

Emulsion Polymerization Induced Self-Assembly of Thermoresponsive Polymer, Poly(N-vinylcaprolactam)

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Electronic Supplementary Information

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1. Synthesis of mCTAs

1. Step: Monomethoxy poly(ethylene glycol) mPEG₁₁₃-OH (20.16 g, 4 mmol) and triethylamine (1.238 g, 12 mmol) were dissolved in 100 ml of anhydrous CH₂Cl₂ in a dry 250 ml three-necked flask placed in an ice bath. A solution of 2-bromopropionyl bromide (1.3 ml, 12 mmol) in 20 ml of anhydrous CH₂Cl₂ was added dropwise to the solution over 2 h. After the addition, the mixture was taken off the ice and stirring was continued for 1 d.

The solution was filtered and 200 ml of CH₂Cl₂ was added. The organic layer was washed with 1 M HCl solution (3 × 80 ml), 1 M NaOH solution (3 × 80 ml), and deionized water (2 × 80 ml) and dried with anhydrous MgSO₄. The solution was concentrated in a rotary evaporator. The polymer was precipitated in 400 ml of cold diethyl ether and dried in vacuum, giving mPEG₁₁₃-Br. Gravimetric yield: 19.4 g (96 %). Product analyzed with ¹H-NMR in DMSO-d₆, 20 mg ml⁻¹.

The same procedure was used for the preparation of mPEG₄₂-Br. Gravimetric yield: 89%.

2. Step: mPEG₁₁₃-Br (5.00 g, 1 mmol) and potassium ethyl xanthogenate (0.480 g, 3 mmol) were mixed with 100 ml of anhydrous CH₂Cl₂, reaction time was 30 min. Solids were filtered off and 50 ml of CH₂Cl₂ were added.

The solution was washed with saturated NaHCO₃ solution (3 × 70 ml) and deionized water (1 × 70 ml). The organic phase was dried with anhydrous MgSO₄ and concentrated to 20 ml at 30 °C using a rotary evaporator. The polymer was precipitated in 400 ml of cold diethyl ether. The product was dried under atmosphere overnight. mPEG₁₁₃-X was obtained. Gravimetric yield: 4.64 g (93%). Product analyzed via ¹H-NMR in DMSO-d₆, 20 mg ml⁻¹.

In the preparation of mPEG₄₂-X from mPEG₄₂-Br, only a 10 min reaction time was used. Longer reaction times seemed to promote difficulties in removing unreacted xanthate from the products, as indicated by impurities in ¹H-NMR spectra. Gravimetric yield: 90%.

