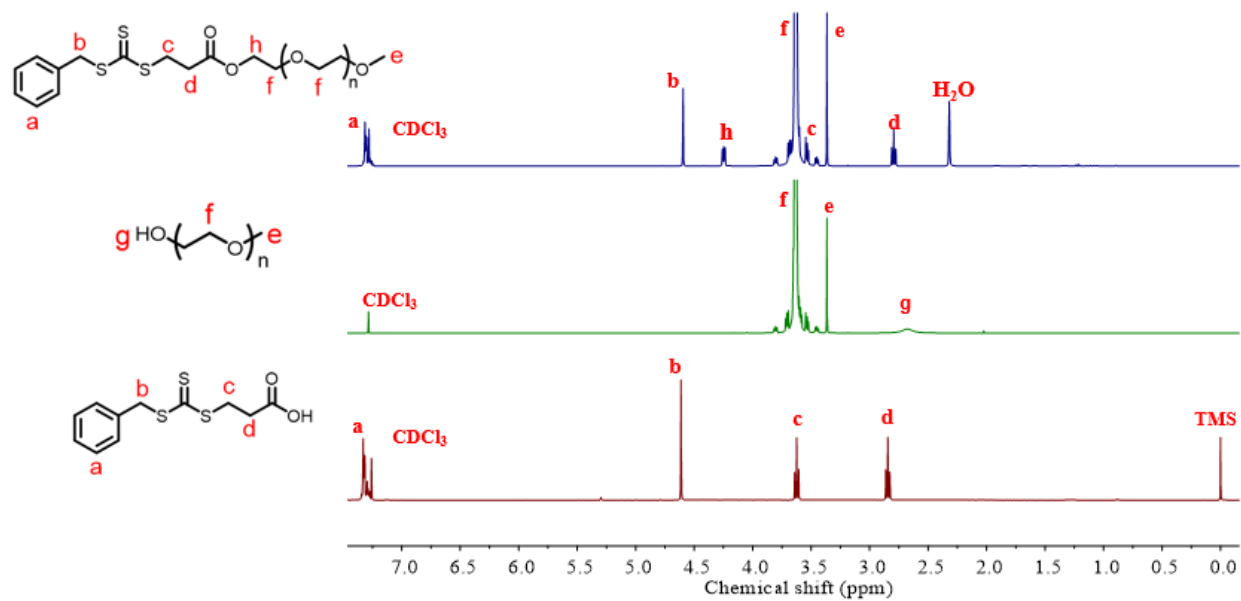was then characterized by THF GPC.

Additional Results

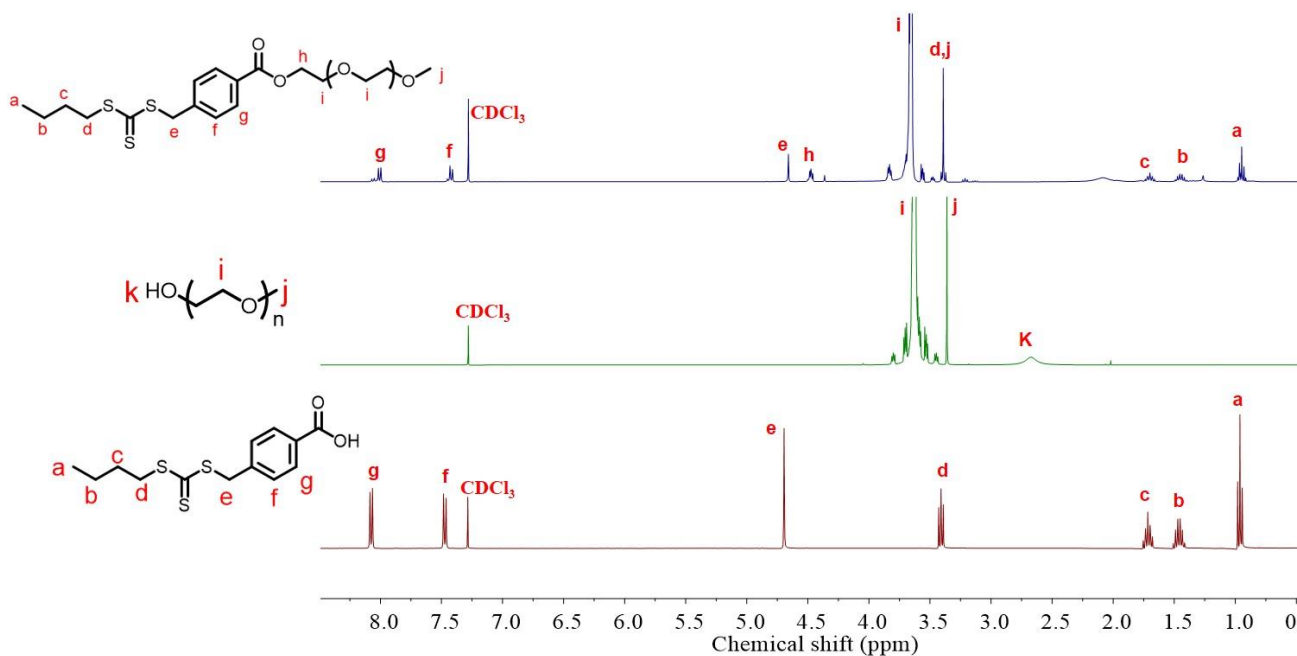Figure S1. ^{1}H NMR spectra of BTPA, mPEG$_{45}$, and mPEG$_{45}$-BTPA.

