Supporting information

Primary sulfonamide-functional polymers with controlled chain architectures by RAFT polymerisation

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1. Materials and methods

Materials

The following chemicals were used as received: sulfanilamide (≥98%, Sigma-Aldrich), acryloyl chloride (≥97%, Sigma-Aldrich), triethylamine (Et_3N, ≥99.5%, Sigma-Aldrich), methyl 2-(butylthiocarbonothioylthio)propanoate (CTA1, 97%, Boron Molecular), 2-(butylthiocarbonothioylthio) propanoic acid (CTA2, 95%, Boron Molecular), 1-ethyl-3-(3'-dimethylaminopropyl) carbodiimide · HCl (EDC*HCl), 4-(dimethylamino)pyridine (DMAP, ≥99%, Sigma-Aldrich), 2,2'-azobis(isobutyramidine) dihydrochloride (AIBA, 97% Sigma-Aldrich), poly(ethylene glycol) methyl ether acrylate (PEGA, average M_n = 480 g mol^{-1}, Sigma-Aldrich), acrylic acid (AA, 99%, Sigma-Aldrich), (trimethylsilyl)diazomethane solution (TMS-CHN_2, 2.0 M in hexanes, Sigma-Aldrich), sodium hydroxide (NaOH, ≥98%, Sigma-Aldrich).

The following chemicals were purified before use: 2,2'-azobis(2-methylproprionitrile) (AIBN, 98%, Sigma-Aldrich) was recrystallized from methanol and dried under vacuum. *N*,*N*-Dimethylacrylamide (DMA, 95%, Sigma-Aldrich) was purified by passing through neutral Al_2O_3. Dimethyl sulfoxide (DMSO, Sigma-Aldrich, HPLC grade) was stored over molecular sieves.

The following solvents were used as received: *n*-pentane (Sigma-Aldrich, HPLC grade), ethyl acetate (EtOAc, Sigma-Aldrich, HPLC grade), tetrahydrofuran (THF, Sigma-Aldrich, HPLC grade), acetone (Sigma-Aldrich, HPLC grade), methanol (MeOH, Sigma-Aldrich, HPLC grade), dichloromethane (DCM, Sigma-Aldrich, HPLC grade), *N*,*N*-dimethylformamide (DMF, Sigma-Aldrich, HPLC grade),

Spectra/Por® dialysis membrane (MWCO 1000 g mol^{-1}) was used for dialysis. D_2O, DMSO-d_6 and $CDCl_3$ were obtained from Eurisotop.

Methods

NMR. Nuclear magnetic resonance spectra (^1H, ^{13}C) were recorded at 25 °C on a Bruker Avance 300 MHz instrument. *J* is reported to ± 0.5 Hz. The resonance multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), dd (doublet of doublets) or m (multiplet). ^{13}C NMR spectra were recorded at 75.47 MHz. Chemical shifts δ are reported in parts per million (ppm) and are referenced to the residual solvent peak (DMSO-d_6: H = 2.5 ppm, $CDCl_3$: H = 7.26 ppm, HDO: H = 4.79 ppm).

Size-exclusion chromatography (SEC). For the polymers analysed in DMF/LiBr average molar masses and molar mass distributions were determined by using 10 mM LiBr solution in DMF as an eluent at a flow rate of 1 mL min^{-1} at 55 °C. Before the analysis, polymers were dissolved in the eluent (final concentration was 10 mg mL^{-1}) and filtrated through a 0.45 µm PTFE filter. Analysis was performed on a system composed of an Agilent technologies guard column (PLGel20 µm, 50 × 7.5 mm) and a set of two KD-804 and KD-805L (SHODEX) columns. Detections were conducted using a Wyatt Optilab® rEX refractive index detector, a Varian ProStar UV detector (dual wavelength analysis at 290 and 254 nm) and a Wyatt MiniDawn TREOS multiangle light scattering detector.

Average molar masses and molar mass distributions were determined by MALS detector for the following polymers: PSPA, PDMA, PPEGA, PDMA-*b*-PSPA, PPEGA-*b*-PSPA, S-PDMA, S-PPEGA, S-PDMA-*b*-PMA.

For the water-soluble polymers average molar masses and molar mass distributions were determined by using water + 0.2 M NaCl + 0.025 M NaH_2PO_4 + 0.025 M Na_2HPO_4 as an eluent at a flow rate of

1 mL min^{-1} at 35 °C. Before the analysis, polymers were dissolved in the eluent (final concentration was 10 mg mL^{-1}) and filtrated through a 0.45 µm cellulose filter. Analysis was performed on a system composed of a SB-G precolumn and a set of two SB-806M HQ and SB-802.5 HQ columns (Shodex). Detections were conducted using a Wyatt Optilab® rEX refractive index detector and a Varian ProStar UV detector (dual wavelength analysis at 290 and 254 nm). The column system was calibrated with PEO standards (ranging from 1080 to 276 300 g mol^{-1}).

Average molar masses and molar mass distributions were determined by PEO calibration for the following polymers: S-PDMA-*b*-PAA, S-PPEGA-*b*-PAA.

Dn/dc values were measured at 620 nm with a PSS DnDc-2010 differential refractometer in DMF/LiBr. Dn/dc_{PSPA} = 0.169 ml g^{-1}, dn/dc_{PPEGA} = 0.042 ml g^{-1}. Dn/dc_{PDMA} = 0.087 ml g^{-1} [1] and dn/dc_{PMA} = 0.044 ml g^{-1} [2] were found in the literature.

Mass spectra. ESI-TOF mass spectra were acquired with a Xevo G2 QTOF mass spectrometer (Waters) and a QTOF Premier (Waters), in electrospray ionization, in positive mode for PSPA and S-PDMA and in negative mode for S-PPEGA. PSPA was dissolved in DMSO and diluted in MeOH, S-PDMA and S-PPEGA were dissolved in MeOH. Then, a solution of NaI (in acetone at 10 mg mL^{-1}) was added.

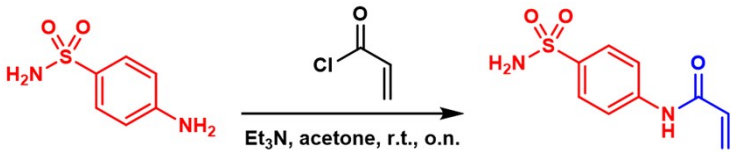
On the Xevo G2 QTOF, the injection was made in Flow Injection Analysis (FIA). The source temperature and desolvation temperature were 110 °C and 350 °C, respectively, and the cone voltage was optimized at 30 V. On the Qtof Premier, the samples are directly infused in the source. The source temperature and desolvatation temperature were 110 °C et 200 °C respectively and the cone voltage was optimised at 50 V. The acquisition software was Masslynx (Waters) and the spectra were processed by using Masslynx and Polymerix 3.0 (Sierra Analytics).

UV-vis. Ultraviolet-visible spectroscopy was performed on an Agilent 8453 UV-visible photodiode array spectrophotometer. Solution absorption spectra were obtained after baseline subtraction using a quartz (1 cm × 1 cm) cuvette filled with the blank solvent.

DLS and Zeta potential. Dynamic light scattering and Zeta potential measurements were conducted using a Zetasizer Nano-ZS (Malvern Instruments, Ltd, UK) with an integrated 4 mW He-Ne laser, λ = 633 nm. Light scattering intensity (at 173°) was measured with instrumental parameters set to constant values for all the samples. The correlation function was analyzed via the cumulant method to get the Z-average size of the colloids and by the general-purpose method (NNLS) to obtain their distribution in size. The apparent equivalent hydrodynamic diameters were then determined using the Stokes-Einstein equation $D = \frac{k.T}{6\pi\eta.Rh}$ where T is the temperature and η the viscosity of the solution. Mean diameter values were obtained from five different runs of the number plot.

2. Synthetic protocols

Synthesis and characterisation of SPA monomer



Sulfanilamide (10 g, 0.058 mol) and triethylamine (7 g, 0.069 mol) were dissolved in acetone (200 ml) under an argon atmosphere. The temperature was decreased to 0 °C and the solution of acryloyl chloride (5.8 g, 0.064 mol) in acetone (50 ml) was added dropwise. The reaction mixture was stirred at room temperature overnight followed by extraction with the mixture of EtOAc and acetone (3 times). The organic phases were combined and washed with a saturated solution of NaCl and dried over $MgSO_4$. Solvents were removed under reduced pressure. The pure product was obtained by recrystallization from MeOH as slightly yellowish crystals (8.1 g, 62%). **^{1}H NMR (300 MHz, DMSO-d_6)** δ (ppm): 10.46 (s, 1H, NH-CO), 7.80 (m, 4H, CH_{ar}), 7.26 (s, 2H, SO_2-NH_2), 6.46 (dd, *J* = 17.0, 9.9 Hz, 1H, CO-CH=CH_2), 6.30 (dd, *J* = 17.0, 2.1 Hz, 1H, CO-CH=CH_2), 5.81 (dd, *J* = 9.9, 2.1 Hz, 1H, CO-CH=CH_2).

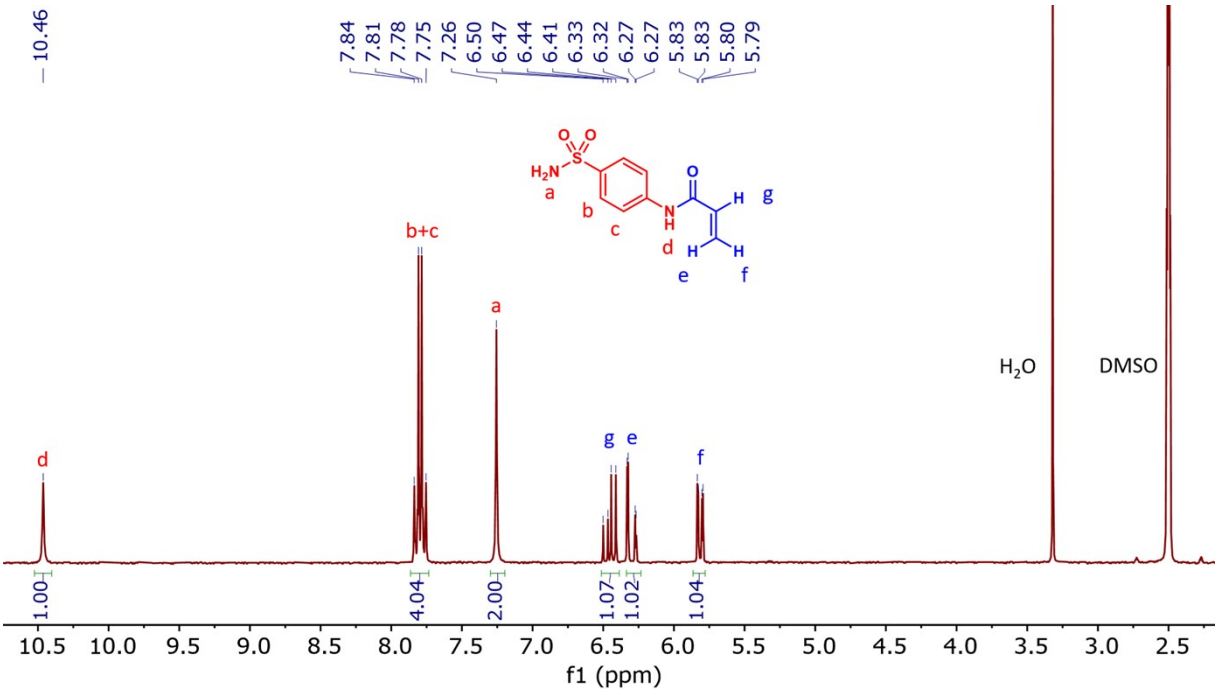


Figure S1. ^{1}H NMR spectrum of SPA (DMSO-d_6)

Synthesis and characterisation of S-CTA

2-(Butylthiocarbonothioylthio) propanoic acid (CTA2, 1 g, 4.2 mmol) was dissolved in DCM (4ml) under argon atmosphere and the temperature was decreased to 0 °C. EDC*HCl (0.97 g, 5.1 mmol) and DMAP (0.062 g, 0.51 mmol) were dissolved in DCM (4 ml) and added dropwise to the solution of the RAFT agent at 0 °C. Sulfanilamide (0.87 g, 5.1 mmol) was dissolved in DMF (12 ml) under an argon atmosphere and the temperature was decreased to 0 °C. The combined solution of RAFT agent, EDC*HCl and DMAP was added dropwise to the sulfanilamide solution and the reaction mixture was stirred for an additional hour at 0 °C. Then the solution was stirred overnight at room temperature followed by extraction with EtOAc (3 times). The organic phases were combined, washed 5 times with a saturated solution of NaCl and dried over $MgSO_4$. The solvent was removed under reduced pressure. Pure compound was obtained after column chromatography (50/50 mixture of EtOAc and *n*-pentane as eluent) in the form of yellow crystals (1.22 g, 74%). **^{1}H NMR (300 MHz, DMSO-d_6)** δ (ppm): 10.74 (s, 1H, NH-CO), 7.75 (m, 4H, $CH_{ar.}$), 7.27 (s, 2H, SO_2-NH_2), 4.89 (q, *J* = 7.0 Hz, 1H, CO-CH-CH_3), 3.39 (t, *J* = 7.3 Hz, 2H, S-CH_2), 1.63 (quint, *J* = 7.3 Hz, 1H, S-CH_2-CH_2), 1.60 (d, *J* = 7.0 Hz, 3H, CO-CH-CH_3) 1.37 (sext, *J* = 7.3 Hz, 2H, S-CH_2-CH_2-CH_2), 0.88 (t, *J* = 7.3 Hz, 3H, S-CH_2-CH_2-CH_2-CH_3). **^{13}C NMR (75 MHz, DMSO-d_6)** δ (ppm): 223 (S-CS-S), 169 (N-CO-CH), 142 (C_{ar}-NH), 139 (C_{ar}-SO_2-NH_2), 127 (CH=C-NH), 119 (CH=C-SO_2-NH_2), 51 (CO-CH-CH_3), 37 (S-CH_2), 30 (S-CH_2-CH_2), 22 (CO-CH-CH_3), 18 (S-CH_2-CH_2-CH_2), 14 (S-CH_2-CH_2-CH_2-CH_3).