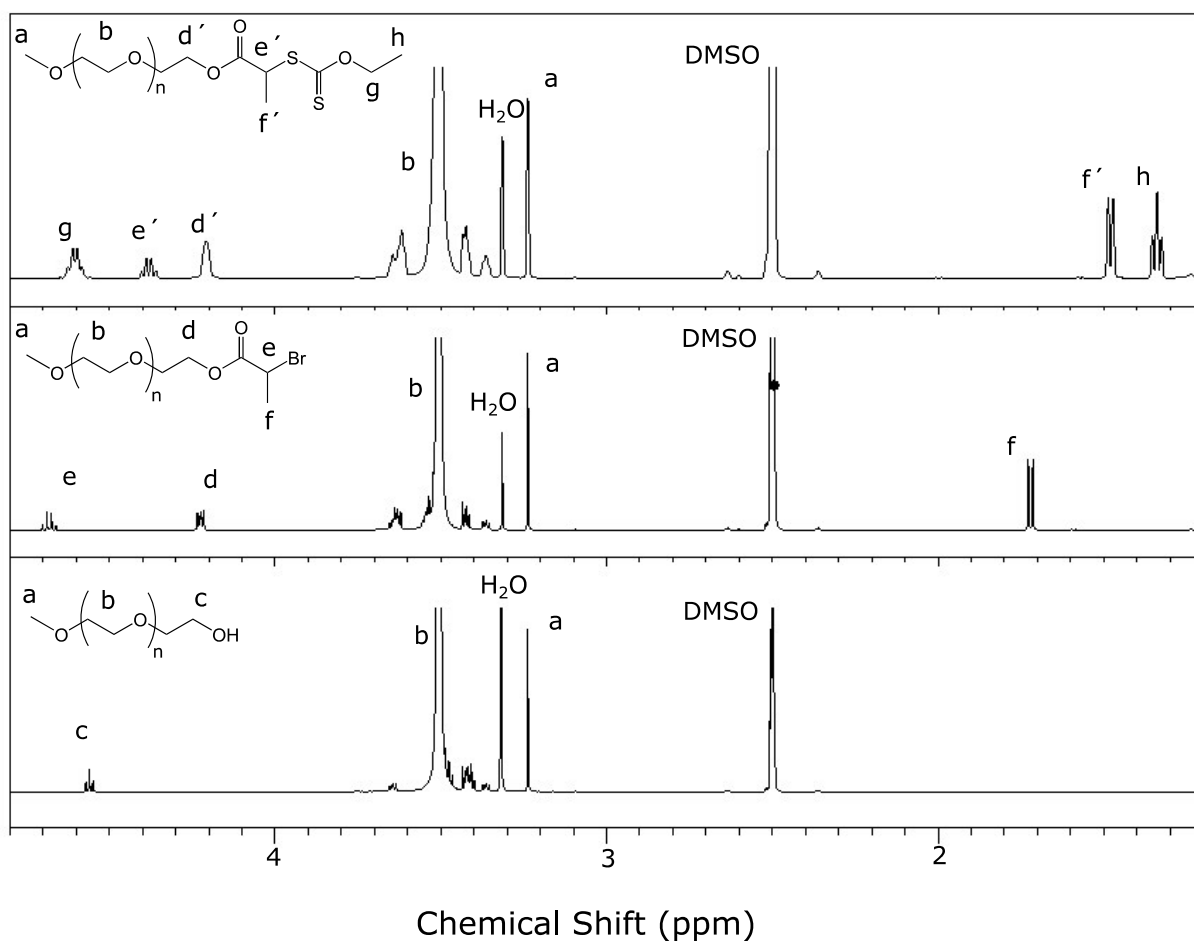


Figure S1. $^1\text{H-NMR}$ spectra

$^1\text{H-NMR}$ (mPEG2000-OH, 500 MHz, DMSO, δ): 4.56 (t, 1H, OH), 3.51 CH_2 (m, 4H per repeating unit of PEG = 181 H), 3.24 (s, CH_3O),

$^1\text{H-NMR}$ (mPEG2000-Br, 500 MHz, DMSO, δ): 1.72 (d, 3H, CH_3), 3.24 (s, 3H, CH_3O), 3.51 CH_2 (m, 4 per repeating unit of PEG), 4.2 (m, 2H, CH_2OCO), 4.69 (q, 1H, CHBr)

$^1\text{H-NMR}$ (mPEG2000-X, 500 MHz, DMSO, δ): 1.34 (t, 3H, $\text{CH}_3\text{CH}_2\text{O}$), 1.48 (d, 3H, CH_3), 3.24 (s, CH_3O), 3.51 CH_2 (m, 4 per repeating unit of PEG), 4.21 (s, 2H, CH_2OCO), 4.39 (q, 1H, CHS), 4.62 (q, 2H CH_2CH_3)

$^1\text{H-NMR}$ (mPEG5000-OH, 500 MHz, DMSO, δ): 4.56 (t, 1H, OH), 3.51 CH_2 (m, 4 per repeating unit of PEG = 452 H), 3.24 (s, 3H CH_3O),

$^1\text{H-NMR}$ (mPEG5000-Br, 500 MHz, DMSO, δ): 1.72 (d, 3H, CH_3), 3.24 (s, 3H CH_3O), 3.51 CH_2 (m, 4H per repeating unit of PEG), 4.2 (m, 2H, CH_2OCO), 4.69 (q, 1H, CHBr)

$^1\text{H-NMR}$ (mPEG5000-X, 500 MHz, DMSO, δ): 1.34 (t, 3 H, $\text{CH}_3\text{CH}_2\text{O}$), 1.48 (d, 3 H, CH_3), 3.24 (s, 3H CH_3O), 3.51 CH_2 (m, 4 per repeating unit of PEG), 4.21 (S, 2H, CH_2OCO), 4.39 (q, 1H, CHS), 4.62 (q, 2H CH_2CH_3)

