Supporting information

The Influence of Mixing on Chain Extension by Photo-Controlled/Living Radical Polymerization under Continuous-Flow Conditions

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1. Materials and characterization methods

1.1. Materials

Methyl acrylate (MA), *N*-isopropyl acrylamide (NIPAM), *N,N*-diethylmethacrylamide (DEA), 4-acryloylmorpholine (AcM), *N,N*-dimethylacrylamide (DMA), and *N*-hydroxyethyl acrylamide (NHEAA) were purchased from Adamas, TCL or Energy Chemical. All liquid monomers were filtered through a plug of basic alumina column before use. NIPAM was recrystallized from *n*-hexane for several times to remove inhibitor. *N,N*-Dimethylformamide (DMF) was freshly distilled from CaH_2. 2-[[(dodecylthio)thioxomethyl]thio]-2-methylpropanoic acid[1] and 5,10,15,20-tetraphenyl-21H,23H-porphine zinc (ZnTPP)[2] were synthesized according to literatures. Azobisisobutyronitrile (AIBN) and other reagents were purchased from TCL, Adamas or Sigma-Aldrich and were used as received without further purification.

1.2. Materials of flow setup

All connectors, tubing, nuts, ferrules and fittings were purchased from IDEX Health and Science. 25 mL syringes were purchased from Shanghai Bolige industry & trade Corporation. Syringe pumps were purchased from Longer company. 13 W white LED the bulbs were purchased from PHILPS light. The tubing reactors and all connection tubings used in all figures were made of PTFE material (1.58 mm OD × 0.8 mm ID). Connections for the tubing reactors and all connection tubings were made of super flangeless ferrules (w/SST ring) and super flangeless nuts (PEEK). Details of equipment configuration are shown in Figure S1. The light intensity at the surface of tubing reactor is about 20 mW/cm^2.

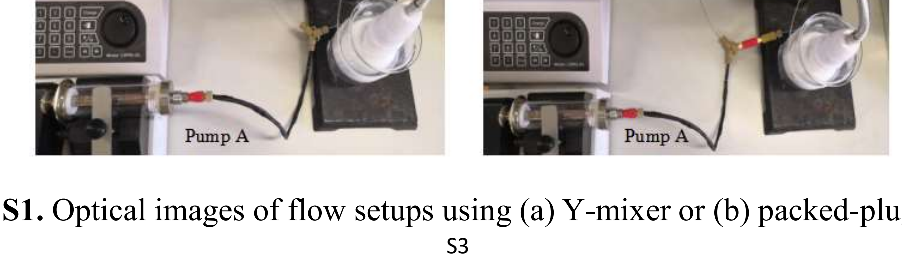

Figure S1. Optical images of flow setups using (a) Y-mixer or (b) packed-plug mixer.

1.3. Materials of mixer setup

A short PTFE tubing (30 mm, 3.17 mm OD × 1.58 mm ID) was first filled with 40 mesh or 100 mesh size SiO2 beads. Two sides of this tubing were packed with quartz cotton (fiber diameter: 3-5 μm) to prevent leaking of SiO2 beads. Then, two pairs of super flangeless nuts (PEEK) and fittings (PEEK) were fitted onto two sides of this tubing to provide connections to the flow setup. The structure of a packed-plug mixer was depicted in Figure S2.

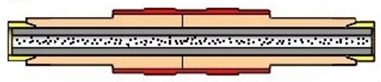

Figure S2. Sectional drawing of the packed plug mixer**.**

1.4. Characterization method

Nuclear magnetic resonance was recorded on Advance III 400 MHz Bruker spectrometer at 298 K. ^{1}H NMR signals were measured relative to the signal of residual chloroform (7.26 ppm) in deuterochloroform ($CDCl_3$) or residual dimethyl sulfoxide (2.54 ppm) in dimethyl sulfoxide-D6.

Size exclusion chromatography (SEC) measurement was conducted in DMF at 50 °C with the elution rate of 0.6 mL/min on a TOSOH instrument which was equipped with a Bryce refractive index detector. One 4 μm superAW2500 gel column and one 4 μm superAW3000 gel column were employed. The calibration was performed with PS standards.

2. Synthesis of macro-CTAs

2.1. Procedure for the synthesis of macro-CTA1

A oven-dried 25 mL schlenk flask equipped with a stir bar was charged with MA (3.01 g, 35 mmol), 2-[[(dodecylthio)thioxomethyl]thio]-2-methylpropanoic acid

(159.0 mg, 0.5 mmol), AIBN (8.2 mg, 0.05 mmol) and 4 mL DMF. After the flask was sealed with a rubber septum, the solution was deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere. Then, the mixture was stirred at 65 °C for 5 h. After reaction, a small aliquot was taken and analyzed with ^{1}H NMR to give monomer conversion. The mixture in the flask was cooled down and added dropwise into 300 mL cold diethyl ether to give a yellow solid. Obtained solid was re-dissolved in minimal amount of acetone and precipitated with cold diethyl ether. This procedure was repeated for three times in total to give macro-CTA1 as a yellow solid. Obtained polymer was characterized with a SEC instrument (M_n = 4.48 kDa, $Đ$ = 1.18).

2.2. Procedure for the synthesis of macro-CTA2

A oven-dried 25 mL schlenk flask equipped with a stir bar was charged with MA (4.30 g, 50 mmol), 2-[[(dodecylthio)thioxomethyl]thio]-2-methylpropanoic acid (159.0 mg, 0.5 mmol), AIBN (8.2 mg, 0.05 mmol) and 4 mL DMF. After the schlenk flask was sealed with a rubber septum, the solution was deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere. Then, the mixture was stirred at 65 °C for 7 h. After reaction, a small aliquot was taken and analyzed with ^{1}H NMR to give monomer conversion. The mixture in the flask was cooled down and dropped into 300 mL cold diethyl ether to give yellow solid. Obtained solid was re-dissolved in minimal amount of acetone and precipitated with cold diethyl ether. This procedure was repeated for three times in total to give macro-CTA2 as a yellow solid. Obtained polymer was characterized with a SEC instrument (M_n = 8.10 kDa, $Đ$ = 1.18).

2.3. Procedure for the synthesis of macro-CTA3

A oven-dried 25 mL schlenk flask equipped with a stir bar was charged with NiPAM (3.33 g, 25 mmol), 2-[[(dodecylthio)thioxomethyl]thio]-2-methylpropanoic acid (159.0 mg, 0.5 mmol), AIBN (8.2 mg, 0.05 mmol) and 4 mL DMF. After the schlenk flask was sealed with a rubber septum, the solution was deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere. Then, the mixture was stirred at 65 °C for 12 h. After reaction, a small aliquot was taken and analyzed with ^{1}H NMR to give monomer conversion. The mixture in the flask was cooled down and dropped into 300 mL cold diethyl ether to give a yellow solid. Obtained solid was re-dissolved in minimal amount of acetone and precipitated with cold diethyl ether. This procedure was repeated for three times in total to give macro-CTA3 as a yellow solid. Obtained polymer was characterized with a SEC instrument (M_n = 5.89 kDa, $Đ$ = 1.17).

3. General procedure for polymerization using a conventional mixer

For related polymerization in Table 1, Figure 4 and Figure 5

An oven-dried vial was charged with a solution of monomer (3.0 M) and ZnTPP (0.3 mM) in DMF. Another oven-dried vial was charged with a solution containing macro-CTA (0.06 M) in DMF. Both solutions were deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere. As shown in Figure S1a, the solution of monomer was loaded into a syringe and fitted onto pump A. The solution from pump A was injected at a flow rate of 40 μL/min. The solution of macro-CTA1 was loaded into another syringe and fitted onto pump B. The solution from pump A was injected at a flow rate of 20 μL/min. Two streams were merged at a Y-mixer, and introduced into a mixing loop of different lengths to reach different mixing times (for 3 min, 36 cm length; for 1.67 min, 20 cm length; for 0.83 min, 10 cm length; for 0 min, no mixing loop). The combined stream was finally delivered into a tubing reactor (volume = 1.8 mL, residence time=30 min) under visible-light irradiation. After reaction, the resulted solution was passed through a back-pressure regulator and was collected for SEC and NMR analysis.

