Electronic Supplementary Material (ESI) for Chemical Communications
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Supporting information

Synthesis of sequence-ordered polymers via sequential addition of monomers in one pot

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Materials

Ethylene dimethacrylate (99%, J&K) and allyl methacrylate (99%, J&K) were distilled before use. 2-Aminoethanethiol (≥99%, Sigma), DL-homocysteine thiolactone hydrochloride (≥98%, Aldrich), acetel chloride (99%, Aladdin), maleimide (98%, J&K), bromine (99.99%, Aladdin), 2,3-dibromomaleimide (97%, Aldrich), 1,3-diaminopropane (>99%, Aldrich), bicyclo[2.2.1]hepta-2,5-diene (98%, Aldrich), benzoin dimethyl ether (DMPA, 99%, Aladdin), tributylphosphine (TBP, 95%, Aladdin), triethylamine (TEA, HPLC grade, >99.5%, Aladdin), methanol-d_4 (99.8%, Aldrich) were used as received. Other reagents were purchased from Sigma and used as received.

Characterizations

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^{1}H NMR and ^{13}C NMR spectra were performed on a Varian spectrometer (400 MHz). Molecular weight and PDI was determined from gel permeation chromatography (GPC) implemented on a Waters 2690 apparatus with Waters ultra-styragel columns HR (500-600K) columns, a Waters 410 refractive index detector. DMF was used as eluent at a flow rate of 1.0 mL min^{-1} and polystyrenes were used as standard.

1. **Synthesis of 2,3-dibromosuccinimide.** Maleimide (2.00 g, 20 mmol) was mixed with 15 mL chloroform, bromine (1.3 mL, 22 mmol) was diluted with 15 mL chloroform and added dropwise to the above suspension within 2 h, and the mixture was refluxed for 3 h. Then the reaction mixture was filtered, the solid was washed with chloroform for three times and purified by silica column to obtain crystal of 2,3-dibromosuccinimide (hexane: ethyl acetate = 3:1, v/v), yield is 51%.

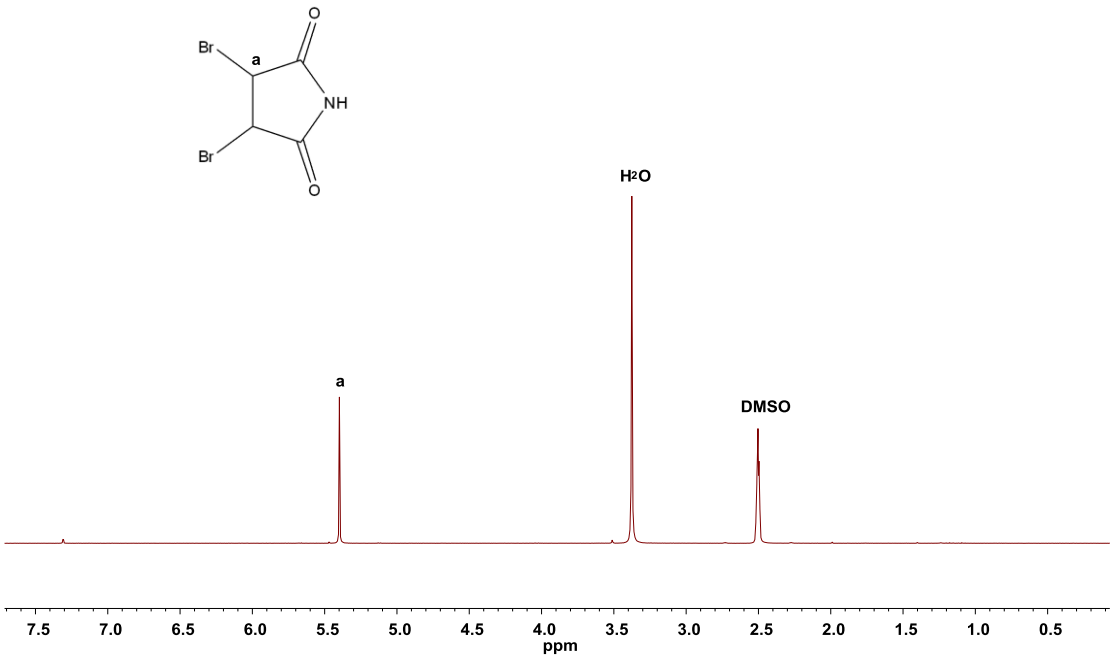


Fig. S1. ^{1}H NMR spectrum of 2,3-dibromosuccinimide.

2. **Synthesis of 2-bromomaleimide.** Dibromosuccinimide (2g, 7.8mmol) was dissolved in 20 mL of tetrahydrofuran. The solution was purged with argon for 10 min. Then triethylamine (1.1mL, 8.0mmol) in 10 mL of tetrahydrofuran was added dropwise over 15 min in an ice bath. The reaction mixture was stirred for another 48 h at room temperature. The solid was filtrated off, and the solvent was evaporated to obtain a yellow solid. The crude product was purified by silica gel column chromatography using 1/5 ethyl acetate/hexane as the fluent to afford a pale white solid. Yield is 39%.

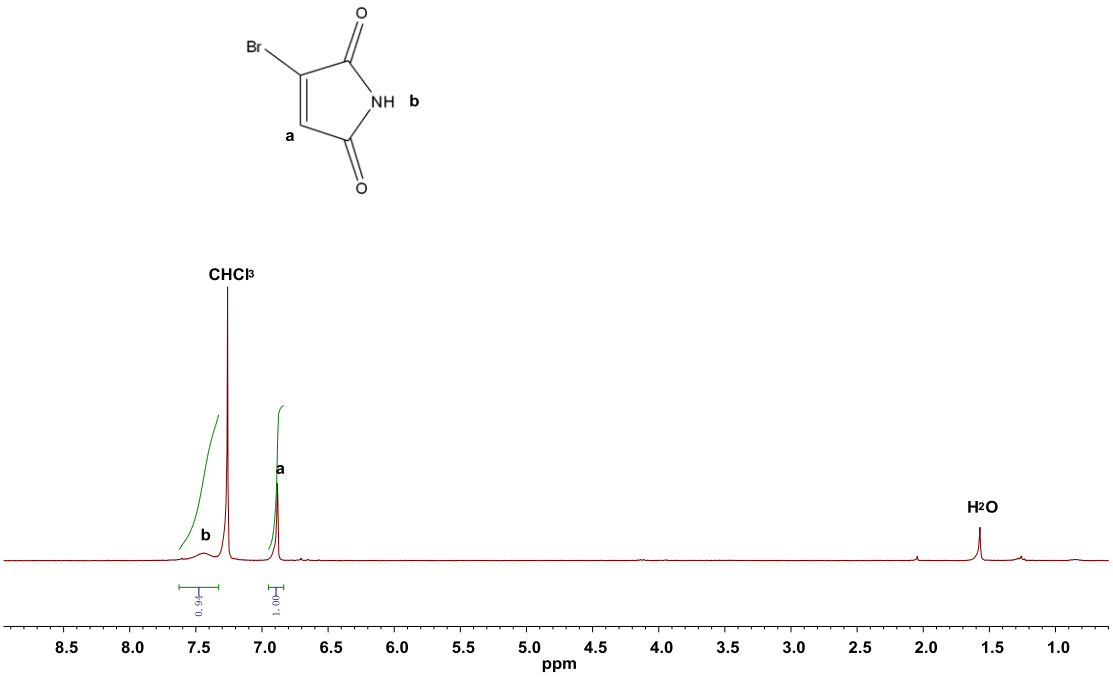


Fig. S2. ^{1}H NMR spectrum of 2-bromomaleimide.

3. **Synthesis of *N*-acethomocysteine thiolactone.** DL-Homocysteine thiolactone hydrochloride (3.07 g, 20 mmol) was mixed with triethylamine (9.70 g, 96 mmol) in 50 mL dichloromethane to form a suspension in ice bath. Acetyl chloride (2.36 g, 30 mmol) was added dropwise in 30 min. The solution was stirred at room temperature for additional 4 h and traced by TLC. The reaction mixture was diluted with 20 mL dichloromethane, filtered, and washed with brine (30 mL × 2) and extracted with dichloromethane (40 mL × 2), the organic phase was dried with Na_2SO_4, and filtered. The resulting solution was subjected to a flash silica chromatography to yield white powder (ethyl acetate as eluent, R_f = 0.60).

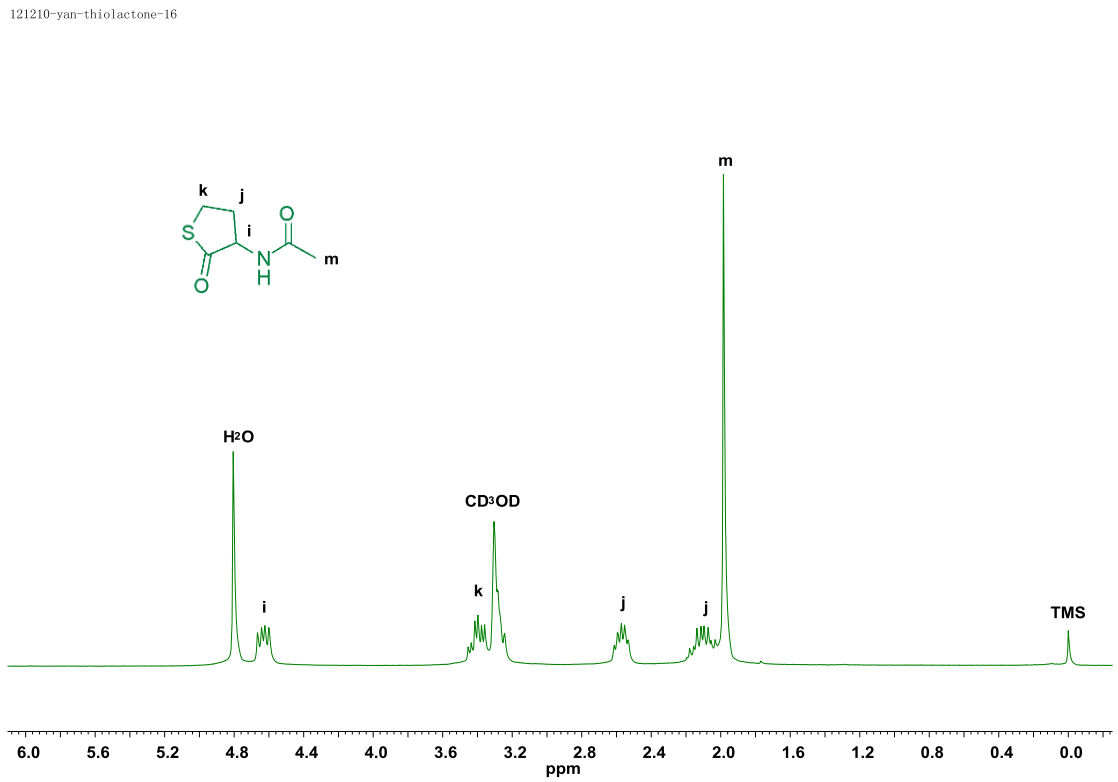
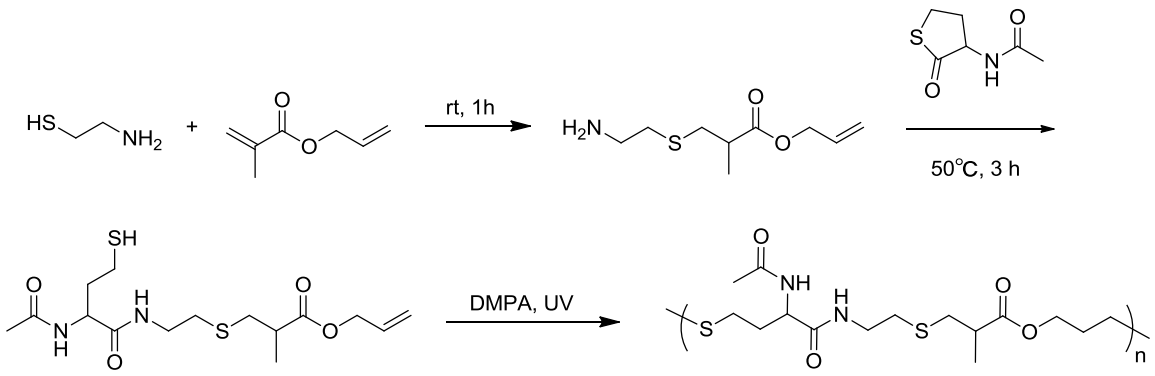


Fig. S3. ^{1}H NMR spectrum of *N*-acethomocysteine thiolactone.