2. $^1\text{H-NMR}$ of a typical product and starting materials

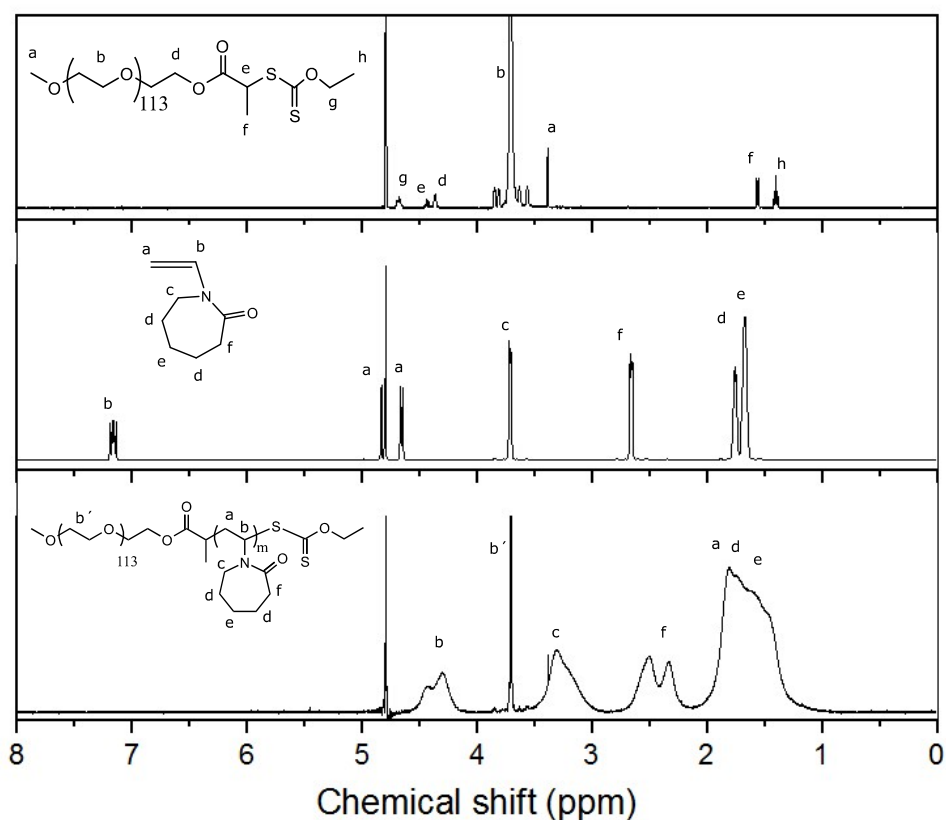


Figure S2. $^1\text{H-NMR}$ spectra of PEG₁₁₃-X (top), NVCL (middle), PEG-b-PNVCL (bottom) with peak assignments