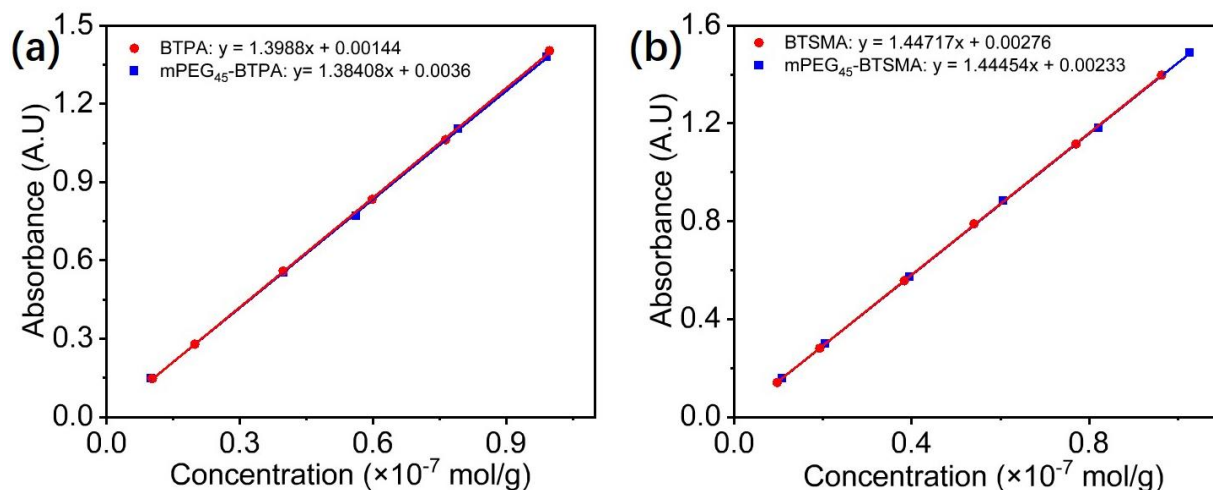Figure S2. ^{1}H NMR spectra of BTSMA, mPEG$_{45}$, and mPEG$_{45}$-BTSMA.