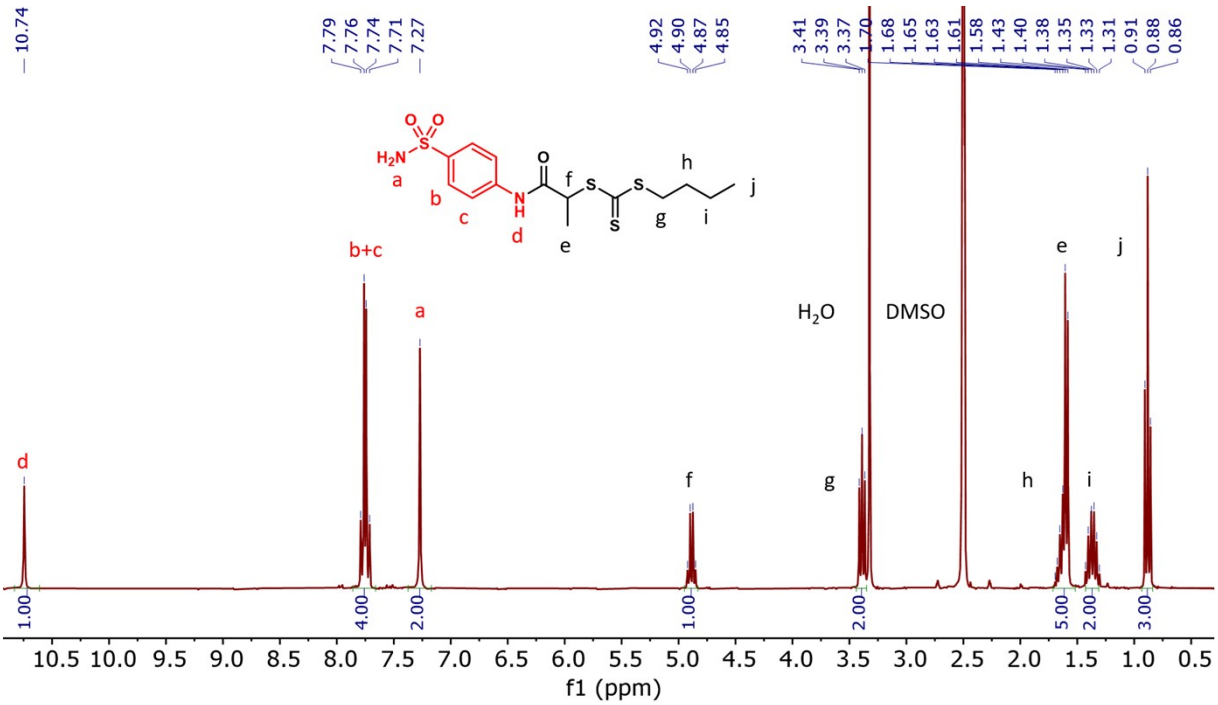


Figure S2. ^{1}H NMR spectrum of S-CTA (DMSO-d_6)

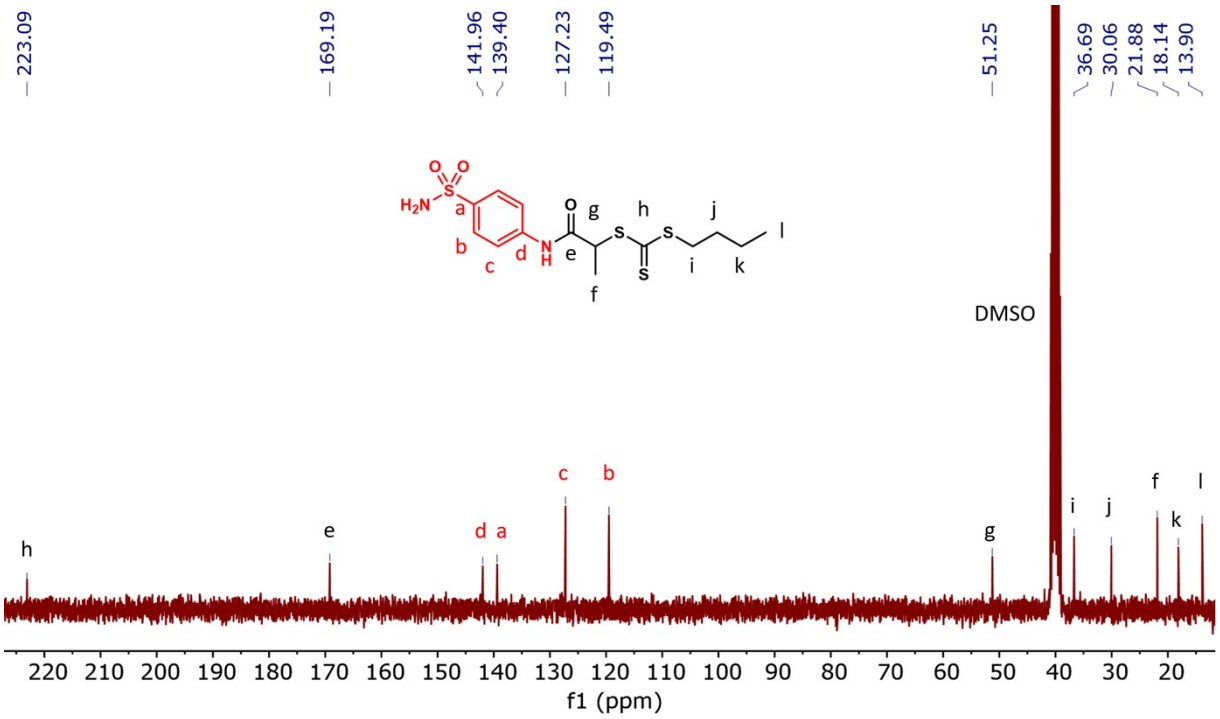
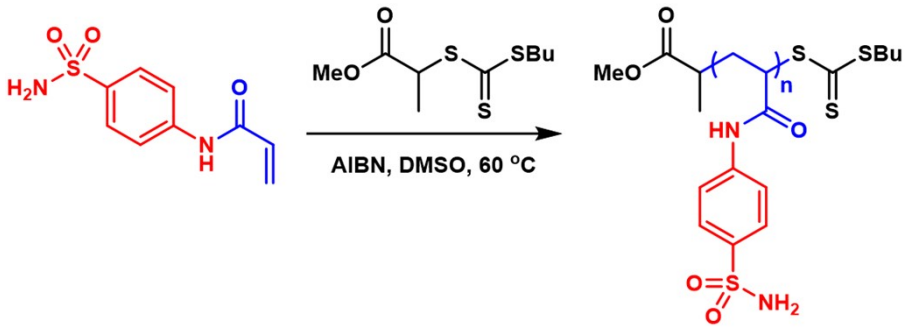


Figure S3. ^{13}C NMR spectrum of S-CTA (DMSO-d_6)

Synthesis and characterisation of PSPA (general procedure)



Methyl 2-(butylthiocarbonothioylthio)propanoate) (CTA1, 7.4 mg, 0.029 mmol), SPA (0.3 g, 1.3 mmol) and AIBN (0.97 mg in stock solution in DMSO, 0.006 mmol) were dissolved in DMSO (total mass = 4.5 g). The solution was transferred to glass ampoules, which were flame sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 60 °C for 4, 6, 8, 16 and 24 h. The polymerisation was stopped by rapid cooling. After opening of the ampoules, the solutions were immediately transferred to an NMR tube for conversion analysis. Samples for SEC analysis were prepared by dilution of solutions with DMF/LiBr. Pure polymers were obtained by precipitation in MeOH as yellowish solid. All polymerisation data is in **Table S1**. **^{1}H NMR (300 MHz, DMSO-d$_6$)** δ (ppm): 10.00 (s, 1H, NH-CO), 7.63 (s, 4H, CH$_{ar}$), 7.16 (s, 2H, SO$_2$-NH$_2$), 2.5-2.1 (s, 1H, CO-CH-CH$_2$), 2.0-1.8 (s, 2H, CO-CH-CH$_2$).

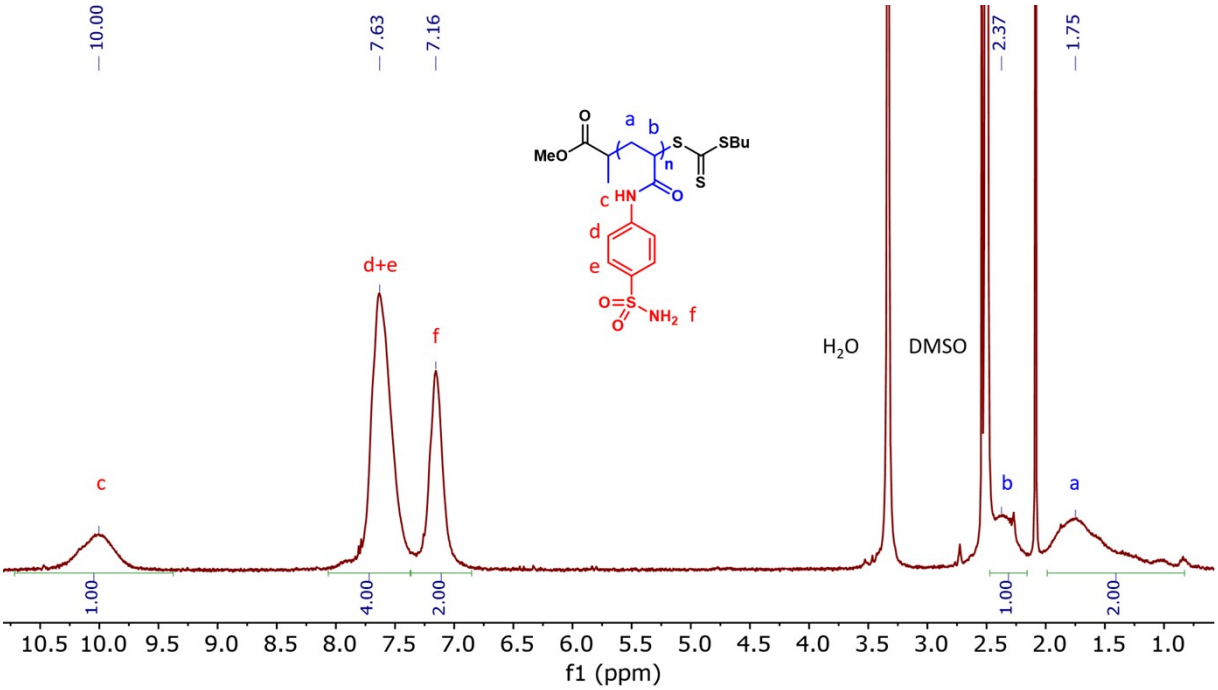
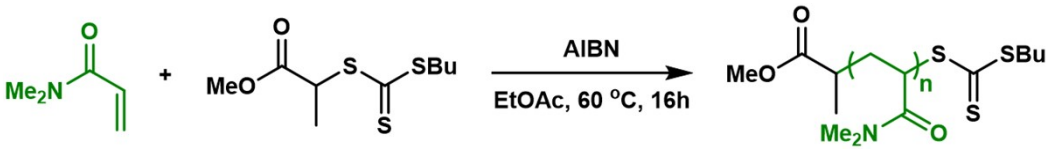


Figure S4. ^{1}H NMR spectrum of PSPA (DMSO-d$_6$)

Synthesis and characterisation of PDMA



General procedure for PDMA synthesis. Methyl 2-(butylthiocarbonothioylthio)propanoate) (CTA1, 84.8 mg, 0.337 mmol), DMA (1 g, 10.1 mmol) and AIBN (11 mg, 0.067 mmol) were dissolved in EtOAc (1 g, 50 wt.%). The solution was transferred to a Schlenk tube, which was sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 60 °C for 16 h. The polymerisation was stopped by rapid cooling. After opening of the Schlenk tube, the solution was immediately transferred to an NMR tube for conversion analysis (99.9 %). Solvent was removed under reduced pressure and yellow solid was obtained in quantitative yield. Sample for SEC analysis was prepared after evaporation and the polymer was used for the next step without any additional purification. M_n = 3.4 kg mol^{-1}, $Đ$ = 1.02 (by SEC-MALS in DMF/LiBr).

For the synthesis of PDMA$_{11.2k}$ the same procedure was adapted with 0.3 g of DMA (3.03 mmol), 7.6 mg of CTA1 (0.03 mmol) and 1.0 mg of AIBN (0.006 mmol) in 0.3 g of EtOAc. Conversion = 99.9 %. M_n = 11.2 kg mol^{-1}, $Đ$ = 1.03 (by SEC-MALS in DMF/LiBr).

