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Supplementary Information for

Passerini Polymerization of α-Lipoic Acid for Dynamically Crosslinking 1,2-Dithiolane-functionalized Polymers

Yasuyuki Nakamura*†[a], Yi-Shen Huang,†[b] Chih-Feng Huang*[b], and Sadaki Samitsu[a]

[a] *Data-driven Polymer Design Group, Research Center for Macromolecules and Biomaterials, National Institute for Materials Science, 1-2-1 Sengen, Tsukuba, Ibaraki 305-0047, Japan. E-mail: NAKAMURA.Yasuyuki@nims.go.jp*

[b] *Department of Chemical Engineering, i-Center for Advanced Science and Technology (iCAST), National Chung Hsing University, 145 Xingda Road, South District, Taichung 40227, Taiwan. E-mail: HuangCF@dragon.nchu.edu.tw*

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1. General information

Materials. Unless otherwise noted, chemicals obtained from commercial suppliers were used as received. Dichloromethane was dried over molecular sieves. Diisopropylamine was dried over KOH pellet.

Instrumental analyses. ^{1}H (400 MHz) nuclear magnetic resonance (NMR) spectra were measured with JEOL ECS-400 for a $CDCl_3$ solution of sample and are reported in ppm (δ) from internal Me_4Si. Gel permeation chromatography (GPC) was performed with Malvern OMNISEC system equipped with RI detector and polystyrene mixed gel columns at 40 °C using THF as an eluent. The GPC was calibrated with PMMA standards. Infrared (IR) spectra were recorded on JASCO FT/IR-6100 with ATR attachment. Differential scanning calorimetry (DSC) was measured on Shimadzu DSC-60Plus under nitrogen atmosphere. The sample was heated at 150 °C for 10 min to erase thermal history, then cooled down, and the temperature cycle was applied at a rate of 10 °C/min. Thermogravimetric (TG) analysis was performed on Hitachi TG/DTA 7300 under nitrogen stream at a heat rate of 10 °C/min.

Rheological measurement. Rheological measurements were carried out on Anton Paar MCR 302 rheometer equipped with 8 mm parallel plate geometry. The temperature sweep measurements were performed in the linear viscoelastic range with dynamic oscillatory mode wit a frequency of 1 Hz and a temperature changing ratio of 3 °C/min. The stress relaxation measurements were carried out with 3% strain and the evolution of stress was monitored. The relaxation modulus $G(t)$ was normalized by the initial relaxation modulus which is at 1 sec after the application of the strain. The relaxation times constant (τ) were obtained at the time $G(\tau) = G_0/e$.

Lap-shear test. A sandwich-shaped lap-shear test specimen with the adhesion are dimensions of approximately 20 × 15 × 0.05 mm was prepared with 20 × 50 × 1 mm SUS329J4L stainless steel plates which were pretreated via sanding, washing with acetone, and drying with N_2 gas. The lap-shear test of the specimen was measured using an Autograph AG-X (Shimadzu) with a 500 N load cell in the tension mode. The crosshead speed was set at 1 mm/min, and the reported values are the medians of five measurements for each epoxy with a standard error. The nominal shear strength was determined using the following equation: $\tau_{\max} = F_{\max}/A$, where $\tau_{\max}$ is the shear strength (MPa), $F_{\max}$ is the maximum load (N), and A is the adhesion surface area of the sample (mm^2). The accurate value of A measured using the broken specimen after the test was used for the calculation of shear strength.

Loading test (the photo in Figure 5). A sandwich-shaped lap-shear test specimen with the adhesion are dimensions of approximately 20 × 4 × 0.06 mm adhesion area was prepared with 20 × 50 × 1 mm SUS329J4L stainless steel plates which were pretreated as the lap-shear test.

Uniaxial tensile test. A dumbbell-shape specimen of **PA-LA/HA** (1/1) was prepared. The tensile properties were measured using a digital force gauge (IMADA) with a 500 N load cell, at a strain rate of 10 mm/min at approximately 20 °C. A constant Poisson ratio of the cross section and the linear relationship between the displacement and the strain during the measurement were assumed. The force-displacement data were combined with the cross-sectional area of the specimen as it transitioned during the measurement to calculate strain and stress.