3. Conversion analysis of a typical product via $^1\text{H-NMR}$

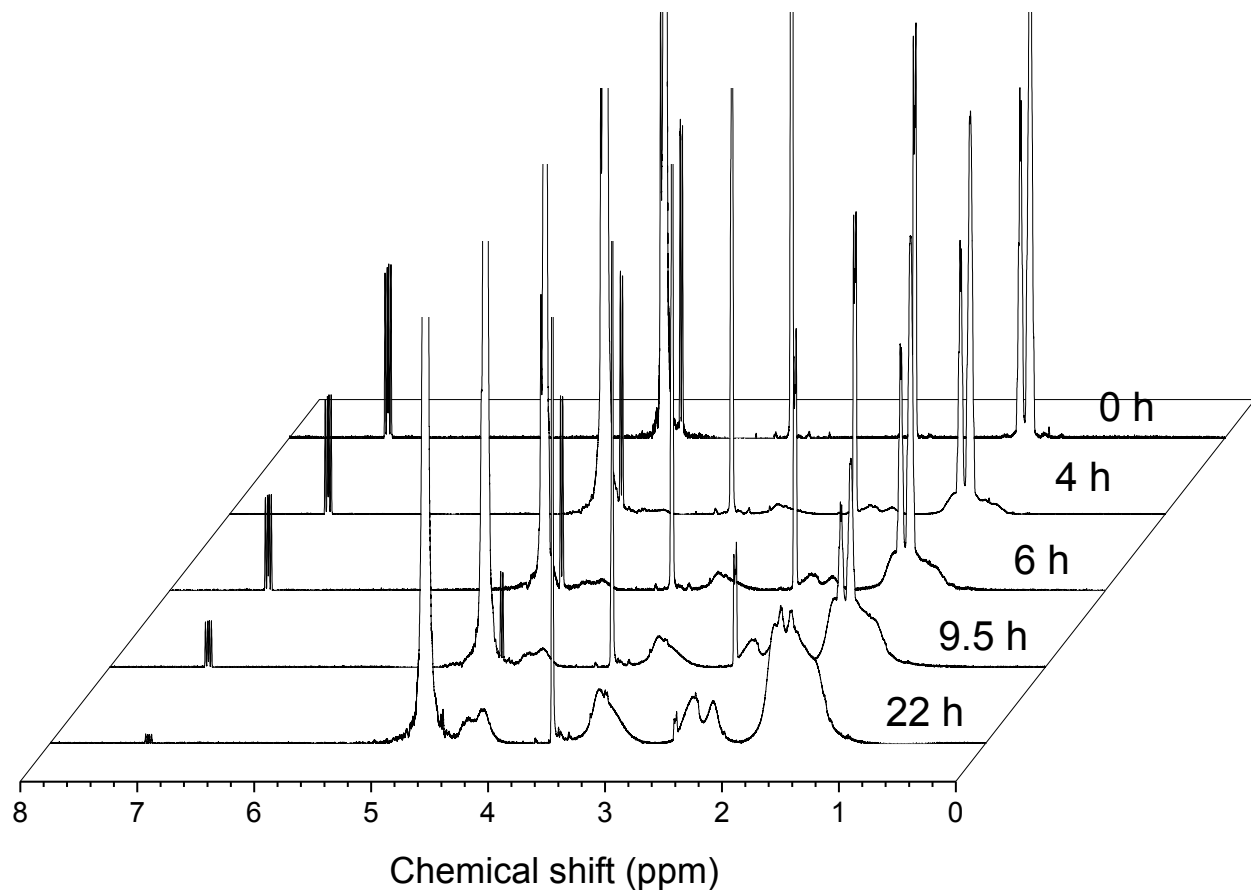


Figure S3. $^1\text{H-NMR}$ spectra of conversion samples taken at different time intervals from reaction mixture (D_2O)

Conversion was calculated from the integrals of $^1\text{H-NMR}$ spectra presented in figure according to equation 1. In short integral coming from a proton of NVCL (at 7 ppm) was compared to a peak assigned to 2 protons from either NVCL or PNVCL repeating unit (2.8 to 2 ppm).

$$Conversion = 1 - \frac{\int_{2ppm}^{2.8ppm} \delta(x) dx}{0.5 \times \int_{6.8ppm}^{7.2ppm} \delta(x) dx}$$

[S1]

4. Kinetics of polymerizations with varying mCTA and initiator concentration

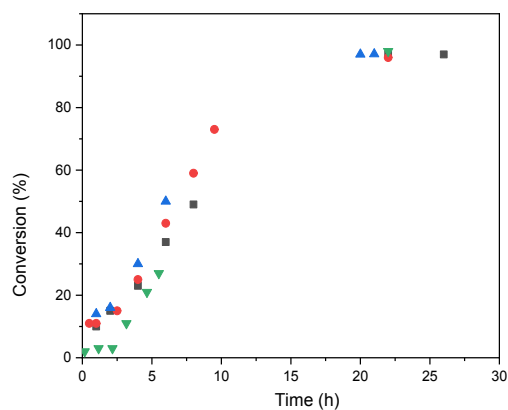


Figure S4. Conversion versus time for polymerizations with varying mCTA and initiator concentrations; DP = ▲ 194, ● 340, ■ 485, or ▼ 980

