Supporting Information

Polymerization of Cyclic Carbamates: A Practical Route to Aliphatic Polyurethanes

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Contents

1. Materials

4-vinyl-1-cyclohexene-1,2-epoxide (mixture of isomers, 98%, TCI), ethyl chloroformate (97%, Sigma-Aldrich), triethylamine (99%, Alfa Aesar), sodium hydride (60 % dispersion in mineral oil, Sigma-Aldrich), benzoyl chloride (98%, TCI), *n*-butyllithium (2.0 M in cyclohexane, Sigma-Aldrich), poly(ethylene glycol) monomethyl ether (mPEG, M_n = 550 Da, TCI), thioglycolic acid (98%, Sigma-Aldrich) and 2,2'-Azobis(isobutyronitrile) (AIBN, 98%, Sigma-Aldrich, recrystallized from anhydrous ethanol) were used as received. THF used for polymerization was distilled over sodium and carefully degassed by three freeze-pump-thaw cycles prior to use.

2. Instruments and Measurements

Nuclear Magnetic Resonance (NMR)

^{1}H NMR spectra and ^{13}C NMR spectra were recorded either on Bruker Avance 300 MHz, Avance III HD 400 MHz or NEO 500 MHz spectrometer at 298 K. 2D NMR (COSY, NOESY, HSQC and HMBC) spectra were recorded on Bruker NEO 500 MHz at 298 K. Deuterated chloroform ($CDCl_3$) was used as the solvent. NMR chemical shifts were recorded in parts per million referenced to the residual solvent proton (δ = 7.26 ppm) for ^{1}H NMR and carbon (δ = 77.1 ppm) for ^{13}C NMR.

Size Exclusion Chromatography (SEC)

The number-average molecular weights (M_n) and molecular weight distributions of polymers (polydispersity index, PDI) were evaluated by size exclusion chromatography (SEC), using Agilent 1260 Infinity Series GPC (ResiPore 3 μm, 300 ×7.5 mm, 1.0 mL min^{-1}, UV (250 nm) and refractive index (RI, PLGPC 220) detector. All measurements were performed with THF as the eluent at a flow rate of 1.0 mL/min at 35 °C. Monodisperse poly(styrene) polymers were used as calibration standards.

Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS)

MALDI-TOF-MS characterization of polymers was performed on UltrafleXtreme

mass spectrometer (Bruker Daltonics, Bremen) using *trans*-2-[3-(4-*tert*-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) as the matrix. All data were processed using FlexAnalysis software (Bruker Daltonics, Bremen). Polymer samples for MALDI analysis were prepared at a concentration of 5 mg/mL in THF. The matrix solution was prepared at a concentration of 10 mg/mL in THF. The sample was prepared by mixing the polymer solution with matrix solution at a volume ratio of 1:5 and allowed to dry at room temperature before analysis.

Attenuated total reflection infrared spectroscopy (ATR-IR)

ATR-IR was used to characterize the infrared absorption spectra of PU samples. The spectra were recorded on a Magna – IR^{TM} 550 spectrometer equipped with a diamond probe. Solid PU samples were put under the probe with pressure and then characterized directly by the instrument.

Gas chromatography (GC)

GC was used to characterize the ratios of diastereomers in the starting vinyl cyclohexene oxide. The GC spectra were recorded on a GC-2010 Plus (SHIMADZU) instrument. Samples were prepared by dissolving in diethyl ether with a concentration of about 2 mg/mL and 2 μL sample solution was injected into the instrument for the analysis.

In situ infrared spectroscopy (*In situ* IR)

In situ IR characterization was performed on METTLER TOLEDO ReactIR 15 analyzer using an attenuated total reflection (ATR) diamond probe in the range 3000-650 cm^{-1}. The reaction mixture containing monomer, co-initiator and THF was added to a 15 mL Schlenk tube in the argon-purged glovebox firstly and cooled to 0 °C. Then the initiator (n-butyllithium) was added to the above solution quickly under argon and sealed with a special cap equipped with the IR probe. IR spectra were recorded by using the iC IR software with a sampling interval of 1 min.

Thermogravimetric analysis (TGA)

TGA measurements were carried out on SDT Q600 TA instrument to analyze the thermal properties of the polyurethane (PU) samples. Samples (5-10 mg) were characterized under a nitrogen atmosphere over the temperature range of 25 to 650 °C, with a heating rate of 20 °C/min.

Differential Scanning Calorimetry (DSC)

Calorimetric measurements of polymers were performed using a Perkin Elmer DSC7 device. The reference cell was kept empty and the sample cell was filled with polymer sample (5 to 10 mg). Samples were scanned over a temperature range between -20 °C and 200 °C with a scanning rate of 5 °C/min or 10 °C/min. Glass temperature (T_g) was measured at the second heating scan.

3. Synthesis and characterization of CHU monomer

As shown in Figure 3, the synthetic process included three steps.

Firstly, 4-vinyl-1-cyclohexene-1,2-epoxide (**1**, 10 g, 0.08 mol) and 25% ammonia (81 mL, 1.20 mol) were added into a 500 mL round-bottom flask and stirred. Ethanol (c.a. 70 mL) was added into the above mixture gradually until the solution became clear. After stirring at room temperature for 48 h, ethanol was removed by rotary evaporation. Then the solution was extracted by dichloromethane (DCM, 3 × 50 mL) and the combined organic layers were dried over anhydrous magnesium sulfate. The solvent was evaporated, and the resulting material was a mixture of compounds **2** and **3** (11.14 g, yield: 98%). ^{1}H NMR ($CDCl_3$): δ 5.73-5.95 (m, 1H, -C*H*=CH_2), 4.94-5.10 (m, 2H, -CH=CH_2), 2.07-2.61 (m, 3H, -CH_2-CH(CH-)-O*H* and -CH_2-CH(CH-)-NH_2).

Secondly, mixture of **2** and **3** (11.14 g, 79 mmol) was dissolved in 80 mL toluene and triethylamine (TEA, 9.98 g, 99 mmol) was added dropwise at 0 °C. Then ethyl chloroformate (10.70 g, 99 mmol) was added dropwise at 0 °C. The mixture was stirred at room temperature for 3 h. Then, toluene was removed by rotary evaporation under vacuum and 120 mL water was added. Then the aqueous solution was extracted with

DCM (3 × 50 mL) and the combined organic layers were dried over anhydrous magnesium sulfate. The solvent was evaporated to afford the crude product, as a mixture of compounds **4** and **5** (15.47 g, yield: 92%). The two products could be separated by column chromatography on a silica gel using toluene and tetrahydrofuran (THF) (40/1,20/1 and 10/1) as the eluent. However, the corresponding mixture can also be used directly for the third step and the separation can be done at last. ^{1}H NMR of **4** ($CDCl_3$): δ5.68-5.95 (m, 1H, -C*H*=CH_2), 4.96-5.22 (m, 2H, -CH=C*H*$_2$), 4.61-4.88 (m, 1H, -N*H*-$COOCH_2CH_3$), 4.10 (q, *J* = 7.2 Hz, 2H, -NH-COOC*H*$_2$$CH_3$), 1.24 (t, *J* = 7.2 Hz, 3H, -NH-$COOCH_2$C*H*$_3$). ^{1}H NMR of **5** ($CDCl_3$): δ5.70-5.88 (1H, -C*H*=CH_2), 4.97-5.11 (2H, -CH=C*H*$_2$), 4.64-4.89 (1H, -N*H*-$COOCH_2CH_3$), 4.10 (q, 2H, -NH-COOC*H*$_2$$CH_3$), 1.22 (t, 3H, -NH-$COOCH_2$C*H*$_3$). ^{13}C{^{1}H} NMR of **5** ($CDCl_3$): δ157.6 (-NH-*C*$OOCH_2CH_3$), 141.5 (-*C*H=CH_2), 114.0 (-CH=*C*H_2), 70.0 (-CH_2*C*H(OH)CH-), 61.1 (-CH_2*C*H(NH-)CH-), 55.0 (-NH-COO*C*H_2CH_3).

Thirdly, mixture of **4** and **5** (10 g, 47 mmol) was dissolved in 80 mL THF and sodium hydride (60 % dispersion in mineral oil, 3.75 g, 94 mmol) was added to the solution. The mixture was heated at reflux overnight. After stopping the reaction, THF was removed by rotary evaporation and 80 mL water was added. Then the aqueous solution was extracted by ethyl acetate (3 × 50 mL). The combined organic layers were dried over anhydrous magnesium sulfate and evaporated under vacuum. Then the resulting crude product was chromatographed on a silica gel using hexane and ethyl acetate with a volume ratio of 20/1 to 4/1 as the eluent. Finally, pure products **6** (white solid, 2.35 g, yield: 30%) and **7** (white solid, 2.90 g, yield: 37%) were obtained. Then compound **7** (50 °C, 0.6 mbar) sublimated to get pure 5-membered cyclic carbamate monomer (CHU). ^{1}H NMR (Figure S1a) ($CDCl_3$): δ5.75-5.97 (m, 1H, H_8), 5.52 (br s, 1H, -H_1), 5.02-5.24 (m, 2H, H_9), 4.02-4.08 (m, 1H, H_3), 3.36-3.31 (m, 1H, H_2), 2.77 (br s, 1H, H_7), 2.23-2.26 (m, 1H, H_5), 1.87-1.95 (m, 3H, H_4, $H_{5'}$, H_6), 1.58-1.67 (m, 2H, $H_{4'}$, $H_{6'}$). ^{13}C{^{1}H} NMR (Figure S1b) ($CDCl_3$): δ161.0 (C_1), 140.5 (C_8), 115.1 (C_9), 80.3 (C_3), 61.3 (C_2), 35.8 (C_7), 32.7 (C_5), 27.2 (C_6), 25.7 (C_4).

The 2D NMR characterization of CHU monomer was shown in Figure S2-S5.