4. General procedure for polymerization using a packed plug

For related polymerization in Table 2, Figure 4 and Figure 5

An oven-dried vial was charged with a solution containing monomer (3.0 M) and ZnTPP (0.3 mM) in DMF. Another oven-dried vial was charged with a solution containing macro-CTA (0.06 M) in DMF. Two solutions were deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere, respectively. As shown in the

Figure S1b, the solution of monomer was loaded in a syringe and fitted onto pump A. The solution from pump A was injected at a flow rate of 40 μL/min. The solution of macro-CTA was loaded in a syringe and fitted onto pump B. The solution from pump A was injected at a flow rate of 20 μL/min. Two streams were merged at a Y-mixer and immediately delivered into a packed plug. After mixing, the solution was finally delivered into tubing reactor (volume = 1.8 mL, residence time = 30 min) under visible-light irradiation. After reaction, the resulted solution was passed through a back-pressure regulator and was collected for SEC and NMR analysis.

5. Polymerization results for experiments in Table 1

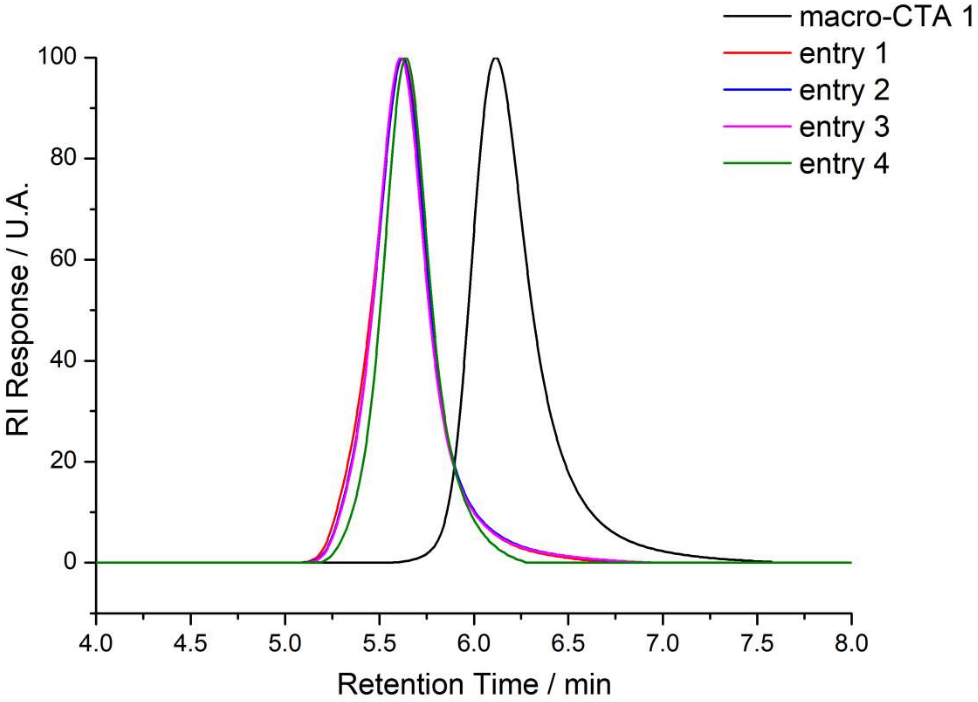

Figure S3. SEC profiles for polymerization from entries 1 to 4 in Table 1.

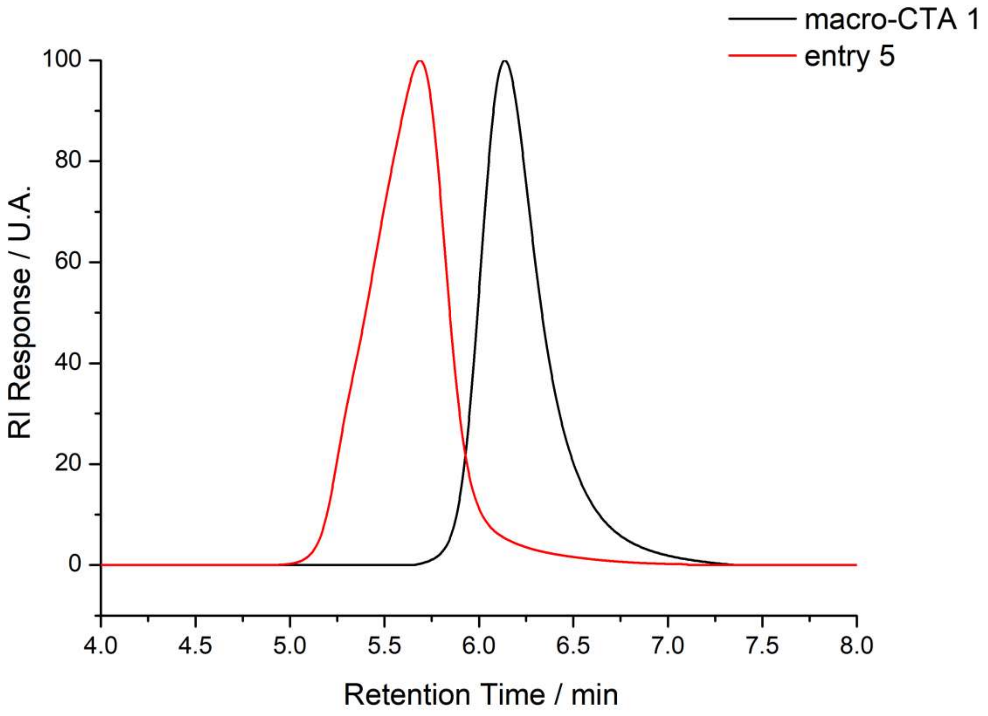

Figure S4. SEC profile for polymerization of entry 5 in Table 1.

6. Polymerization results for experiments in Figure 4b

Table S1. Results of photopolymerization in flow using macro-CTA2.[a]

monomer	mixer	conv. (%)	$M_{n,calc}$[b] (kDa)	$M_{n,SEC}$[c] (kDa)	$Đ$[c]
DMA	Y-mixer	75	14.9	14.9	1.60
	Packed plug	81	17.1	19.2	1.24
DEA	Y-mixer	82	18.4	17.9	1.53
	Packed plug	88	19.1	19.3	1.25
AcM	Y-mixer	90	20.6	14.5	1.41
	Packed plug	95	21.8	22.3	1.18
NHEAA	Y-mixer	75	17.5	19.2	1.89
	Packed plug	77	17.7	21.6	1.33

[a] [M]/[CTA]/[PC] = 100/1/0.01, room temperature, DMF, 13 W white LEDs, residence time = 30min. Conversions were determined by 1H NMR analysis. Flow

rates for solutions of macro-CTA1 and monomer are 20 and 40 µL/min, respectively. [b] $M_{\mathrm{n,calc}}$ was determined by conversion. [c] $M_{\mathrm{n,SEC}}$ and $Đ$ were determined by SEC measurement.

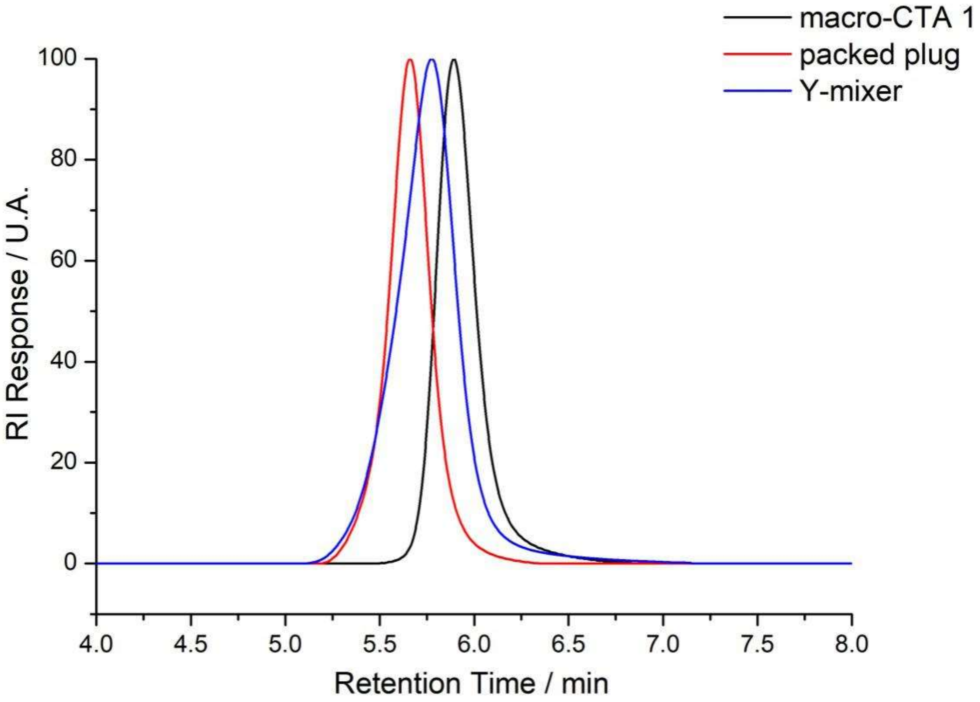

Figure S5. SEC profiles for polymerization of DMA in Figure 4b.