4. **The reparation of ABC sequence-ordered polymers.** 2-Aminoethanethiol (23.0 mg, 0.298 mmol) and allyl methacrylate (37.5 mg, 0.298 mmol) were dissolved in 0.55 mL methanol under argon atmosphere and stirred at room temperature for 1 h. Then *N*-acethomocysteine thiolactone (47.4 mg, 0.298 mmol) was added and the reaction mixture was left at 50℃ for 3 h. Subsequently,, tributylphosphine (5 μL) was utilized to reduce the possible coupled disulfide bonds at room temperature for 1 h, and photoinitiator benzoin dimethyl ether (DMAP, 2.1 mg) was added to the reaction mixture and subjected to UV irradiation (Fusion UV) for 30 min. The polymer was purified by precipitating into diethyl ether to obtain white viscous solids. The entire reaction process was monitored by ^{1}H NMR and 13C NMR as shown in Fig. S5-S7.



Scheme S1.

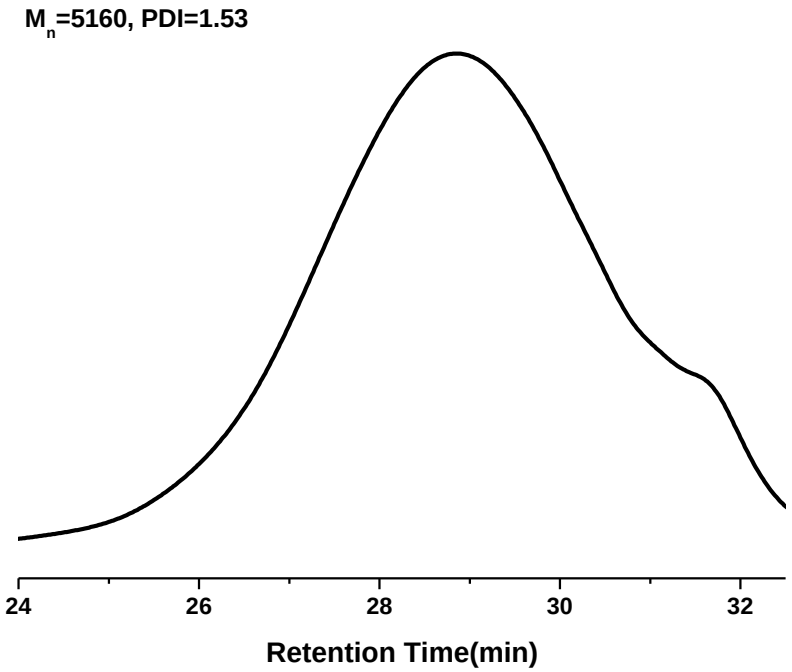
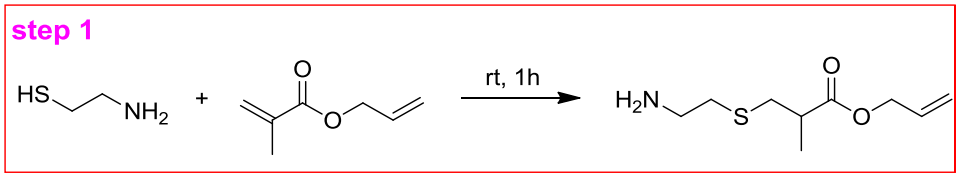
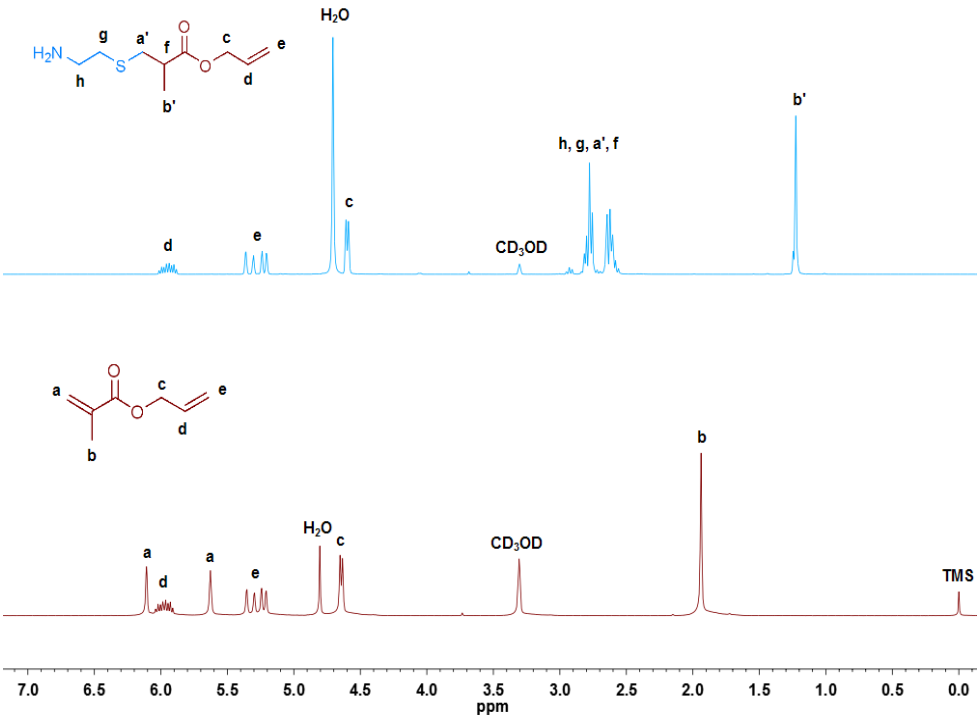


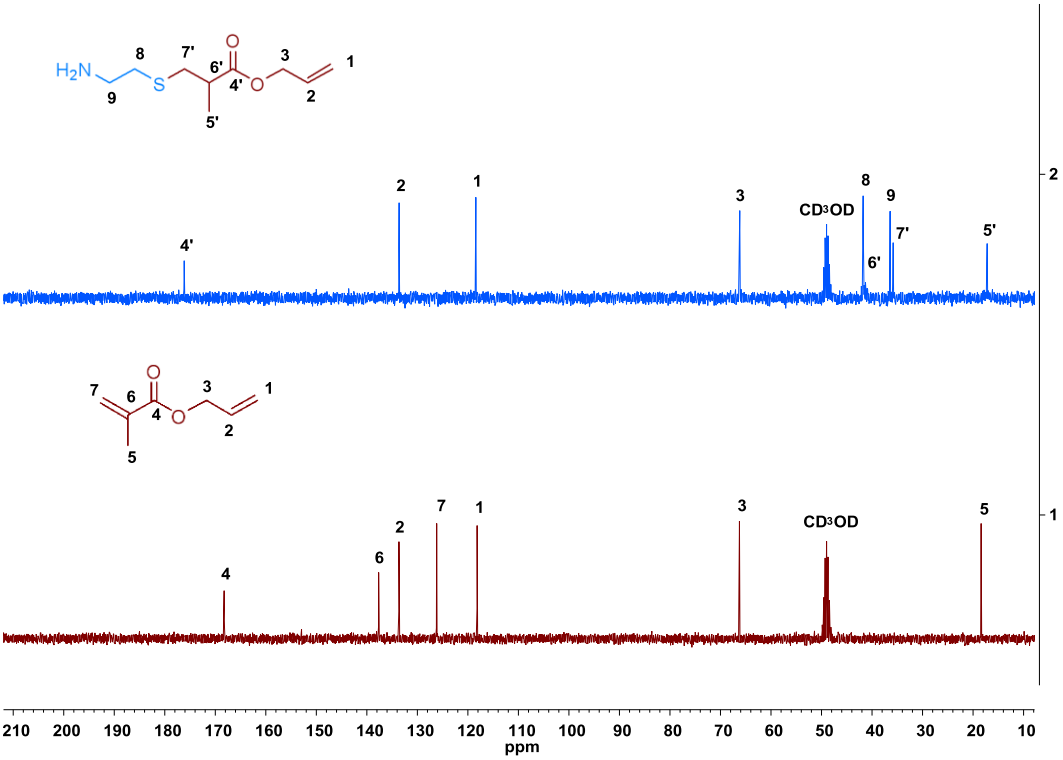
Fig. S.4 GPC curve of ABC sequenced copolymer.