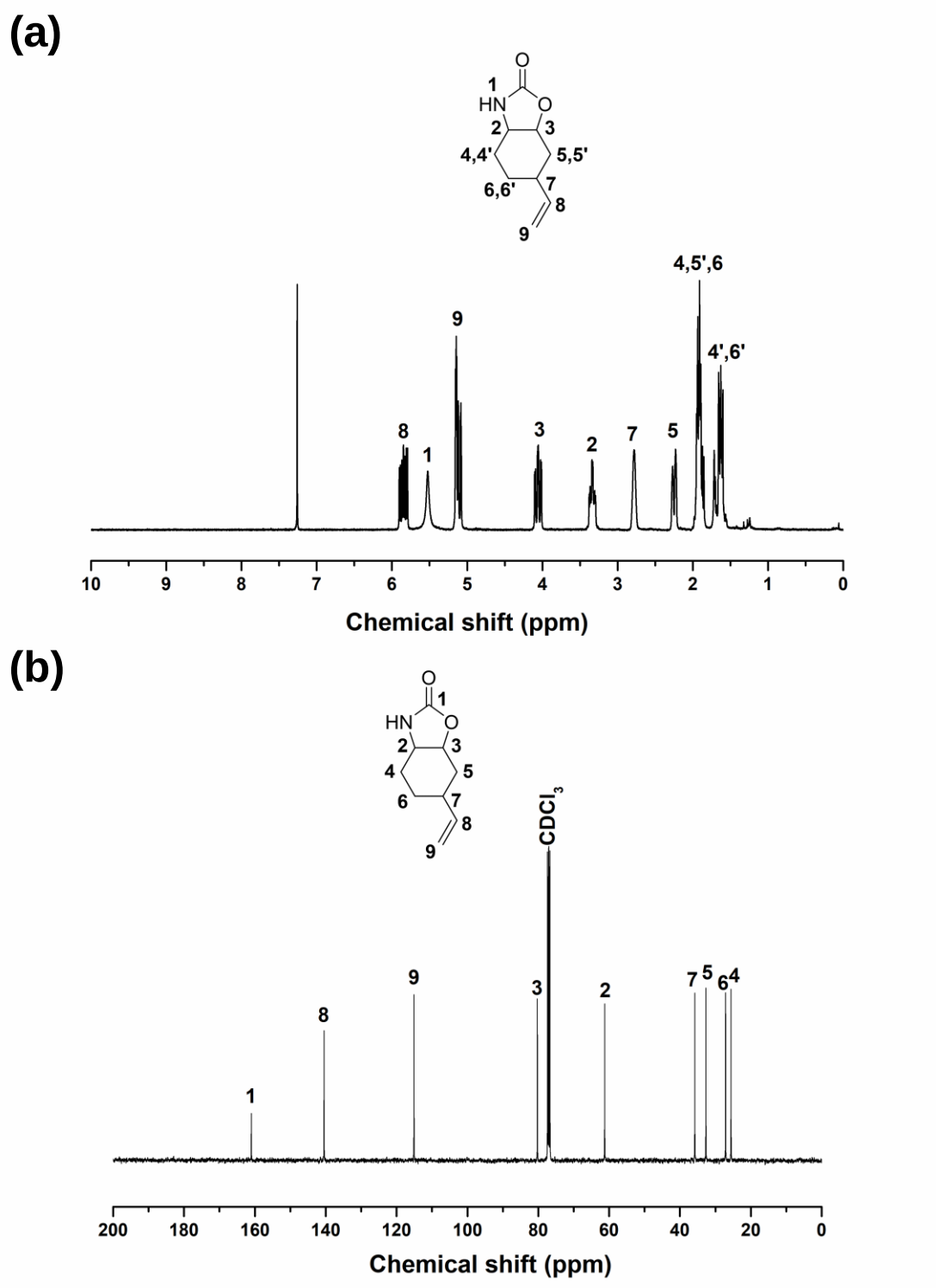


Figure S1. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of CHU monomer. $CDCl_3$, 300 MHz, 298 K.

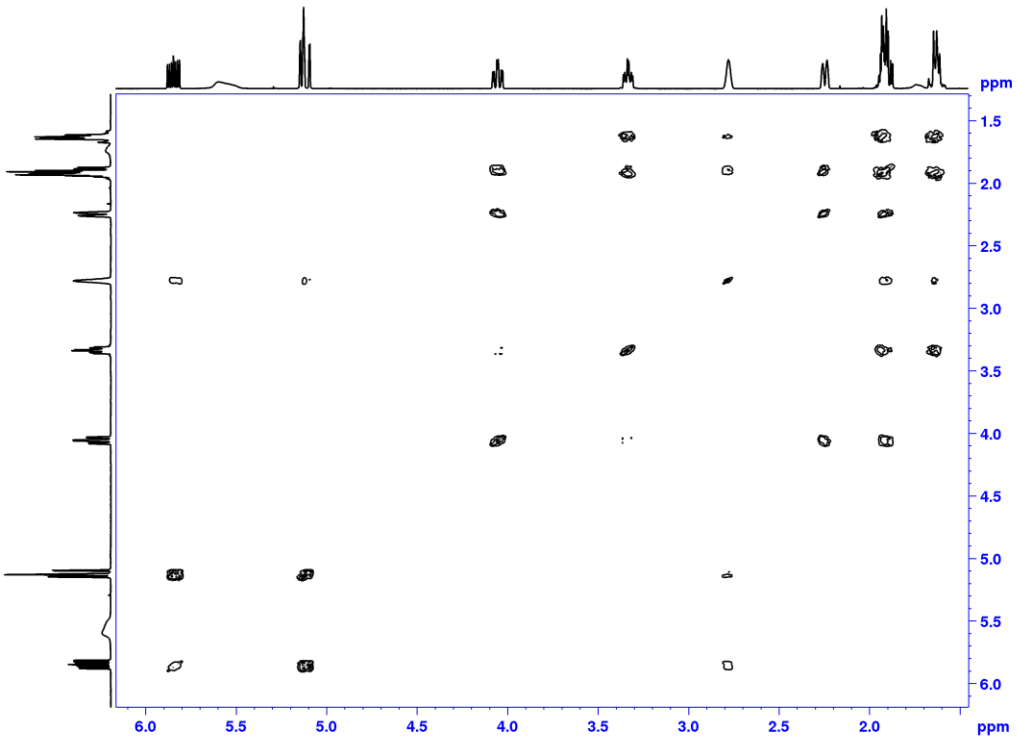


Figure S2. 2D COSY spectrum of CHU monomer. $CDCl_3$, 500 MHz, 298 K.

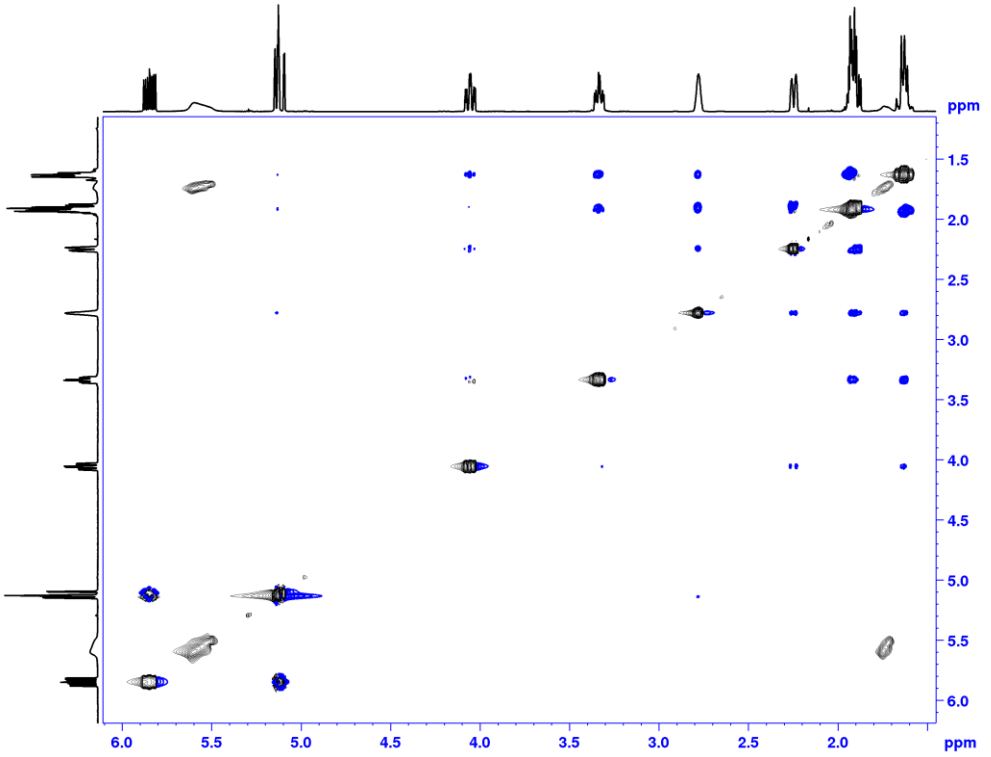


Figure S3. 2D NOESY spectrum of CHU monomer. $CDCl_3$, 500 MHz, 298 K.