5. M_n of the high molecular weight PNVCL via $^1\text{H-NMR}$

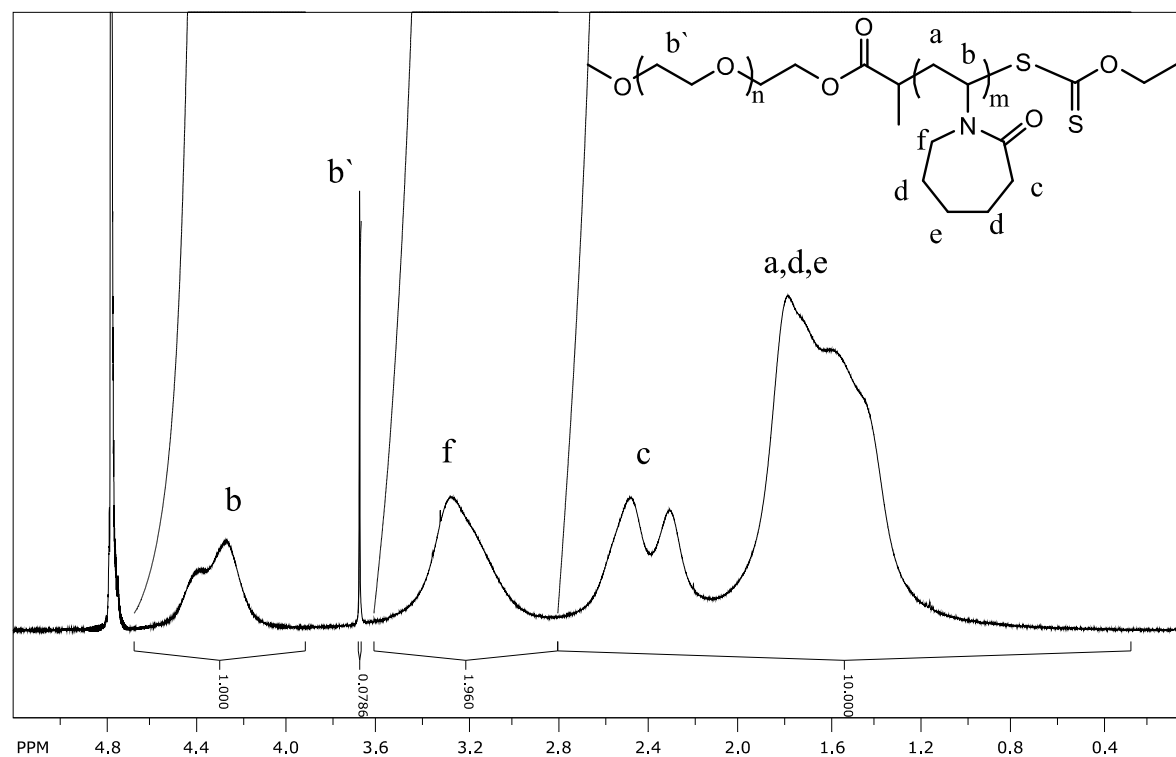


Figure S5. $^1\text{H-NMR}$ spectra of high molecular weight PNVCL in D_2O

$$M_n = \frac{n \text{ of repeating units of VCL}}{n \text{ of PEG chains}} * M(\text{NVCL}) + M_n(\text{mCTA}) = \frac{\int b \, dx}{\int b' \, dx / (113 * 4)} * 139.19 \text{ g/mol} + 5000 \text{ g/mol}$$

[S2]

$$M_n = \frac{1}{0.078 / (113 * 4)} * 139.19 \text{ g/mol} + 5000 \text{ g/mol} = 810 \, 000 \text{ g/mol}$$