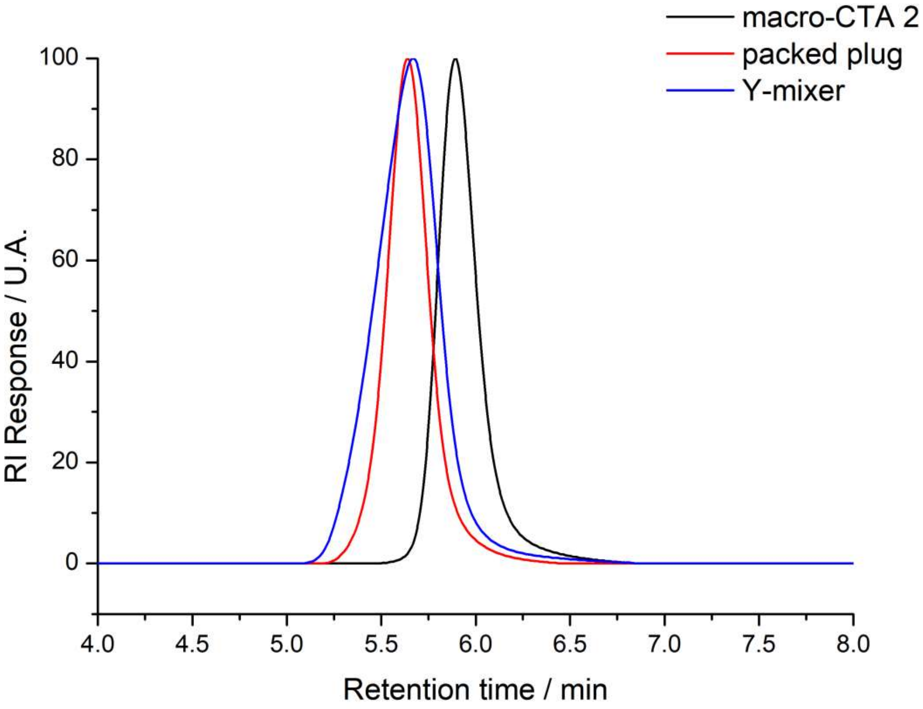

Figure S6. SEC profiles for polymerization of DEA in Figure 4b.

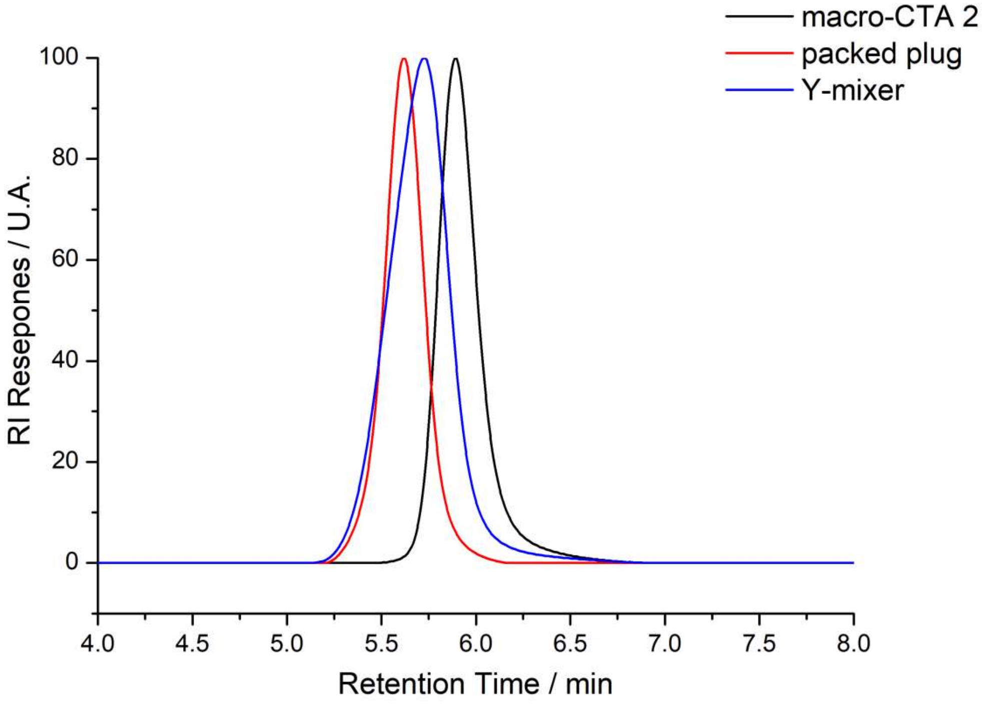

Figure S7. SEC profiles for polymerization of AcM in Figure 4b.

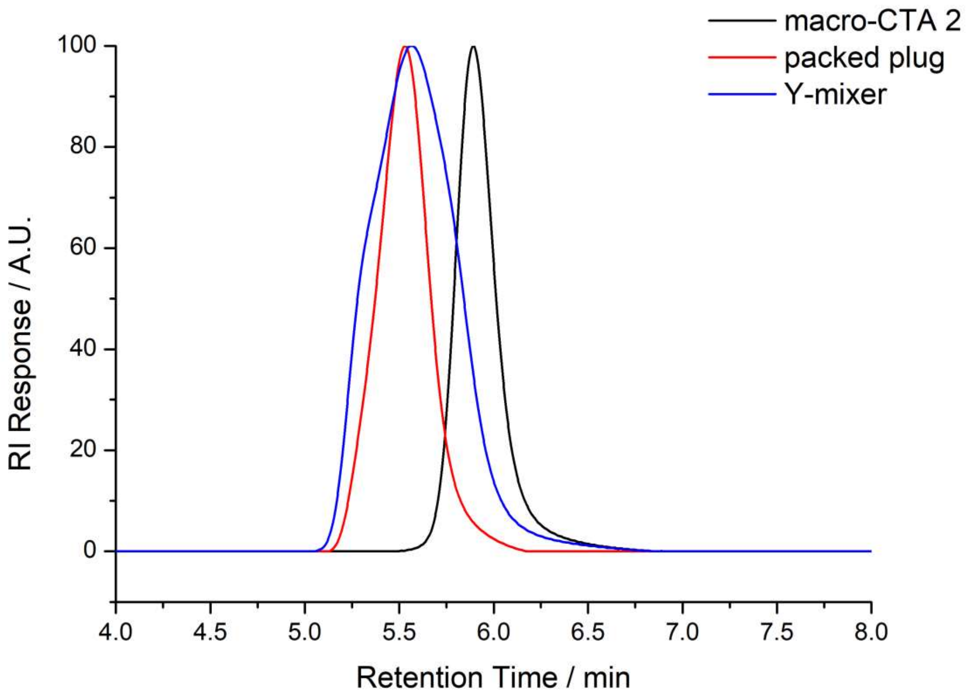

Figure S8. SEC profiles for polymerization of NHEAA in Figure 4b.

7. Polymerization results for experiments in Figure 5

Table S2. Results of photopolymerization under flow conditions using macro-CTA3.[a]

monomer	mixer	conv. (%)	$M_{n,calc}$[b] (kDa)	$M_{n,SEC}$[c] (kDa)	$Đ$[c]
DMA	Y-mixer	78	13.6	12.8	1.57
	Packed plug	87	17.5	18.6	1.24
DEA	Y-mixer	80	15.8	13.5	1.60
	Packed plug	91	18.4	19.1	1.28
AcM	Y-mixer	91	18.7	12.7	1.41
	Packed plug	98	19.7	20.8	1.24
NHEAA[d]	Y-mixer	73	15.2	17.1	1.44
	Packed plug	79	17.1	20.4	1.36

[a] [M]/[CTA]/[PC] = 100/1/0.01, room temperature, DMF, 13 W white LEDs, residence time is 30min. Conversions were determined by 1H NMR analysis. Flow

rates for solutions of macro-CTA1 and monomer are 20 and 40 μL/min, respectively. [b] $M_{n,calc}$ values were determined by conversion. [c] $M_{n,sec}$ and $Đ$ were determined by the SEC measurement. [d] the flow rates of the monomer solution and the CTA solution are 20 μL/min and 10μL/min respectively, residence time is 30 min.