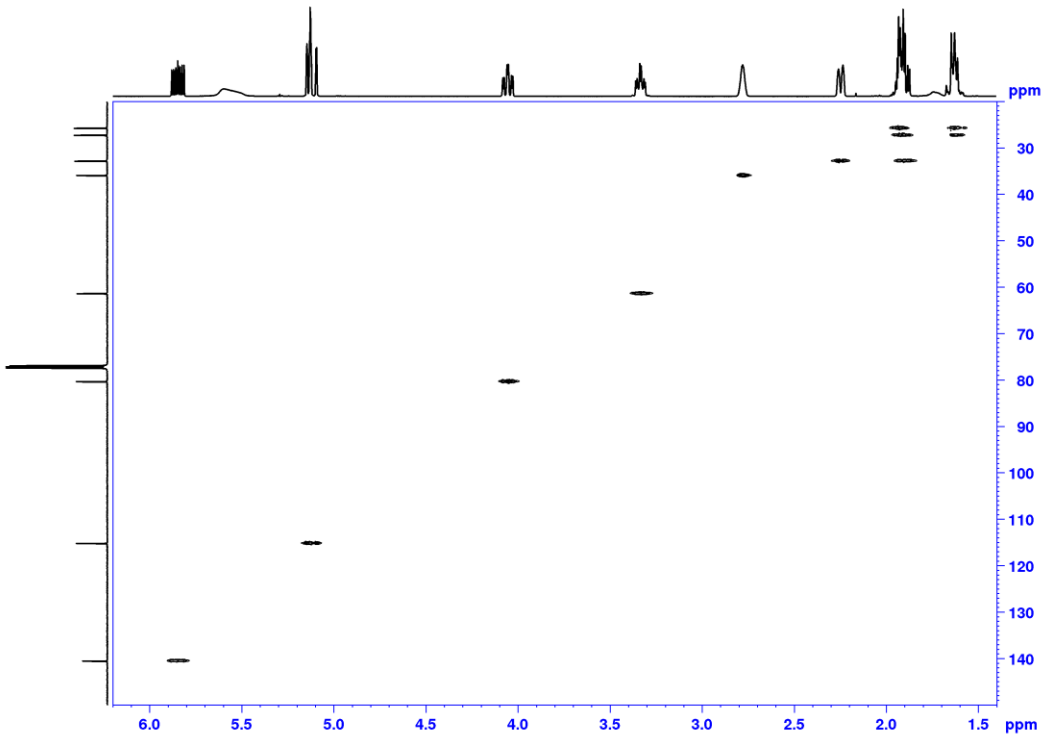


Figure S4. 2D HSQC spectrum of CHU monomer. $CDCl_3$, 500 MHz, 298 K.

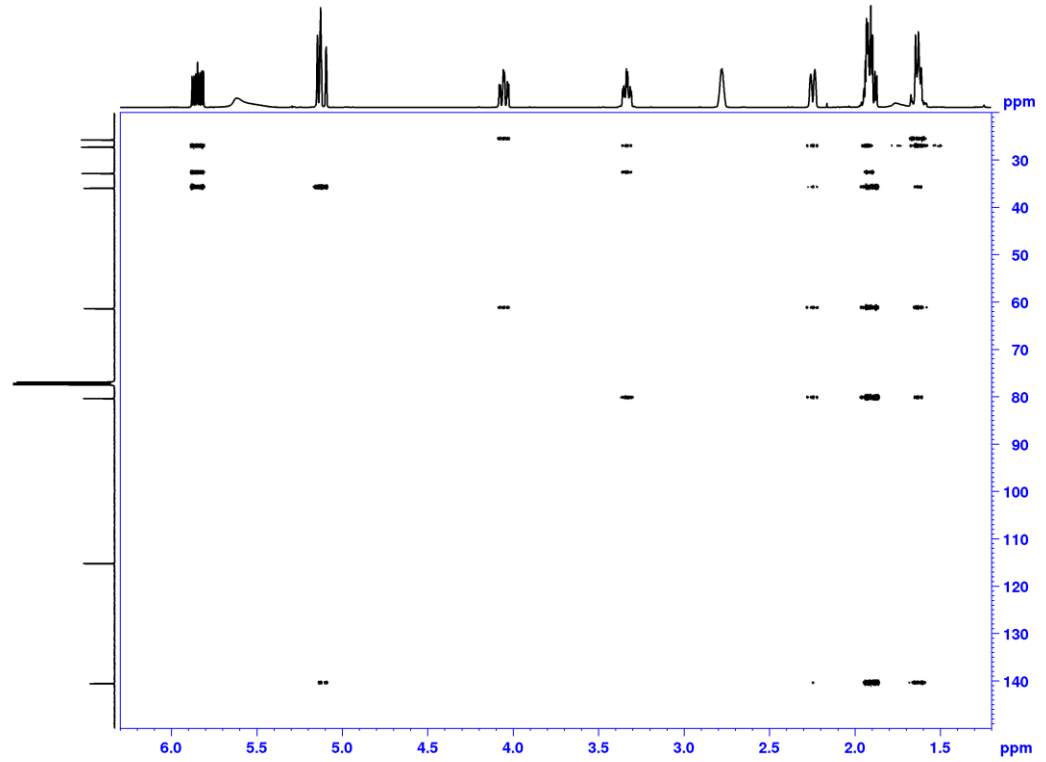


Figure S5. 2D HMBC spectrum of CHU monomer. $CDCl_3$, 500 MHz, 298 K.

4. Synthesis and characterization of CHU-derived imide I1 (co-initiator)

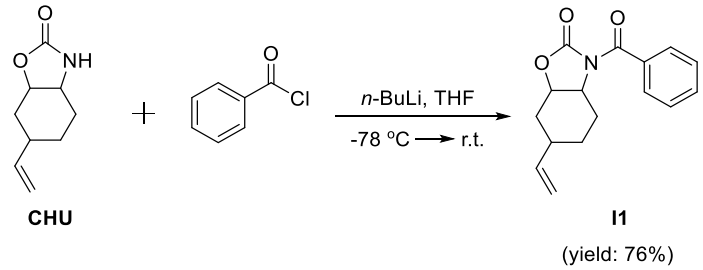


Figure S6. Synthetic route to CHU-derived imide **I1**.

The CHU-derived imide **I1** (co-initiator) was synthesized through the one step reaction between CHU monomer and benzoyl chloride (Figure S6). The typical synthesis process was as follows: CHU (0.50 g, 3.0 mmol) was dissolved in dry THF (10 mL) and the solution was cooled to -78 °C. Then *n*-butyllithium (2.0 M in cyclohexane, 1.65 mL, 3.3 mmol) was added slowly and the mixture was stirred at -78 °C for 30 min. A solution of benzoyl chloride (0.51 g, 3.6 mmol) in dry THF (20 mL) was subsequently added dropwise to the above mixture and the reaction mixture was stirred overnight while warming to the room temperature. After stopping the reaction, silica gel was added directly into the reaction mixture. Removed the solvent by rotary evaporation to afford the dried silica gel with crude product adhered to. Then the crude product was chromatographed on a silica gel using petroleum ether and ethyl acetate with a volume ratio of 1/1 as the eluent. Finally, pure CHU-derived imide **I1** (white solid, 0.62 g, yield: 76 %) was obtained after recrystallization from acetone. The ^{1}H NMR and ^{13}C NMR spectra of **I1** were shown in Figure S7.

^{1}H NMR (Figure S7a) ($CDCl_3$): δ 7.74-7.76 (m, 2H, H_{12}), 7.56 (tt, J = 7.4, 1.2 Hz, 1H, H_{14}), 7.41-7.45 (m, 2H, H_{13}), 5.89 (ddd, J = 17.4, 10.7, 5.0 Hz ,1H, H_8), 5.15-5.22 (m, 2H, H_9), 4.20-4.26 (m, 1H, H_3), 3.80 (td, J = 11.4, 3.4 Hz, 1H, H_2), 2.84-2.89 (m, 1H, H_7), 2.57 (dq, J = 12.2, 3.4 Hz 1H, H_4), 2.33-2.38 (m, 1H, H_5), 1.99-2.05 (m, 1H, H_6), 1.97 (td, J = 12.2, 5.4 Hz, 1H, $H_{5'}$), 1.76-1.84 (m, 1H, $H_{6'}$), 1.57-1.66 (m, 1H, $H_{4'}$).

^{13}C{^{1}H} NMR (Figure S7b) ($CDCl_3$): δ 171.1 (C_{10}), 154.8 (C_1), 140.3 (C_8), 133.1 (C_{11}

and C_{14}), 129.8 (C_{12}), 128.1 (C_{13}), 115.5 (C_9), 77.8 (C_3), 63.7 (C_2), 35.6 (C_7), 32.6 (C_5), 27.2 (C_6), 24.4 (C_4).

