

Electronic Supplementary Information

Controlled synthesis of thermoresponsive polymers derived from L-proline via RAFT polymerization

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Experimental Section

Materials. L-Proline methyl ester hydrochloride (Kokusan Chemical) was used as received. AIBN (Kanto Chemical, 97%) was purified by recrystallization from methanol. N,N-Dimethylacrylamide (DMA, Kanto Chemical, >97%) was distilled under vacuum. Chlorobenzene (Kanto Chemical, > 99.5%) was dried with P₂O₅ and then distilled under vacuum. N-Acryloyl-L-proline methyl ester (A-Pro-OMe) was prepared by the reaction of acryloyl chloride with L-proline methyl ester hydrochloride according to a method reported previously.¹ Other materials were used without further purification.

Synthesis of Chain Transfer Agent (CTA). Benzyl dithiobenzoate (BDB) used mainly in this study was synthesized according to the procedure reported in the literature.² Finally, the purification of BDB was conducted by sublimation under high vacuum to give red oil. Syntheses of other chain transfer agents, benzyl 1-pyrrolicarbodithioate (CTA 2)³ and O-ethyl-S-(1-phenylethyl) dithiocarbonate (CTA 3),^{4,5} were carried out according to the procedures reported in the literatures.

Polymerization. A representative example is as follows: AIBN (3.28 mg, 0.020 mmol) and BDB (9.78mg, 0.040 mmol) were placed in a dry glass ampule equipped with a magnetic stirring bar, and then 1.0 M chlorobenzene solution of A-Pro-OMe (0.27 g, 1.5 mmol) was added the ampule. After the solution was degassed by three freeze-evacuate-thaw cycles, the ampule was flame-sealed off under vacuum, and it was allowed to stand at 60 °C for 20 h. The characteristic

pale red color kept constant during the polymerization. The reaction was stopped by rapid cooling with liquid nitrogen. The reaction mixture was precipitated from chlorobenzene in a large excess of diethyl ether and isolated by filtration. The resulting product was dried under vacuum at 50 °C. For the determination of the monomer conversion, the ¹H NMR spectrum of the polymerization mixture was measured in CDCl₃ at room temperature, and the integration of the monomer C=C-H peak at around 5.7 ppm was compared with the sum of N-CH–COO peak intensity of the polymer and the monomer at around 4.0-5.0 ppm. Additionally, the polymer yields were gravimetrically determined from the ether-insoluble polymer sample. The resulting polymer was soluble in most organic solvents, such as dichloromethane, acetone, dioxane, DMF, and DMSO, while insoluble in diethylether and hexane. The theoretical number-average molecular weight on conversion is defined as follows:

$$M_n(\text{theor}) = \frac{[\text{Monomer}]_0}{[\text{CTA}]_0} \times M_{\text{Monomer}} \times \text{conv.} + M_{\text{CTA}} \quad (1)$$

where M_{CTA} and M_{Monomer} are molecular weights of chain transfer agent and monomer, and $[\text{Monomer}]_0$ and $[\text{CTA}]_0$ are the initial concentrations of monomer and chain transfer agent, respectively.

A representative example of the copolymerization is as follows: 1.8 mL of chlorobenzene solution of A-Pro-OMe (0.49 g, 2.7 mmol) and N,N-dimethylacrylamide (DMA, 0.03 g, 0.3 mmol) were placed in a dry ampule containing AIBN (4.93 mg, 0.030 mmol) and BDB (14.7 mg, 0.060 mmol), and then the solution was degassed by three freeze-evacuate-thaw cycles. The polymerization was conducted at 60 °C for 20 h. The reaction mixture was precipitated from chlorobenzene in a large excess of diethyl ether and isolated by filtration. The copolymer composition was determined using ¹H NMR spectroscopy by a comparison of peaks associated with the two comonomers. The peak at 4.0-5.0 ppm is attributed the methine proton (NCHCOO, 1H) of the A-Pro-OMe unit, whereas the peaks at 2.9-3.1 ppm correspond to the methyl protons (NCH₃, 6H) of the DMA unit.

Instrumentation. ¹H and ¹³C NMR spectra were recorded with a JEOL EX-270 and a Varian INOVA-500.