^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 3.2-2.8 (m, 6H, N(C<u>H</u>$_3$)$_2$), 2.8-2.3 (m, 1H, CO-C<u>H</u>-CH$_2$), 1.9-1.2 (m, 2H, CO-CH-C<u>H</u>$_2$), 0.92 (m, 3H, S-CH$_2$-CH$_2$-CH$_2$-C<u>H</u>$_3$).

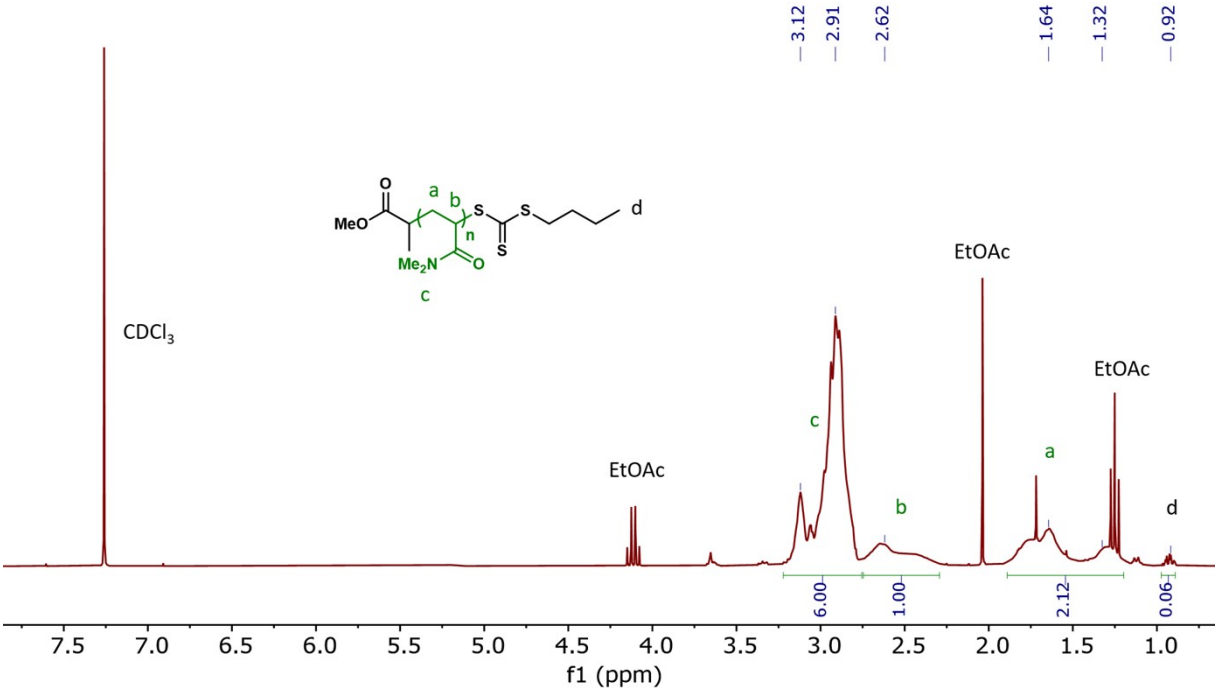
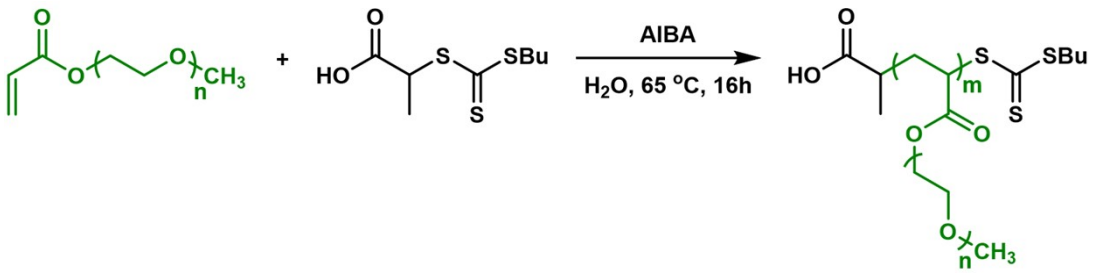


Figure S5. ^{1}H NMR spectrum of PDMA (CDCl$_3$)

Synthesis and characterisation of PPEGA



2-(Butylthiocarbonothioylthio) propanoic acid) (CTA2, 0.1 g, 0.417 mmol), PEGA (1 g, 2.08 mmol) and AIBA (11.3 mg, 0.042 mmol) were dissolved in H_2O (5 g, 83.3 wt.%). The solution was transferred to a Schlenk tube, which was sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 65 °C for 16 h. The polymerisation was stopped by rapid cooling. After opening of the Schlenk tube, the solution was immediately transferred to an NMR tube for conversion analysis (99.9 %). Obtained polymer was purified by dialysis (MWCO = 1000 g mol^{-1}) and lyophilization. A yellow viscous oil was obtained (0.82 g, 82 %) and analysed by SEC. M_n = 3.3 kg mol^{-1}, $Đ$ = 1.09 (by SEC-MALS in DMF/LiBr). **^{1}H NMR (300 MHz, D_2O)** δ (ppm): 4.4-4.2 (m, 2H, COO-C<u>H</u>$_2$), 4.0-3.4 (m, 34H, O-C<u>H</u>$_2$-C<u>H</u>$_2$), 3.40 (s, 3H, O-CH$_2$-CH$_2$-O-C<u>H</u>$_3$), 2.9-2.2 (m, 1H, CO-C<u>H</u>-CH$_2$), 2.2-1.1 (s, 2H, CO-CH-C<u>H</u>$_2$), 1.21 (m, 2H, S-CH$_2$-CH$_2$-CH$_2$), 0.97 (m, 3H, S-(CH$_2$)$_3$-C<u>H</u>$_3$).

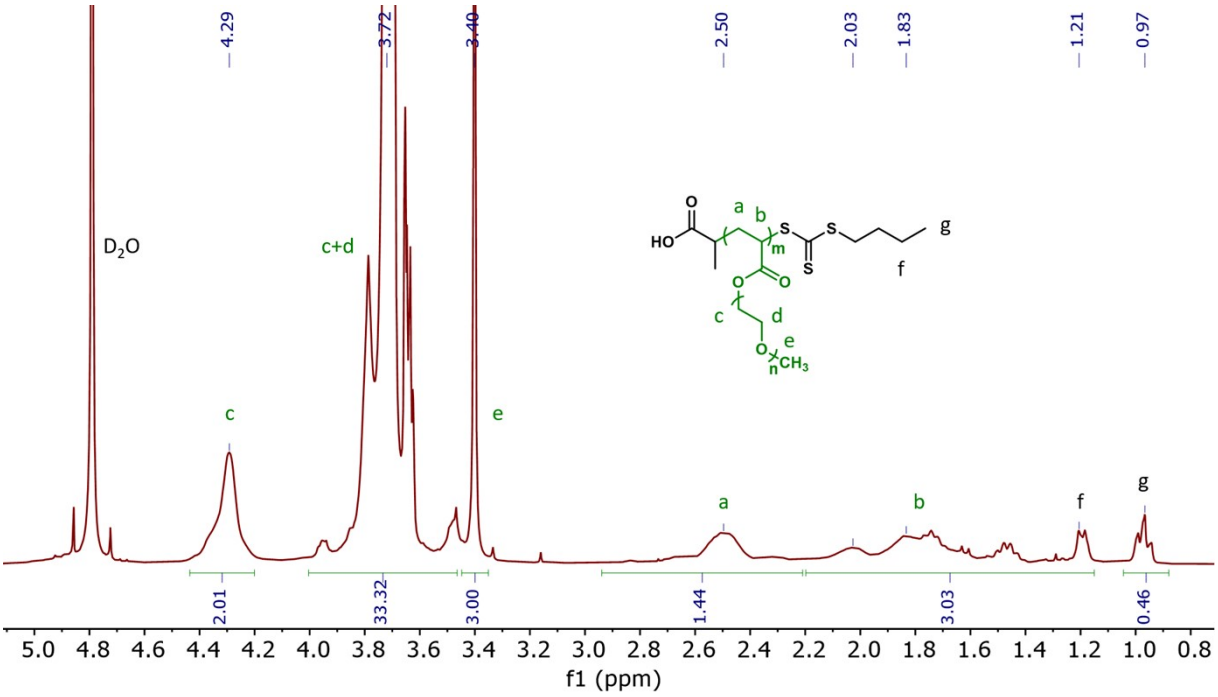
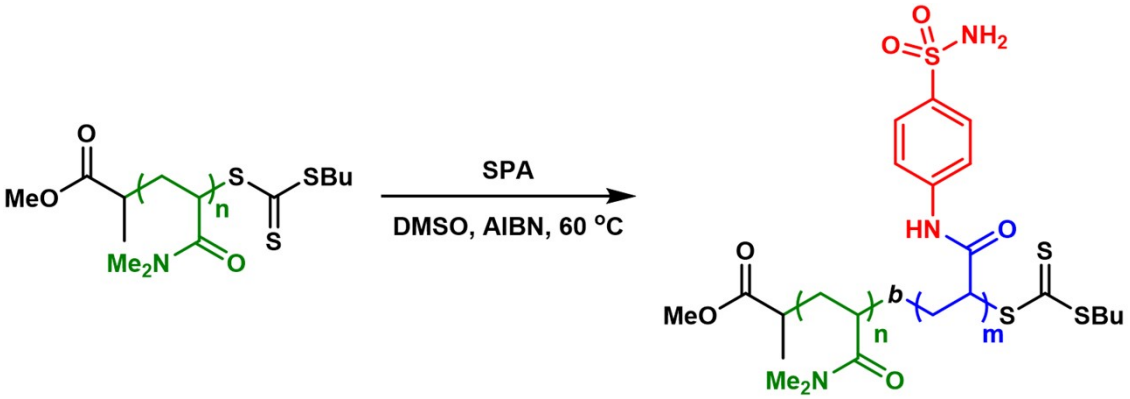


Figure S6. ^{1}H NMR spectrum of PPEGA (D_2O)

Synthesis and characterisation of PDMA-b-PSPA



General procedure for PDMA-b-PSPA synthesis. The $PDMA_{3.4k}$ macro-RAFT agent (53.7 mg, 0.016 mmol), SPA (0.19 g, 0.84 mmol) and AIBN (0.65 mg in stock solution in DMSO, 0.004 mmol) were dissolved in DMSO (total mass = 3.15 g, 93.75 wt.%). The solution was transferred to glass ampoules, which were flame sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 60 °C for 4, 6, 8, 16 and 24 h. The polymerisation was stopped by rapid cooling. After opening of the ampoules, the solutions were immediately transferred to an NMR tube for conversion analysis. Samples for SEC analysis were prepared by dilution of solutions with DMF/LiBr. Pure polymers were obtained by precipitation in MeOH as yellowish solid. All polymerisation data is in **Table S2**.

For the synthesis of $PDMA_{11.2k}$-*b*-$PSPA_{1.9k}$ the same procedure was adapted with 123.9 mg of $PDMA_{5.5k}$ (0.011 mmol), 40.0 mg of SPA (0.177 mmol) and 0.36 mg of AIBN (0.002 mmol) in 0.6 g of DMSO. Conversion = 90 %. M_n = 13.1 kg mol^{-1}, $Đ$ = 1.31 (by SEC-MALS in DMF/LiBr).

^{1}H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 10.01 (s, 1H, NH-CO), 7.62 (s, 4H, CH_{ar}), 7.15 (s, 2H, SO_2-NH_2), 3.2-2.6 (m, 6H, $N(CH_3)_2$), 2.5-1.9 (m, 1H, CO-CH-CH_2), 1.9-0.9 (m, 2H, CO-CH-CH_2).