6. SEC Chromatogram of the high molecular weight PNVCL

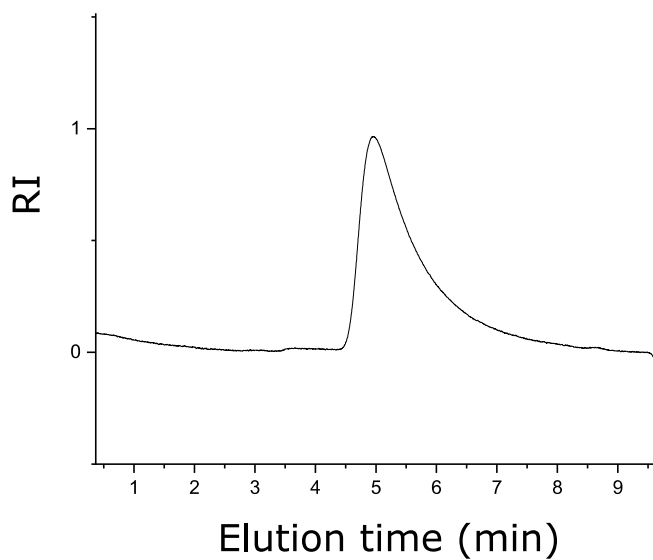


Figure S6. SEC chromatogram of the high molecular weight PNVCCL in THF

7. M_w of the high molecular weight PNVCCL via SLS

Refractive index increment (dn/dc) was determined for the high molecular weight polymer in THF with Wyatt Optilab rEX differential refractometer at 25 °C 633 nm. The obtained dn/dc value was 0.137.

The M_w measurements were performed using a setup with Brookhaven Instruments BI-200SM goniometer, a BIC-TurboCorr digital pseudo-cross-correlator, and a BI-CrossCorr detector and a red 637 nm BI-mini L140 operated with 50 mW power was used as light source and. Sample cell was connected to a Lauda RC 6 CP thermostat and temperature was set to 25 °C. Goniometer alignment was checked before measurements and calibration was done at 90° with toluene. Zimm-plot software was used for M_w determination.

$M_w = 1\,270\,000 \pm 49\,000$ g/mol.

Second virial coefficient (A_2) = $2.43 \cdot 10^{-4}$ cm³mol/g²

$R_g = 59.8$ nm

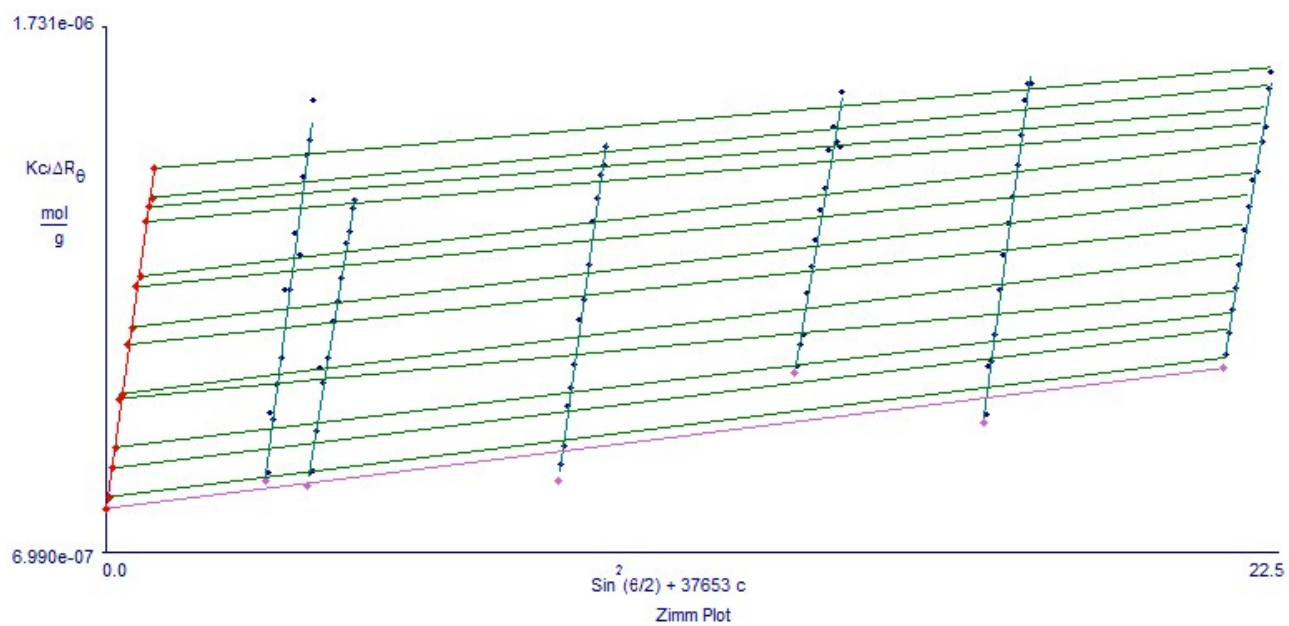


Figure S7. Zimm plot for high M_n PVCL

8. LS data of polymerizations with varied total concentration

$$[M_0] / [mCTA] / [I] = 500 / 1 / 0.3$$

[NVCL] ₀ (g/ml)	Conv. (%)	Mn _{theory} (g/mol)	Mn _{SEC} (g/mol)	Đ (M _n /M _w)	Dh* (nm)	R _g / R _h * (nm)
0.1	97	72 500	72 300	1.5	225	0.76
0.2	98	73 200	71 400	1.4	220	0.74
0.3	98	73 200	72 100	1.3	245	0.78