Figure S3. (a) Linear plots obtained for BTPA and mPEG$_{45}$-BTPA by UV-vis spectroscopy at a wavelength of 310 nm. (b) Linear plots obtained for BTSMA and mPEG$_{45}$-BTSMA by UV-vis spectroscopy at a wavelength of 310 nm.
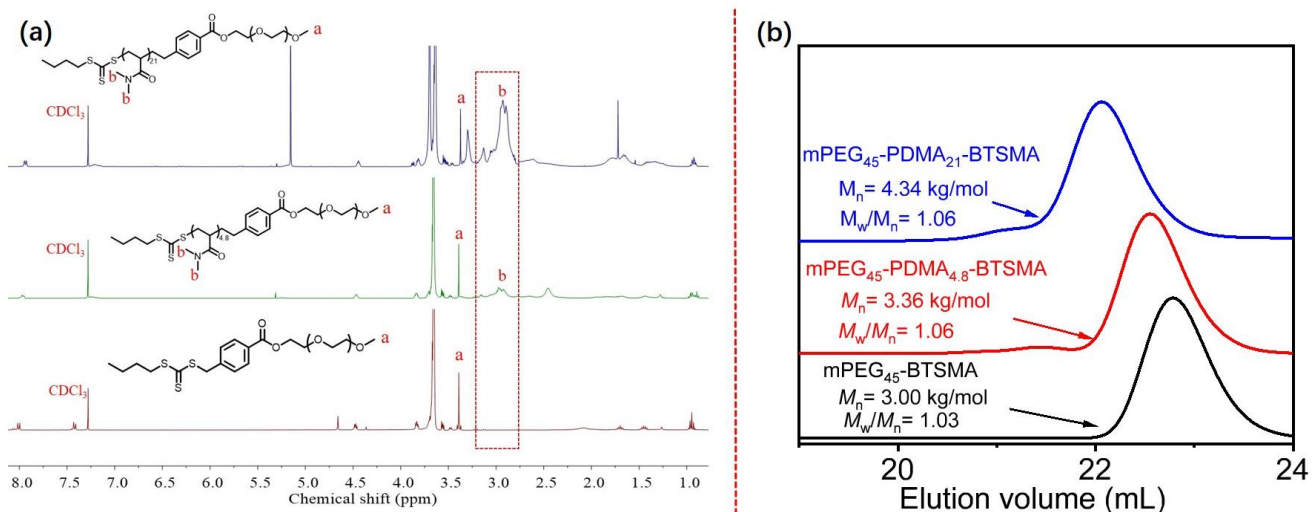