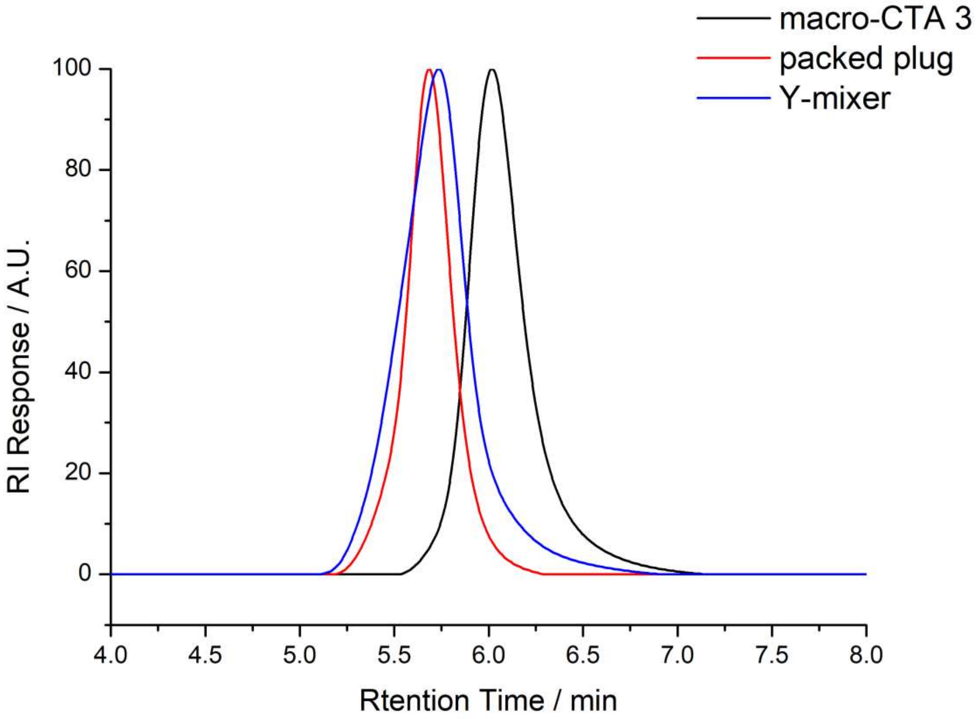

Figure S9. SEC profiles for polymerization of DMA in Figure 5.

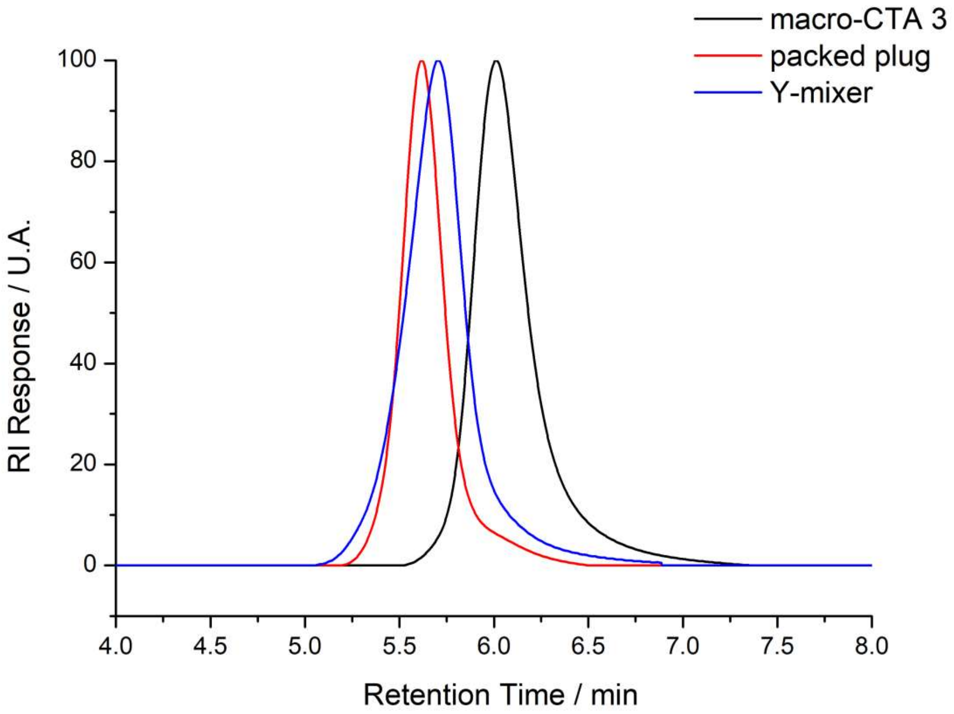

Figure S10. SEC profiles for polymerization of DEA in Figure 5.

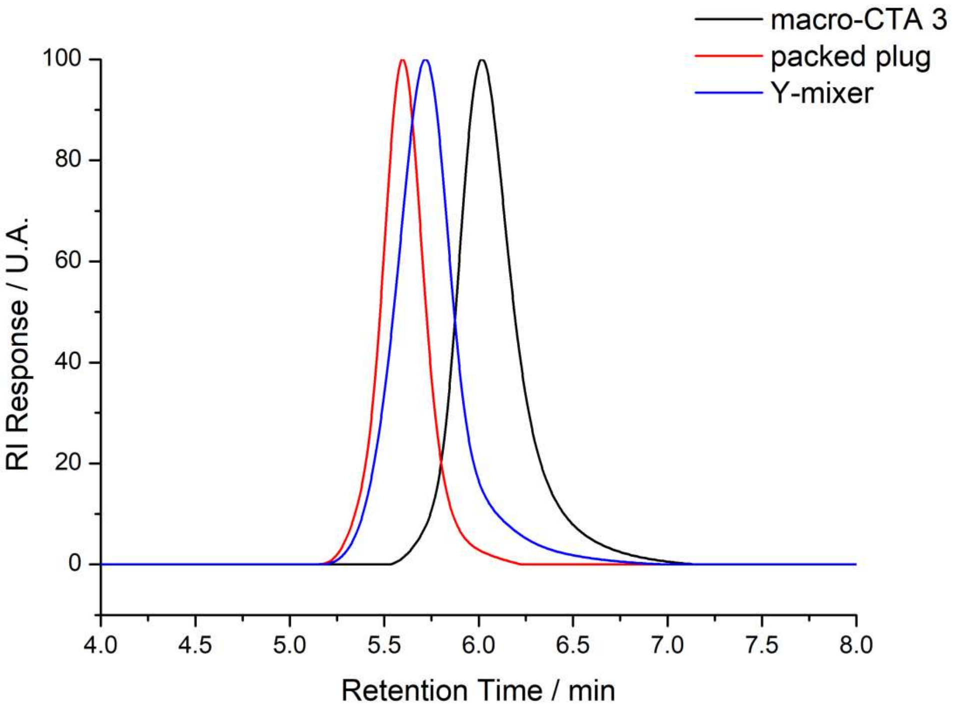

Figure S11. SEC profiles for polymerization of AcM in Figure 5.

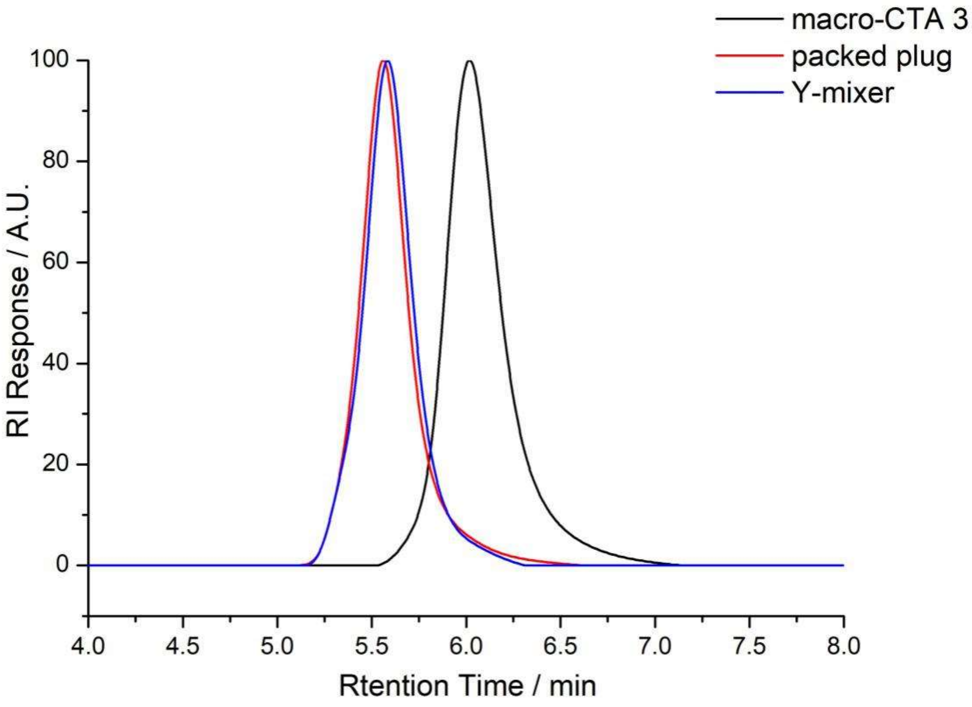

Figure S12. SEC profiles for polymerization of NHEAA in Figure 5.