^{1}H NMR spectra



^{13}C NMR spectra



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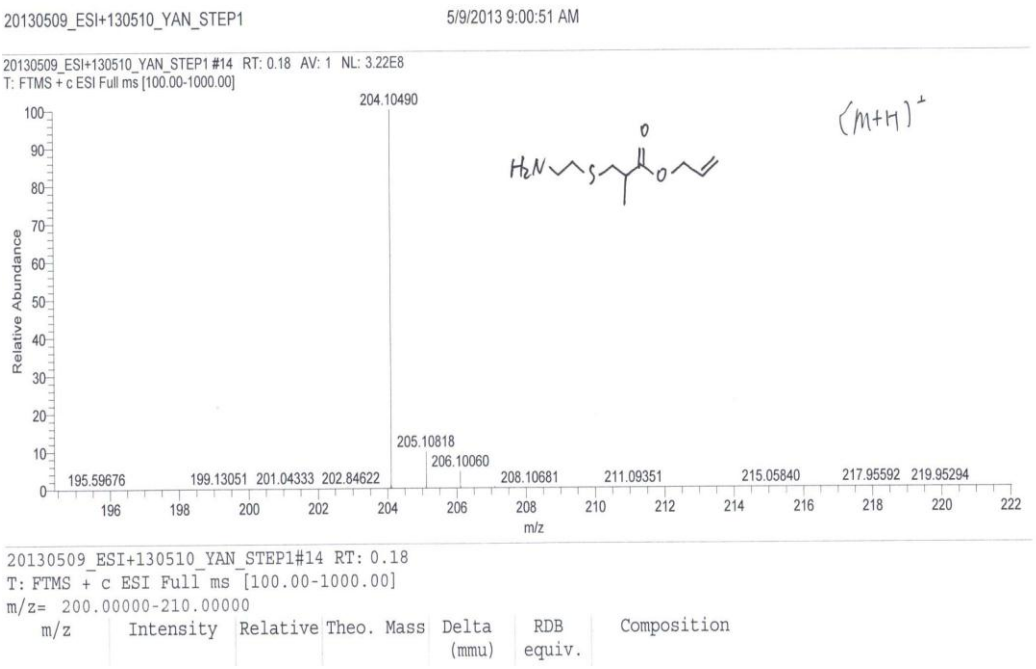
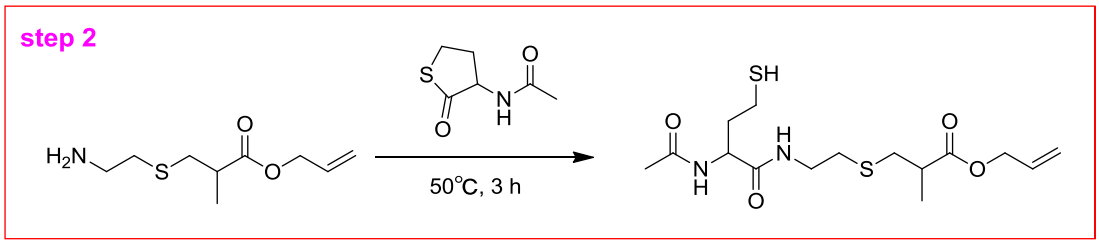
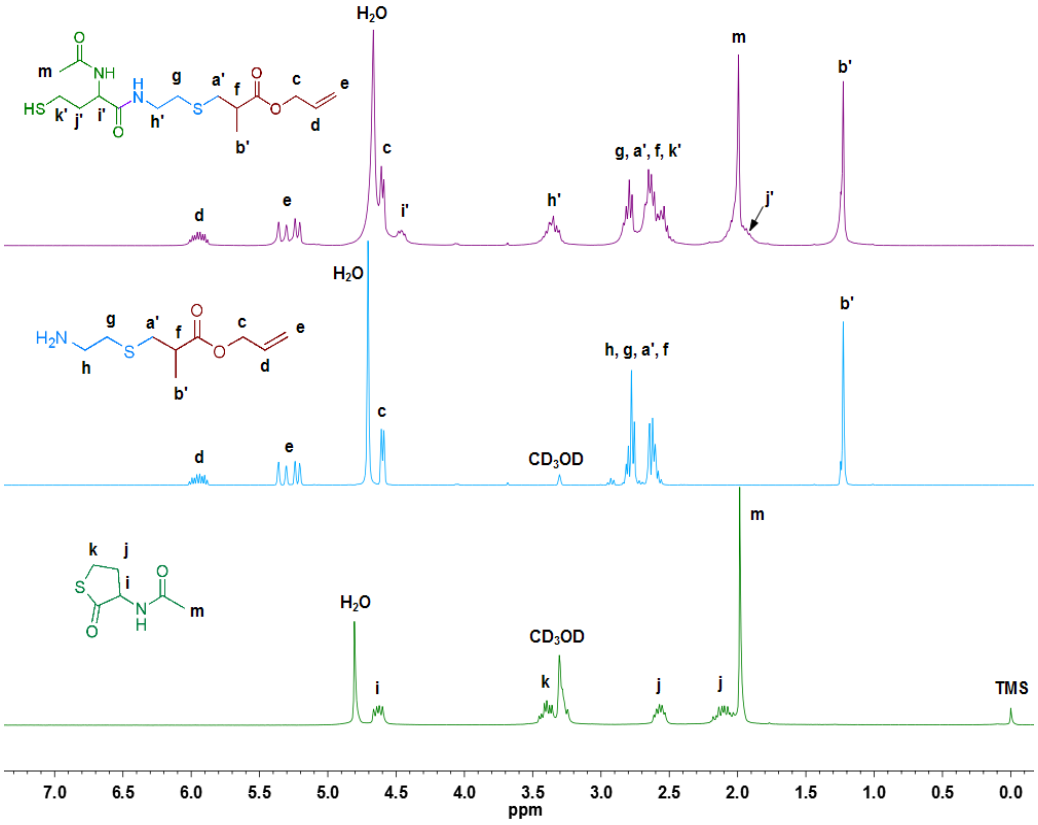


Fig. S5.



^{1}H NMR spectra



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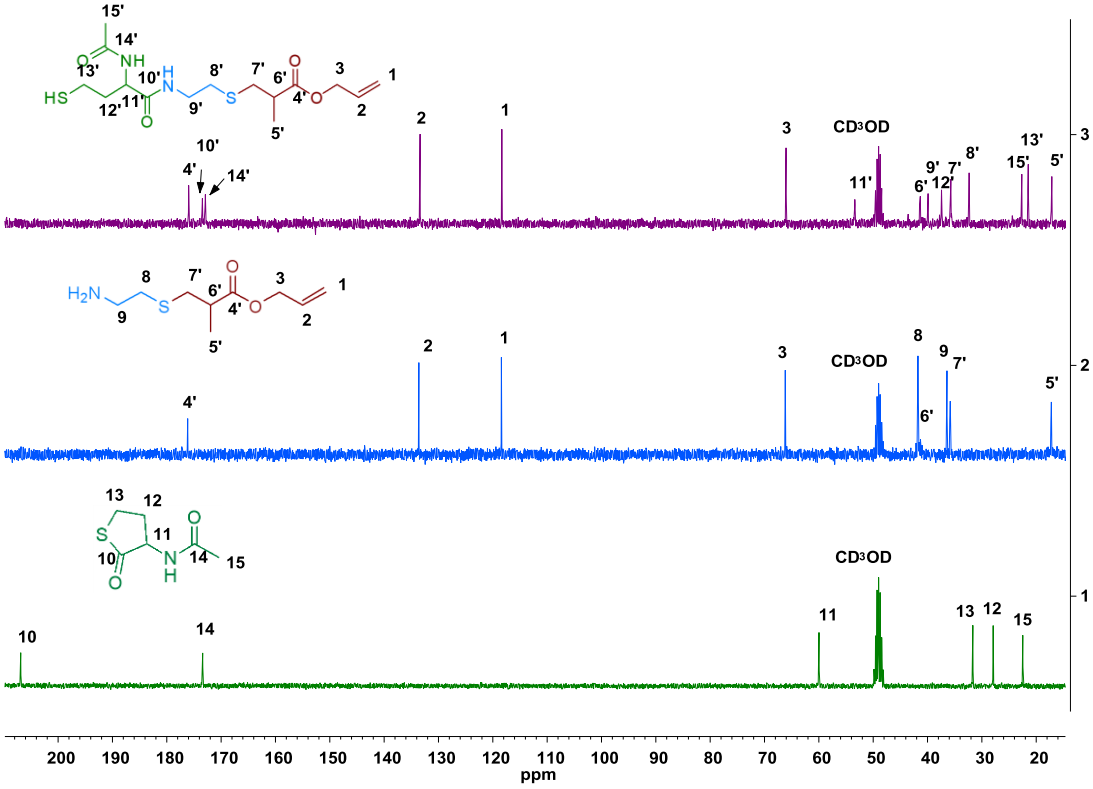

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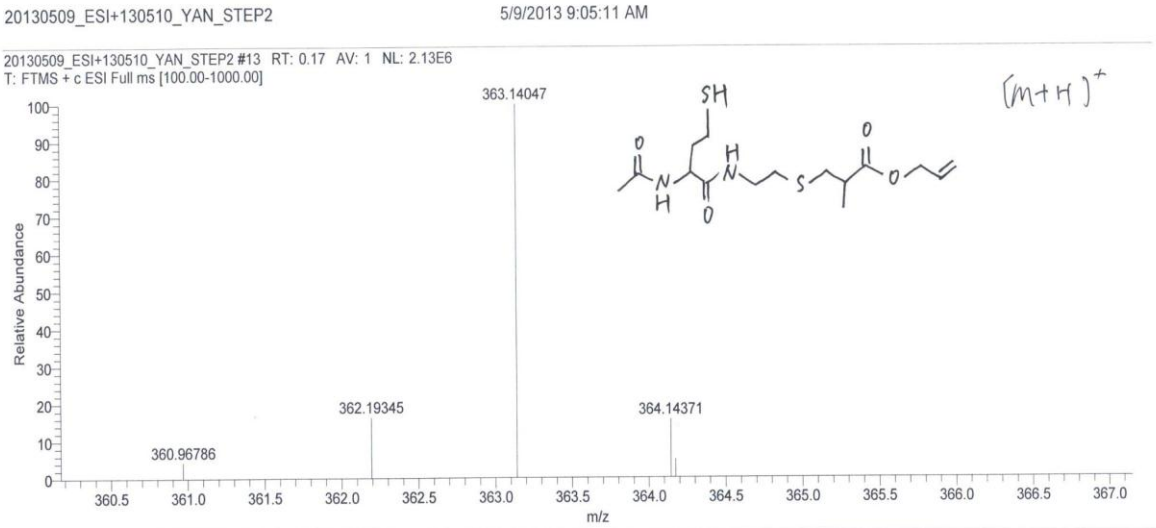

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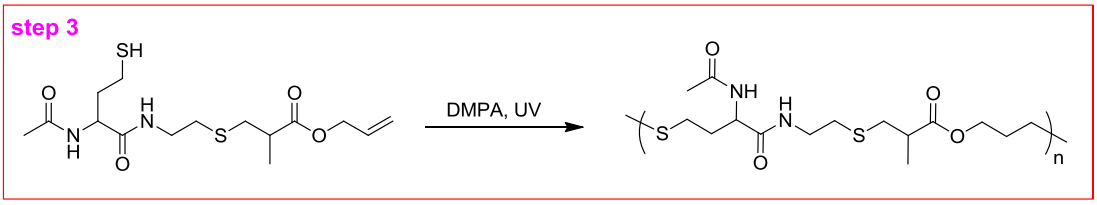
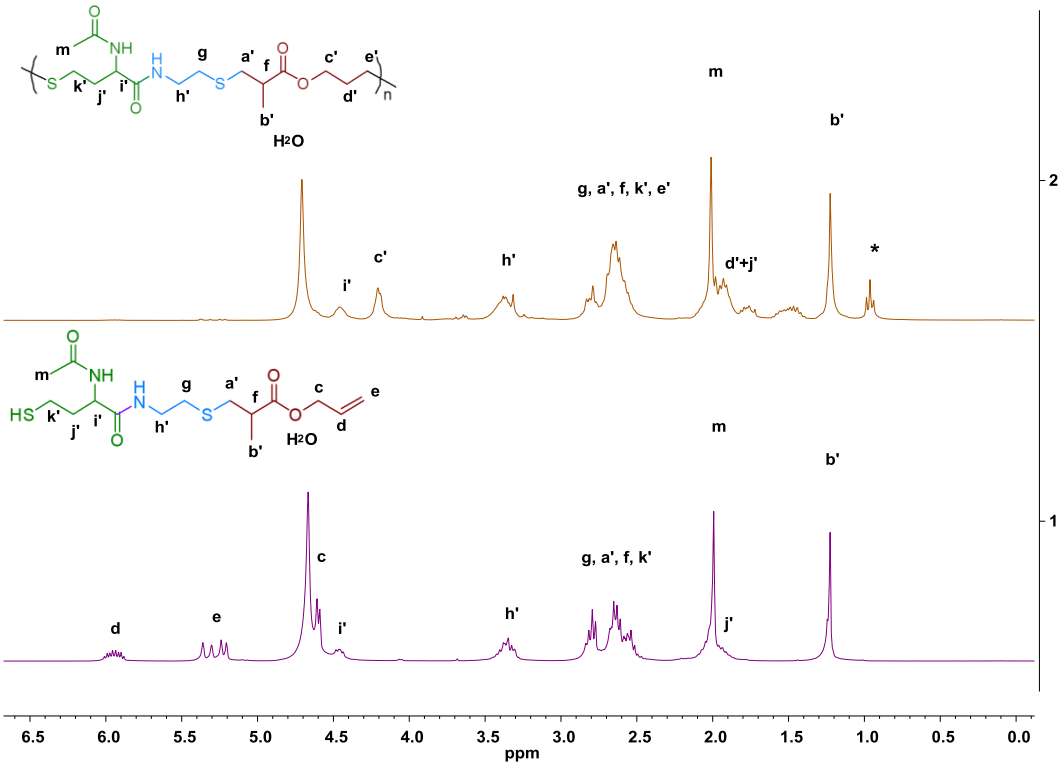
Fig. S6.