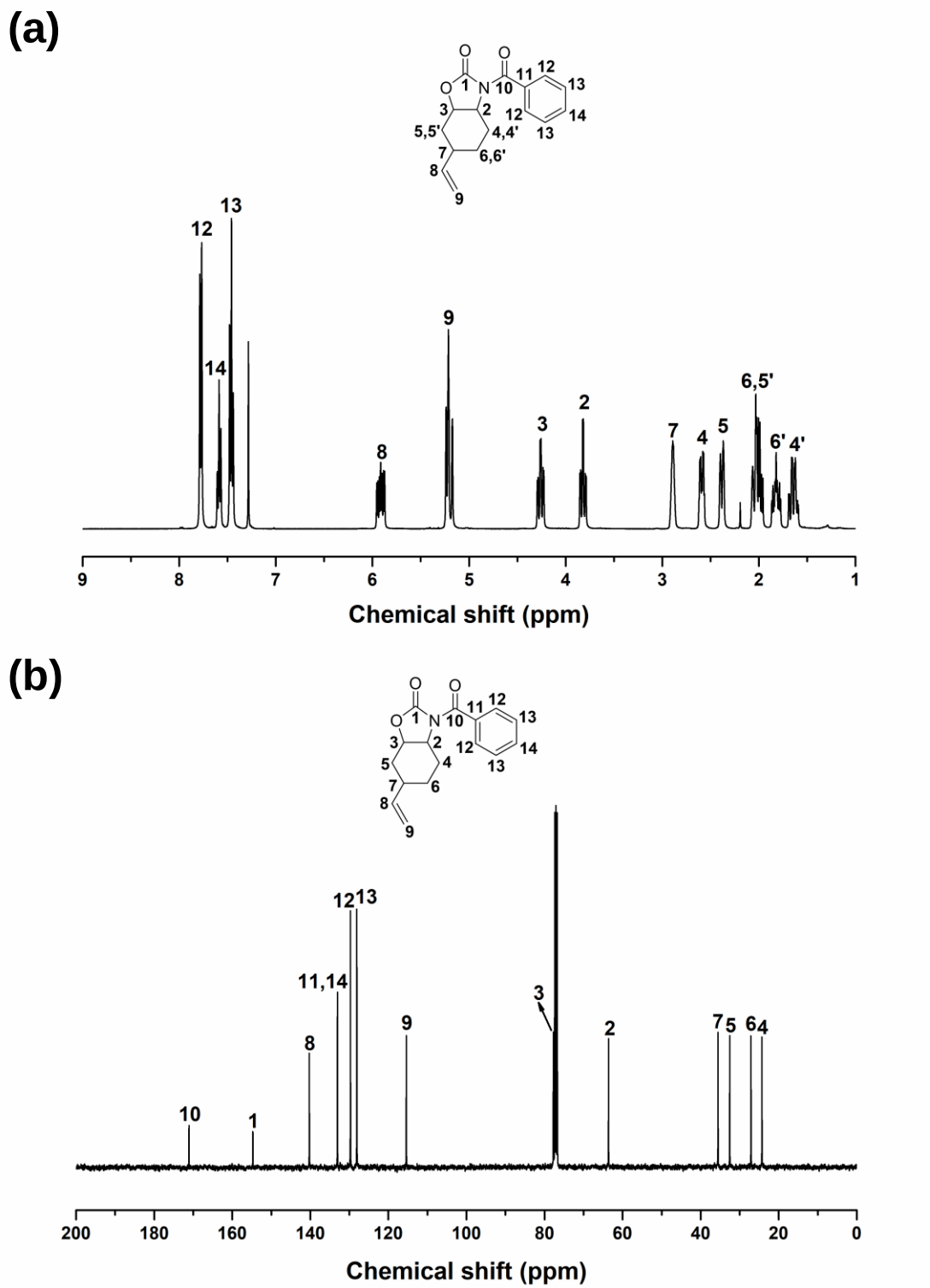


Figure S7. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of CHU-derived imide **I1**. $CDCl_3$, 400 MHz, 298 K.

5. Stereochemistry analysis of CHU monomer

For CHU synthesis, it is important to know more about the stereoselectivity of the reaction. Stereochemistry of CHU is complicated because there are three chiral stereogenic centers in its molecular structure and the whole synthetic steps from 4-vinyl-1-cyclohexene-1,2-epoxide to the final CHU are non-stereoselective. If we consider that all configurations are possible for the three chiral centers in CHU, it is a mixture of eight stereoisomers. Although it is not our current research subject to resolve these stereoisomers, we need to know the possible types and ratios of stereoisomers in CHU monomer.

The starting material, 4-vinyl-1-cyclohexene-1,2-epoxide, was purchased from chemical supplier as a mixture of isomers. It can exist as eight stereoisomers at most since it had three chiral centers. However, GC (gas chromatography) characterization showed only two signal peaks with a ratio of about 6:4 (Figure S9). So, we speculated that it might be a mixture of four stereoisomers or two racemic mixtures of diastereomers (Figure S8). This explained why there were two signal peaks in the GC spectrum. ^{13}C NMR characterization of 4-vinyl-1-cyclohexene-1,2-epoxide also showed two signals for the methine carbon atoms with a ratio of about 6:4 (Figure S10), which further confirmed it was a mixture of two racemic mixtures of diastereomers.

The reaction between 4-vinyl-1-cyclohexene-1,2-epoxide and ammonia in ethanol gave rise to two constitutional isomers (**2** and **3**, Figure S8). Considering that this reaction is a S_N2 nucleophilic reaction,[1,2] the addition of ammonia on the epoxide ring was a *trans* addition and the produced NH_2 group and OH group in compound **2** or **3** should have opposite orientation *versus* the cyclohexane ring. So, **2** and **3** existed as four stereoisomers. After the following two non-stereoselective synthetic steps from **3**, CHU was synthesized as a mixture of four stereoisomers in which the orientation of C-O and C-N bonds connected to the cyclohexane ring kept consistent with those in **2** and **3**, as shown in Figure S8. Similarly, the four stereoisomers were also two pairs of diastereomers. To confirm this, the pure CHU was characterized by HPLC (high-performance liquid chromatography) but we were not able to detect it as the detector of

HPLC was a UV detector. So, we used a CHU derivative that substituted the H atom on the NH group with a benzoyl group (co-initiator **I1** for the AROP) for the HPLC characterization. The result showed two signal peaks with a ratio of about 6:4 (see Figure S11), which confirmed our previous results. In the following work, CHU was considered as a mixture of stereoisomers to synthesize PUs by AROP.

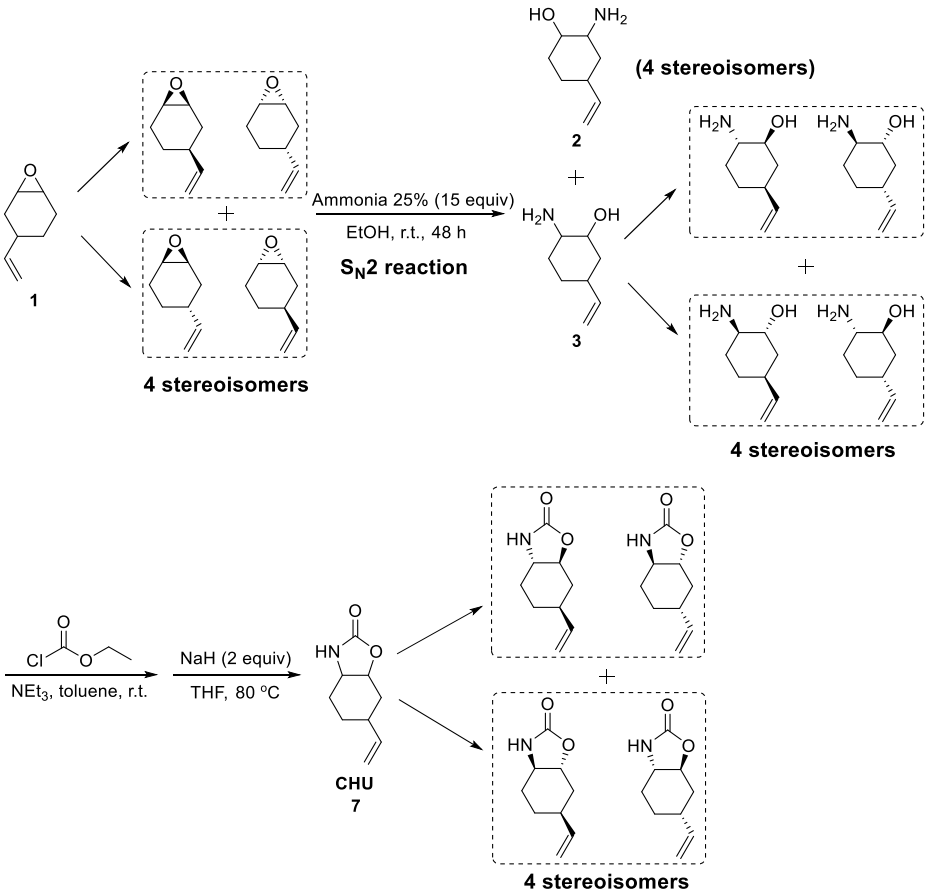
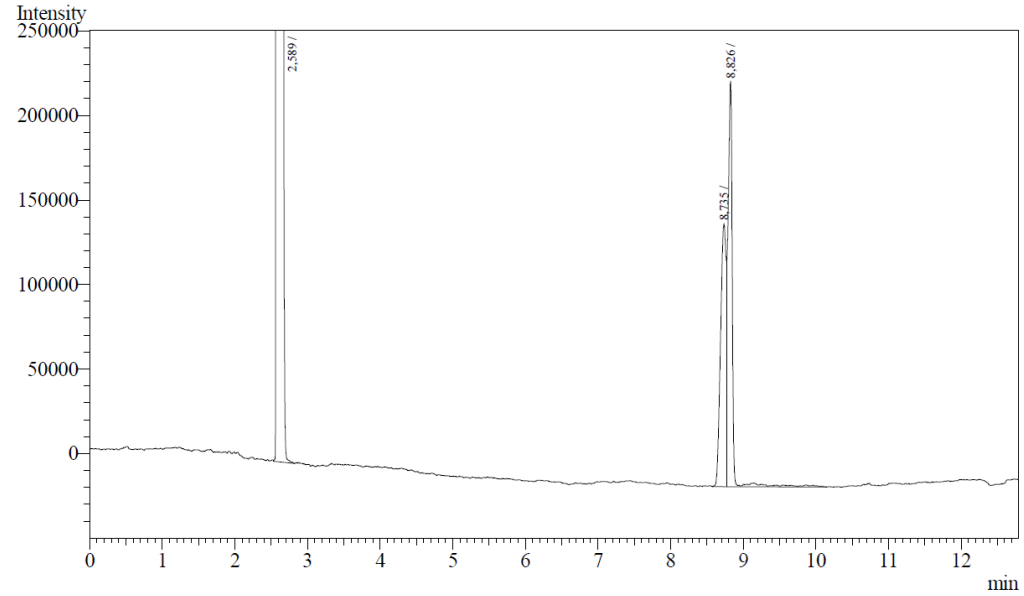


Figure S8. Stereochemistry study of CHU monomer.



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	2,589	108763336	37596889	0,000		V		
2	8,735	837332	155547	0,000				
3	8,826	974107	239151	0,000		SV		
Total		110574775	37991587					

Figure S9. GC spectrum of 4-vinyl-1-cyclohexene-1,2-epoxide (mixture of isomers). Injection temperature: 260 °C. The column temperature was increased from 80 °C to 160 °C with a rate of 2 °C/min.