8. Polymerization results for experiments in Figure 6

General procedure

An oven-dried vial was charged with a solution containing DMA (25 wt% to 61 wt%) and ZnTPP (0.6 mM to 0.24 mM) in DMF. Another oven-dried vial was charged with a solution containing macro-CTA1 (13 wt% to 53 wt%) in DMF. Two solutions were deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere, respectively. As shown in Figure S1, solutions of monomer and macro-CTA1 were loaded into two syringes, and fitted onto pump A and pump B, respectively. For pump A, flow rate = 20 μL/min to 50 μL/min; for pump B, flow rate = 10 μL/min to 40 μL/min (see Figure 6 for details). Two streams were combined at a Y-mixer or a packed plug. After mixing, combined mixture was introduced into a tubing reactor (volume = 1.8 mL, total flow rate = 60 μL/min) exposed to visible-light irradiation. After reaction, the resulted solution passed through a back-pressure regulator, and was collected for SEC and NMR measurements.

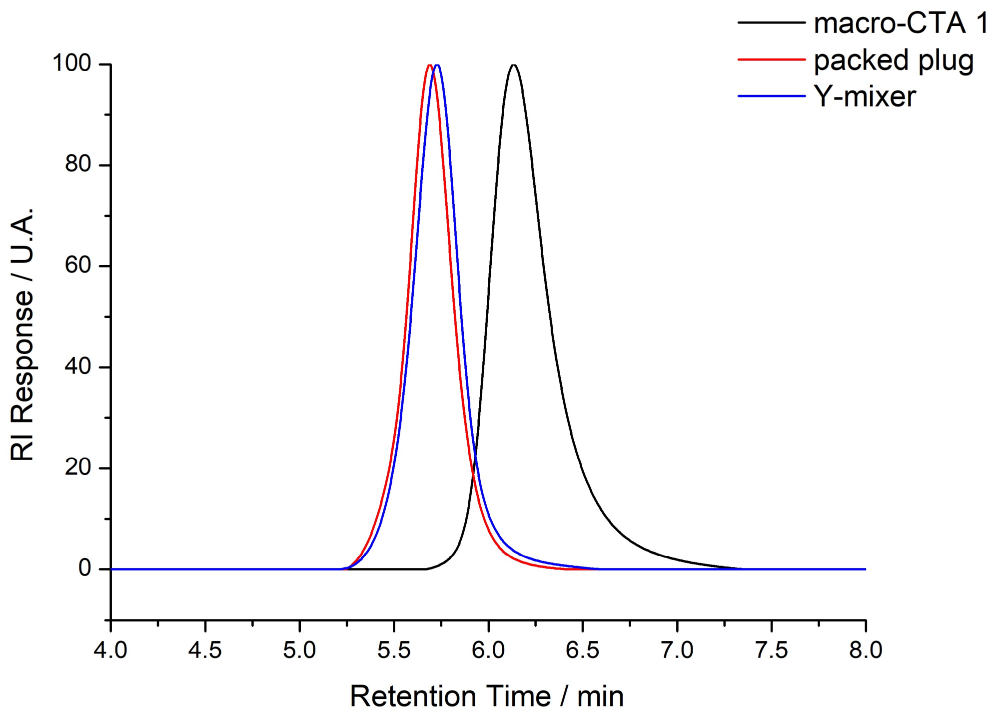

Figure S13. SEC profiles for polymerization in Figure 6a.

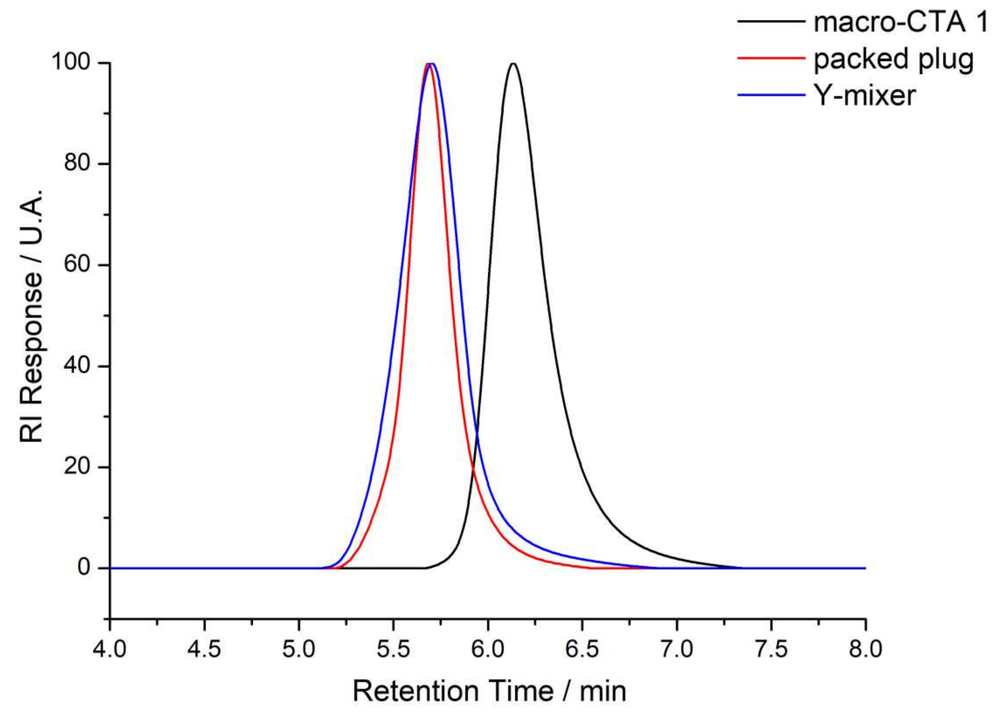

Figure S14. SEC profiles for polymerization in Figure 6b.

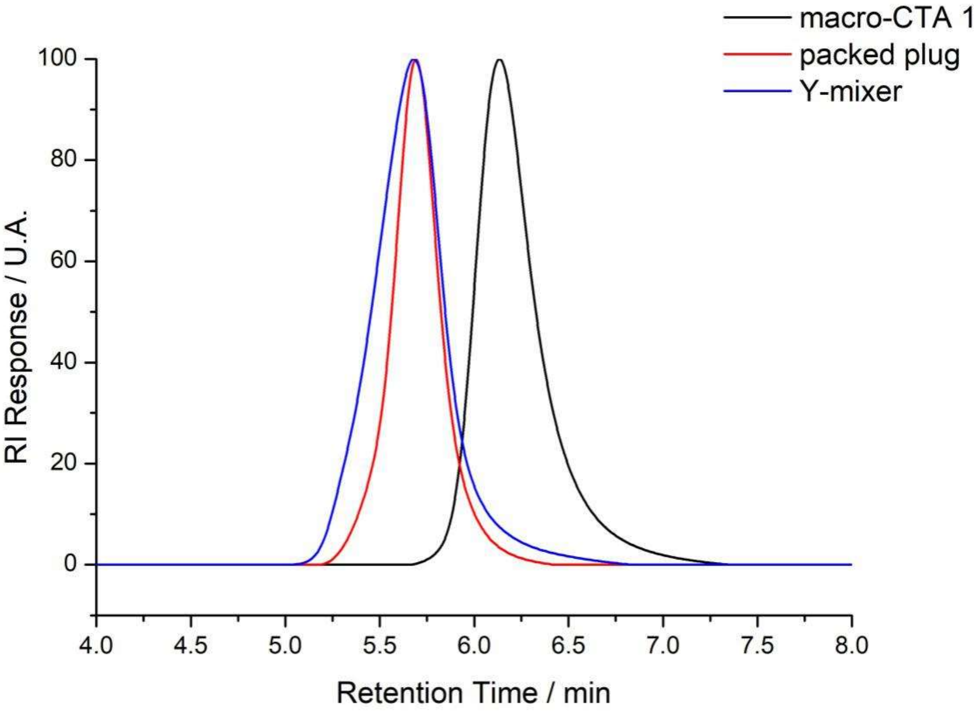

Figure S15. SEC profiles for polymerization in Figure 6c.