^{1}H NMR spectra



^{13}C NMR spectra

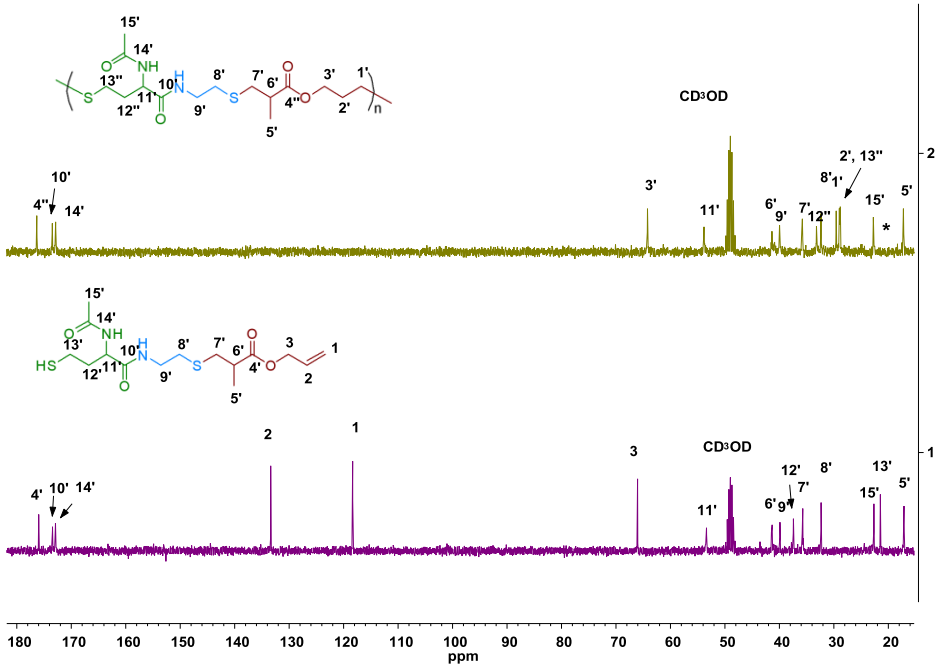
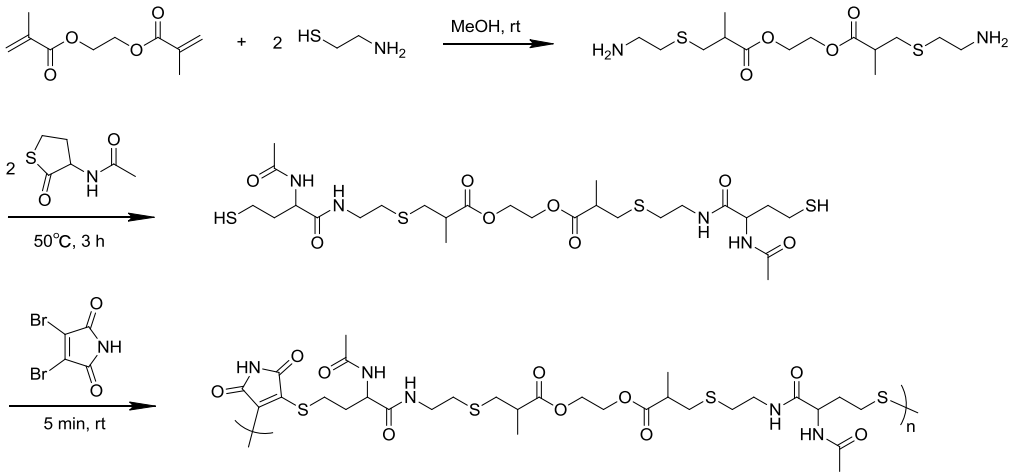


Fig. S7.

5. The preparation of CBABCD sequenced copolymers.



Scheme 2

2-Aminoethanethiol (24.7 mg, 0.320 mmol) and ethylene dimethacrylate (31.7 mg, 0.160 mmol) were dissolved in 1.0 mL methanol under argon atmosphere and stirred at room temperature for 1 h. Then *N*-acethomocysteine thiolactone (50.9 mg, 0.320 mmol) was added and the reaction mixture was left at 50℃ for 3 h. Subsequently, 2,

3-dibromomaleimide (40.8 mg, 0.16 mmol) was added into the reaction mixture, the solution turned into yellow immediately and stirred at room temperature for additional 1 h. The polymer was obtained as white yellow solid by precipitating into diethyl ether. The entire reaction process was monitored by ^{1}H NMR and ^{13}C NMR as shown in Fig. S9-S11.

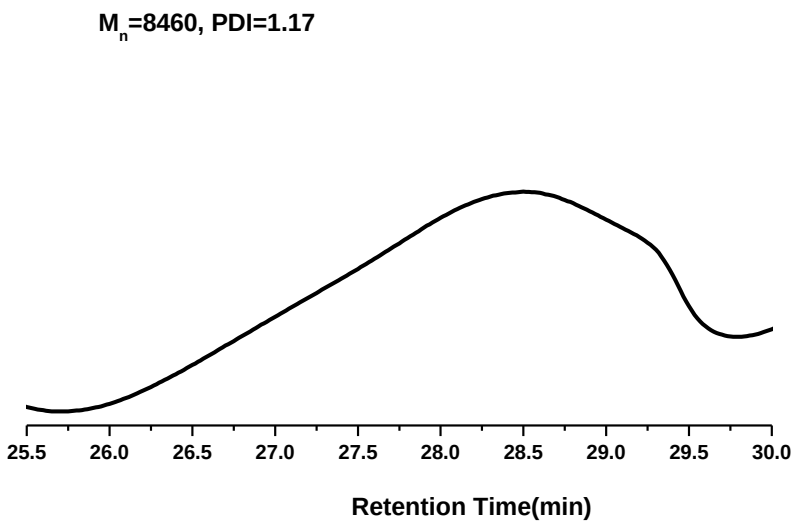
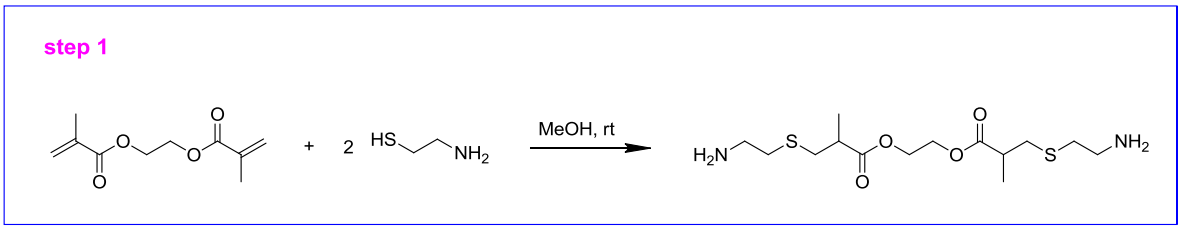
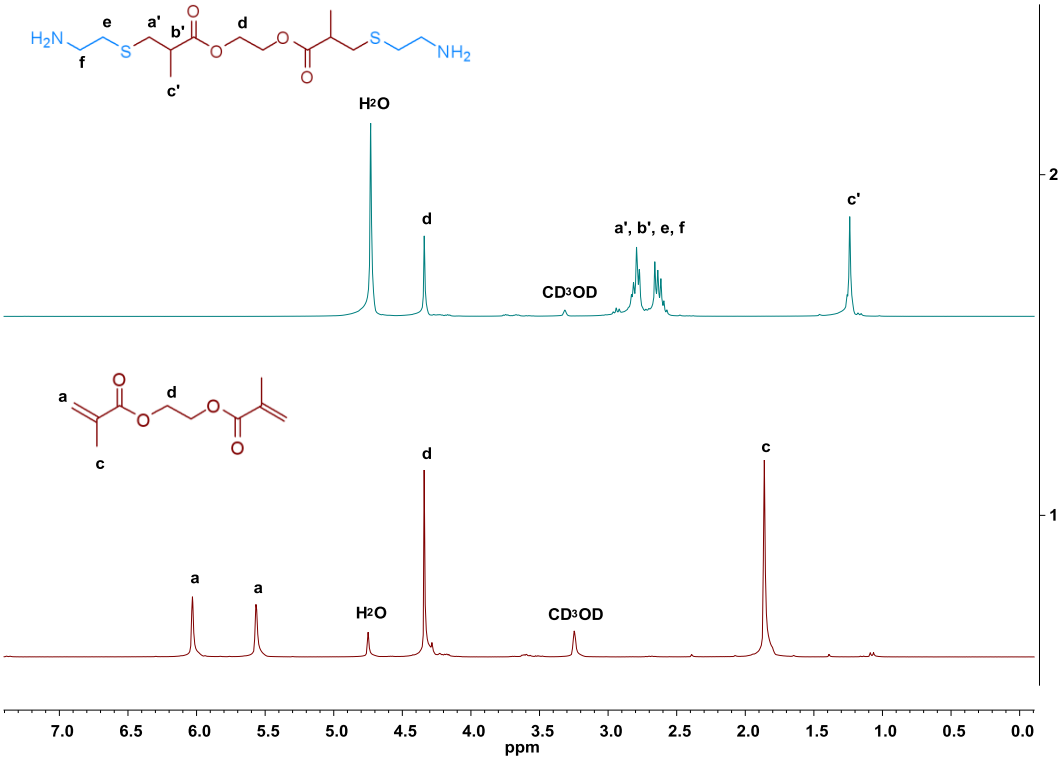


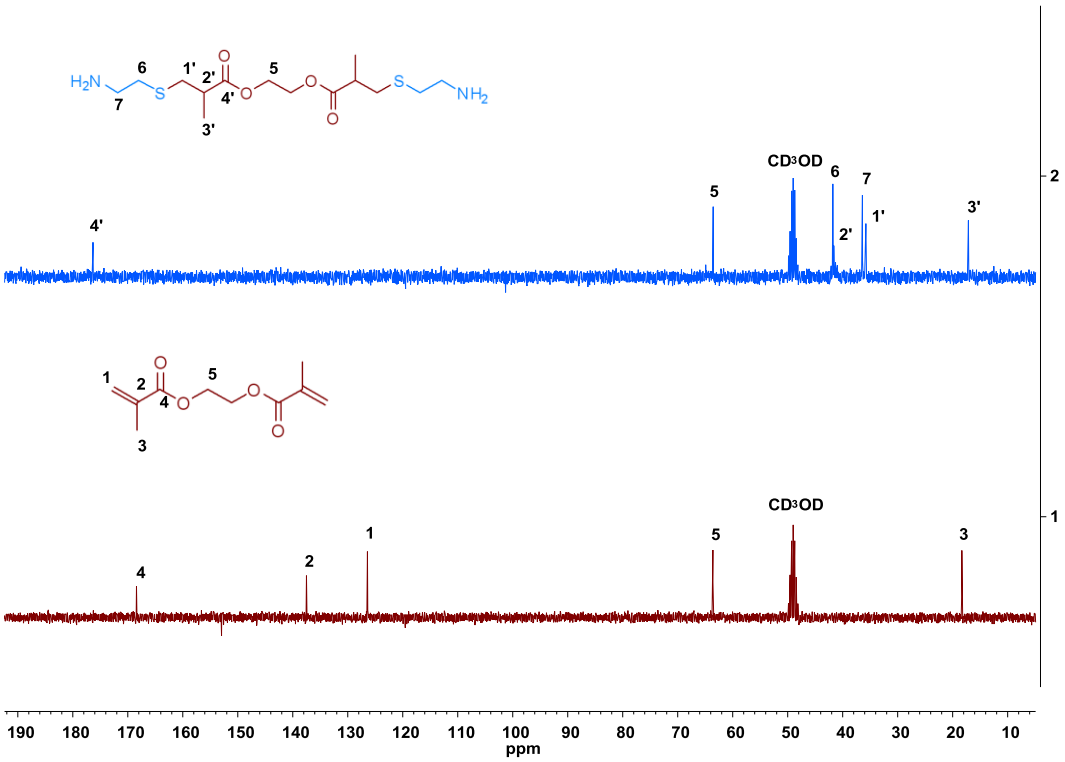
Fig. S.8 GPC curve of CBABCD sequenced copolymer.