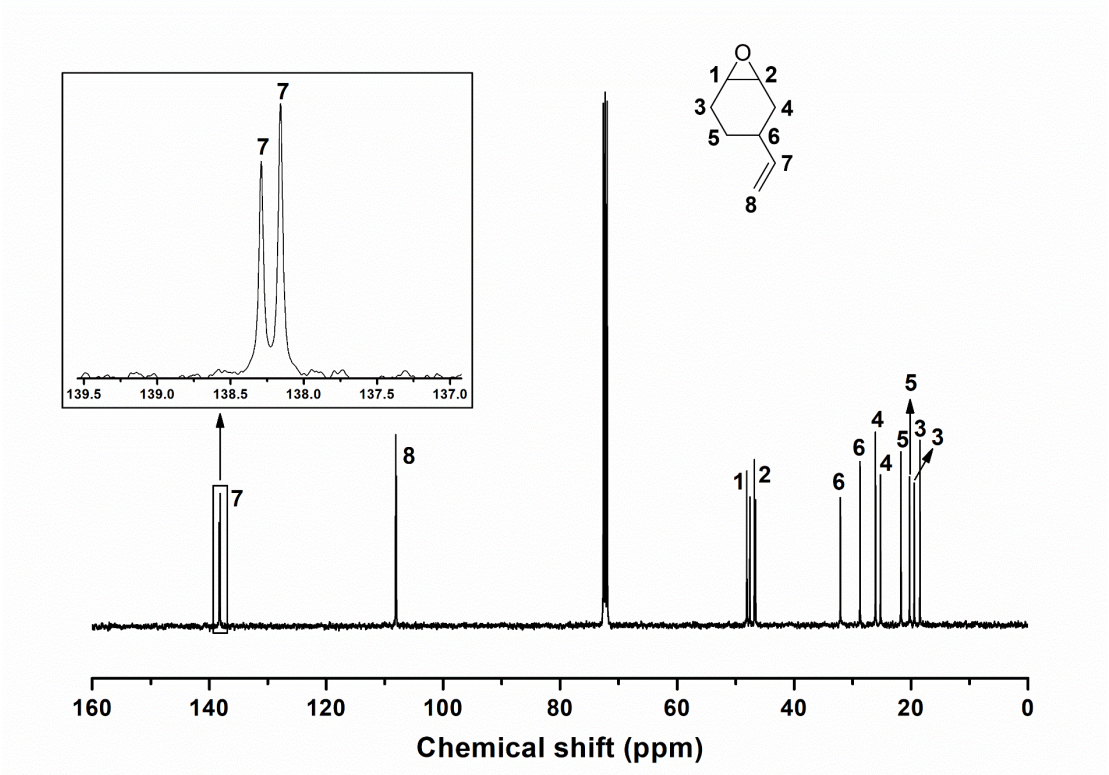


Figure S10. ^{13}C NMR spectrum of 4-vinyl-1-cyclohexene-1,2-epoxide (mixture of isomers). $CDCl_3$, 400 MHz, 298 K.

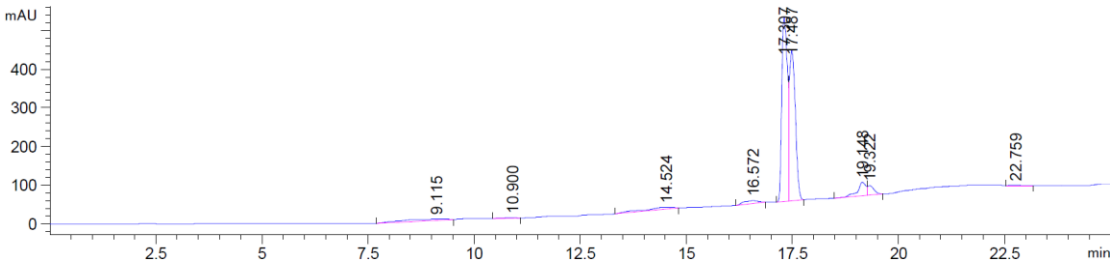


Figure S11. HPLC spectrum of CHU-derived imide **I1**. The eluent was the mixture of acetonitrile and water.

6. Polymerization

All polymerizations were carried out under argon in a 15 mL Schlenk tube equipped with a Teflon coated stirring bar. The typical polymerization process was as follows: In the glove box, the Schlenk tube was charged with appropriate amounts of CHU monomer, co-initiator and THF to reach the desired monomer to co-initiator ratio and monomer concentration. The Schlenk tube was kept for 20 min in the refrigerator of -40 °C in the glove box. Then appropriate amount of *n*-butyllithium was added and the Schlenk tube was transferred outside of the glove box quickly. The mixture was stirred at 0 °C for a certain time. The polymerization was stopped by adding a small amount of methanol. The mixture was then poured drop-by-drop into *n*-hexane (15 mL) to precipitate the crude PU polymer. The precipitate was collected by centrifugation. After being re-dissolved in THF and reprecipitated in *n*-hexane twice more, the pure polymer was collected and dried under vacuum at room temperature for 24 h. The NMR, GPC, MALDI-TOF mass spectrometry, ATR-IR, TGA and DSC characterization results of the synthesized PU polymers were shown in Figure S12-S17.

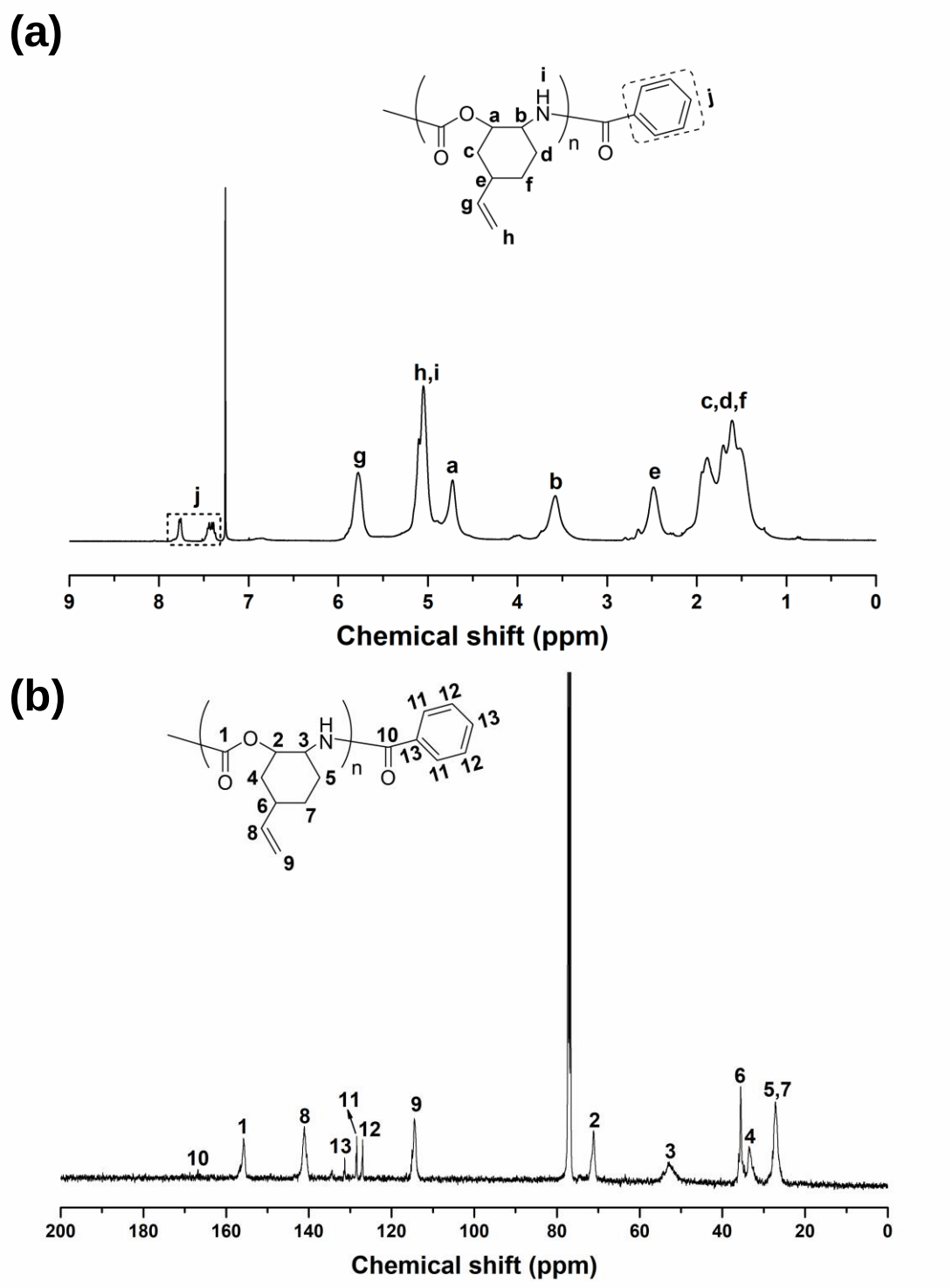


Figure S12. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of PU (polymer from entry 7 in Table 1). $CDCl_3$, 400 MHz, 298 K.

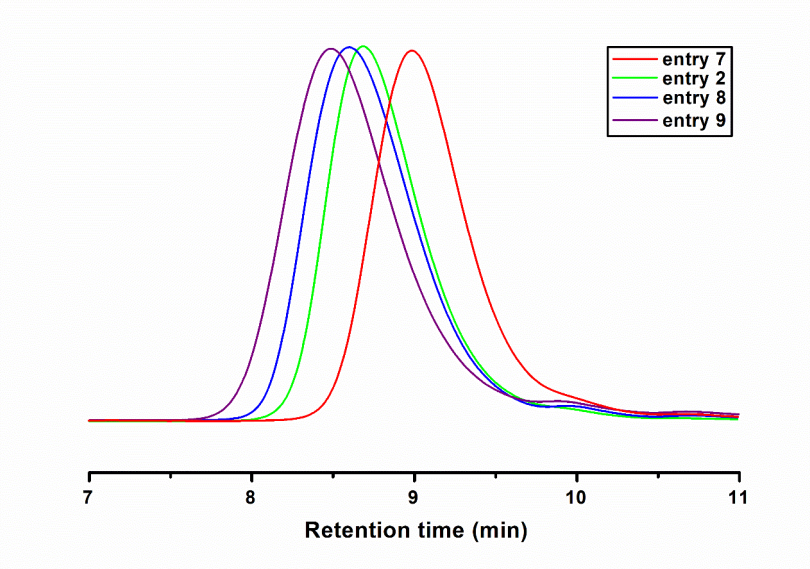


Figure S13. GPC curves of PUs from Table 1 with THF as the eluent.