2. Synthetic procedures.

1,6-Diisocyanohexane: A mixture of 1,6-hexanediamine (12.4 g, 0.106 mol) and ethyl formate (117 g, 1.6 mol) was reflexed for 18 h with stirring. The resulting suspension was cooled down to room temperature, and the residual ethyl formate was evaporated under reduced pressure. The obtained while powder of *N*,*N*'-(hexamethylene)diformamide was used without further purification. To the crude *N*,*N*'-(hexamethylene)diformamide (18.0 g), diisopropylamine (127 mL, 1.6 mol) and dichloromethane (130 mL) was added and the mixture was cooled with a cold bath at -3 °C under nitrogen atmosphere with stirring. $POCl_3$ (27.5 mL, 0.30 mol) was added dropwise over the period of 3 h with monitoring the temperature of the reaction mixture. The cold bath was removed, and the reaction mixture was stirred for 2 h. Then the mixture was slowly added to a mixture of K_2CO_3 (70 g) and ice water (300 mL), and washed with additional dichloromethane. The organic phase was separated and washed with water two times, dried with Na_2SO_4. The solvent was evaporated under reduced pressure to give a crude product. The purification was carried out with silica-gel column chromatography using ethyl acetate and hexane as the eluents to give the target compound as pale-yellow liquid (9.8 g, 68% yield).

Passerini reaction of α-lipoic acid: To a solution of α-lipoic acid (0.3 g, 1.45 mmol) in $CHCl_3$ (0.5 mL), butanal (0.13 mL, 1.45 mmol) and 1,6-diisocyanohexane (0.99 g, 0.73 mmol) was added. The resulting mixture was heated at 40 °C for 1 h with stirring. The reaction mixture was analyzed by ^1H NMR (Figure S1).

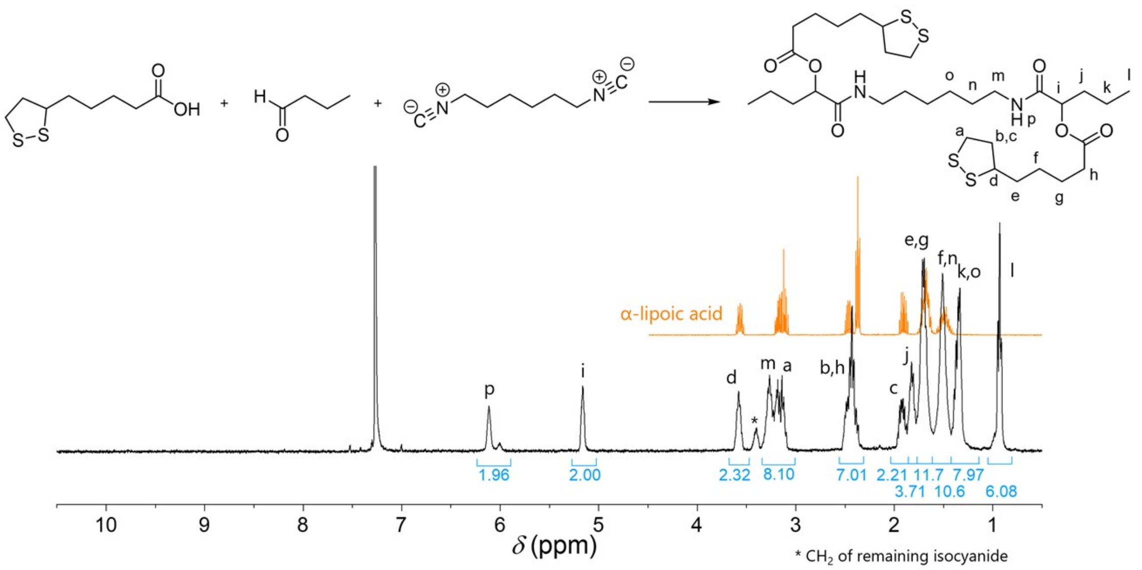


Figure S1. Synthetic scheme and ^1H NMR spectrum of the crude product of the reaction of α-lipoic acid, butanal and 1,6-diisocyanohexane. The chemical shifts of the signals assigned to 1,2-dithiolane group in the product was nicely overlapped with those of α-lipoic acid, which indicated the retention of 1,2-dithiolane structure under the Passerini reaction conditions.