^{1}H NMR spectra



^{13}C NMR spectra



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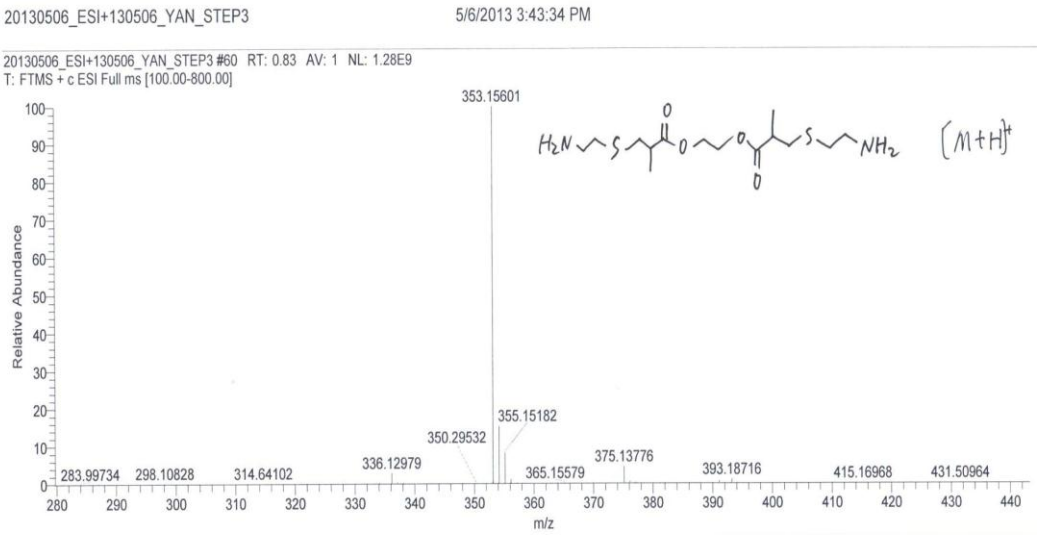

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m/z	Intensity	Relative	Theo. Mass	Delta (mmu)	RDB equiv.	Composition
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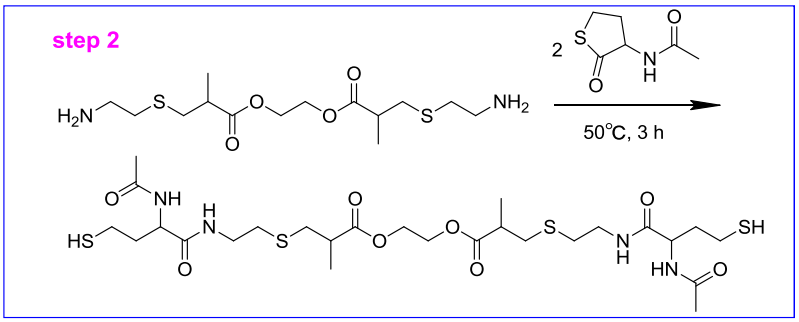
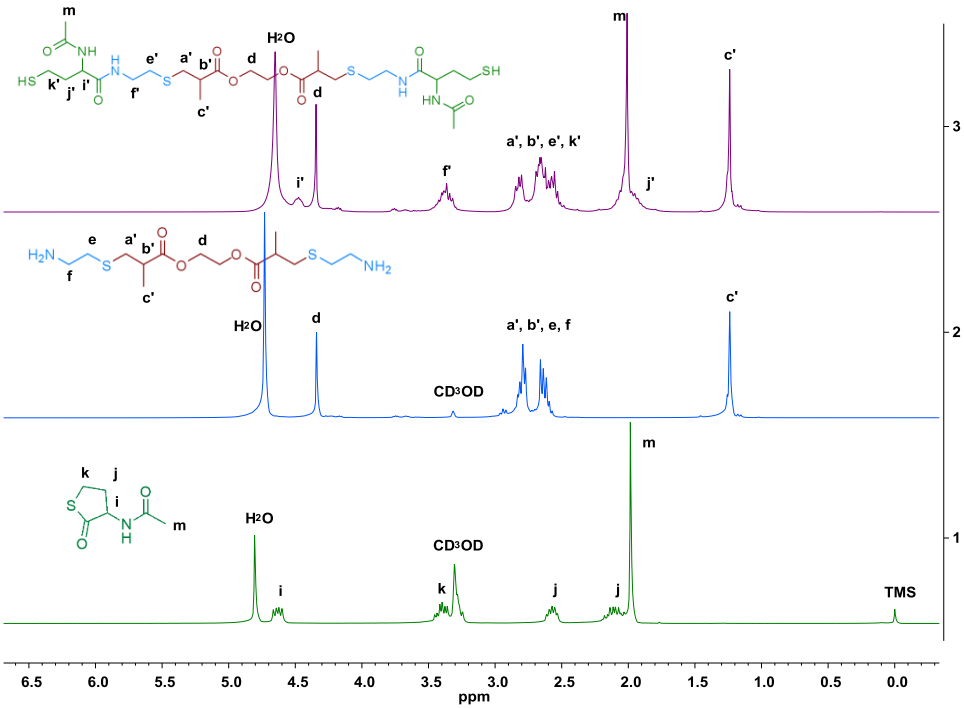
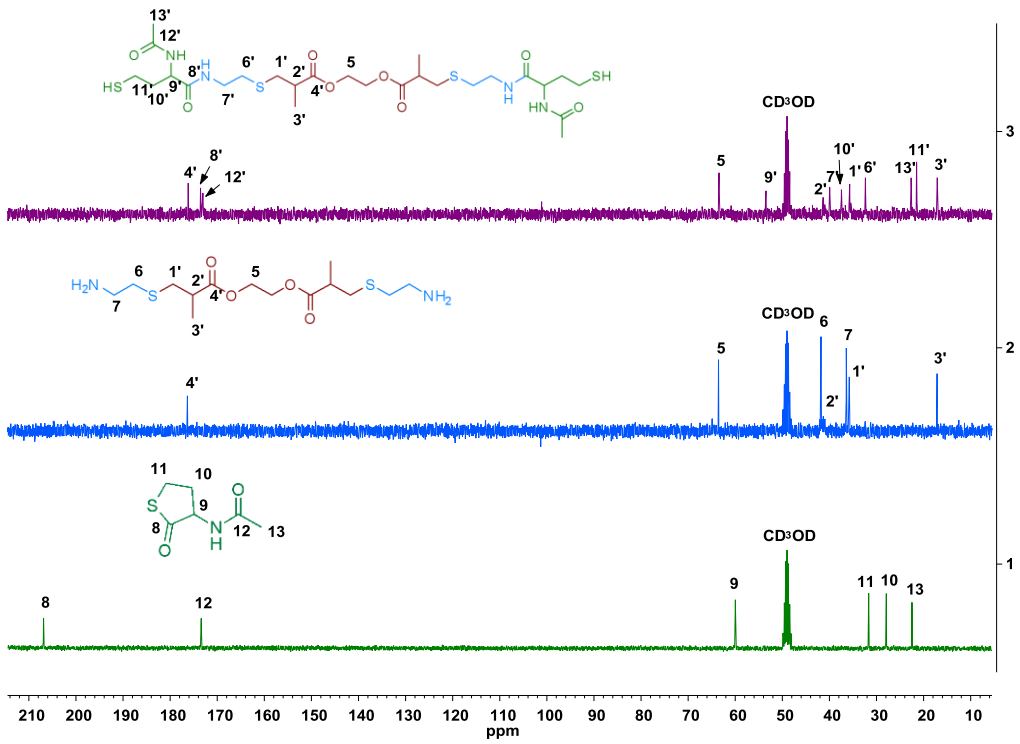
Fig. S9



^{1}H NMR spectra



^{13}C NMR spectra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CD3OD
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ppm

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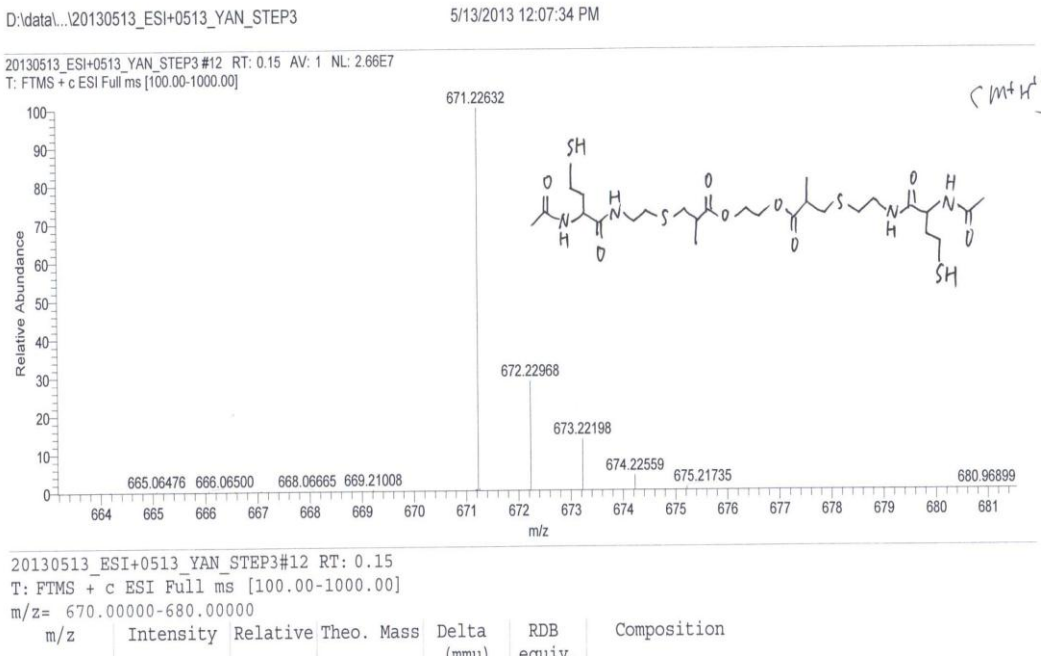
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Relative Abundance
m/z
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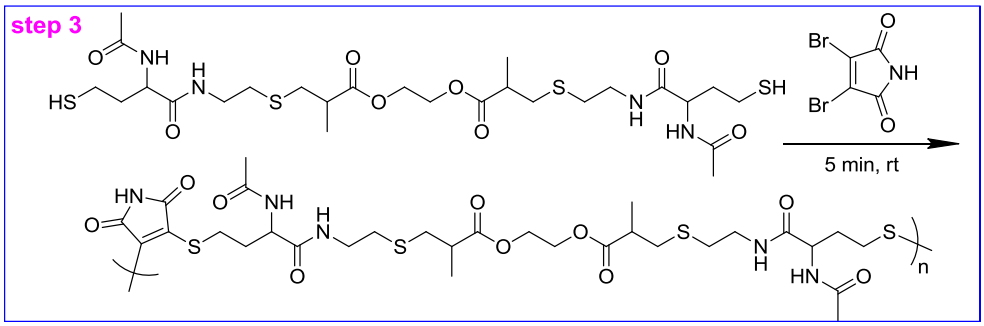
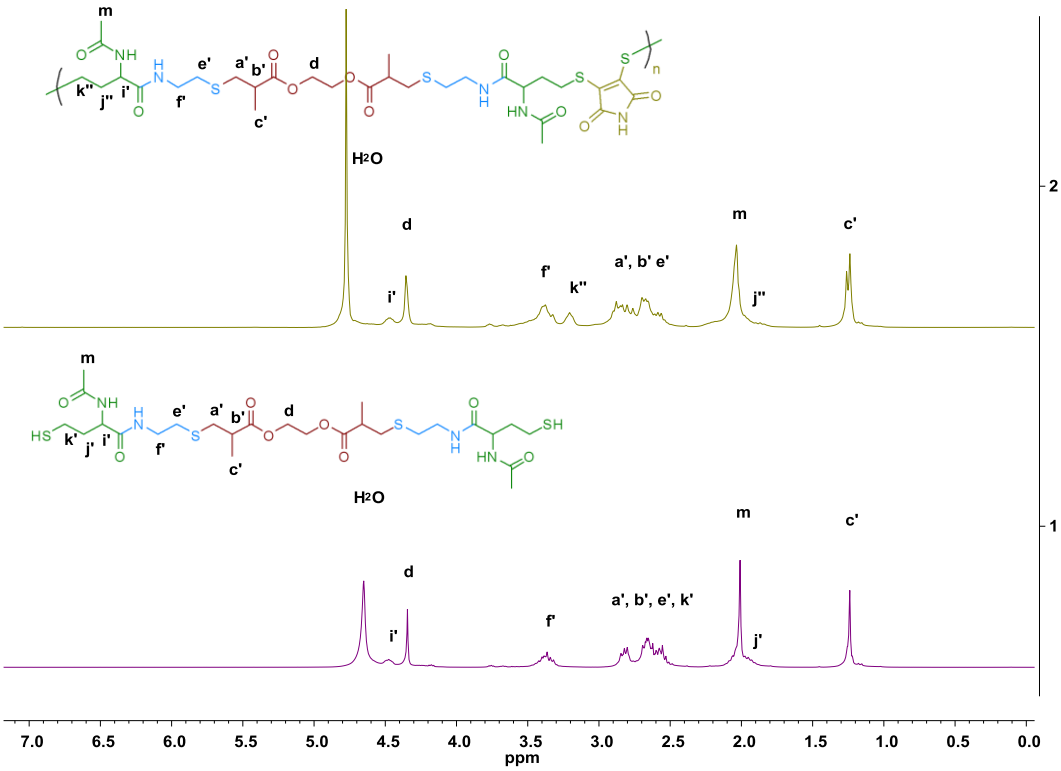
m/z Intensity Relative Theo. Mass Delta RDB Composition