Figure S4. (a) ^{1}H NMR spectra of mPEG$_{45}$-BTSMA and mPEG$_{45}$-PDMA$_n$-BTSMA (n = 4.8, 21). (b) THF SEC traces of mPEG$_{45}$-BTSMA and mPEG$_{45}$-PDMA$_n$-BTSMA (n = 4.8, 21).
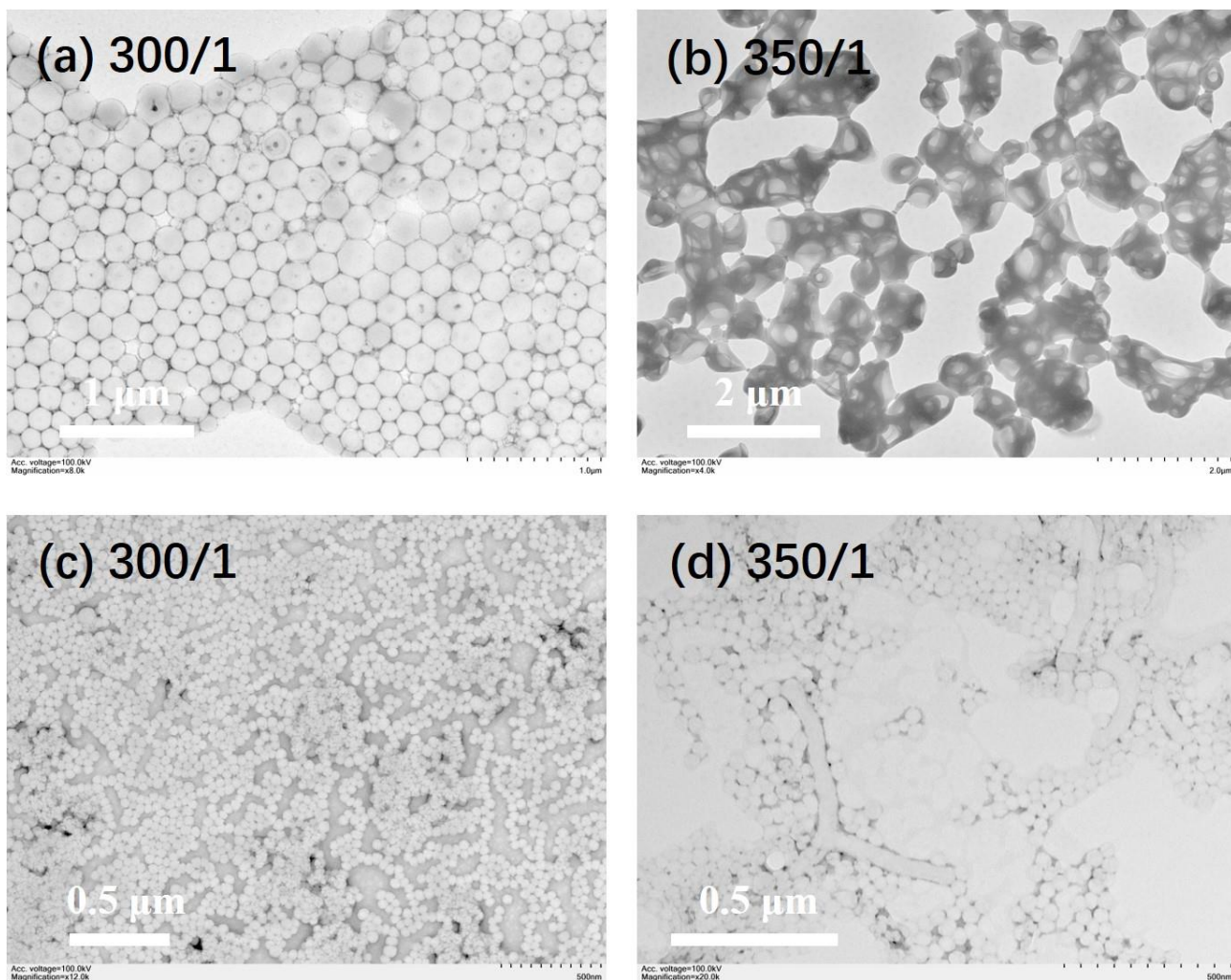
Figure S5. (a, b) TEM images of block copolymer nanoparticles prepared by RAFT dispersion polymerization of *tert*-butyl acrylate (*t*BA, 20% w/w) in ethanol/water (60/40, w/w) using mPEG$_{45}$-BTPA-PDMA$_{20}$ with different [*t*BA]/[mPEG$_{45}$-BTPA-PDMA$_{20}$] ratios: (a) 300/1, (b) 350/1. (c, d) TEM images of block copolymer nanoparticles prepared by RAFT dispersion polymerization of *tert*-butyl acrylate (*t*BA, 20% w/w) in ethanol/water (60/40, w/w) using mPEG$_{45}$-PDMA$_{21}$-BTSMA with different [*t*BA]/[mPEG$_{45}$-PDMA$_{21}$-BTSMA] ratios: (a) 300/1, (b) 350/1.
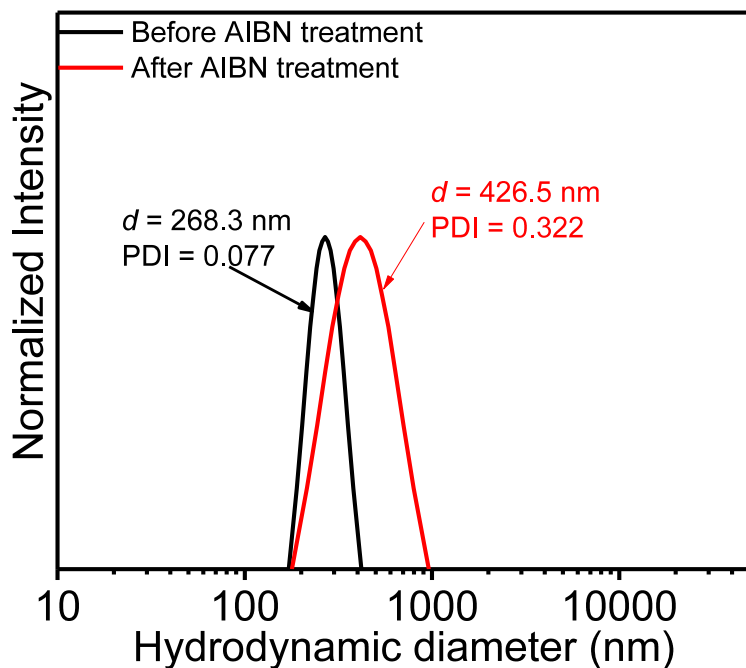
Figure S6. DLS data of mPEG$_{45}$-BTPA-PSt$_{300}$-PDMA$_{20}$ block copolymer nanoparticles before and after treating with 100-fold AIBN at 70 °C.

REFERENCE

(1)   Dag, A.; Zhao, J.; Stenzel, M. H. Origami with ABC Triblock Terpolymers Based on Glycopolymers: Creation of Virus-Like Morphologies. *ACS Macro Lett.* **2015**, *4* (5), 579–583. https://doi.org/10.1021/acsmacrolett.5b00163.

(2)   Ercole, F.; Harrisson, S.; Davis, T. P.; Evans, R. A. The Application of a Photochromic Probe to Monitor the Self-Assembly of Thermosensitive Block Copolymers. *Soft Matter* **2011**, *7* (6), 2687–2696. https://doi.org/10.1039/C0SM00746C.