Passerini polymerization of α-lipoic acid, a general procedure: To a solution of α-lipoic acid (2.73 g, 13 mmol) in THF (4.6 mL), glutaraldehyde (5.6 M solution in water, 1.07 mL, 6 mmol) and 1,6-diisocyanohexane (0.816 g, 6 mmol) was added. The resulting mixture was heated at 40 °C for 20 h with stirring. During the heating, the aliquot of the reaction mixture was taken to analyze the progress with ^{1}H NMR and GPC. The reaction mixture was diluted with THF (15 mL), and poured dropwise into vigorously stirred diethyl ether. The precipitate was collected by suction filtration, and dried under reduced pressure to give the target polymer (2.91 g, 75% yield). The molecular weight was analyzed by GPC (Mn = 6590, $Đ$ = 1.95).

The detail of each polymer synthesis was summarized in Table S1 below. After about 24 h, the progress of the polymerization monitored by GPC analysis was slow and the extended time has no significant effects on the polymer molecular weight and the yield. On the other hand, excessive extension of reaction time resulted in gelation of the reaction mixture making reaction monitoring difficult.

Table S1. The detail of the synthesis of PA-LA and PA-LA/HA. The entry (run) numbers in this table are the same as those in Table 1 in the main text.[a]

Run	Carboxylic acid[b]	Solvent	[Carboxylic acid] (M)[c]	Time (h)	Conversion: CHO, NC (%)[d]	Yield (%)	M_n[e]	$Đ$[e]
1	LA	THF	2.0	20	97, 100	75	6590	1.95
2	LA	THF[f]	1.0	40	88, 100	66	2980	2.29
3	LA	THF	2.5	20	98, 100	80	8740	2.01
4	LA	$CHCl_3$	2.0	20	-[f]	-	-	-
5	LA/HA (1/1)	THF	2.0	24	99, 100	75	8860	1.98
6	LA/HA (1/2)	THF	2.0	48	98, 100	72	8750	2.02
7	LA/HA (1/4)	THF	2.0	48	98, 100	77	8920	2.00
8[g]	LA/HA (1/1)	THF	2.0	20	99, 100	74	6980	1.85

[a] [Carboxylic acid]:[glutaraldehyde]:[1,6-diisocyanohexane]=2.2:1:1. [b] Molar ratio is given for LA and HA mixture. [c] Concentration of the sum of LA and HA. [d] Conversions of aldehyde and isocyanide groups calculated by the ^{1}H NMR signal intensity of CHO in the starting dialdehyde. [e] Calculated against PMMA standards. [f] The reaction mixture became a gel during the reaction. [g] The product of this entry was used in the decrosslinking experiment.