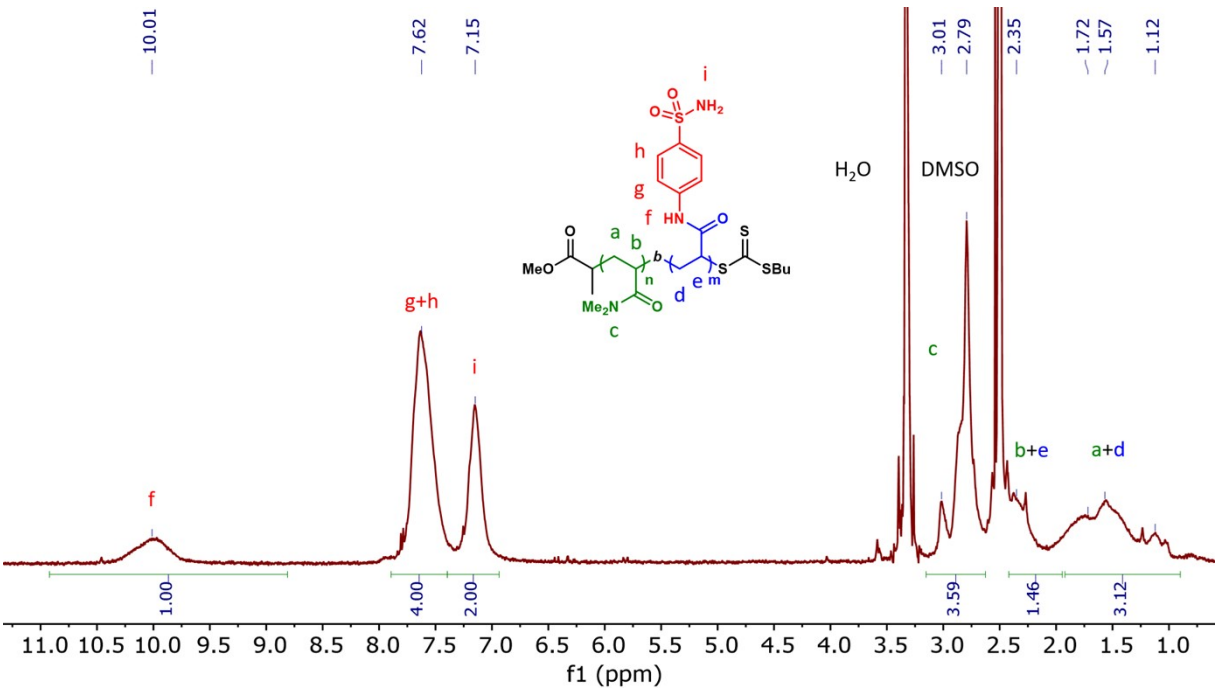
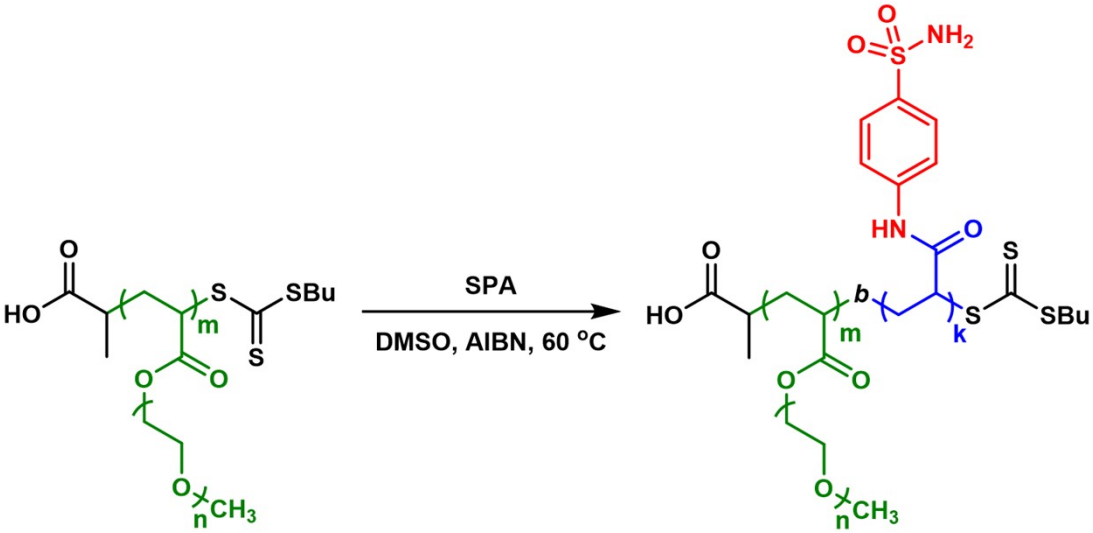


Figure S7. ^{1}H NMR spectrum of PDMA-*b*-PSPA (DMSO-d$_6$)

Synthesis and characterisation of PPEGA-b-PSPA



Macro RAFT agent ($PPEGA_{3.3k}$) (53.7 mg, 0.016 mmol), SPA (0.19 g, 0.84 mmol) and AIBN (0.65 mg (in stock solution in DMSO), 0.004 mmol) were dissolved in DMSO (total mass = 2.85 g, 93.75 wt.%). The solution was transferred to glass ampoules, which were flame sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 60 °C for 2, 4, 6, 16 and 24 h. The polymerisation was stopped by rapid cooling. After opening of the ampoules, the solutions were immediately transferred to an NMR tube for conversion analysis. Samples for SEC analysis were prepared by dilution of solutions with DMF/LiBr. Pure polymers were obtained by precipitation in MeOH as yellowish solid. All polymerisation data is in **Table S3**. **^{1}H NMR (300 MHz, DMSO-d_6)** δ (ppm): 10.02 (s, 1H, NH-CO), 7.62 (s, 4H, CH_{ar}), 7.14 (s, 2H, SO_2-NH_2), 4.09 (m, 2H, COO-CH_2), 3.6-3.4 (m, 34H, O-CH_2-CH_2), 3.23 (s, 3H, O-CH_2-CH_2-O-CH_3), 2.5-2.1 (m, 1H, CO-CH-CH_2), 2.1-0.9 (m, 2H, CO-CH-CH_2).

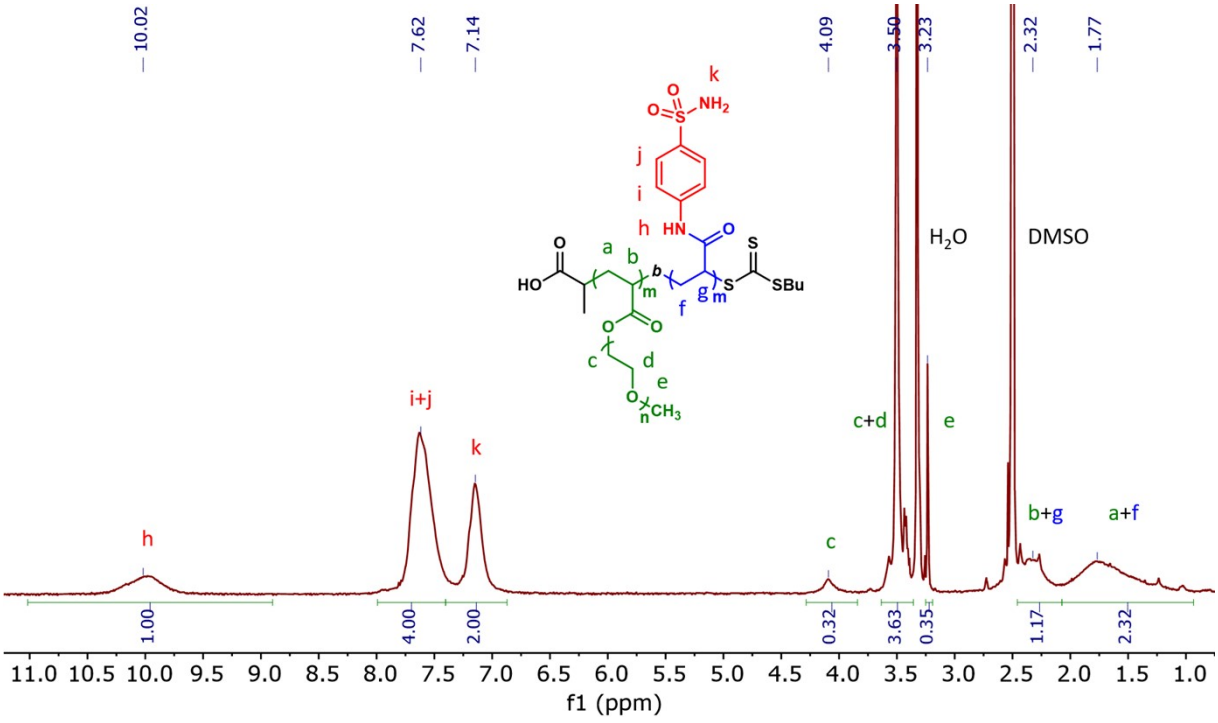
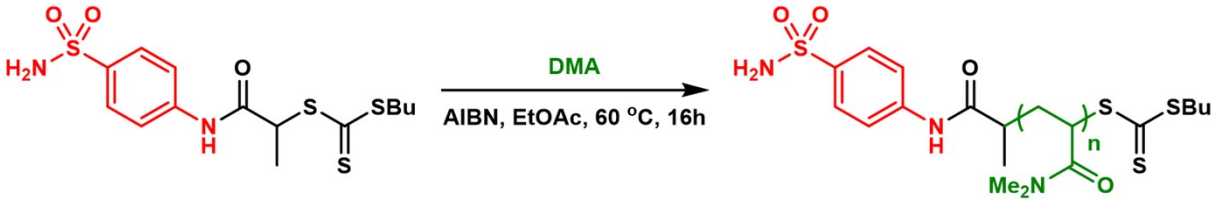


Figure S8. ^{1}H NMR spectrum of PPEGA-*b*-PSPA (DMSO-d_6)

Synthesis and characterisation of S-PDMA$_{4.0k}$



S-CTA (26.0 mg, 0.066 mmol), DMA (0.2 g, 2.02 mmol) and AIBN (2.1 mg, 0.013 mmol) were dissolved in EtOAc (0.2 g, 50 wt.%). The solution was transferred to a glass ampoule, which was flame sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 60 °C for 16 h. The polymerisation was stopped by rapid cooling. After opening of the ampoule, the solution was immediately transferred to an NMR tube for conversion analysis (99.9 %). Solvent was removed under reduced pressure. A yellow solid was obtained in a high yield after dialysis (MWCO = 1000 g mol^{-1}) and lyophilization (0.18 g, 90 %) and was analysed by SEC. M_n = 4.0 kg mol^{-1}, $Đ$ = 1.03 (by SEC-MALS in DMF/LiBr).

^{1}H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 10.21 (m, 1H, NH-CO), 7.74 (s, 4H, CH$_{ar}$), 7.23 (s, 2H, SO$_2$-NH$_2$), 5.07 (m, 1H, S-CH-CH$_3$), 3.2-2.6 (m, 6H, N(CH$_3$)$_2$), 2.5-1.9 (m, 1H, CO-CH-CH$_2$), 1.7-1.0 (m, 2H, CO-CH-CH$_2$), 0.88 (m, 3H, S-(CH$_2$)$_3$-CH$_3$).

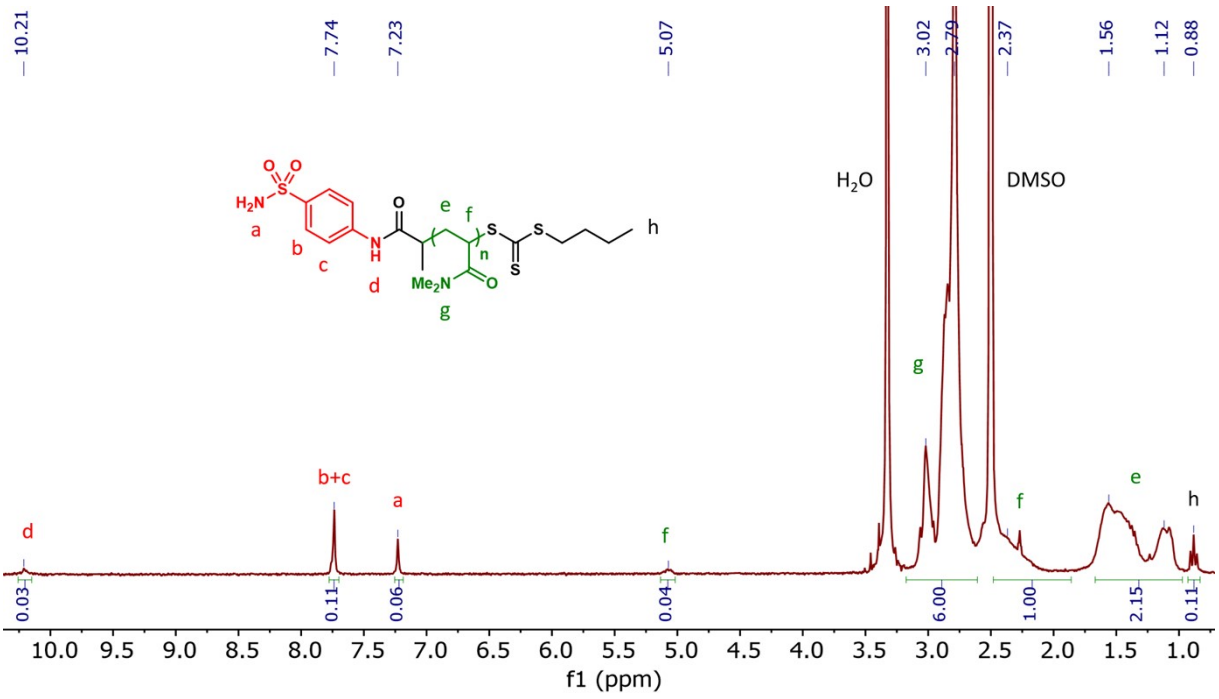


Figure S9. ^{1}H NMR spectrum of S-PDMA$_{4.0k}$ (DMSO-d$_6$)

Synthesis and characterisation of S-PDMA$_{4.0k}$-b-PAA$_{8.0k}$

S-PDMA$_{4.0k}$ (0.1 g, 0.025 mmol), AA (0.25 g, 3.47 mmol), NaOH (69.4 mg, 1.74 mmol) and AIBA (1.3 mg, 0.005 mmol) were dissolved in water (2.5 g, 90.9 wt.%). The solution was transferred to the Schlenk tube, which was sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 65 °C for 24 h. The polymerisation was stopped by rapid cooling. After opening of the Schlenk tube, the solution was immediately transferred to an NMR tube for conversion analysis (70.2 %). The obtained polymer was purified by dialysis (MWCO = 1000 g mol^{-1}) and lyophilization. A white solid was obtained (0.18 g, 64 %) and analysed by SEC. M_n = 12.0 kg mol^{-1}, $Đ$ = 1.15 (by SEC$_{aq.}$-RI with PEO calibration).