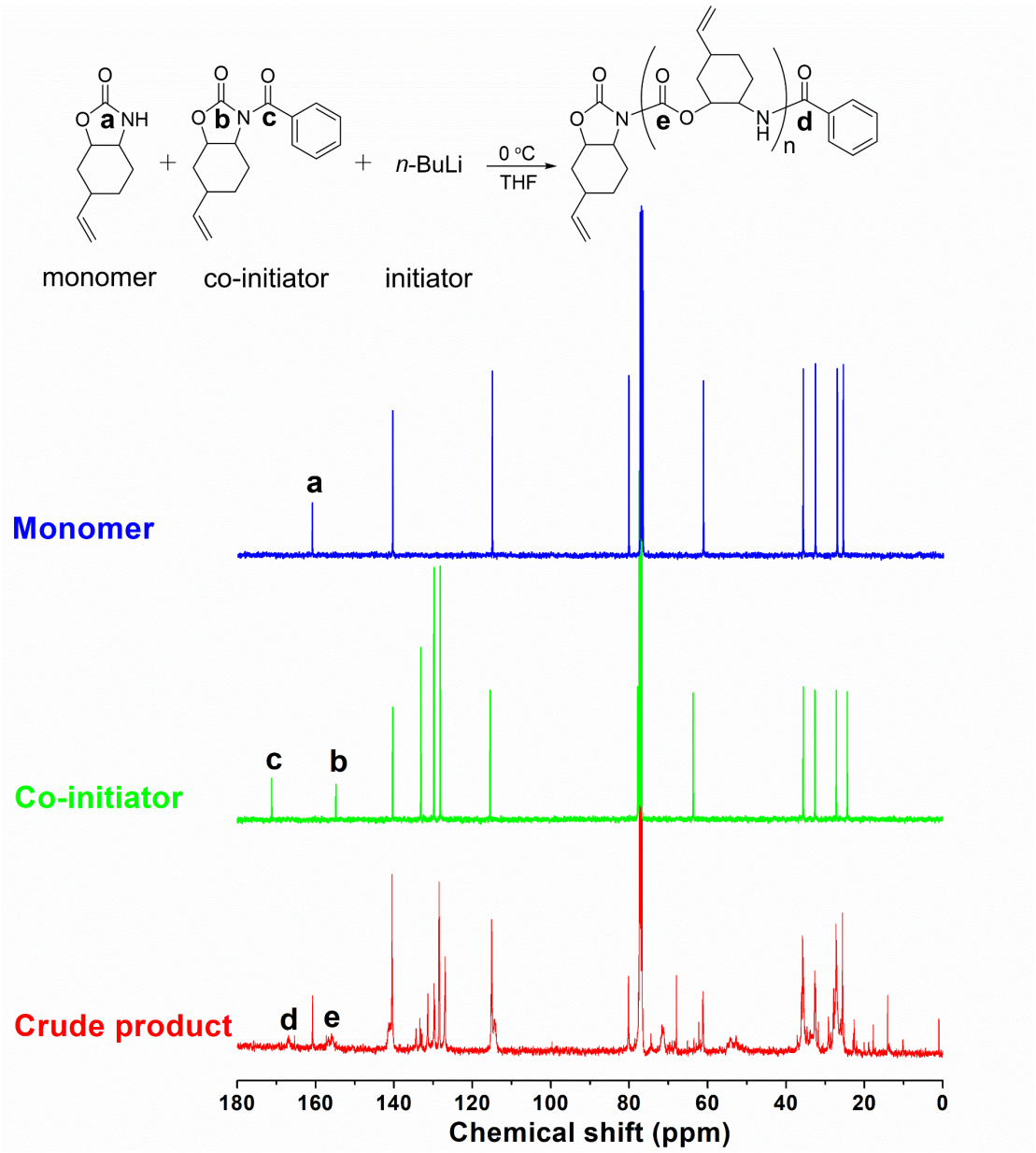


Figure S14. ^{13}C NMR spectra of monomer, co-initiator and the crude product in the *in situ* IR experiment to monitor the 1/1/1 (monomer, initiator, co-initiator) reaction.

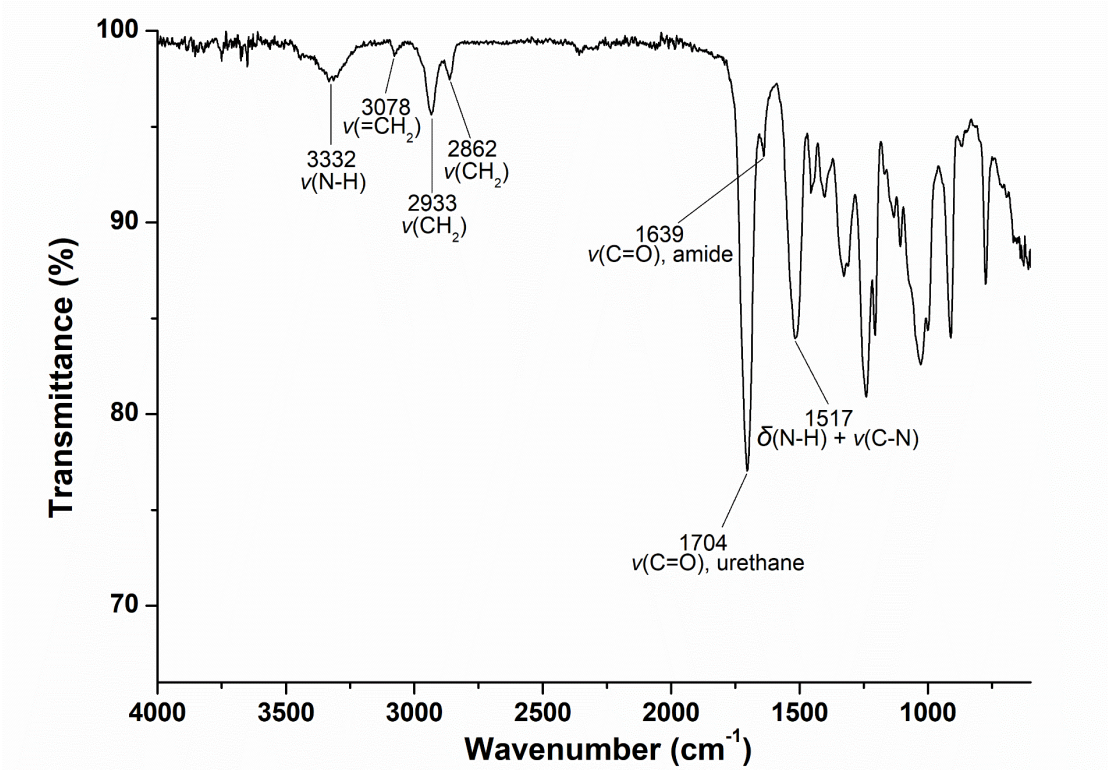


Figure S15. ATR-IR spectrum of PU (polymer from entry 2 in Table 1).

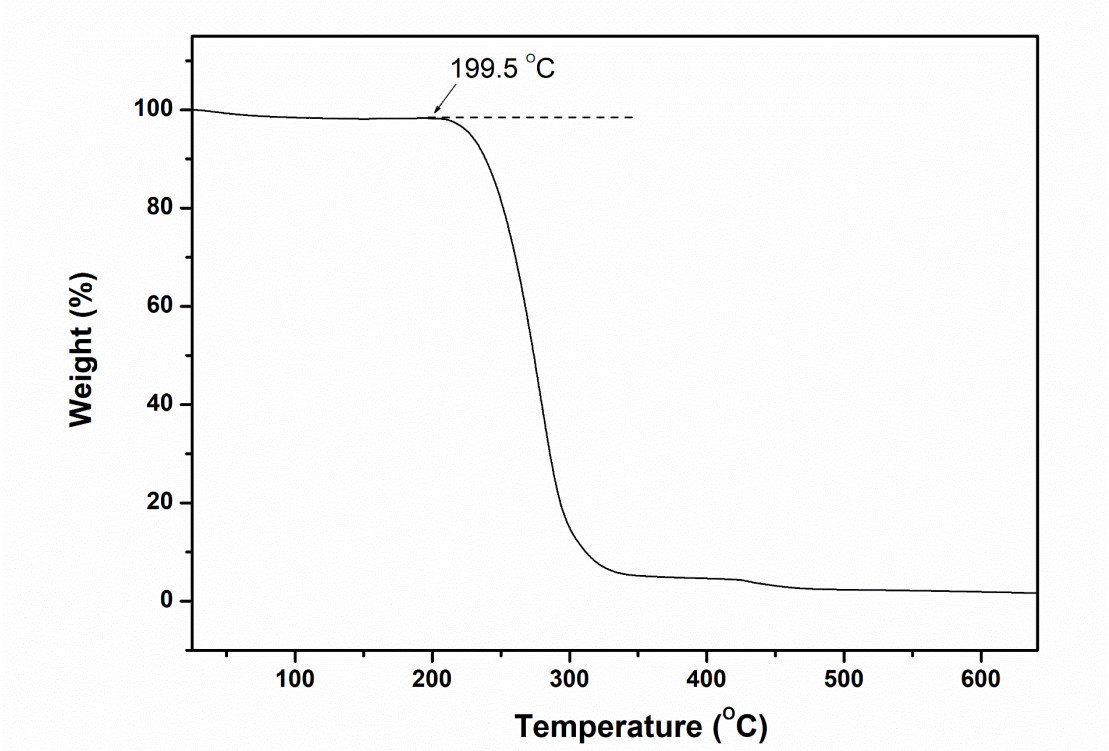


Figure S16. TGA curve of PU (polymer from entry 2 in Table 1).