3. Instrumental analysis

3.1 IR

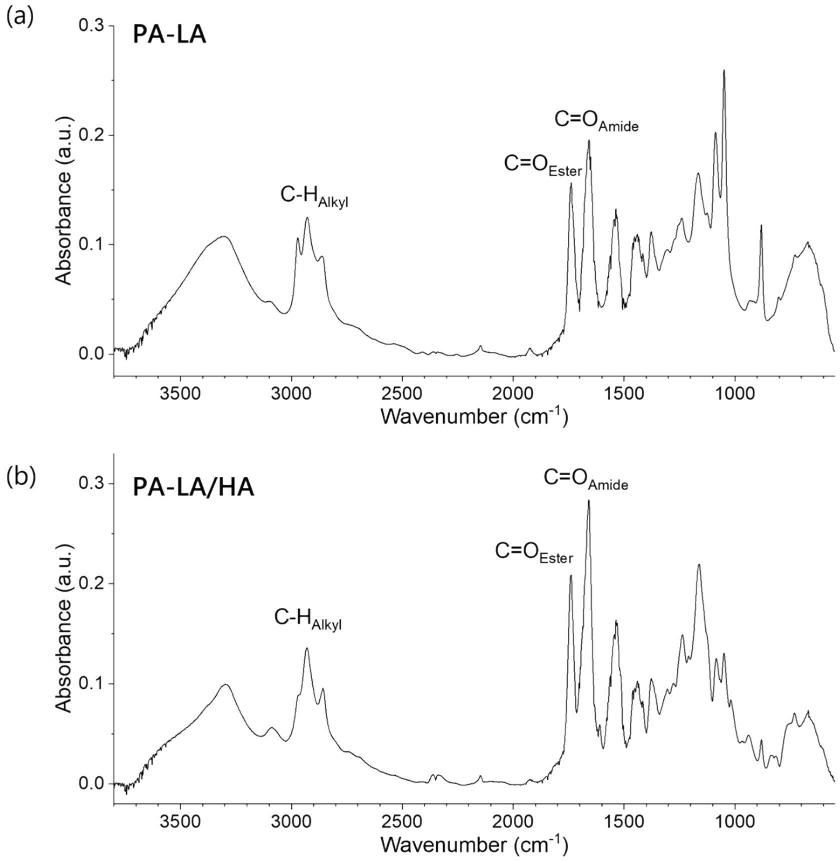


Figure S2. ATR-IR spectra of (a) **PA-LA** (Table 1, run 1) and (b) **PA-LA/HA** (1/1) (Table 1, run 5).

3.2 NMR

NMR spectral analysis of **PA-LA** (Figure 2) and **PA-LA/HA** (Figure S2) showed aldehyde proton signal with a slightly different chemical shift from that of the starting aldehyde (glutaraldehyde), and thus which was assigned to the polymer chain end aldehyde group. On the other hand, no signal was observed for α-CH_2 of isocyanide group. A control experiment confirmed that isocyanide group retains in this reaction condition if the reactants are absent. From these results, it was indicated that the chain end structure of the polymer is an aldehyde group derived from glutaraldehyde. For more solid experimental evidence, MALDI-TOF-MS analysis was performed for these polymers, however, it was difficult to obtain a spectrum that allowed structural identification.

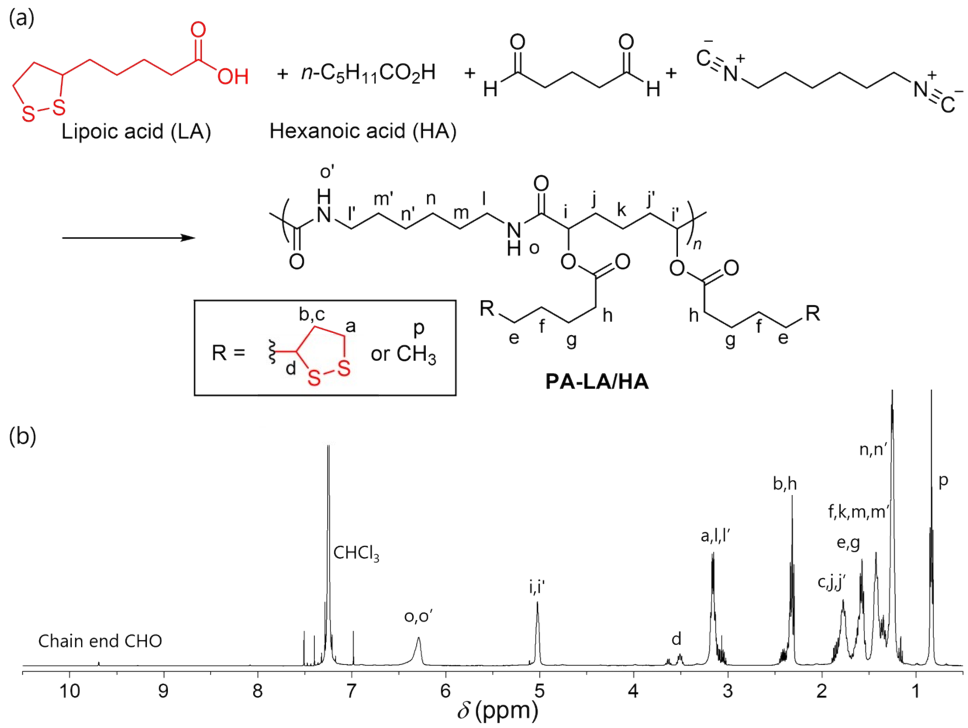
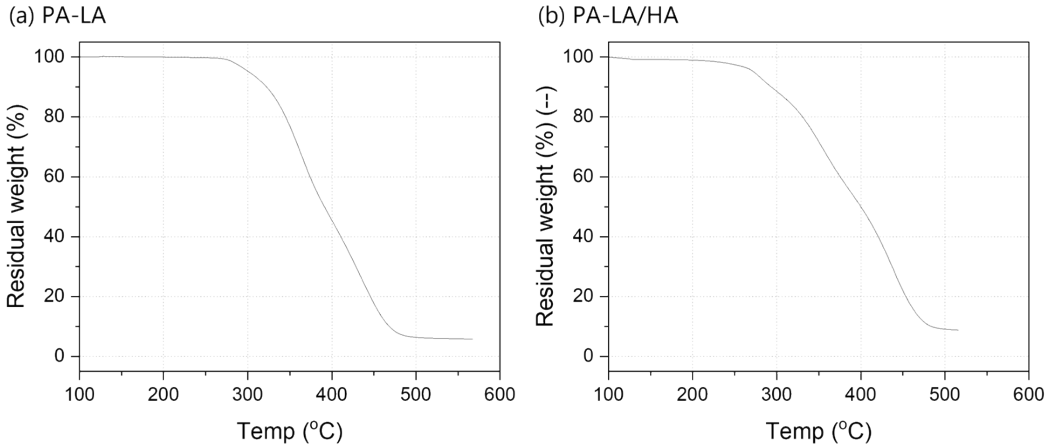