^{1}H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 13.9-11.0 (s, COOH), 10.21 (m, 1H, NH-CO), 7.74 (s, 4H, CH$_{ar}$), 7.23 (s, 2H, SO$_2$-NH$_2$), 3.0-2.7 (m, 6H, N(CH$_3$)$_2$), 2.4-1.9 (m, 1H, CO-CH-CH$_2$), 1.8-1.0 (m, 2H, CO-CH-CH$_2$), 0.88 (m, 3H, S-(CH$_2$)$_3$-CH$_3$)

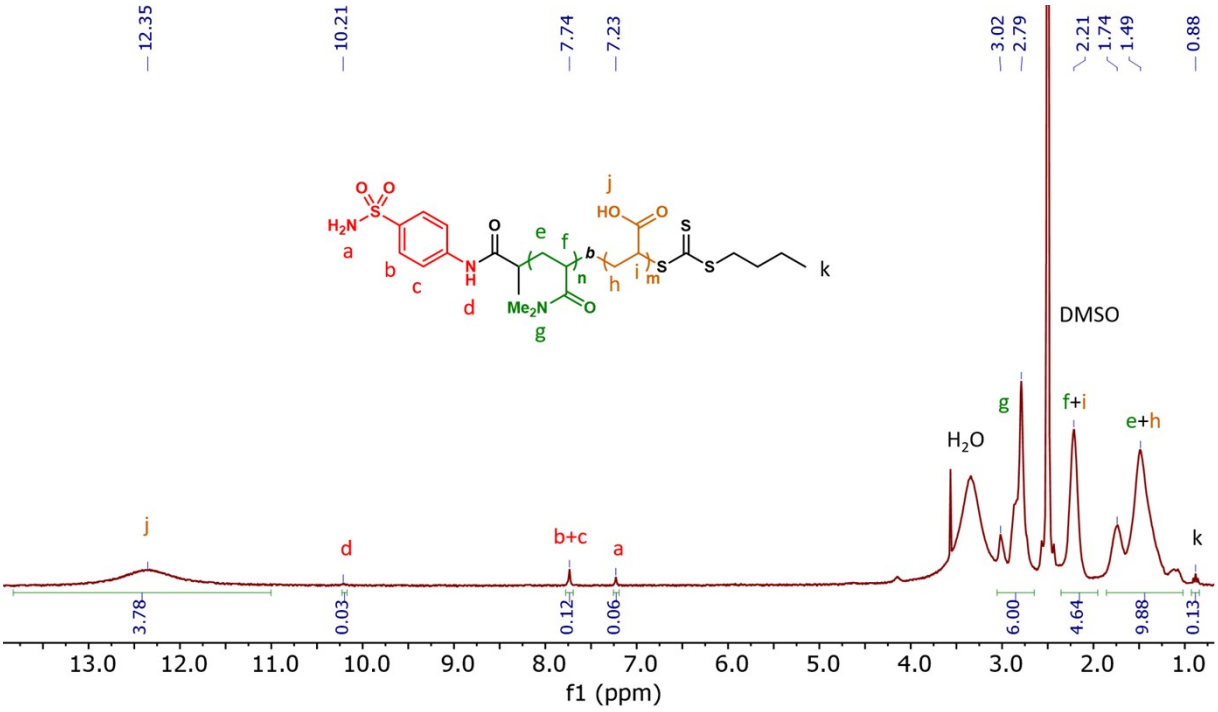
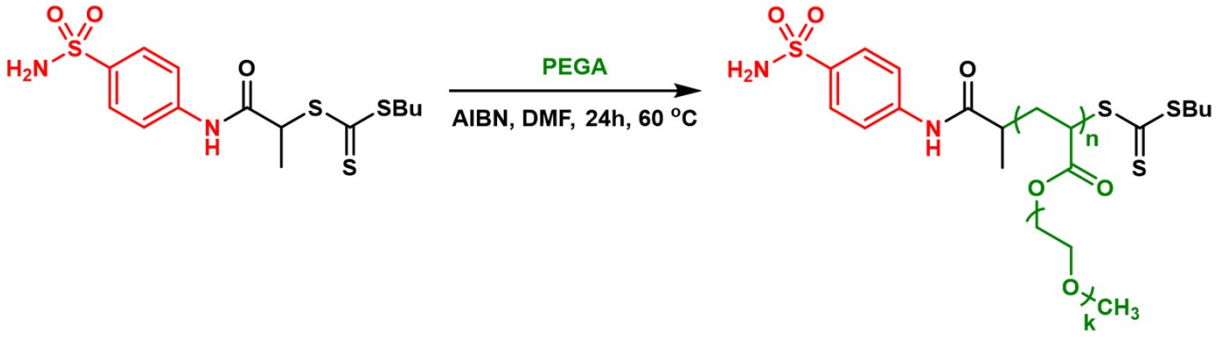


Figure S10. ^{1}H NMR spectrum of S-PDMA$_{4.0k}$-*b*-PAA$_{8.0k}$ (DMSO-d$_6$)

Synthesis and characterisation of S-PPEGA$_{3.4k}$



S-CTA (32.7 mg, 0.083 mmol), PEGA (0.2 g, 0.42 mmol) and AIBN (2.7 mg, 0.016 mmol) were dissolved in DMF (0.5 g, 71.4 wt.%). The solution was transferred to a glass ampoule, which was flame sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 60 °C for 24h. The polymerisation was stopped by rapid cooling. After opening of the ampoule, the solution was immediately transferred to an NMR tube for conversion analysis (99.9 %). The obtained polymer was purified by dialysis (MWCO = 1000 g mol^{-1}) and lyophilization. A yellow viscous oil was obtained (0.19 g, 83 %) and analysed by SEC. M_n = 3.4 kg mol^{-1}, $Đ$ = 1.07 (by SEC-MALS in DMF/LiBr).

^{1}H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 10.14 (m, 1H, NH-CO), 7.74 (s, 4H, CH$_{ar}$), 7.21 (s, 2H, SO$_2$-NH$_2$), 4.74 (m, 1H, S-CH-CH$_3$), 4.3-3.9 (m, 2H, COO-CH$_2$), 3.8-3.3 (m, 34H, O-CH$_2$-CH$_2$), 3.24 (s, 3H, O-CH$_2$-CH$_2$-O-CH$_3$), 2.4-1.9 (m, 1H, CO-CH-CH$_2$), 1.9-1.2 (s, 2H, CO-CH-CH$_2$), 1.09 (m, 2H, S-CH$_2$-CH$_2$-CH$_2$), 0.88 (m, 3H, S-(CH$_2$)$_3$-CH$_3$).

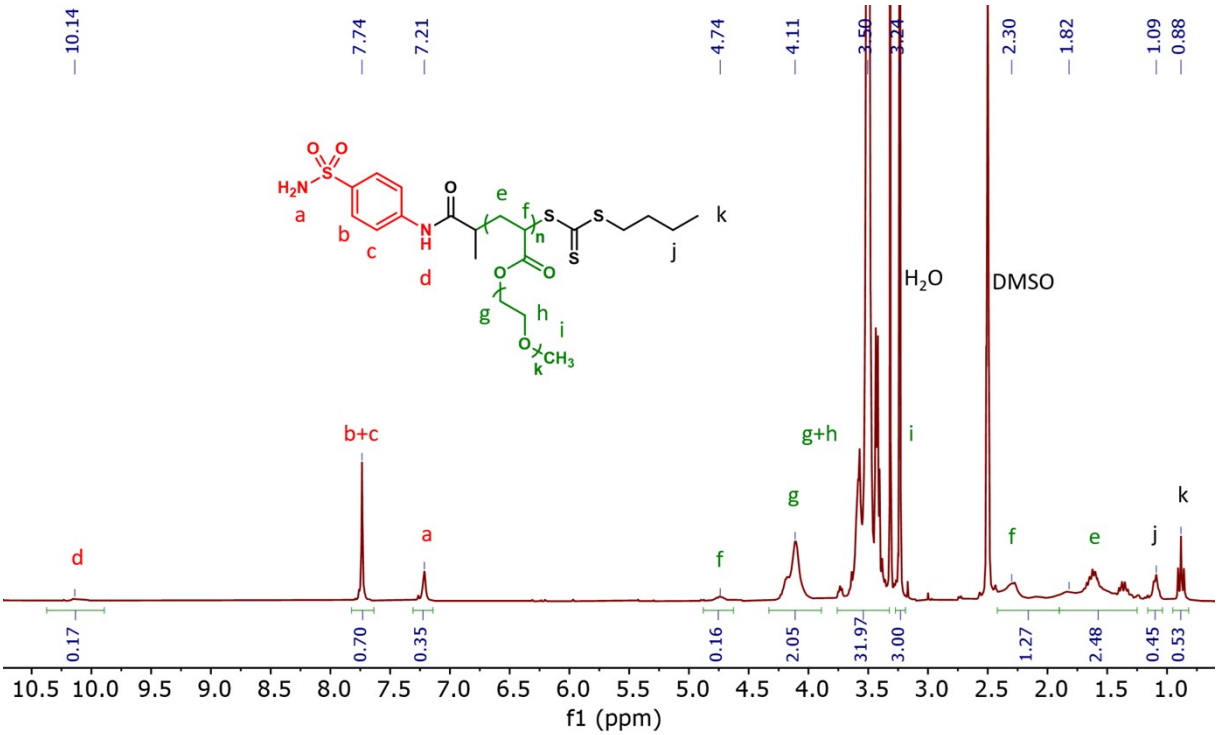
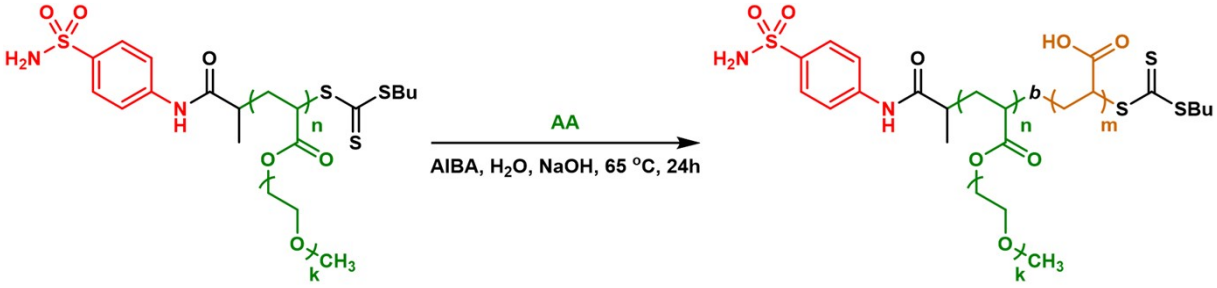


Figure S11. ^{1}H NMR spectrum of S-PPEGA$_{3.4k}$ (DMSO-d$_6$)

Synthesis and characterisation of S-PPEGA$_{3.4k}$-b-PAA$_{8.1k}$



S-PPEGA$_{3.4k}$ (0.1 g, 0.029 mmol), AA (0.3 g, 4.17 mmol), NaOH (83.3 mg, 2.08 mmol) and AIBA (1.6 mg, 0.006 mmol) were dissolved in water (3 g, 90.9 wt.%). The solution was transferred to the Schlenk tube, which was sealed after degassing by three freeze-pump-thaw cycles and immersed in an oil bath at 65 °C for 24h. The polymerisation was stopped by rapid cooling. After opening of the Schlenk tube, the solution was immediately transferred to an NMR tube for conversion analysis (89.5 %). The obtained polymer was purified by dialysis (MWCO = 1000 g mol^{-1}) and lyophilization. A white solid was obtained (0.26 g, 71 %) and analyzed by SEC. M_n = 11.5 kg mol^{-1}, $Đ$ = 1.07 (by SEC$_{aq.}$-RI with PEO calibration).

^{1}H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 13.6-11.0 (s, COO<u>H</u>), 10.11 (m, 1H, N<u>H</u>-CO), 7.73 (s, 4H, C<u>H</u>$_{ar}$), 7.21 (s, 2H, SO$_2$-N<u>H</u>$_2$), 4.3-3.9 (m, 2H, COO-C<u>H</u>$_2$), 3.8-3.0 (m, 34H, O-C<u>H</u>$_2$-C<u>H</u>$_2$), 3.23 (s, 3H, O-CH$_2$-CH$_2$-O-C<u>H</u>$_3$), 2.4-2.0 (s, 1H, CO-C<u>H</u>-CH$_2$), 1.9-1.0 (s, 2H, CO-CH-C<u>H</u>$_2$), 0.88 (m, 3H, S-(CH$_2$)$_3$-C<u>H</u>$_3$).