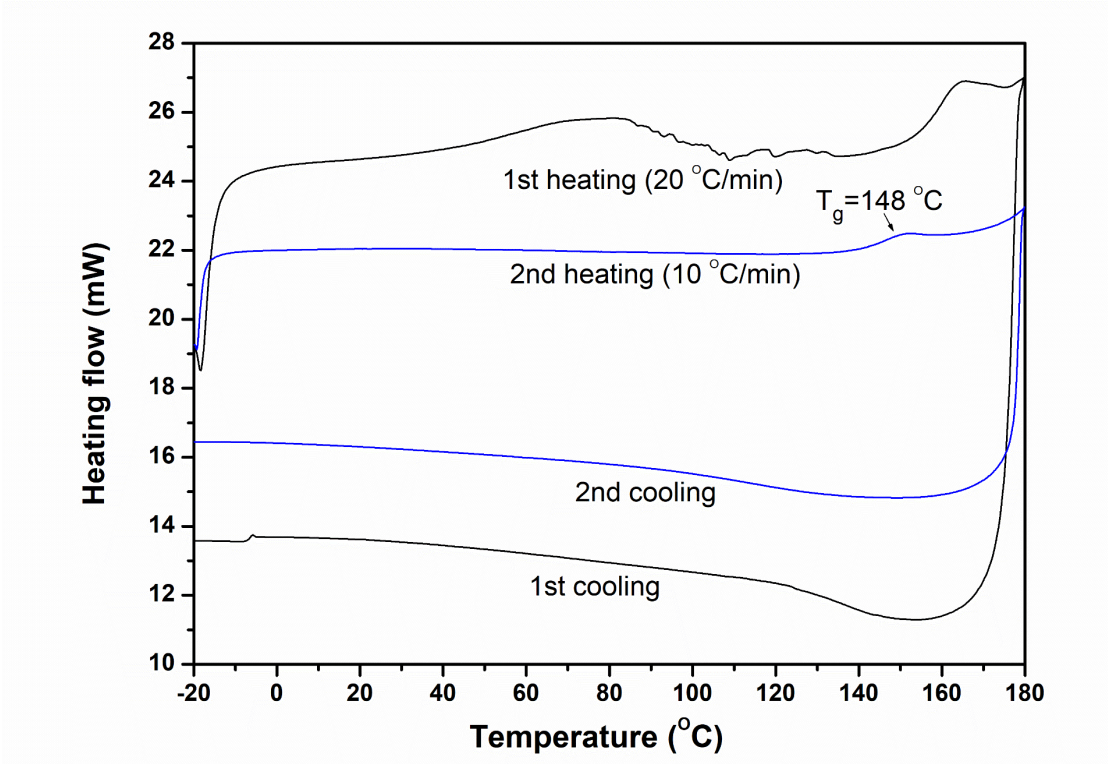


Figure S17. DSC curves of PU (polymer from entry 2 in Table 1).

7. Evidence of ROP mechanism

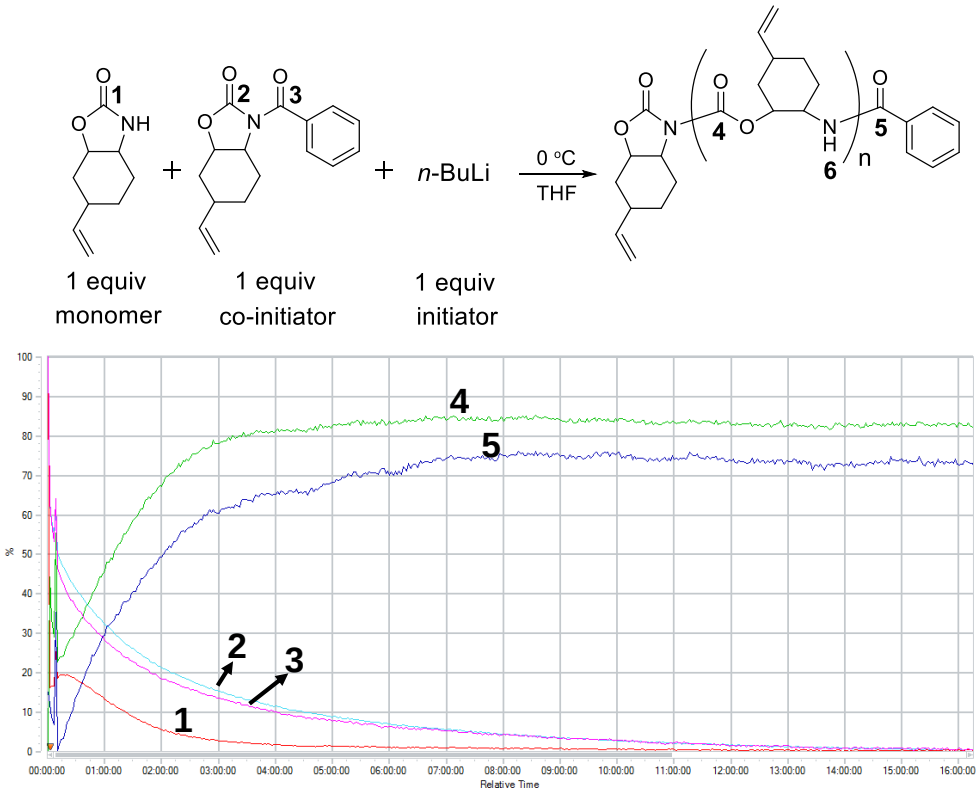


Figure S18. Evolutions of characteristic IR peaks *versus* time by *in situ* IR experiment.

8. ROP kinetics

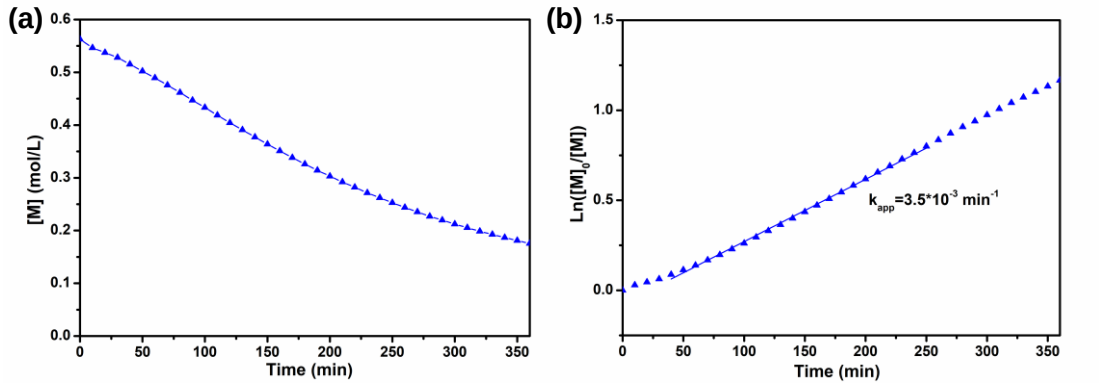


Figure S19. (a) Monomer concentration as a function of time with the molar ratio of monomer, initiator and co-initiator being 30/1/1 monitored by *in situ* IR. The initial monomer concentration was 0.564 M. Initial concentrations of initiator and co-initiator were 0.0188 M. (b) Semilogarithmic plot of the data used to generate part (a).

9. Synthesis of amphiphilic PU-*g*-PEG graft copolymer

9.1 Synthesis of thiol-terminated mPEG (mPEG-SH)

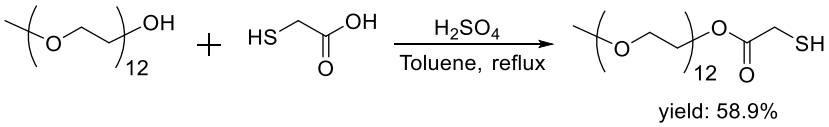


Figure S20. Synthetic scheme of mPEG-SH.

Thiol-terminated mPEG was prepared through the esterification reaction between $mPEG_{12}$-OH and thioglycolic acid with sulfuric acid as the catalyst (Figure S20). The typical synthesis process was as follows: $mPEG_{12}$-OH (3.30 g, 6 mmol) and thioglycolic acid (1.66 g, 18 mmol) were dissolved in dry toluene (10 mL). Then conc. sulfuric acid (2 drops) was added to the mixture and the reaction flask was equipped with an azeotropic distillation apparatus. The mixture was refluxed at 130 °C for 16 h. After stopping the reaction by cooling to the room temperature, toluene was removed under reduced pressure. Pure $mPEG_{12}$-SH (colorless viscous liquid, 2.20 g, yield: 58.9%) was obtained by recrystallization of the crude product once from the mixture of THF and diethyl ether. The ^{1}H NMR spectrum of mPEG-SH was shown in Figure S21.

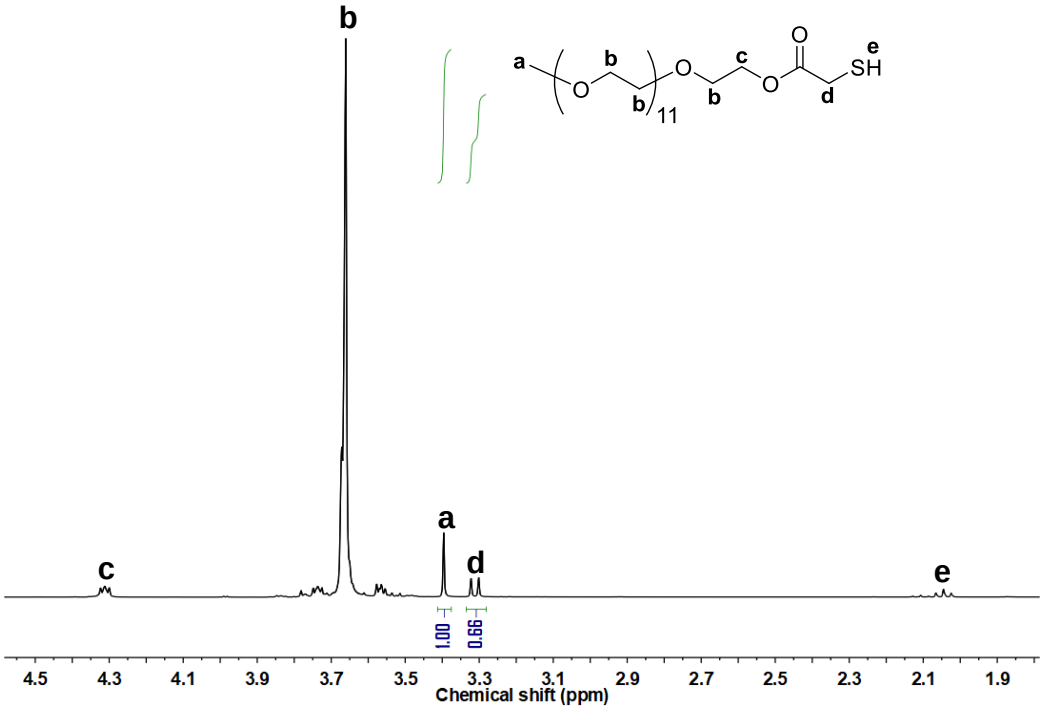


Figure S21. ^{1}H NMR spectrum of mPEG-SH. $CDCl_3$, 400 MHz, 298 K.