Number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) were estimated by conventional GPC using a Tosoh HPLC HLC-8220 system equipped with refractive index and ultraviolet detectors at 40 °C. The column set was as follows: three consecutive hydrophilic vinyl polymer-based gel columns [TSK-GELs (bead size): SuperAW5000 (7 μm), SuperAW4000 (6 μm), SuperAW3000 (4 μm), 15 cm each] and a guard column [TSK-guardcolumn Super AW-H, 3.5 cm]. The system was operated at a flow rate of 0.6 mL/min,

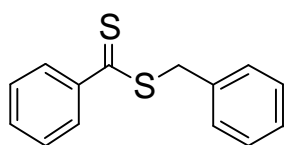
using N,N-dimethylformamide (DMF) containing 10 mM LiBr as an eluent. Polystyrene standards were employed for calibration.

The phase separation temperatures of the aqueous solutions of the polymers (1.0 mg/mL) were measured by monitoring the transmittance of a 500 nm light beam through a quartz sample cell. The transmittance was recorded on a JASCO V-550-DS UV-vis spectrophotometer equipped with temperature controller system (JASCO EHC-477S and EHC477T). The temperature was increased at a rate of ca. 0.5 °C/min, and the sample was allowed to equilibrate for 3-5 min at each temperature (every 0.5 °C). On average, the heating and cooling rates were ca. 0.1 °C/min. The cloud points of the polymers were defined as the inflection point (usually approximated as 50 % transmission) in the turbidity curve.

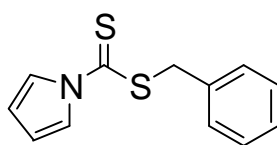
Table S1. RAFT polymerization of A-Pro-OMe using different chain transfer agents (CTAs)^a

run	CTA	conv. ^b (%)	M _n (M _w /M _n) ^c
1	-	-	131000 (2.90)
2	BDB	99	5500 (1.15)
3	CTA2	92	8300 (1.30)
4	CTA3	99	9400 (1.64)

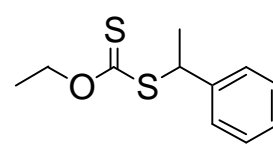
^a Conditions; A-Pro-OMe (0.27 g, 1.5 mmol), AIBN (1.3 mol%), CTA (2.7 mol%), chlorobenzene (1.0 M), 60 °C, 20 h. ^b Determined by ¹H-NMR spectroscopy. ^c Estimated by SEC [DMF, LiBr (10 mM)].



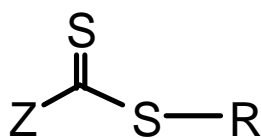
BDB



CTA 2



CTA 3



General structure of CTA

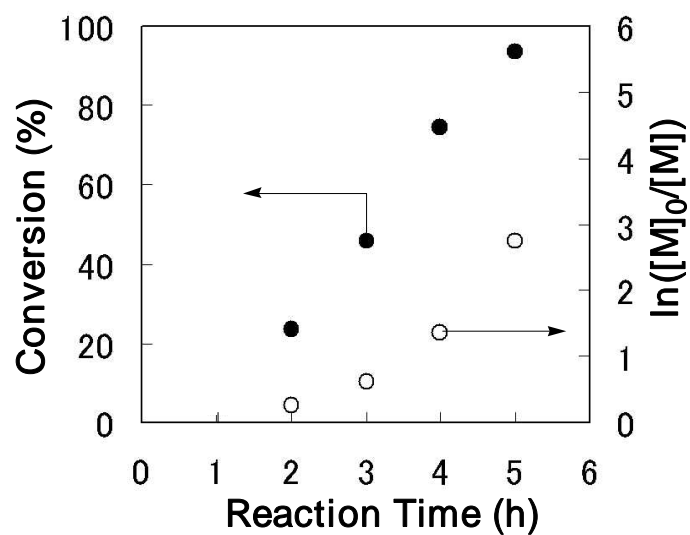


Figure S1. Time-conversion and the first-order kinetic plots for the polymerization of A-Pro-OMe with AIBN in the presence of BDB in chlorobenzene at 60°C; $[M]_0 = 1.0$ M, $[M]_0/[BDB]_0 = 112.4$, $[BDB]_0/[AIBN]_0 = 2/1$.