Figure S3. Synthetic scheme (a) and ^{1}H NMR spectrum of **PA-LA/HA** (1/2) (b). The data of the polymer in Table 1 run 6 is shown.

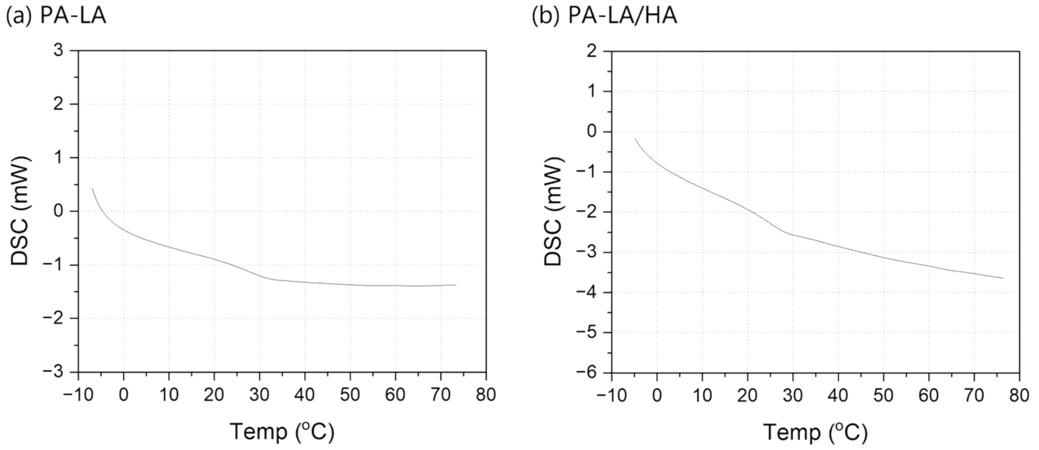
3.3 TG



	PA-LA	**PA-LA/HA**
$T_{\mathrm{deg},5\%}$ (°C)	302	278
$T_{\mathrm{deg},10\%}$ (°C)	322	295

Figure S4. TG analysis profiles of (a) **PA-LA** (Table 1, run 1) and (b) **PA-LA/HA** (1/1) (Table 1, run 5).

3.4 DSC



	PA-LA	**PA-LA/HA**
T_g (°C)	29	24

Figure S5. DSC profiles of (a) **PA-LA** (Table 1, run 1) and (b) **PA-LA/HA** (1/1) (Table 1, run 5).