Fig. S10



^{1}H NMR spectra



^{13}C NMR spectra

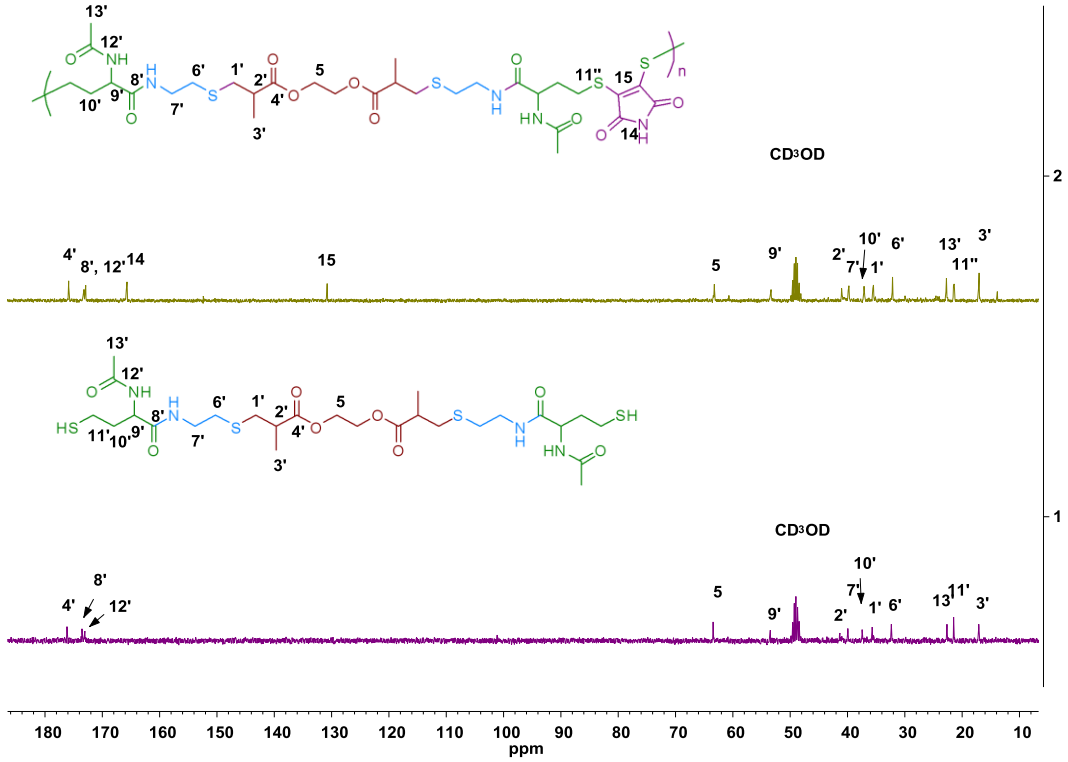
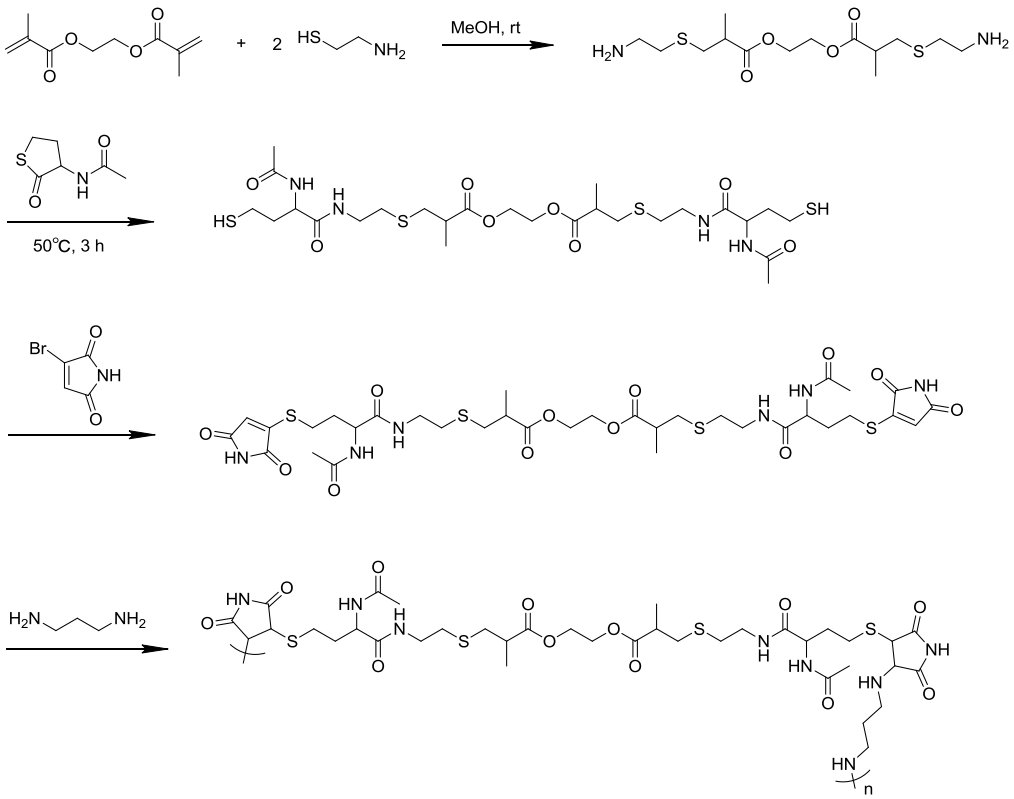


Fig. S11

6. **The preparation of DCBABCDE sequenced copolymers.** 2-Aminoethanethiol (24.5. mg, 0.318 mmol) and ethylene dimethacrylate (31.5 mg, 0.159 mmol) were dissolved in 1.0 mL methanol under argon atmosphere and stirred at room temperature for 1 h. Then *N*-acethomocysteine thiolactone (50.6 mg, 0.318 mmol) was added and the reaction mixture was left at 50℃ for 3 h. Subsequently, 2-bromomaleimide (56.0 mg, 0.318 mmol) was added into the mixture under argon protection, the solution turned into yellow immediately and stirred at room temperature for 30 min. Lastly, 1,3-diaminopropane (11.9 mg, 0.159 mmol) was added to react with the double bonds of maleimide. The final polymer was obtained by precipitating into diethyl ether as white viscous solid. The entire reaction process was monitored by ^{1}H NMR and ^{13}C NMR as shown in Fig.

S13-S16.



Scheme 3

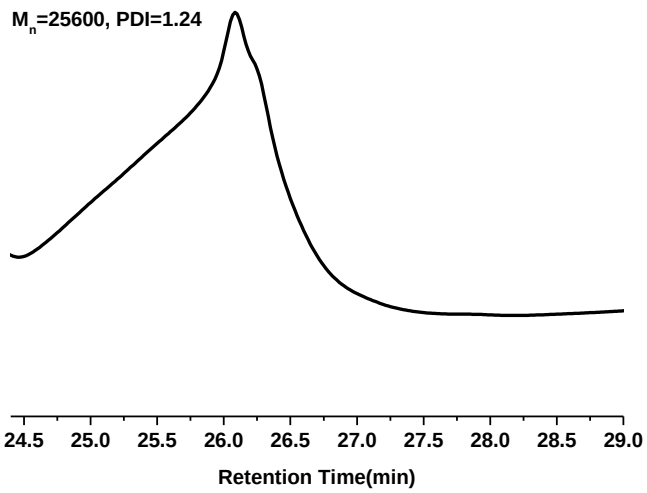
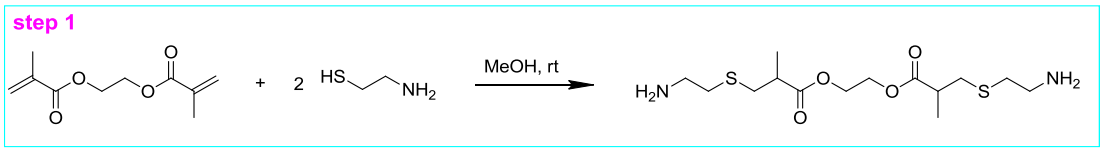
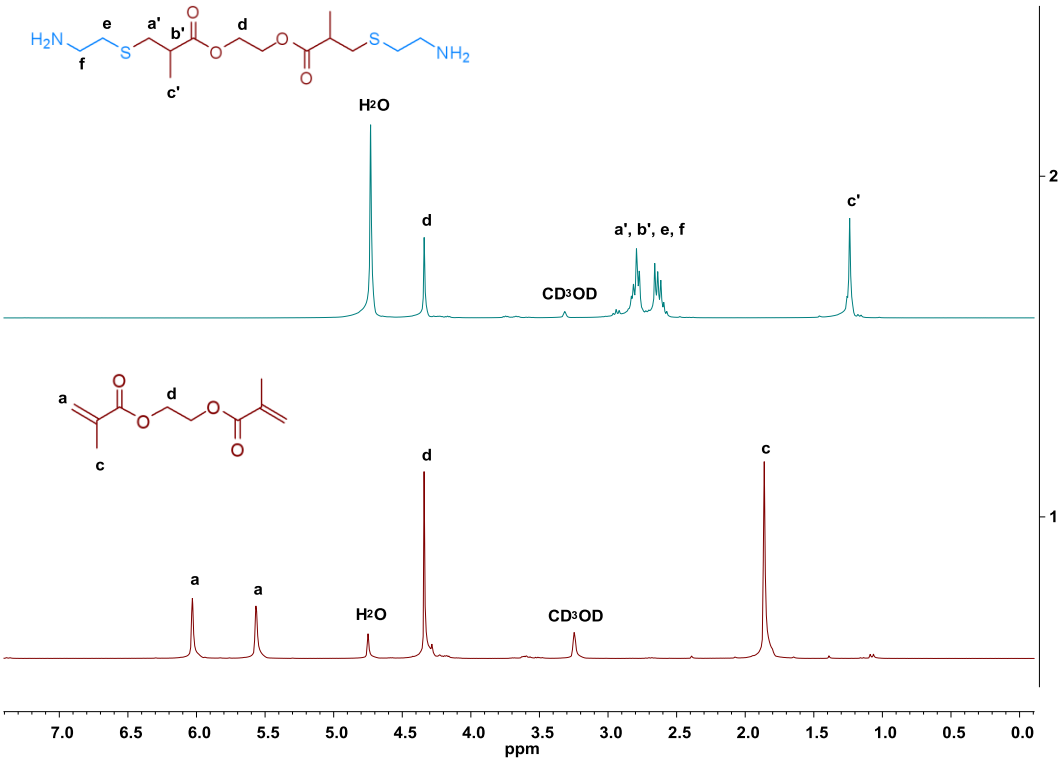


Fig. S.12 GPC curve of DCBABCDE sequenced copolymer.