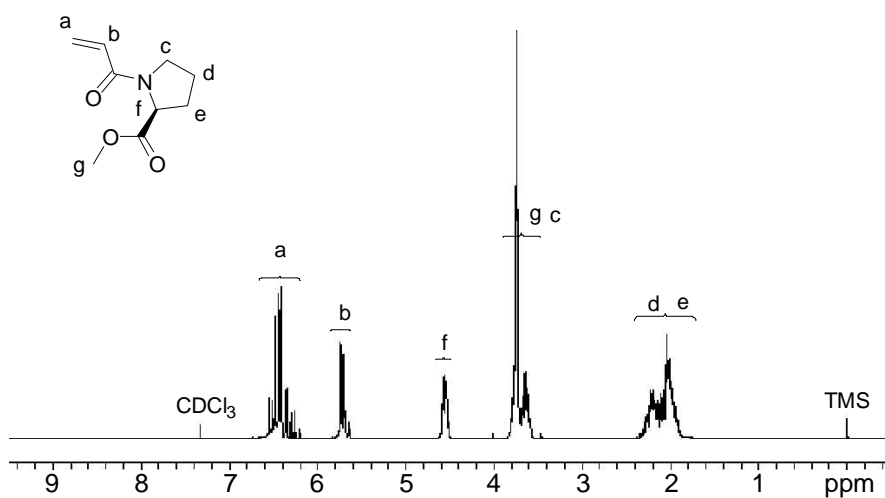


Figure S2. $^1\text{H-NMR}$ spectrum (270 MHz, CDCl_3) of A-Pro-OMe.

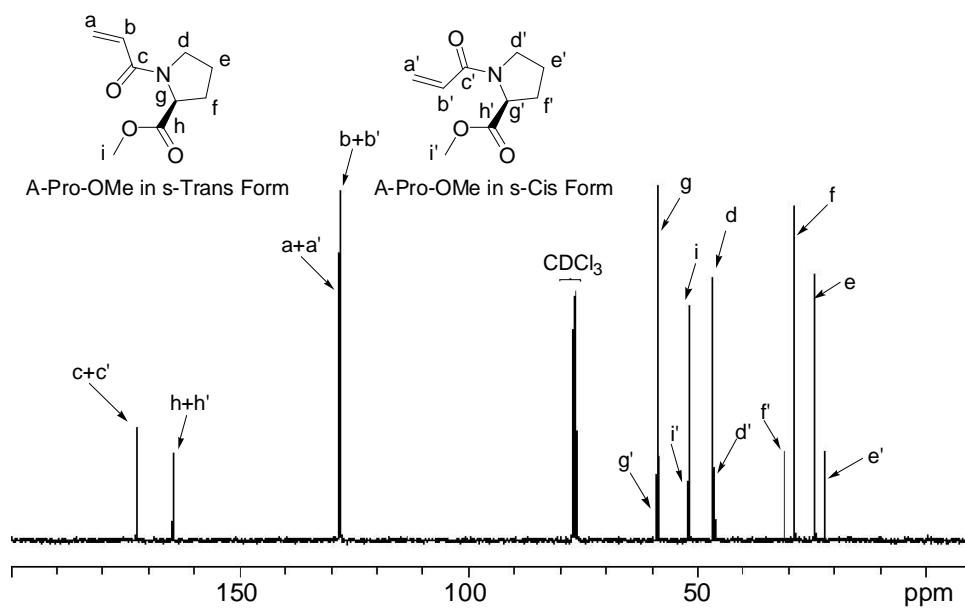


Figure S3. $^{13}\text{C-NMR}$ spectrum (270 MHz, CDCl_3) of A-Pro-OMe.