3.5 Rheology measurements

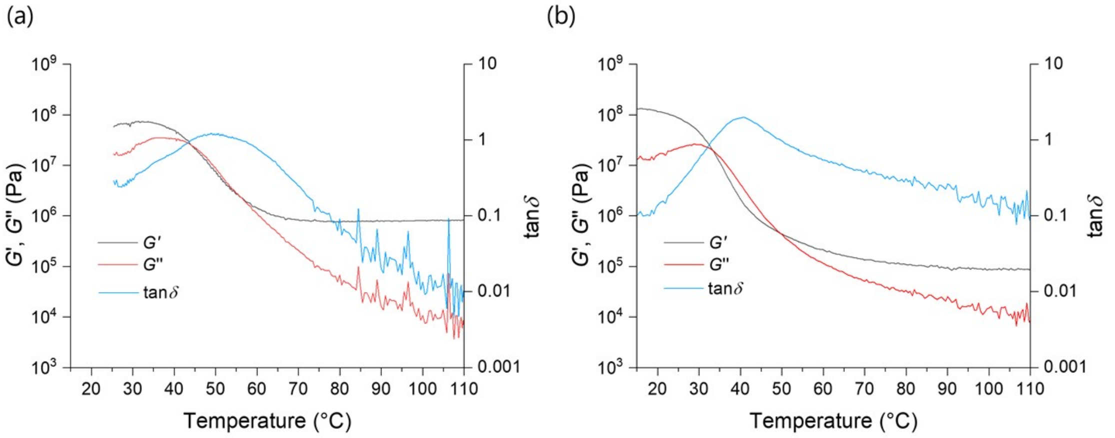


Figure S6. Rheological analysis of the crosslinked **PA-LA** (Table 1, run 1) and **PA-LA/HA** (1/1) (Table 1, run 5) with temperature-sweep.

The difference in crosslink density calculated from these measurements (8 folds) appears to be greater than the difference in the number of 1,2-dithiolane groups in **PA-LA** and **PA-LA/HA** (2 folds). Considering that the 1,2-dithiolane undergoes a concentration-induced crosslinking, the propensity for crosslinking density might be dependent on the density of 1,2-dithiolane groups in polymer chain.

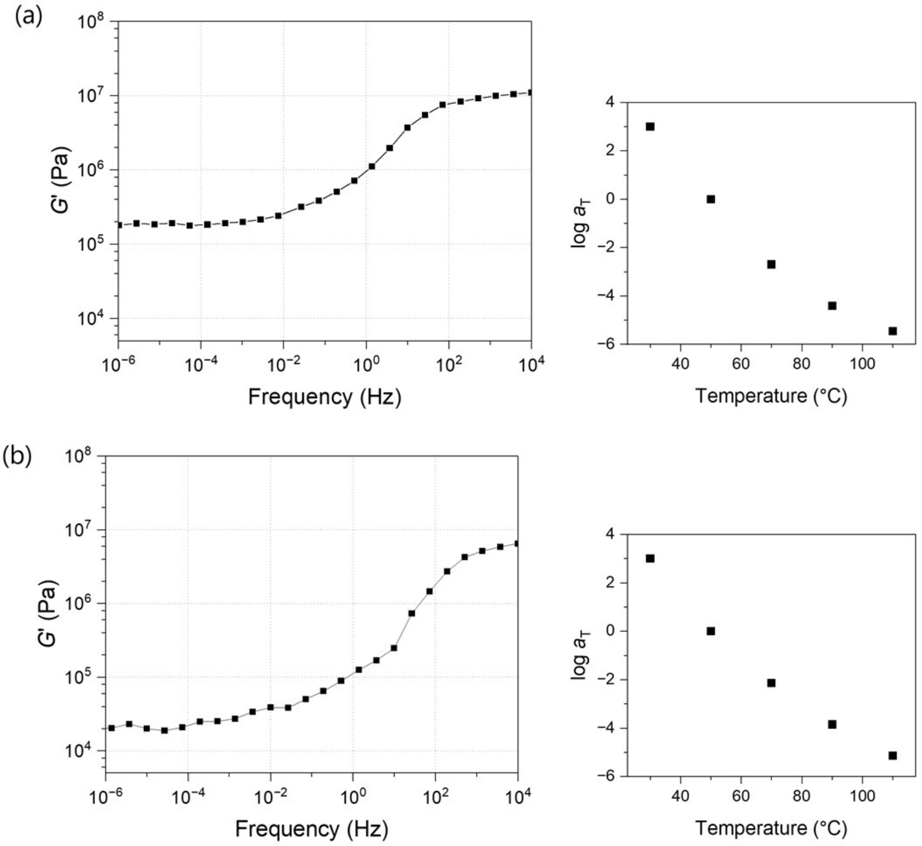


Figure S7. Master curves of the crosslinked **PA-LA** (Table 1, run 1) and **PA-LA/HA** (1/1) (Table 1, run 5).