Table S1. Effect of polymerization concentration, with LS data

*measured at 50 °C from diluted particle dispersion before cooling

9. DLS data of polymerizations with varied initiator concentration

Table S2. Synthesis of polymers with different initiator concentrations, with LS data

C₀(NVCL) = 0.1 g / ml i.e [M]₀ = 0.718 mol / l

[M ₀]:[CTA]:[I]	Conv. (%)	Mn _{theory} (g/mol)	Mn _{SEC} (g/mol)	Đ (M _n /M _w)	Dh* (nm)	R _g / R _h * (nm)
500/1/0.3	97	72 500	72 300	1.5	220	0.77
500/1/0.6	99	73 900	74 700	1.2	225	0.80
500/1/0.9	100	74 600	75 700	1.2	210	0.82

*measured at 50 °C from particle diluted dispersion before cooling

10. Cryo-TEM images of the high M_n polymer particles

This cryo-EM sample was imaged with FEI Tecnai F20 microscope and micrographs were recorded with Gatan US4000 CCD camera.

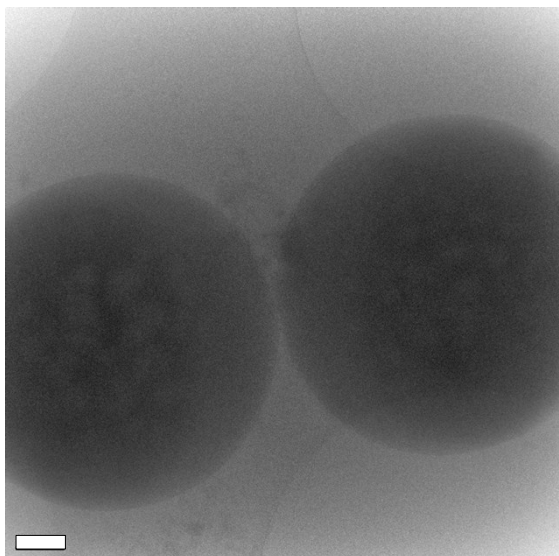


Figure S8. Cryo-TEM image of high M_n polymer particle, scale bar is 200 nm wide.

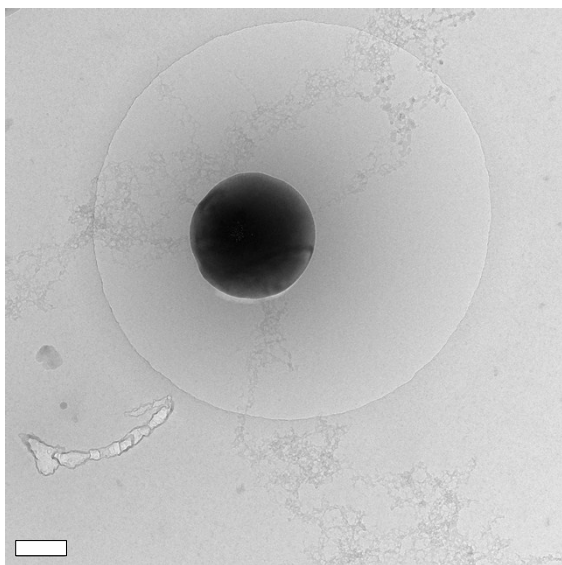


Figure S9. Another cryo-TEM image of high M_n polymer particle, scale bar is 200 nm wide.