9. Polymerization results for experiments in Figure 7

General procedure

An oven-dried vial was charged with a solution containing DMA (3.0 M) and ZnTPP (0.6 mM) in DMF. Another oven-dried vial was charged with a solution containing macro-CTA1 (the concentration of macro-CTA1 was kept in a range of 0.03 M to 0.12 M to maintain the [monomer]/[CTA] ratio = 200/1 to 50/1) in DMF. Two solutions were deoxygenated through three freeze-pump-thaw cycles under N_2 atmosphere, respectively. As shown in Figure S1, solutions of monomer and macro-CTA1 were loaded into two syringes, and fitted onto pump A and pump B, respectively. For pump A, flow rate = 40 μL/min; for pump B, flow rate = 20 μL/min. Two streams were combined at a Y-mixer or a packed plug. After mixing, combined mixture was introduced into a tubing reactor (volume = 1.8 mL, total flow rate = 60 μL/min) exposed to visible-light irradiation. After reaction, the resulted solution passed through a back-pressure regulator, and was collected for SEC and NMR measurements.

Table S3. Results of photopolymerization under flow with different ratios of [monomer]/[CTA].[a]

[M]/[CTA]/[PC]	conc.$_{\mathrm{M}}$ (wt%)	conc.$_{\mathrm{CTA}}$ (wt%)	conv. (%)	$M_{\mathrm{n,calc}}$[b] (kDa)	$M_{\mathrm{n,SEC}}$[c] (kDa)	$Đ$[c]
50/1/0.005	31	53	77	8.3	9.6	1.19
65/1/0.0065	31	40	76	9.5	11.2	1.23
100/1/0.01	31	28	75	11.9	13.6	1.21
130/1/0.013	31	20	74	14.5	16.3	1.25
200/1/0.01	31	13	74	18.5	22.1	1.26

[a] room temperature, macro-CTA1, DMF, 13 W white LEDs, residence time is 30min. Conversions were determined by 1H NMR analysis. Flow rates for solutions of macro-CTA1 and monomer are 20 and 40 µL/min, respectively. [b] $M_{\mathrm{n,calc}}$ values were determined by conversion. [c] $M_{\mathrm{n,SEC}}$ and $Đ$ were determined by the SEC measurement.

10. ^{1}H NMR spectra of block polymers

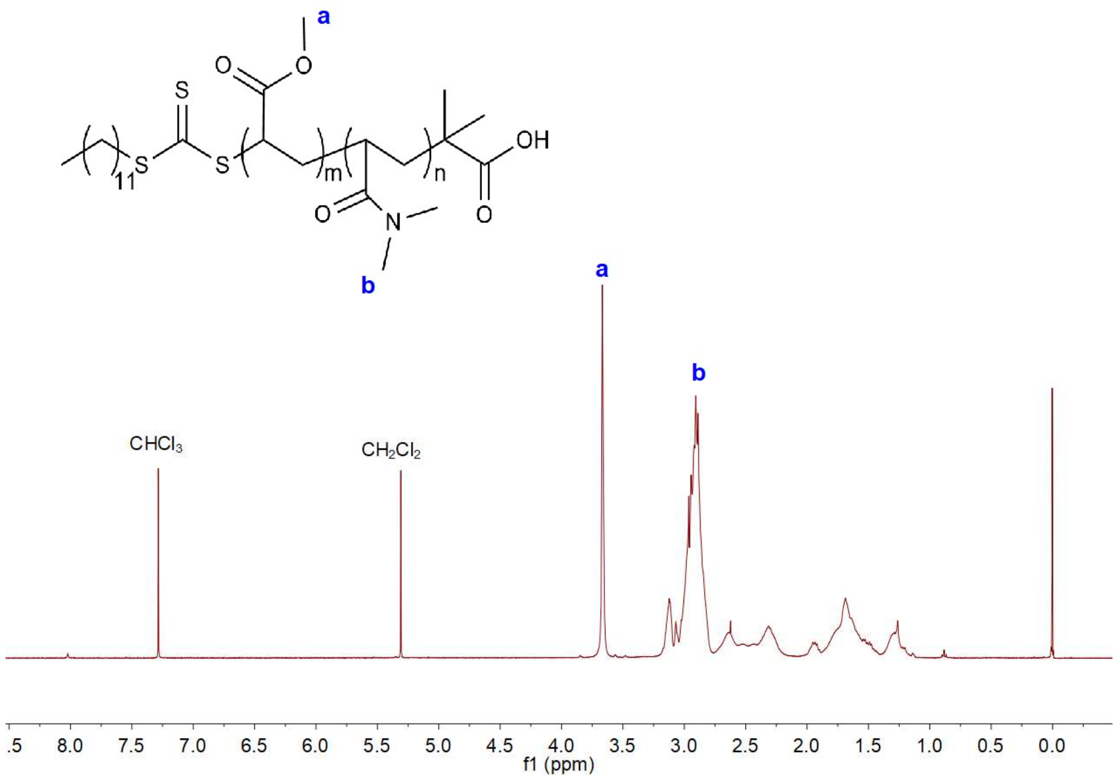

Figure S16. ^{1}H NMR spectrum of PMA-*b*-PDMA.

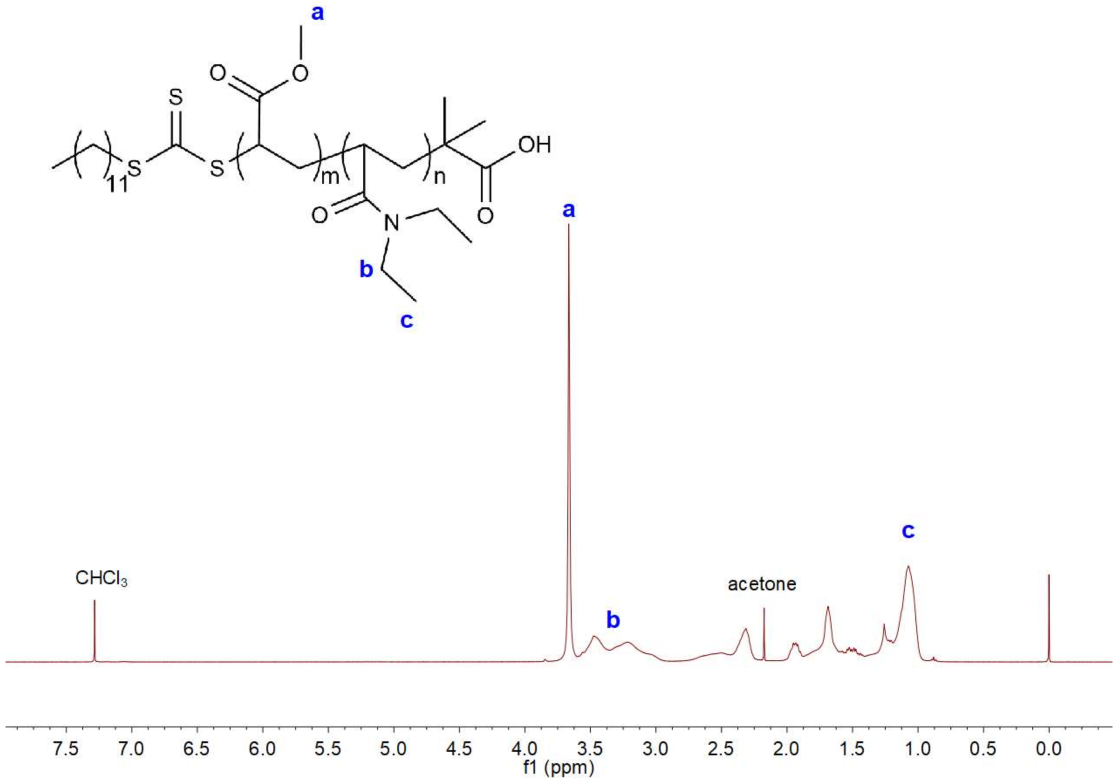

Figure S17. ^{1}H NMR spectrum of PMA-*b*-PDEA.