^{1}H NMR spectra



^{13}C NMR spectra

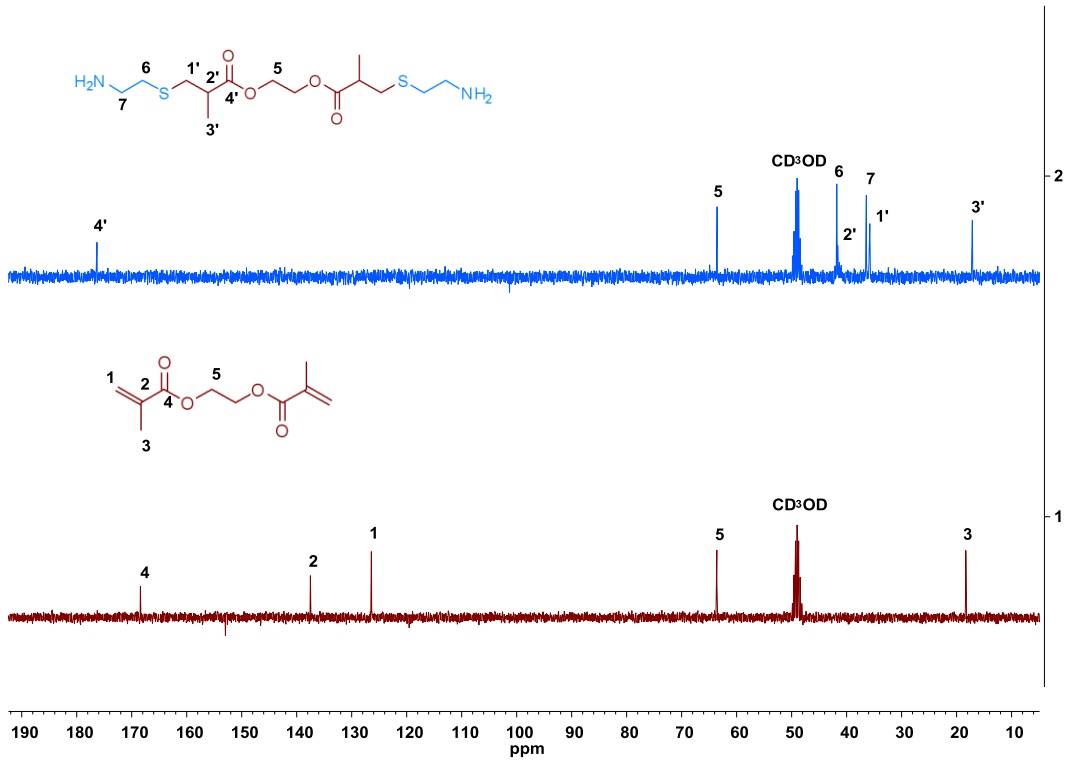
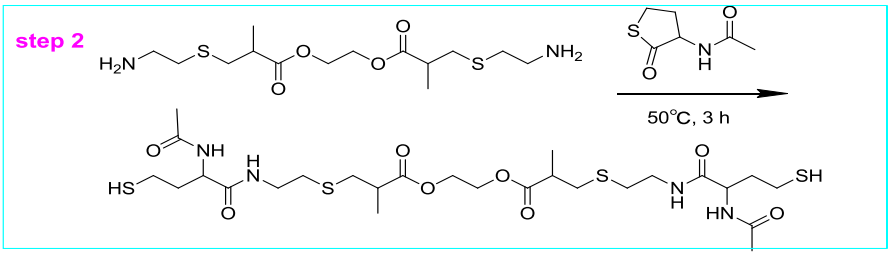
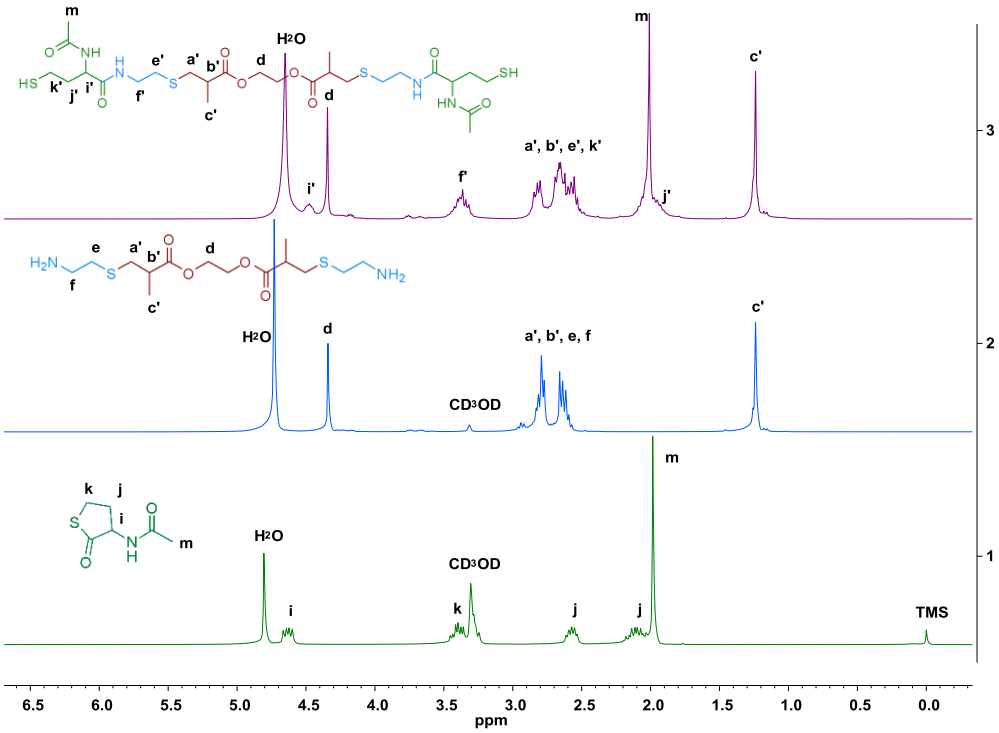


Fig. S13



^{1}H NMR spectra



^{13}C NMR spectra

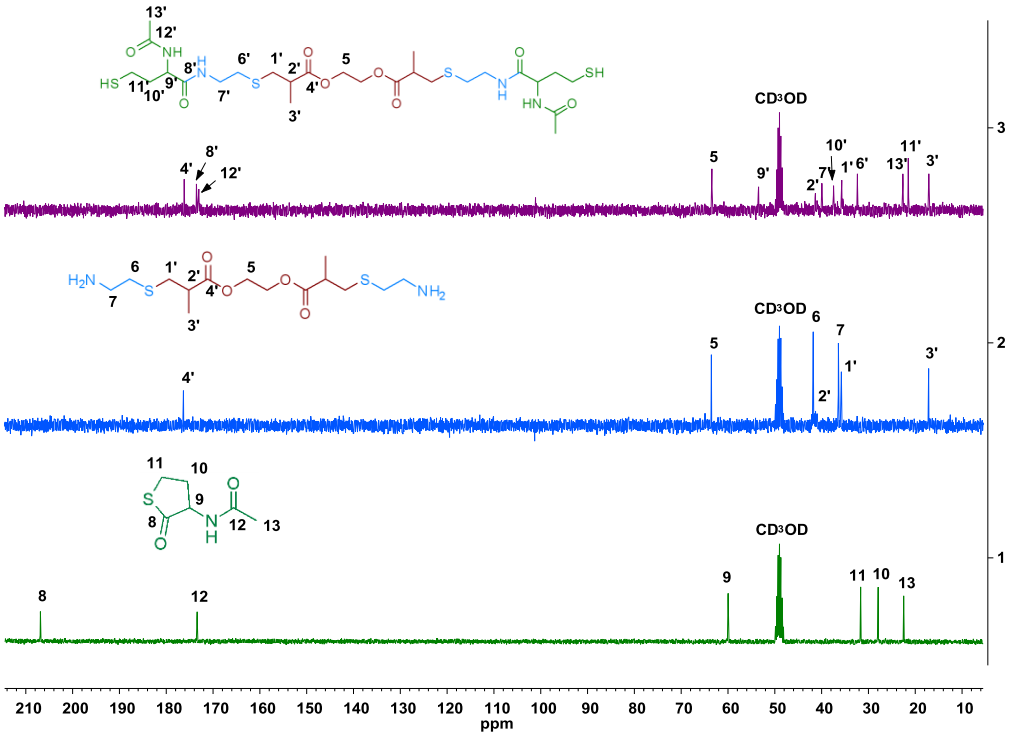
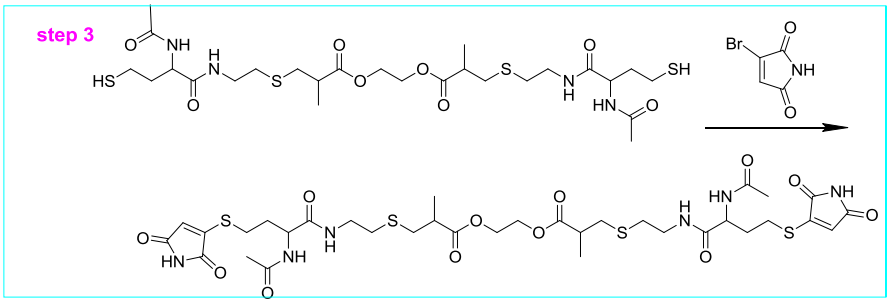
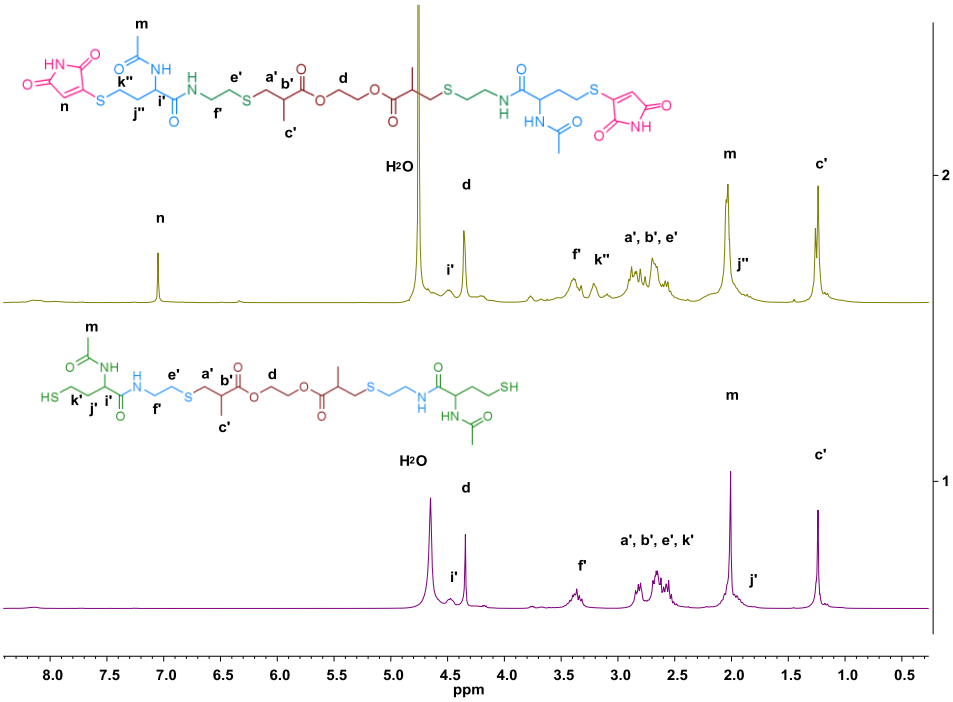