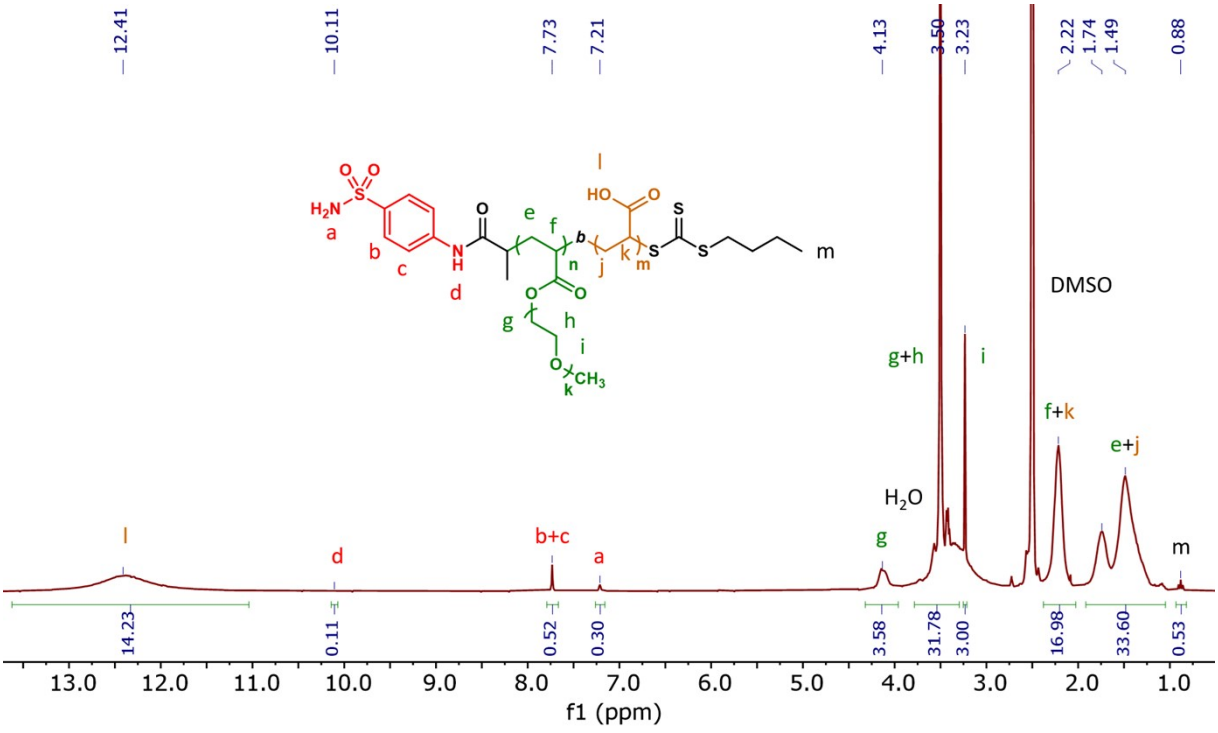


Figure S12. ^{1}H NMR spectrum of S-PPEGA$_{3.4k}$-*b*-PAA$_{8.1k}$ (DMSO-d$_6$)

3. Polymerisation data

Table S1. *SPA homopolymerisations*

Entry	[M]/[CTA]/[I]	Time, h	Conversion, % [a]	$M_{n(th)}$, kg mol^{-1} [b]	$M_{n(SEC)}$, kg mol^{-1} [c]	$Đ$ (M_w/M_n) [c]
1	45/1/0.2	4	15.8	1.9	3.6	1.23
2	45/1/0.2	6	40.5	4.4	5.2	1.38
3	45/1/0.2	8	69.6	7.3	8.0	1.32
4	45/1/0.2	16	90.0	9.4	10.1	1.33
5	45/1/0.2	24	95.0	9.9	10.3	1.33
6	90/1/0.2	4	20.9	4.6	9.8	1.37
7	90/1/0.2	8	34.7	7.4	12.1	1.50
8	90/1/0.2	16	76.9	16.1	18.7	1.50
9	90/1/0.2	24	85.9	18.0	21.0	1.50
10	90/1/0.2	55	90.8	19.0	22.4	1.50
11	225/1/0.2	8	13.3	7.0	13.9	1.48
12	225/1/0.2	16	29.5	15.1	31.4	1.69
13	225/1/0.2	24	38.2	19.5	33.8	1.62
14	225/1/0.2	72	57.1	29.1	58.0	1.63
15	45/-/0.2	24	91.9	-	81.5	1.87

Reaction conditions: M = SPA (6.25 wt.% in DMSO); CTA = methyl 2-(butylthiocarbonothioylthio)propanoate (CTA1); I = AIBN; temperature = 60 °C. [a] Determined by ^{1}H NMR. [b] Determined by formula $M_{n(th)} = (m_{(mon.)} * conv._{(mon.)} * M_{(RAFT\ agent)} / m_{(RAFT\ agent)}) + M_{(RAFT\ agent)}$. [c] Determined by SEC-MALS in DMF/LiBr.

Table S2. *PDMA-b-PSPA synthesis*

Entry	[M]/[CTA]/[I]	Time, h	Conversion, % [a]	$M_{n(th)}$, kg mol^{-1} [b]	$M_{n(SEC)}$, kg mol^{-1} [c]	$Đ$ (M_w/M_n) [c]
1	50/1/0.2	4	52.9	9.6	10.5	1.34
2	50/1/0.2	6	73.7	12.1	11.6	1.44
3	50/1/0.2	8	82.0	13.1	12.5	1.37
4	50/1/0.2	16	88.9	13.9	12.3	1.45
5	50/1/0.2	24	93.5	14.5	12.5	1.42

Reaction conditions: M = SPA (6.25 wt.% in DMSO); CTA = $PDMA_{3.4k}$; I = AIBN; temperature = 60 °C. [a] Determined by ^{1}H NMR. [b] Determined by formula $M_{n(th)} = (m_{(mon.)} * conv._{(mon.)} * M_{(RAFT\ agent)} / m_{(RAFT\ agent)}) + M_{(RAFT\ agent)}$. [c] Determined by SEC-MALS in DMF/LiBr.

Table S3. *PPEGA-b-PSPA synthesis*

Entry	[M]/[CTA]/[I]	Time, h	Conversion, % [a]	$M_{n(th)}$, kg mol^{-1} [b]	$M_{n(SEC)}$, kg mol^{-1} [c]	$Đ$ (M_w/M_n) [c]
1	50/1/0.2	2	23.7	5.3	9.0	1.35
2	50/1/0.2	4	42.3	7.4	10.3	1.45
3	50/1/0.2	6	53.0	8.6	11.0	1.47
4	50/1/0.2	16	83.5	12.0	15.2	1.53
5	50/1/0.2	24	93.0	13.1	15.7	1.53

Reaction conditions: M = SPA (6.25 wt.% in DMSO); CTA = $PPEGA_{3.3k}$; I = AIBN; temperature = 60 °C. [a] Determined by ^{1}H NMR. [b] Determined by formula $M_{n(th)} = (m_{(mon.)} * conv._{(mon.)} * M_{(RAFT\ agent)} / m_{(RAFT\ agent)}) + M_{(RAFT\ agent)}$. [c] Determined by SEC-MALS in DMF/LiBr.

4. SEC traces

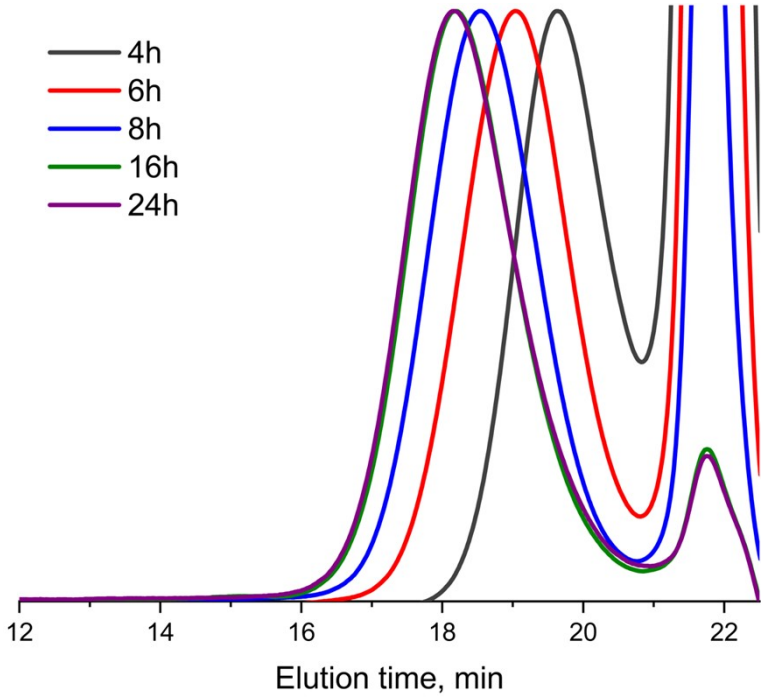


Figure S13. SEC-RI (DMF/LiBr) chromatograms of PSPA during polymerisation with targeted M_n of 10 kg mol^{-1} (**Table S1** (entry 1-5))

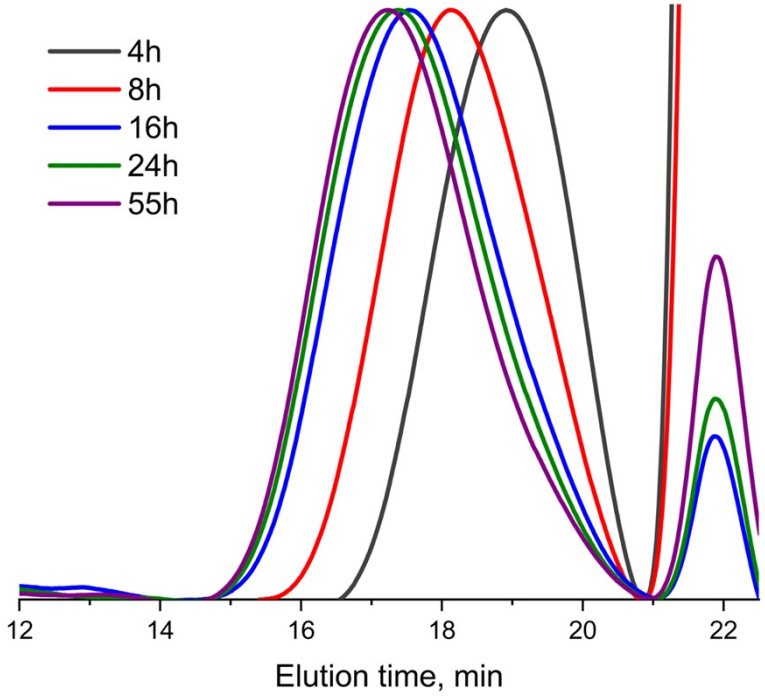


Figure S14. SEC-RI (DMF/LiBr) chromatograms of PSPA during polymerisation with targeted M_n of 20 kg mol^{-1} (**Table S1** (entry 6-10))

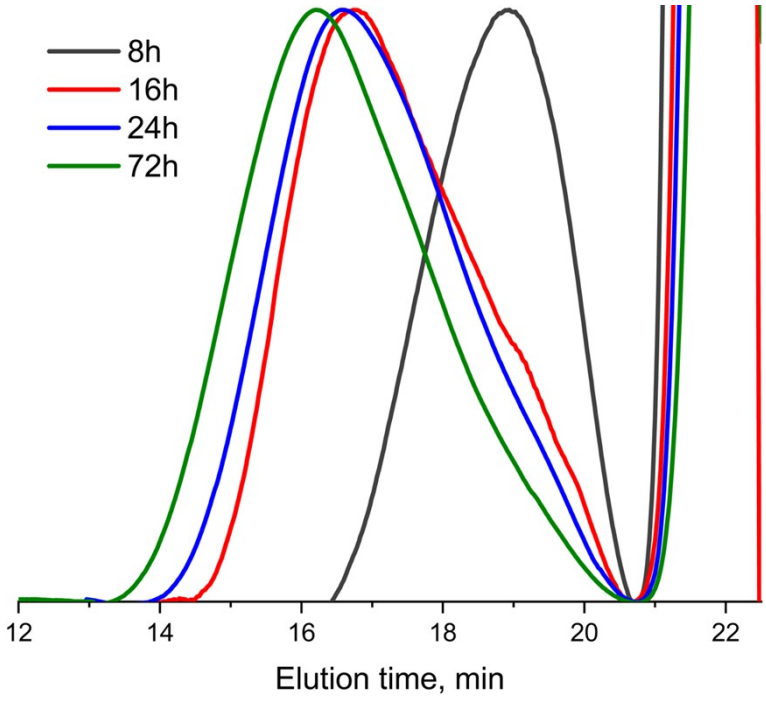


Figure S15. SEC-RI (DMF/LiBr) chromatograms during PSPA polymerisation with targeted M_n of 50 kg mol^{-1} (**Table S1** (entry 11-14)) in DMF/LiBr