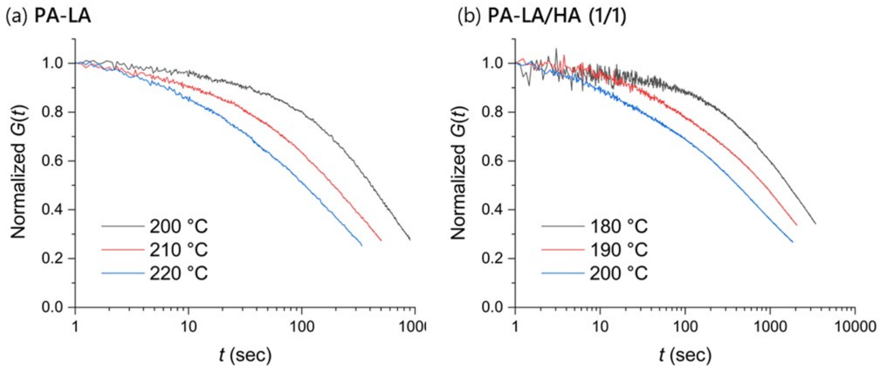


Figure S8. Stress relaxation measurements for **PA-LA(/HA)** samples.

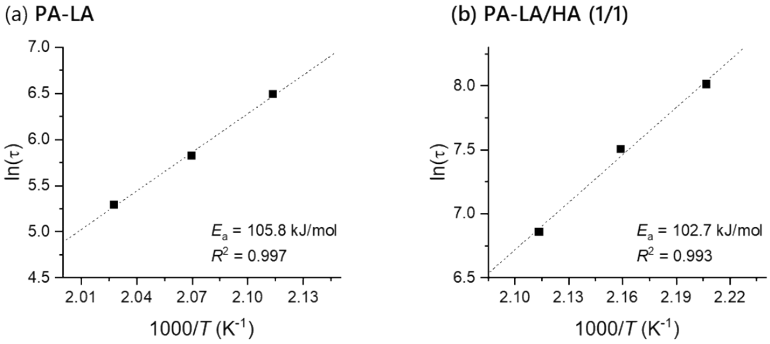


Figure S9. Relaxation time (τ) – $1/T$ plot for **PA-LA(/HA)** samples.

4. Uniaxial tensile test (Preliminary result)

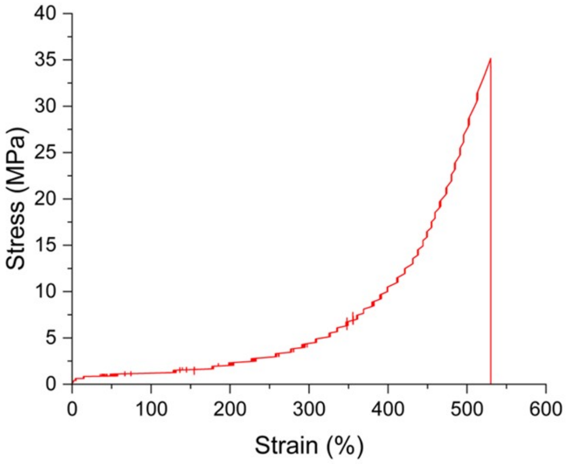


Figure S10. Stress-strain curve for PA-LA/HA (1/1) sample (Table 1, run 5). The staircase-like curve is due to the resolution limitation of our force gauge. In our preliminary experiments, the strain and the stress of the break was 529% and 35.2 MPa. PA-LA/HA does not have a rubbery character, while has elastomeric properties. The observed stress increasing with the strain might indicate the potential mechanism such as inter-chain interaction or crystallization associated with the sample stretching.