11. Solubility of NVCL to H_2O and to TRIS buffer (100 mM, pH = 7.4)

Solubility of NVCL to TRIS buffer (100 mM, pH = 7.4) at 22 °C and at 50 °C were tested. At 22 °C, 5 ml of TRIS was mixed with 500 mg of NVCL at room temperature for 2 days to get saturated solution. Insoluble material was separated via centrifugation (2h, 10 000 rcf). 0.1 ml of supernatant was diluted with 1 ml D₂O. The amount of dissolved NVCL was determined via ¹H-NMR by comparing integral from TRIS protons with integral from NVCL (1 of the ¹H-NMR spectra presented as figure S10). Experiment was performed in triplicate.

Solubility of NVCL to 100mM TRIS at 22 °C is 35 ± 2 g/L.

Solubility of NVCL to TRIS buffer at 50 °C was tested by mixing 5 ml of TRIS with 500 mg of NVCL for 4 h to get saturated solution. At 50 C, the monomer is liquid and the mixing time was deemed sufficient via number of test with different mixing times. Supernatant was separated via centrifugation (30 min, 3773 rcf, at 50 °C). 0.1 ml of supernatant was diluted with 1 ml D₂O. The amount of dissolved NVCL was determined by comparing integral from TRIS protons with integral from NVCL. Experiment was performed in triplicate.

Solubility of NVCL to 100mM TRIS at 50 °C is 36 ± 2 g/L.

Solubility of NVCL to H₂O was tested at 22 °C. Test was same as with TRIS at 22 °C. Only difference was that after centrifugation supernatant was mixed in 1 to 1 ration with 100 mM TRIS. 0.1 ml of the mixture was diluted with 1 ml D₂O. The amount of dissolved NVCL was determined via ¹H-NMR by comparing integral from TRIS protons with integral from NVCL. Experiment was done in triplicate.

Solubility of NVCL to H₂O at 22 °C is 15 ± 2 g/L.

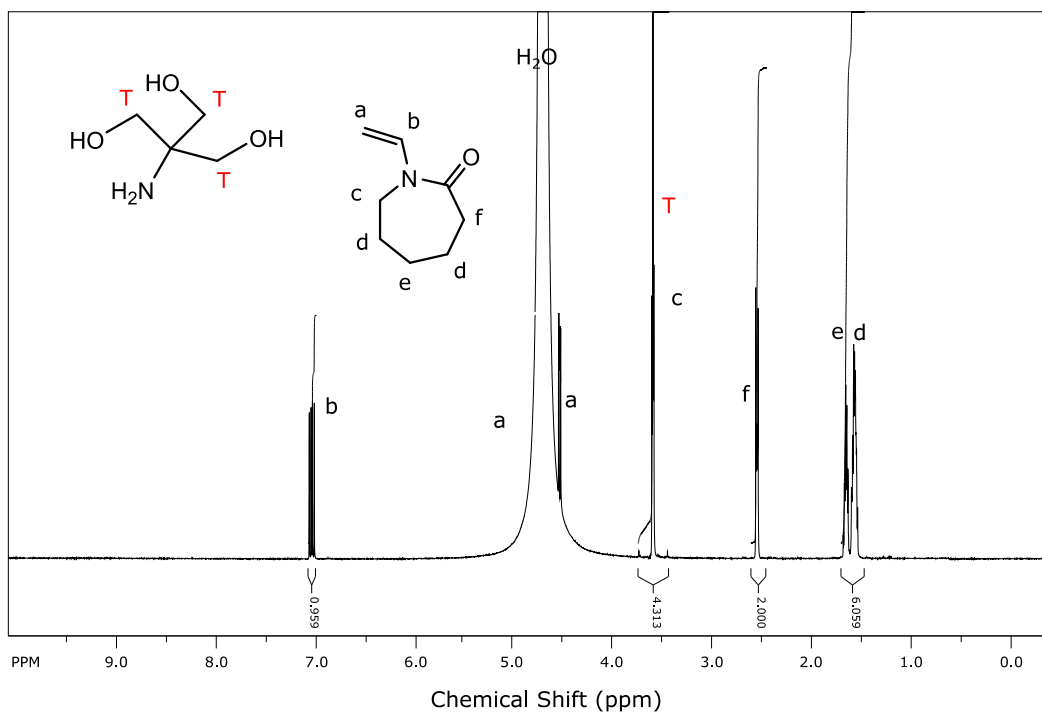


Figure S10. $^1\text{H-NMR}$ spectrum from solubility test