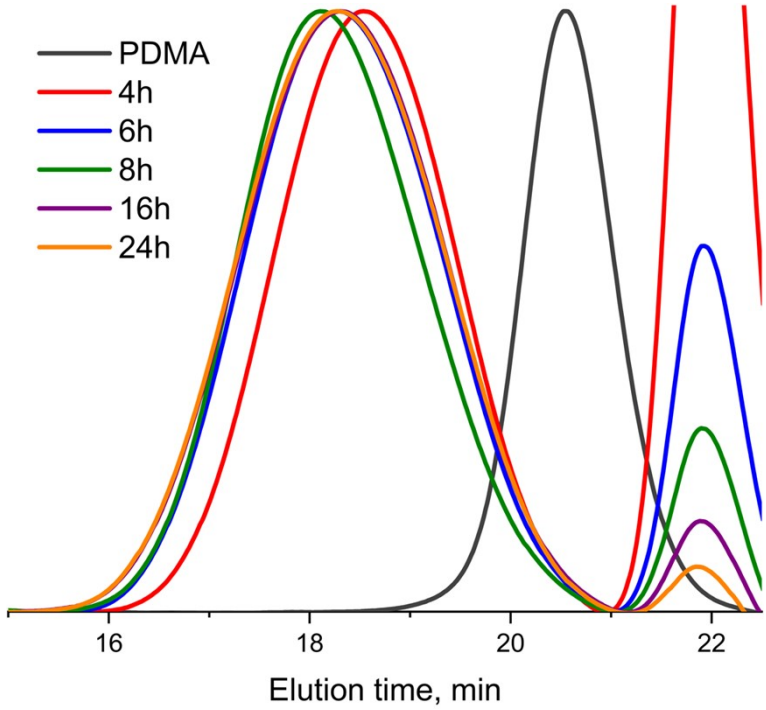


Figure S16. SEC-RI (DMF/LiBr) chromatograms of PDMA-*b*-PSPA (**Table S2** (entry 1-5))

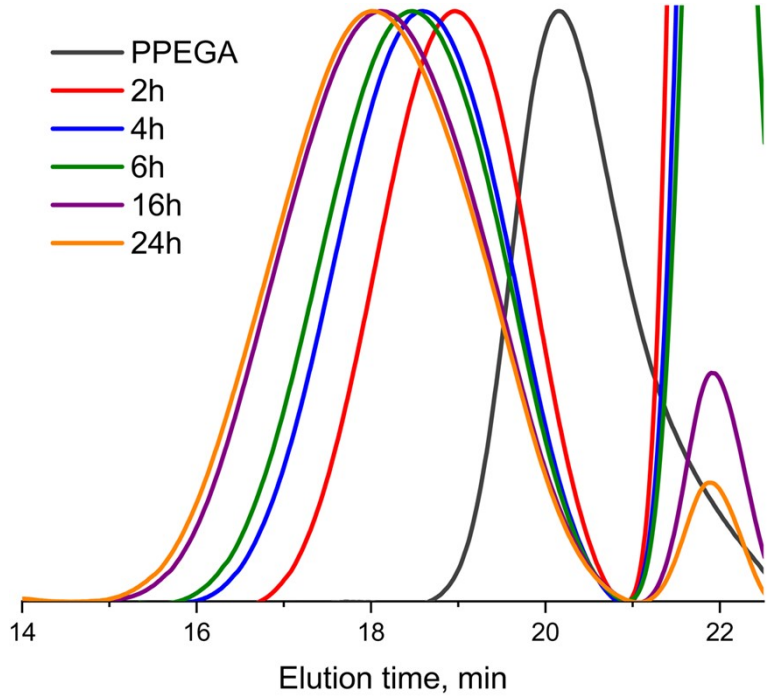


Figure S17. SEC-RI (DMF/LiBr) chromatograms of PPEGA-*b*-PSPA (**Table S3** (entry 1-5))

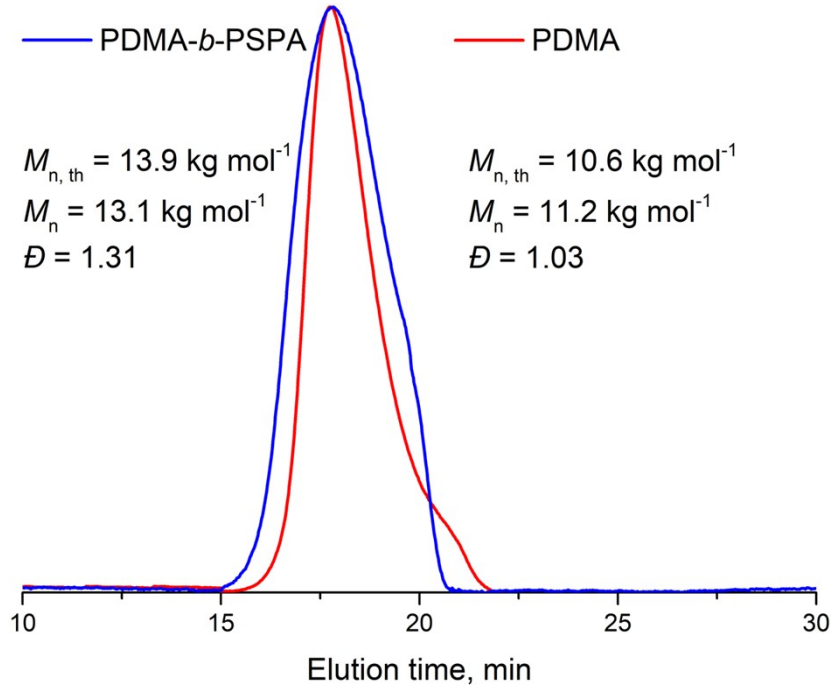


Figure S18. SEC-RI (DMF/LiBr) chromatograms of $PDMA_{11.2k}$ and corresponding $PDMA_{11.2k}$-*b*-$PSPA_{1.9k}$

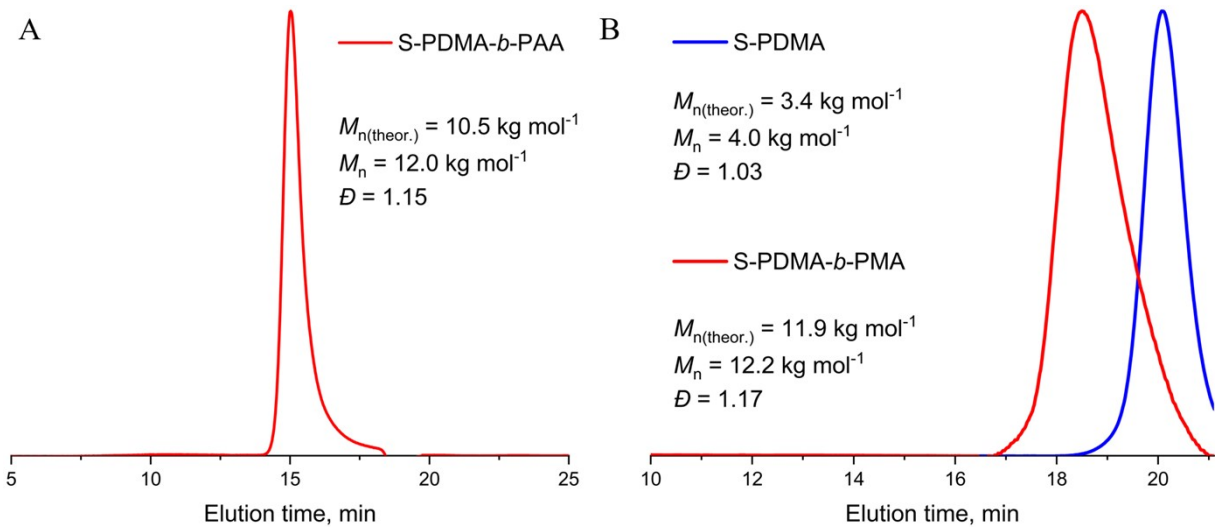


Figure S19. Aqueous SEC-RI chromatograms of S-PDMA$_{4.0k}$-*b*-PAA$_{8.0k}$ (a) and S-PDMA$_{4.0k}$ with the corresponding S-PDMA$_{4.0k}$-*b*-PMA$_{9.2k}$ in DMF/LiBr after methylation (b). Methylation procedure was reproduced from the literature[3]

5. ESI-MS spectra

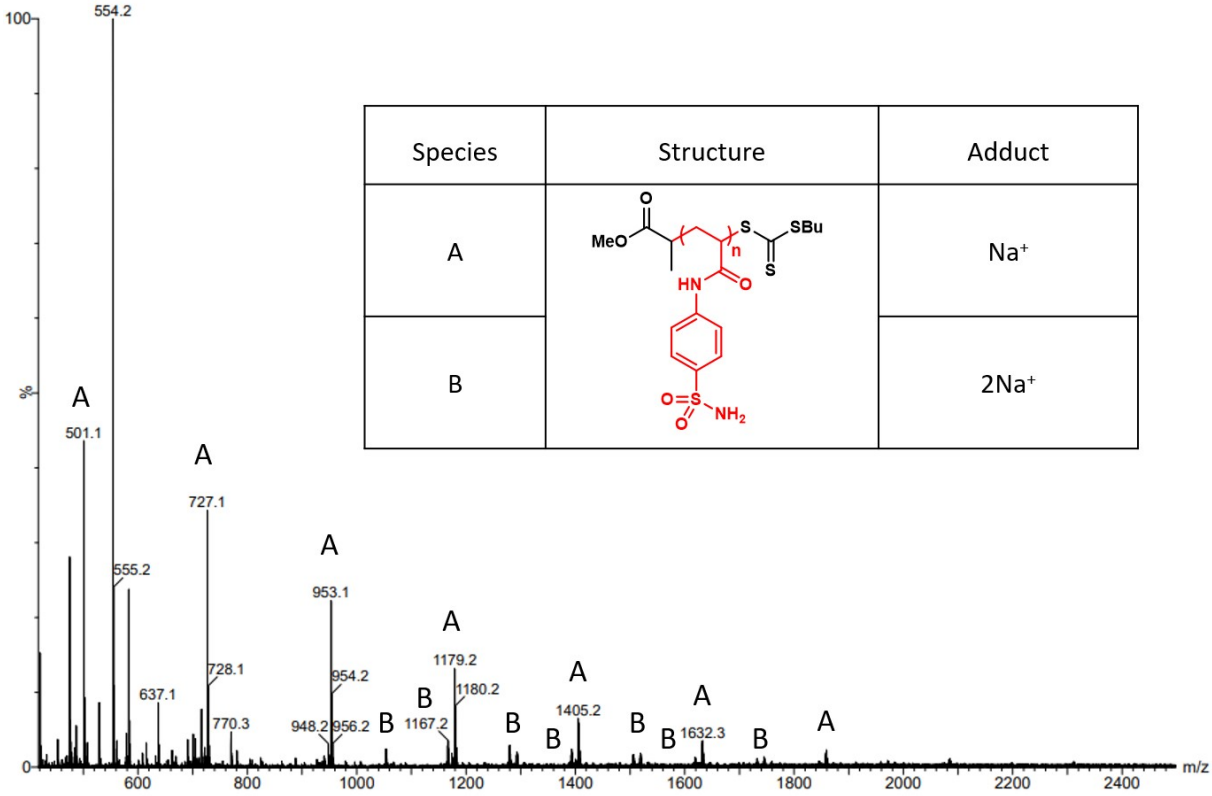


Figure S20. ESI-MS spectrum of PSPA (**Table S1**, entry 1, M_n = 3.6 kg mol^{-1}, $Đ$ = 1.23 (by SEC-MALS in DMF/LiBr))

α end	ω end	DP_n	Cation	$M_{n,th}$	$M_{n,exp}$
MeO-C(=O)-CH-CH_3	BuS-C(=S)-S	1	Na^+	501.063	501.063
MeO-C(=O)-CH-CH_3	BuS-C(=S)-S	2	Na^+	727.104	727.106
MeO-C(=O)-CH-CH_3	BuS-C(=S)-S	3	Na^+	953.145	953.148
MeO-C(=O)-CH-CH_3	BuS-C(=S)-S	8	$2Na^+$	1053.171	1053.174
MeO-C(=O)-CH-CH_3	BuS-C(=S)-S	9	$2Na^+$	1166.191	1166.197
MeO-C(=O)-CH-CH_3	BuS-C(=S)-S	10	$2Na^+$	1279.212	1279.217

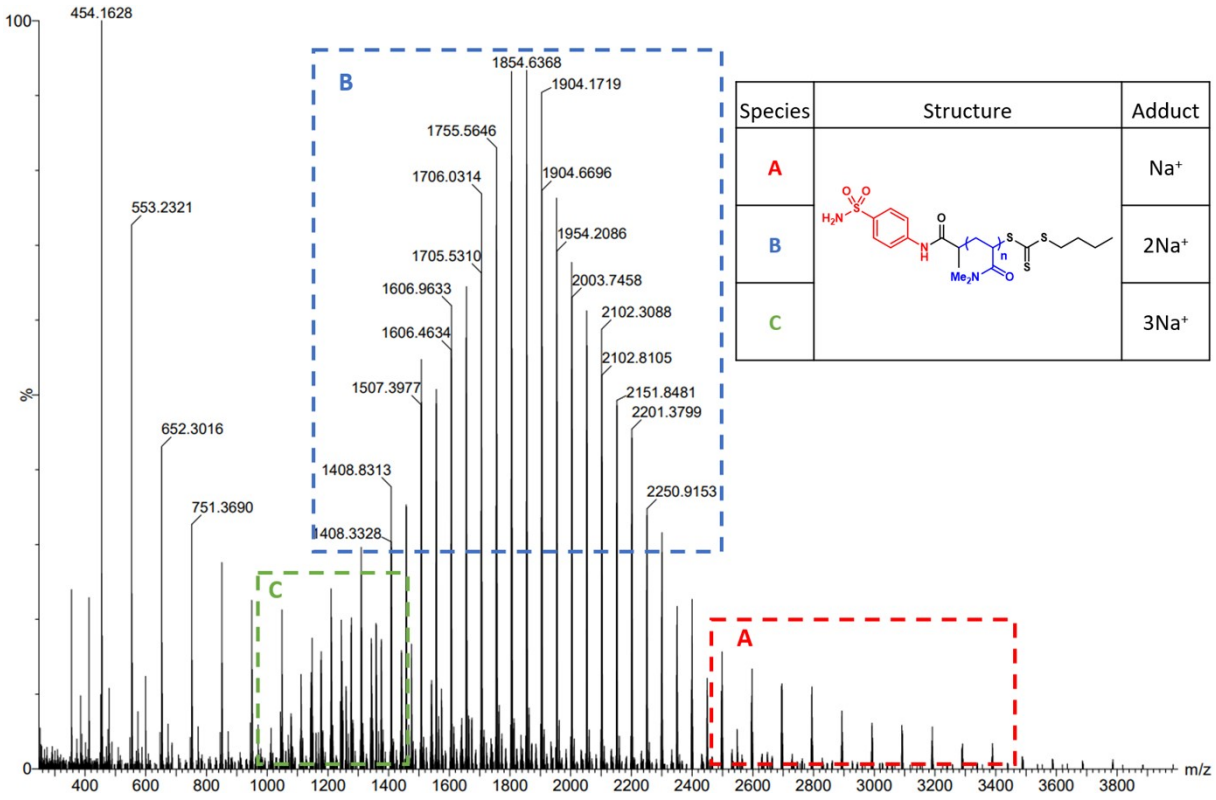


Figure S21. ESI-MS spectrum of S-PDMA (**Table S1**, entry 1, M_n = 3.6 kg mol^{-1}, $Đ$ = 1.23). A, B and C are respectively the mono-, bis- and tris-Na$^+$ adducts.