5. Self-healing test (Preliminary results)

A **PA-LA/HA** (1/1) specimen with the dimension of approximately 20 × 8 × 1 mm was prepared by molding under heat and pressure. After pulling and bending the specimen with tweezers, the specimen was cut into two pieces, contacted at the cut surface, and heated at 135 °C for 15 minutes. The resulting specimen were checked for healing by pulling and bending (Figure S8).

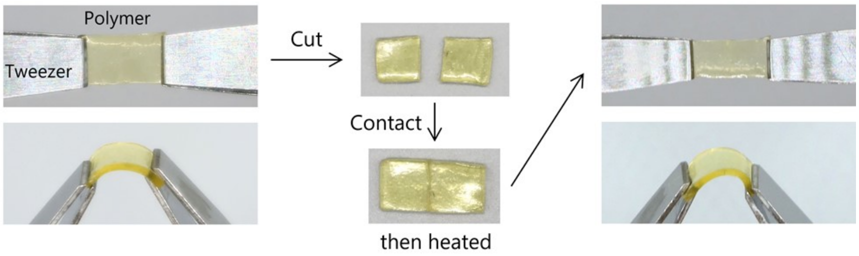


Figure S11. Self-healing test of **PA-LA/HA** (1/1) sample.

6. Decrosslinking experiment

Decrosslinking of a crosslinked PA-LA, a general procedure: A crosslinked PA-LA (50 mg, the amount of S-S moiety was 3.3×10^{-4} mol) was added $CHCl_3$ (1 mL), benzyl thiol (1.0×10^{-5} mol, a 0.3 M $CHCl_3$ stock solution was used) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.0×10^{-5} mol, a 0.3 M $CHCl_3$ stock solution was used). The mixture was heated at 40 °C for 3 h with stirring. The solution of decrosslinked **PA-LA** was analyzed by GPC.

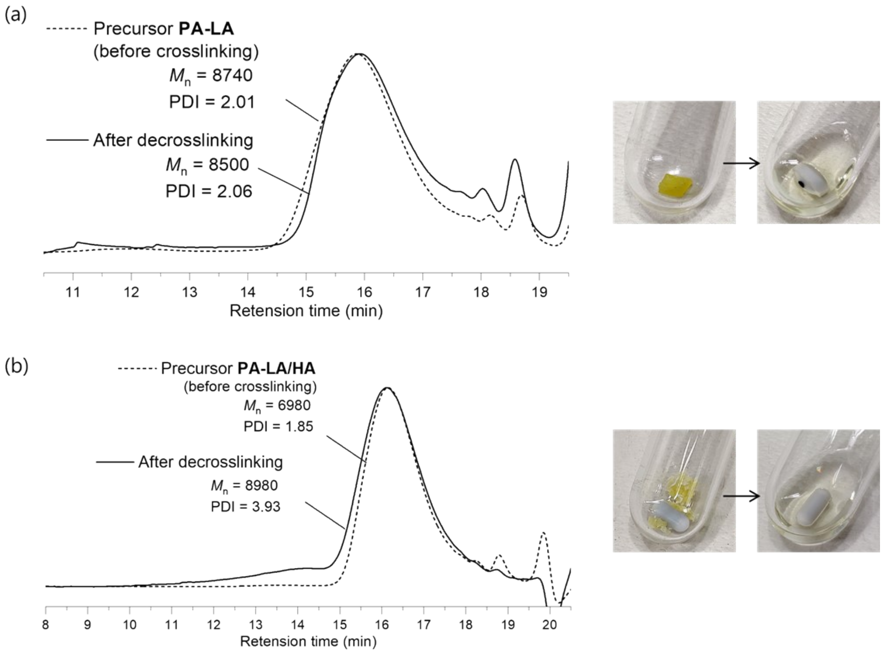


Figure S12. GPC profiles in the decrosslinking of (a) **PA-LA** (Table 1, run 3) and (b) **PA-LA/HA** (1/1) (Table S1, run 8). There was a high molecular weight components that are estimated to be linked multiple polymer chains in the decrosslinking reaction of crosslinked **PA-LA/HA**. The GPC traces of precursors were measured at the time of polymer synthesis.