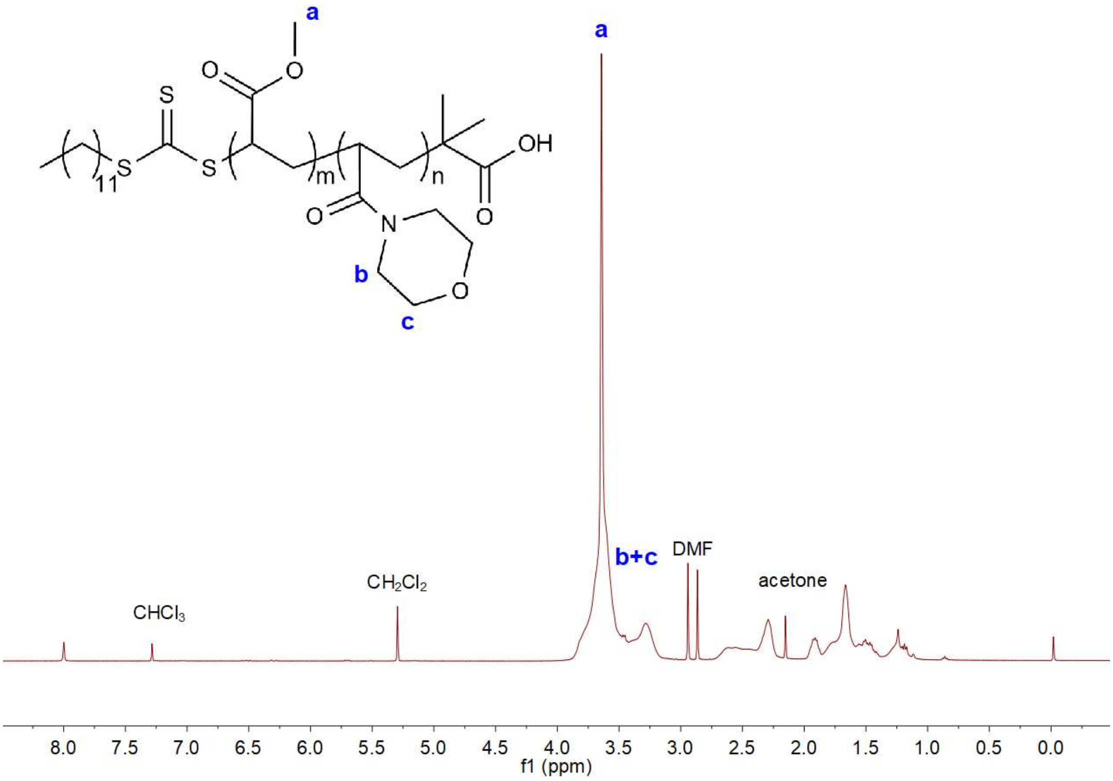

Figure S18. ^{1}H NMR spectrum of PMA-*b*-PAcM.

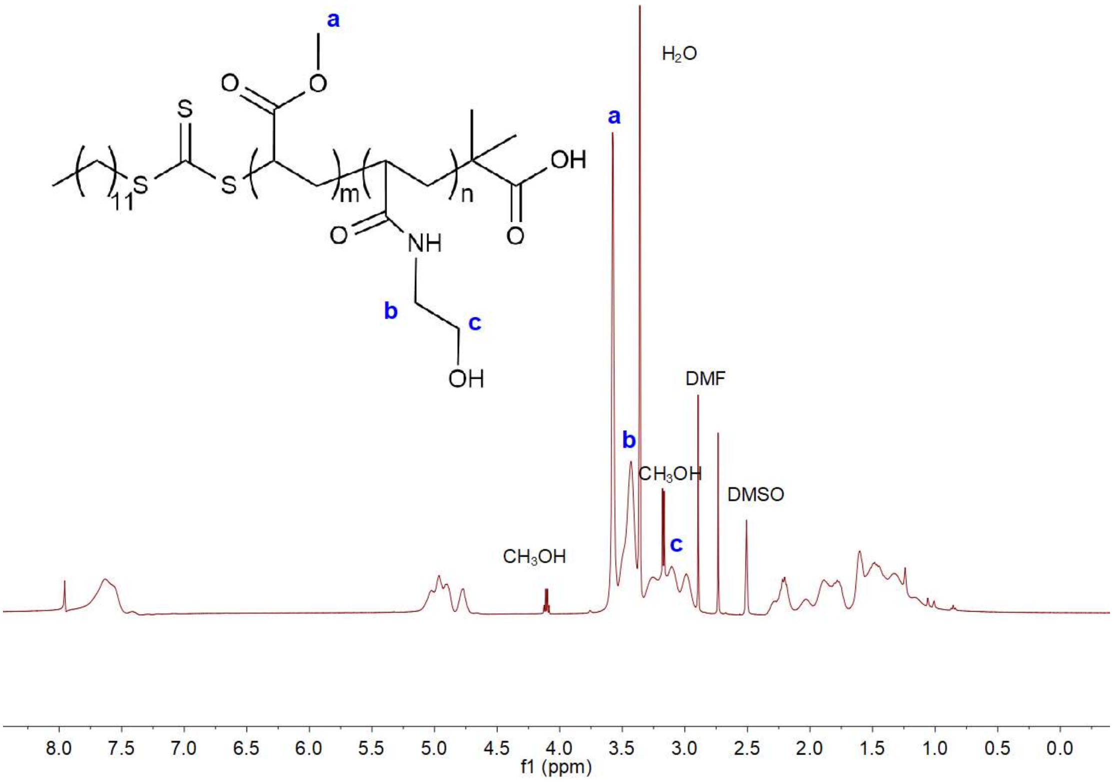

Fig S19. ^{1}H NMR spectrum of PMA-*b*-PNHEAA.

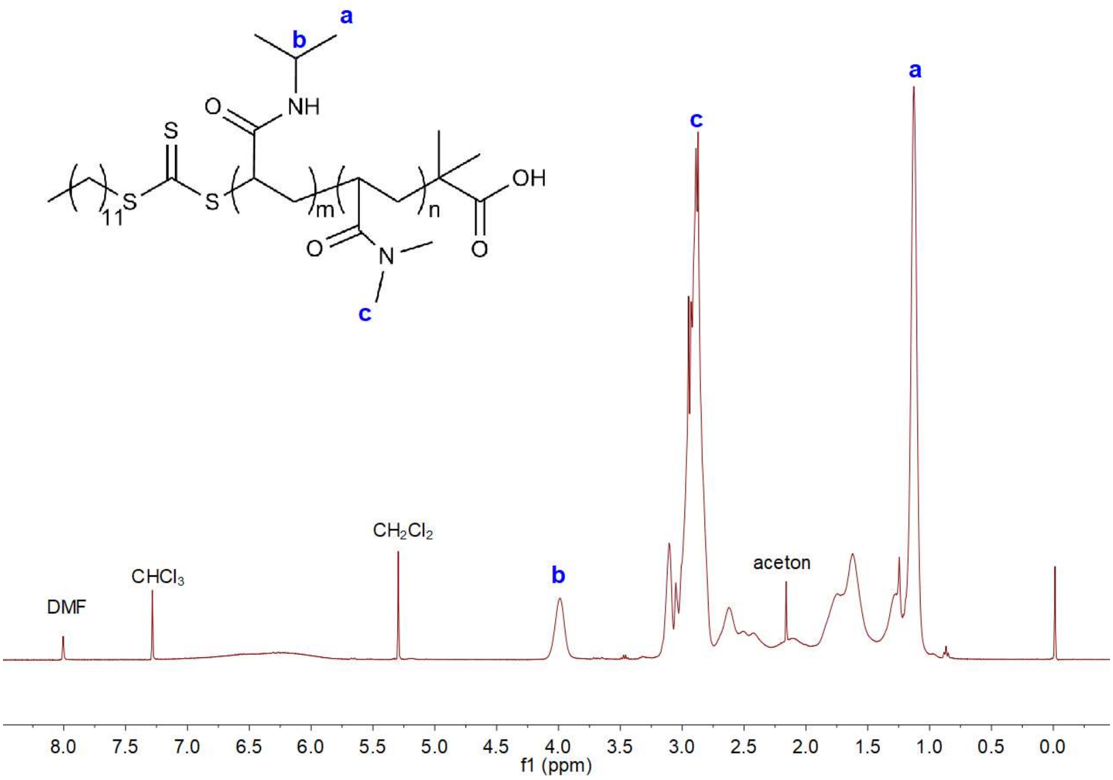

Figure S20. ^{1}H NMR spectrum of PNIPAM-*b*-PDMA.