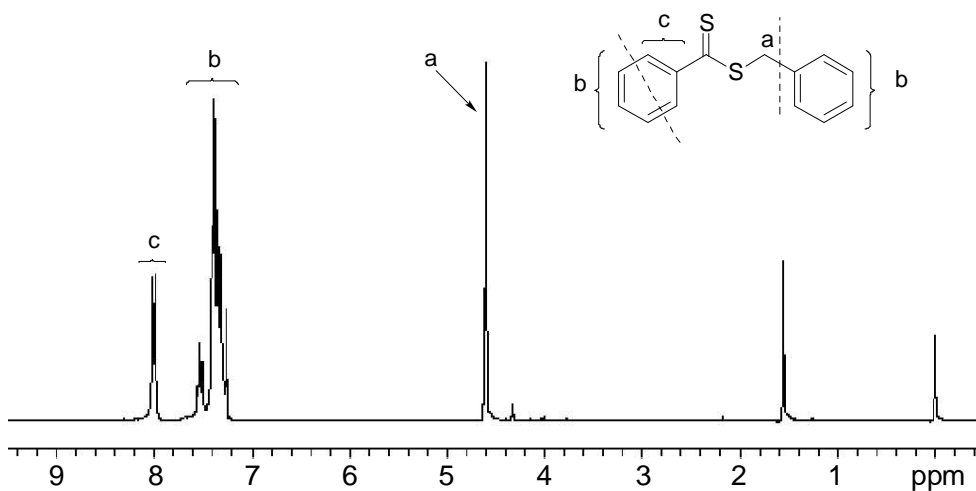


Figure S4. $^1\text{H-NMR}$ spectrum (270 MHz, CDCl_3) of benzyl dithiocarbonate (BDB).

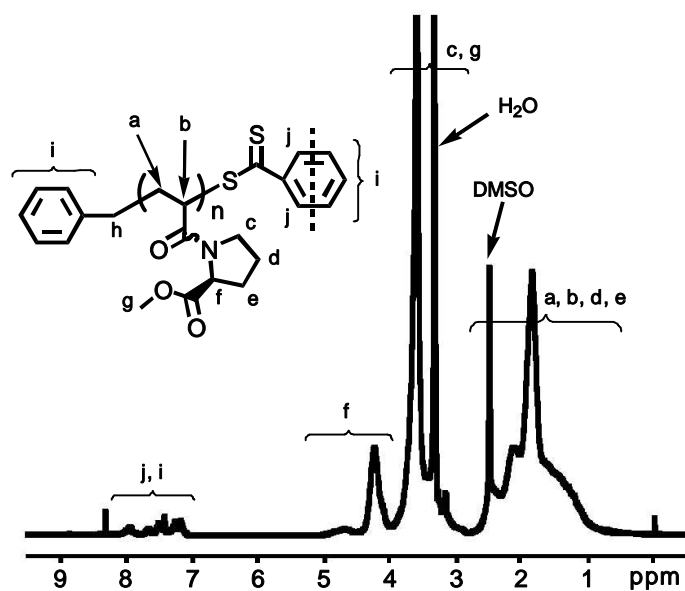


Figure S5. $^1\text{H-NMR}$ spectrum (270 MHz, DMSO-d_6) of poly(A-Pro-OMe) (run 2 in Table S1).

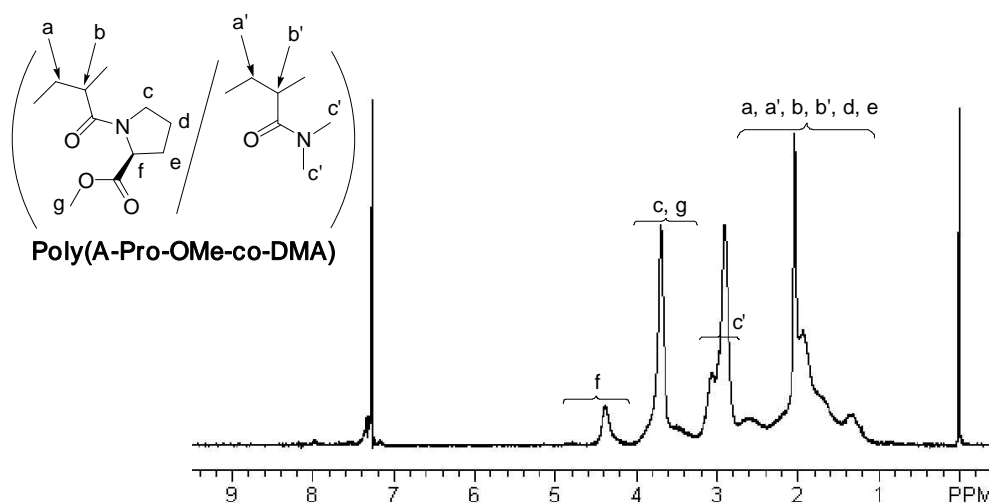


Figure S6. ¹H-NMR spectrum (270 MHz, CDCl₃) of the copolymers, poly(A-Pro-OMe-co-DMA) (Sample, see Table 1, M_n = 6800, M_w/M_n = 1.22, A-Pro-OMe : DMA = 83 : 17).

References

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