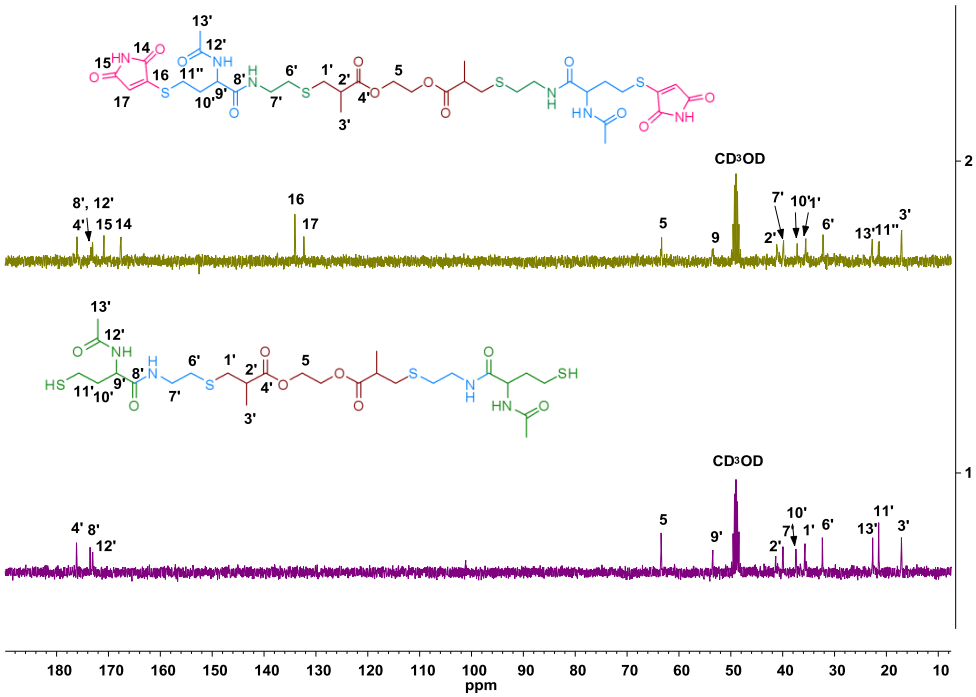
Fig. S14



^{1}H NMR spectra



^{13}C NMR spectra



HR-MS

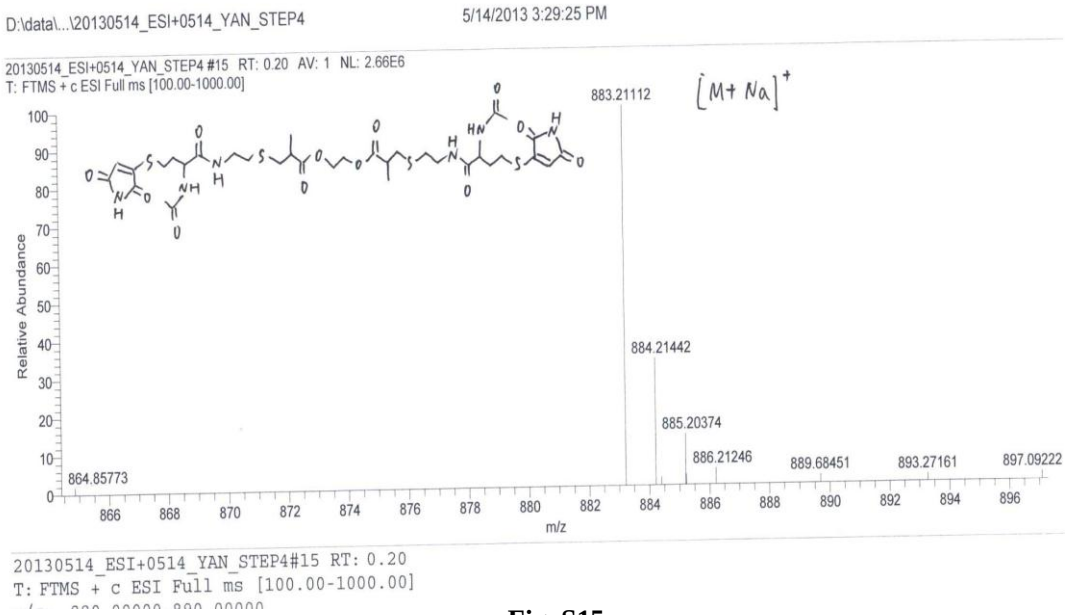
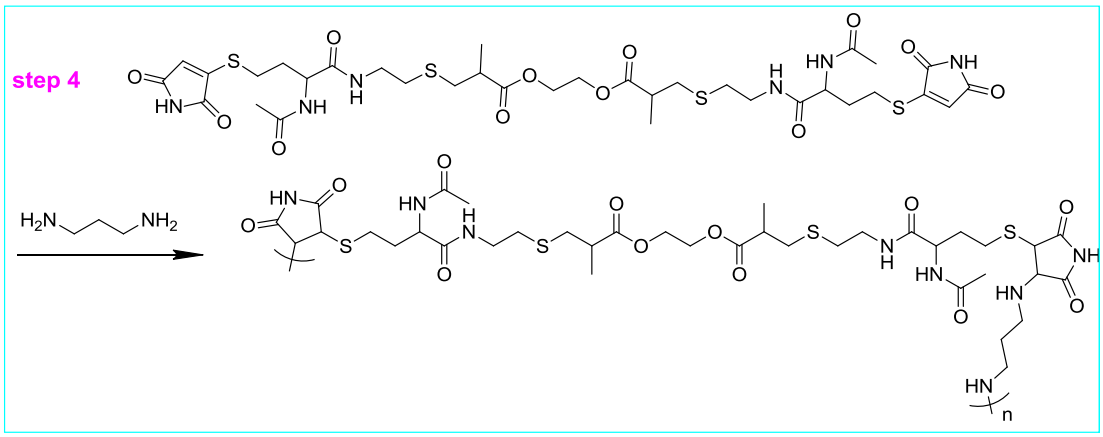
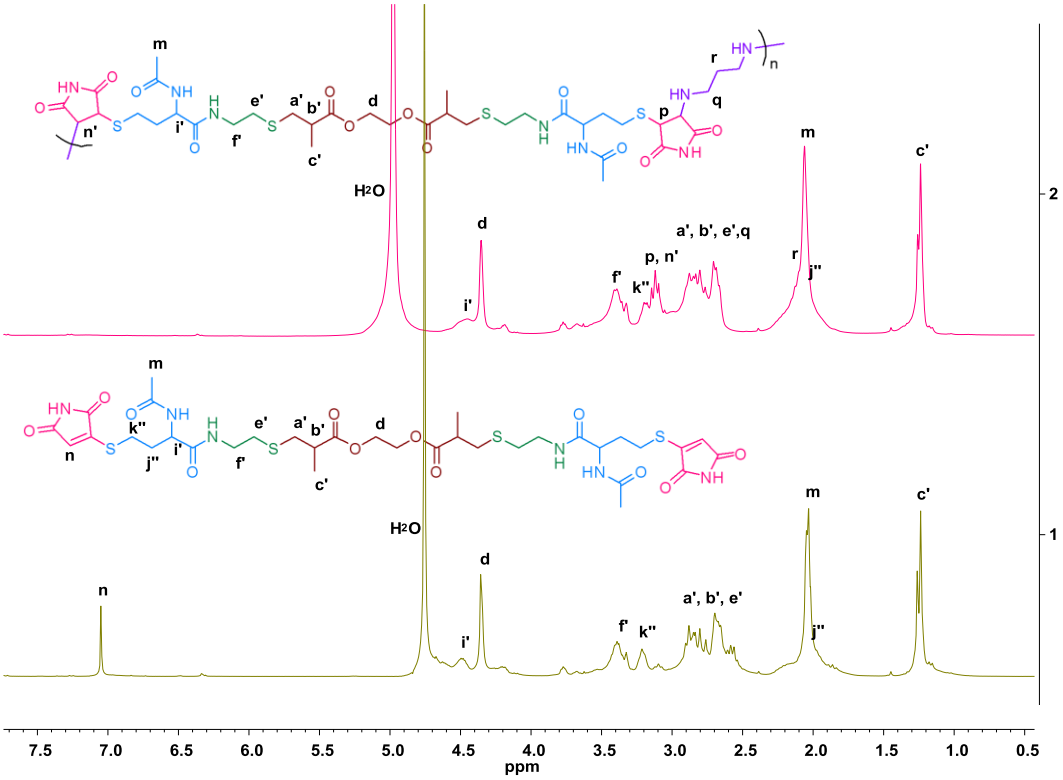
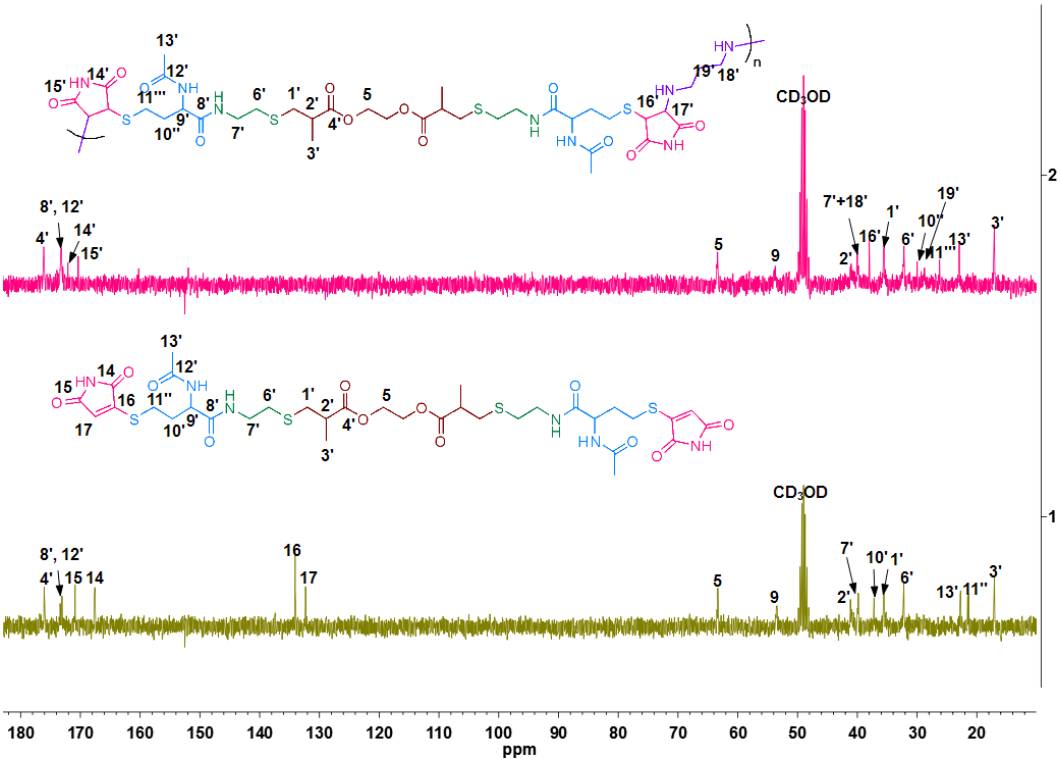


Fig. S15



^{1}H NMR spectra



^{13}C NMR spectra