9.2 Synthesis of amphiphilic PU-*g*-PEG graft copolymer

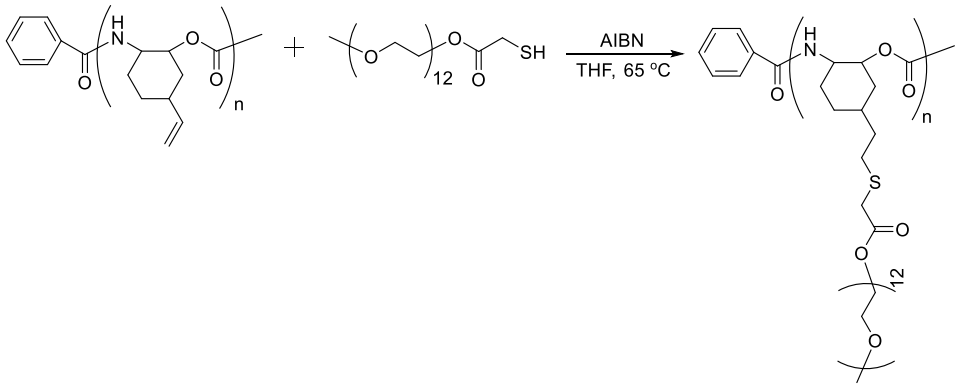


Figure S22. Synthetic scheme of amphiphilic PU-*g*-PEG graft copolymer.

The amphiphilic PU-*g*-PEG graft copolymer was prepared by the radical-mediated thiol-ene reaction of a linear PU homopolymer backbone with vinyl groups attached on each repeating unit and $mPEG_{12}$-SH, which was a grafting onto strategy to prepare graft copolymer (Figure S22). The PU homopolymer was prepared *via* the AROP of CHU monomer firstly. The typical synthesis of PU-*g*-PEG graft copolymer with a hydrophilic ratio of 56.6% by thiol-ene coupling reaction was as follows: PU (M_n = 2400 Da, 30 mg, c.a. 0.175 mmol vinyl groups), $mPEG_{12}$-SH (437 mg, 0.7 mmol), AIBN (34.5 mg, 0.21 mmol) and 2 mL dry THF were added to a 15 mL Schlenk tube equipped with a Teflon coated stirring bar. After deoxygenation by three freeze-pump-thaw cycles, the reaction mixture was stirred at 65 °C for 24 h. The reaction was stopped by cooling to the room temperature. The crude product was purified by dialysis against ethanol in a 3500 Da cut off cellulose bag for 5 days to remove unreacted $mPEG_{12}$-SH, and the ethanol was changed twice a day. The ethanol solution in the dialysis bag was collected and pure PU-*g*-PEG graft copolymer (colorless viscous liquid, 82 mg, yield: 59.0 %) was obtained by removing the ethanol under high vacuum.

The pure product was carefully characterized by ^{1}H NMR spectroscopy and GPC (Figure S23 and S24). By comparing the ^{1}H NMR spectra of PU and PU-*g*-PEG, the proton signals at δ 5.78 (peak a) and 2.48 ppm (peak b) attributed respectively to “CH” groups on the vinyl moiety and cyclohexane completely disappeared after the reaction (Figure S23). This result indicated that the grafting ratio of PEG side chains was 100%.

In addition, new ^{1}H resonances at δ 4.28 ppm (peak e), 3.64 ppm (peak d), 3.37 ppm (peak c), 3.24 ppm (peak f) and 2.64 ppm (peak g) appeared on the ^{1}H NMR spectrum of the obtained PU-*g*-PEG product, which were assigned to the protons of the PEG side chains. Finally, the GPC curve of PU-*g*-PEG showed a unimodal distribution and the retention time shifted to the left compared to the GPC curve of PU (Figure S24). All these characterization results confirm that pure amphiphilic graft copolymer PU-*g*-PEG with high grafting density was obtained by the thiol-ene coupling reaction of PU and mPEG-SH.

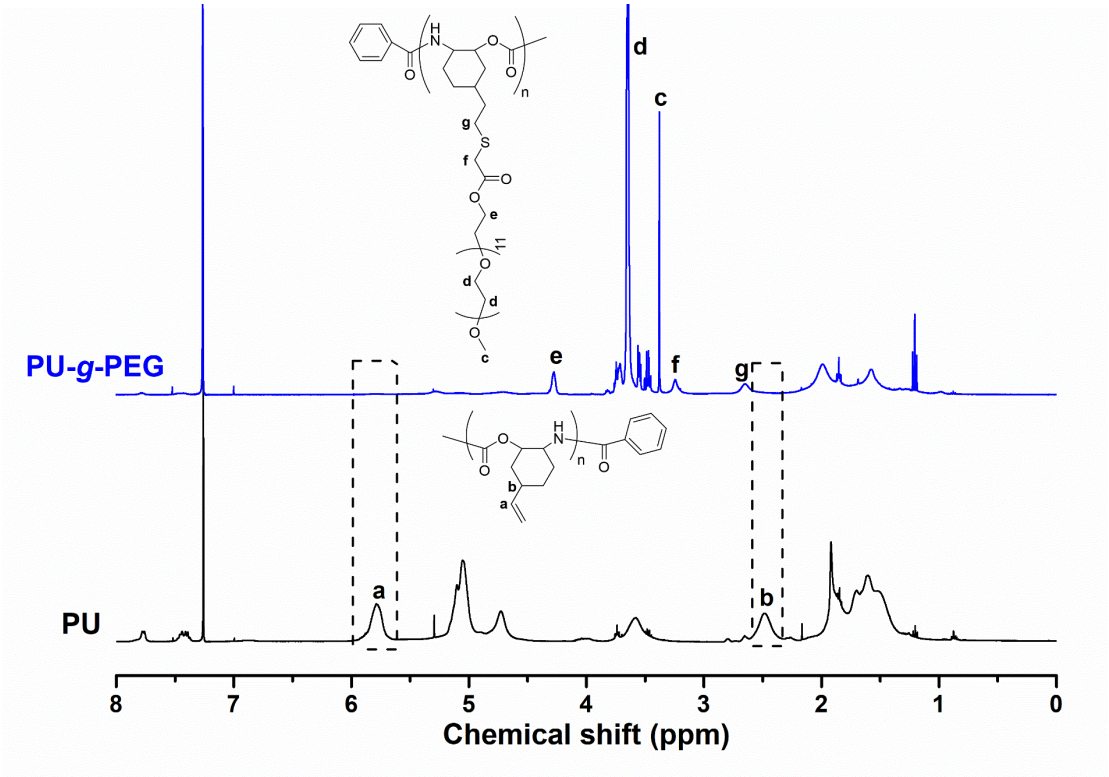


Figure S23. ^{1}H NMR spectra of the amphiphilic graft copolymer PU-*g*-PEG and PU backbone.

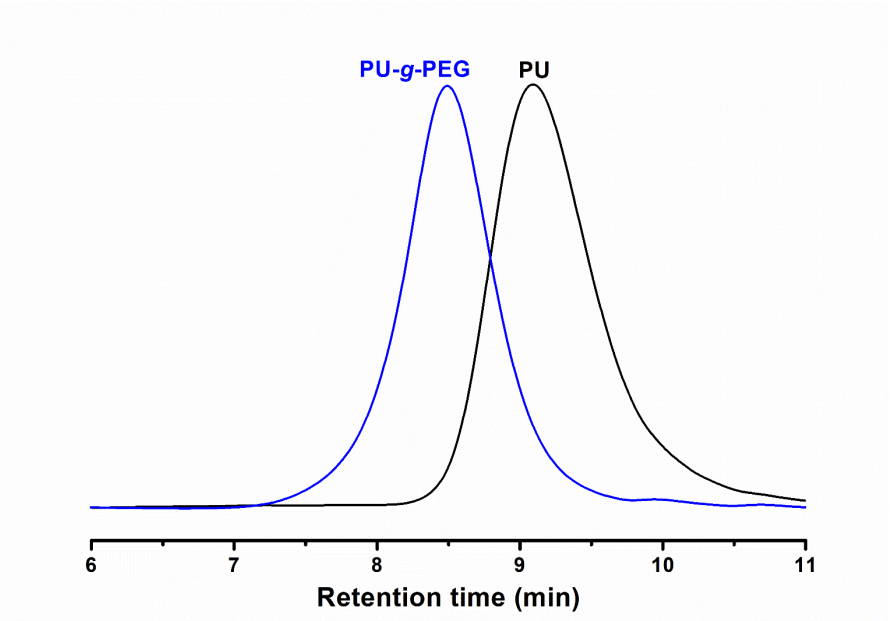


Figure S24. GPC traces of the amphiphilic graft copolymer PU-*g*-PEG and PU backbone with THF as the eluent.

References

1. McManus, S. P.; Larson, C. A.; Hearn, R. A. *Synth. Commun.* **1973**, *3*, 177-180.

2. Hawkins, L. R.; Bannard, R. A. B. *Can. J. Chem.* **1958**, *36*, 220-227.