α end	ω end	DP_n	Cation	$M_{n,th}$	$M_{n,exp}$
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	23	Na^+	2695.5774	2695.9747
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	24	Na^+	2794.7061	2794.9071
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	25	Na^+	2893.8343	2893.8974
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	32	$2Na^+$	1805.3739	1805.4032
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	33	$2Na^+$	1854.6361	1854.6368
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	34	$2Na^+$	1904.1701	1904.1719
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	33	$3Na^+$	1244.2881	1244.2697
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	34	$3Na^+$	1277.3312	1277.3213
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	35	$3Na^+$	1310.3747	1310.3698

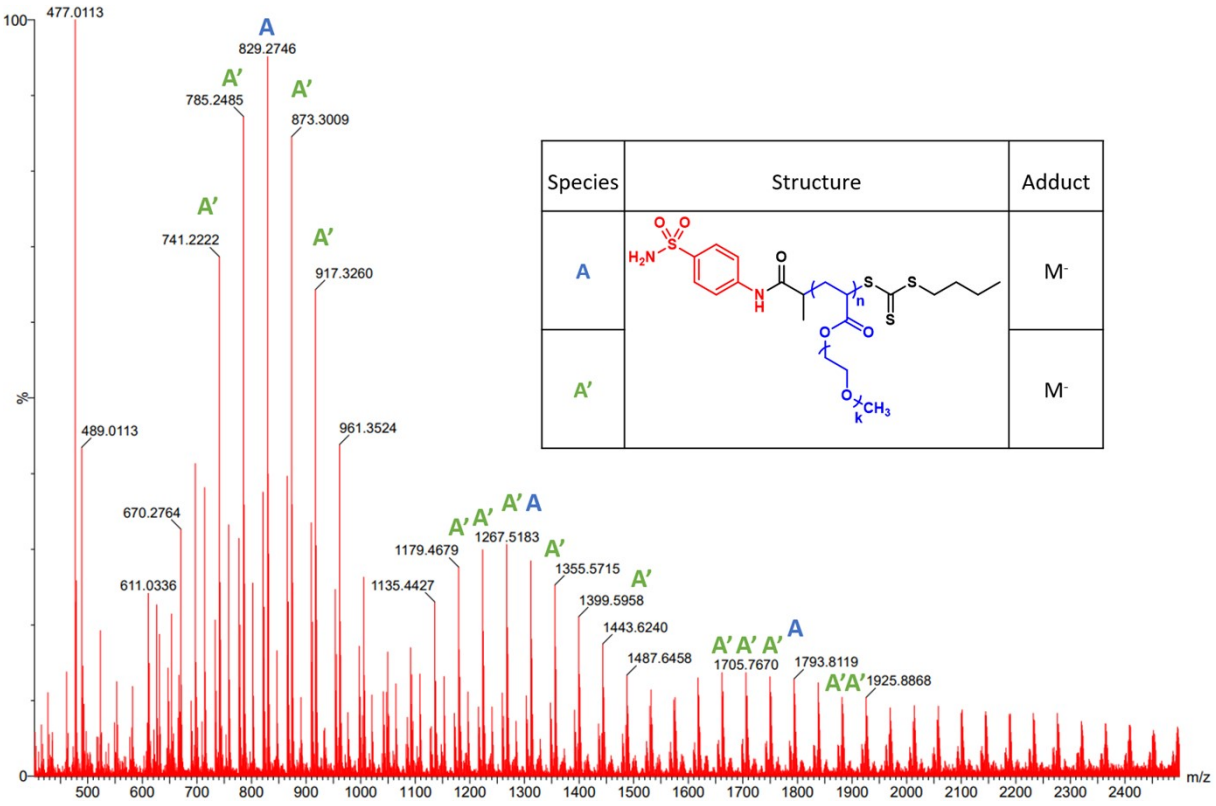


Figure S22. ESI-MS spectrum of S-PPEGA (M_n = 3.4 kg mol^{-1}, $Đ$ = 1.07 (by SEC-MALS in DMF/LiBr)). Two fragmentations are observed, **A** populations correspond to the different DPs of PEGA with the difference of 482 Da. **A'** populations correspond to the different DPs of the ethylene oxide units (-CH_2-CH_2-O) with the difference of 44 Da

α end	ω end	DP_n	Anion	$M_{n,th}$	$M_{n,exp}$
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	1 (k = 9)	-	829.2744	829.2746
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	2 (k = 9)	-	1311.5471	1311.5455
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	3 (k = 9)	-	1793.8198	1793.8119
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	1 (k = 8)	-	785.2481	785.2485
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	1 (k = 10)	-	873.3005	873.3009
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	2 (k = 8)	-	1267.5209	1267.5183
NH_2-SO_2-C_6H_4-NH- C(=O)-CH-CH_3	BuS-C(=S)-S	2 (k = 7)	-	1223.4946	1223.4943

6. UV-vis spectra

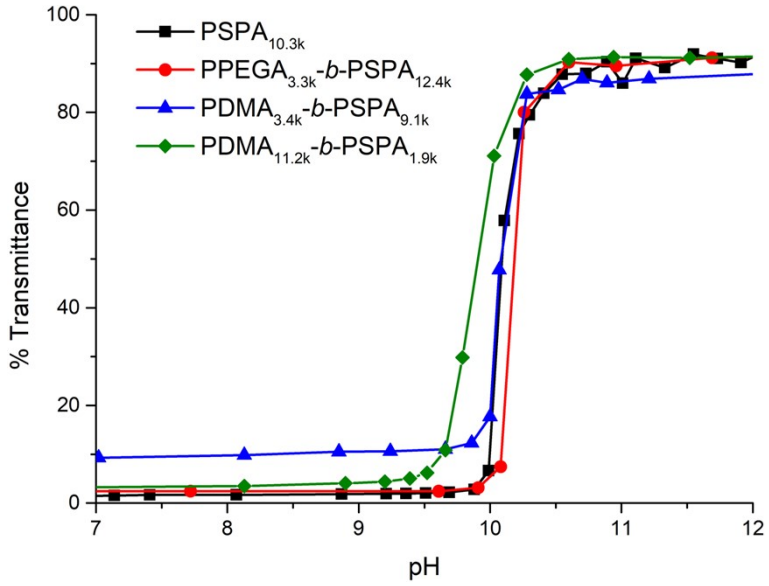


Figure S23. Measurement of pH-dependent solubility transition of $PSPA_{10.3k}$, $PPEGA_{3.3k}$-*b*-$PSPA_{12.4k}$ $PDMA_{3.4k}$-*b*-$PSPA_{9.1k}$ and $PDMA_{11.2k}$-*b*-$PSPA_{1.9k}$. Percent transmittance was measured using a UV−vis spectrophotometer (λ = 500 nm).

7. Mono-angle DLS

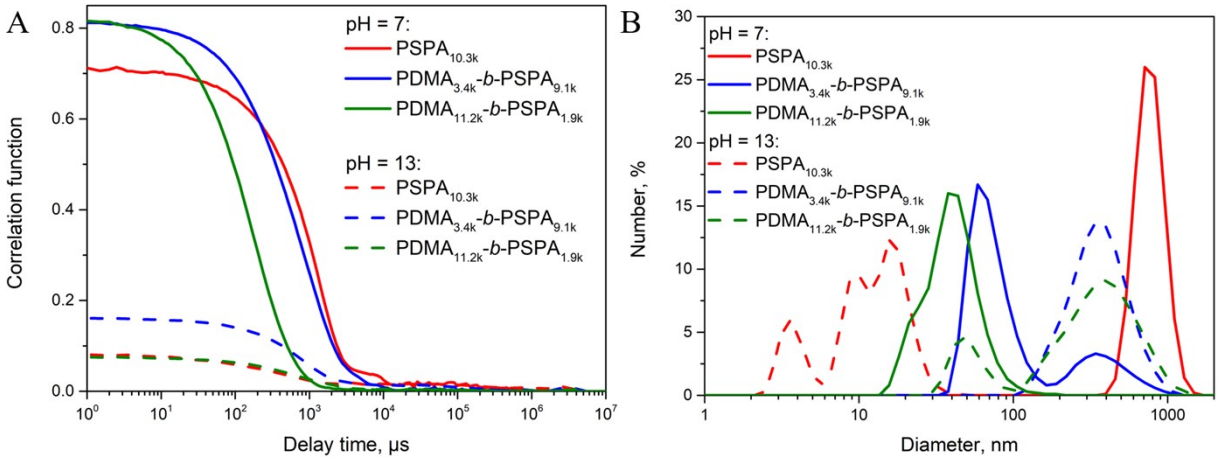


Figure S24. Correlation functions (A) and corresponding distribution average size in number (NNLS method) (B) of $PSPA_{10.3k}$, $PDMA_{3.4k}$-*b*-$PSPA_{9.1k}$ and $PDMA_{11.2k}$-*b*-$PSPA_{1.9k}$ at pH 7 and 13. High values of correlograms at pH 7 show the formation of large aggregates, while low values at pH 13 show that the polymers are completely soluble (A). The second population for $PDMA_{3.4k}$-*b*-$PSPA_{9.1k}$ shows the non-ideal size distribution at pH 7 (B)

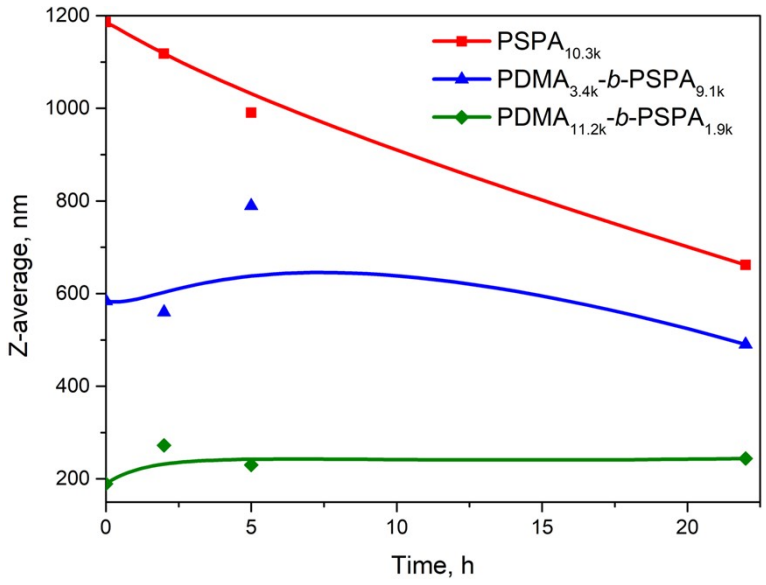


Figure S25. Dependence of Z-average sizes of the colloidal structures of the studied polymers at pH 7 as a function of time. Lines are just guide for the eye

8. Literature

(1) Despax, L.; Fitremann, J.; Destarac, M.; Harrisson, S. Low Concentration Thermoresponsive Hydrogels from Readily Accessible Triblock Copolymers. *Polym. Chem.* **2016**, *7* (20), 3375–3377. https://doi.org/10.1039/C6PY00499G.

(2) Lamb, J. R.; Qin, K. P.; Johnson, J. A. Visible-Light-Mediated, Additive-Free, and Open-to-Air Controlled Radical Polymerization of Acrylates and Acrylamides. *Polym. Chem.* **2019**, *10* (13), 1585–1590. https://doi.org/10.1039/C9PY00022D.

(3) Couvreur, L.; Lefay, C.; Belleney, J.; Charleux, B.; Guerret, O.; Magnet, S. First Nitroxide-Mediated Controlled Free-Radical Polymerization of Acrylic Acid. *Macromolecules* **2003**, *36* (22), 8260–8267. https://doi.org/10.1021/ma035043p.