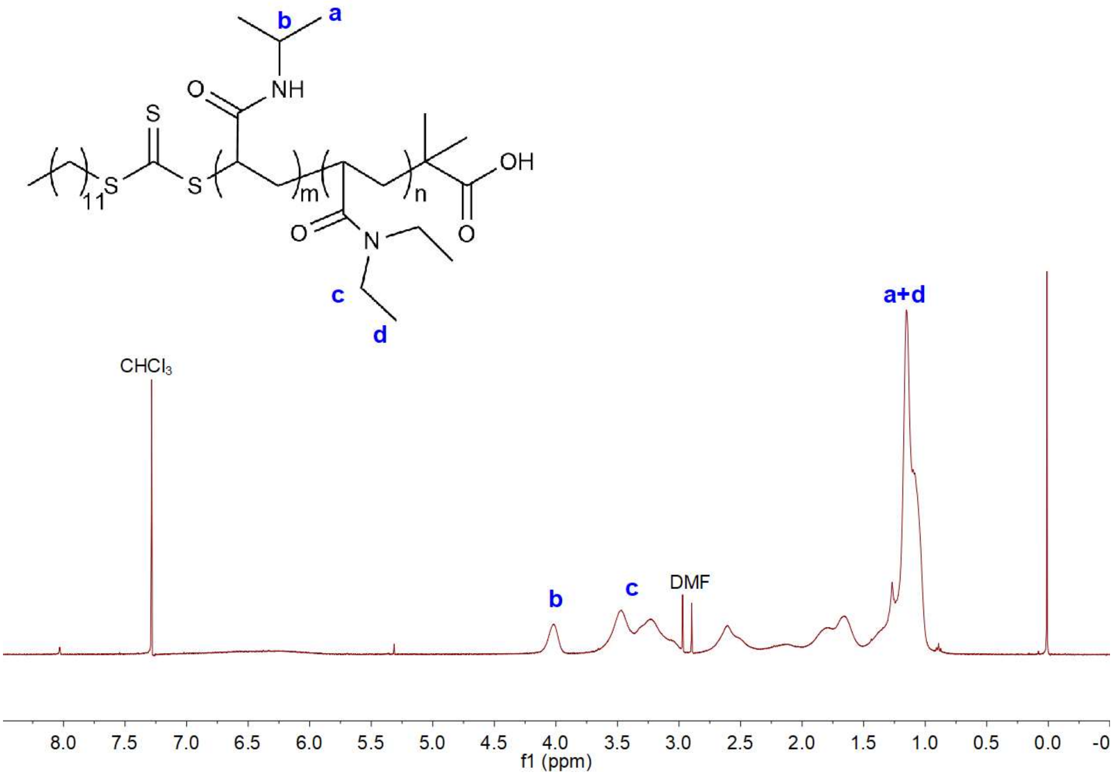

Figure S21. ^{1}H NMR spectrum of PNIPAM-*b*-PDEA.

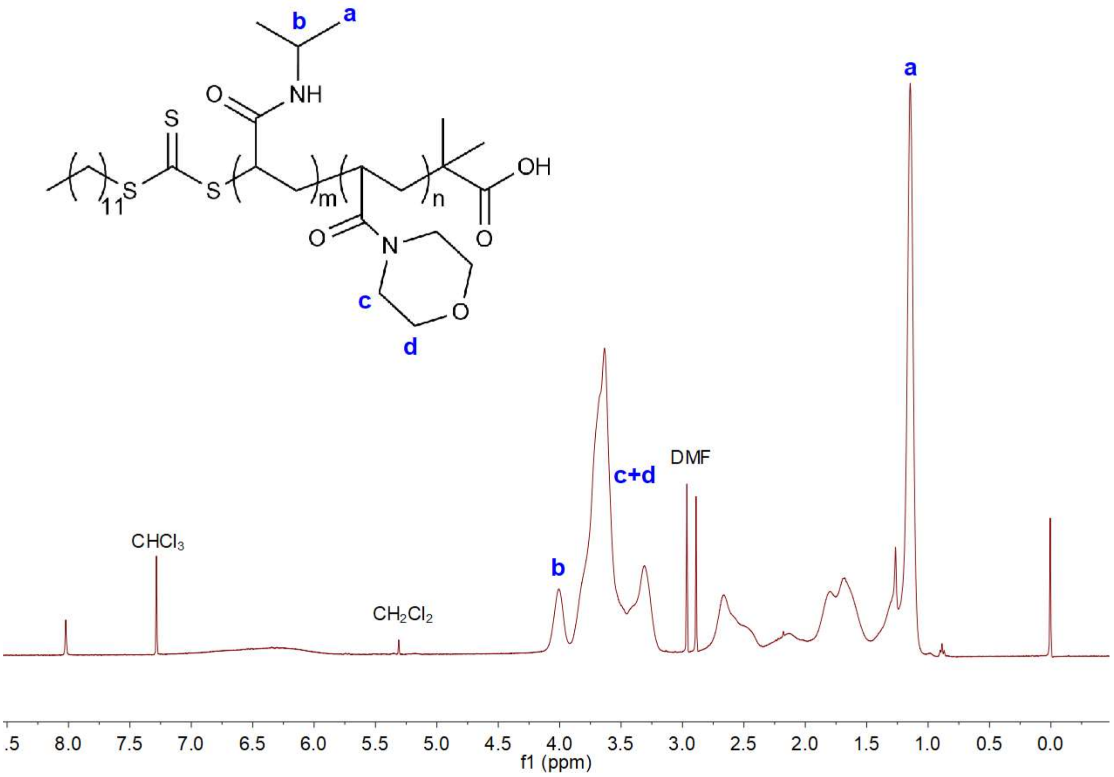

Figure S22. ^{1}H NMR spectrum of PNIPAM-*b*-PAcM.

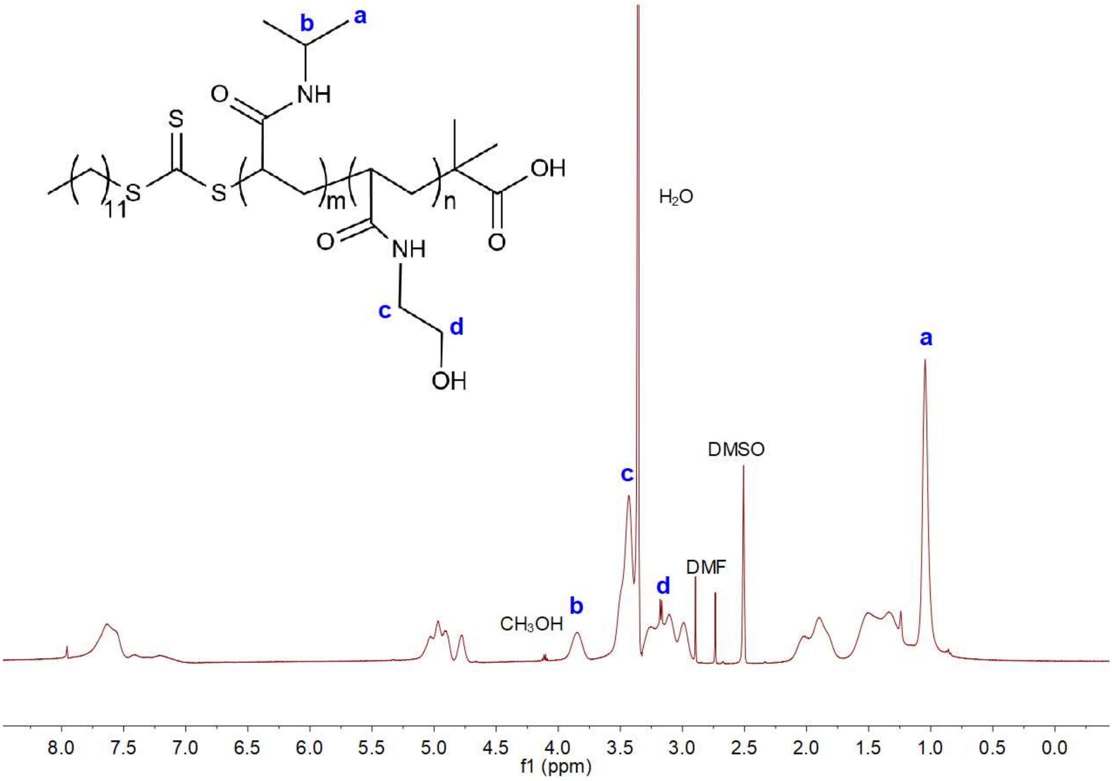

Figure S23. ^{1}H NMR spectrum of PNIPAM-*b*-PNHEAA.

Reference

[1] Jared Skey, Rachel K. O’Reilly. *Chem Comm*, 2008, **35**, 4183-4185

[2] Olsson S, Dahlstrand C, Gogoll A. *Dalton Transactions*, 2018, **47**, 11572.