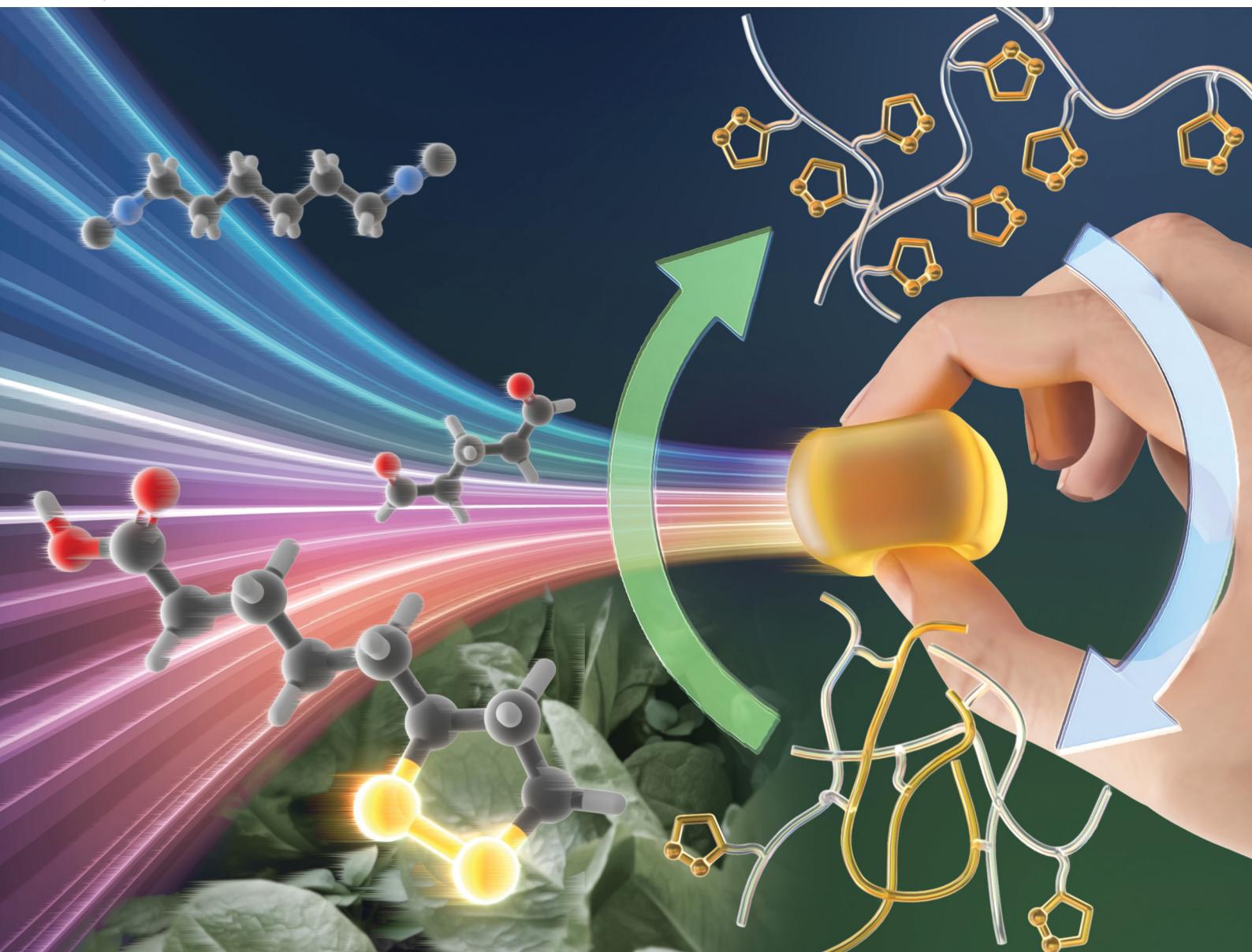


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Passerini polymerization using naturally occurring α -lipoic acid as a raw material yields polyamides with 1,2-dithiolane functional groups in a one-step reaction. The polyamide exhibits characteristics of an adaptable dynamically crosslinked network through reversible ring-opening reaction of 1,2-dithiolane, enabling self-healing, reusable strong adhesion, and regeneration through decrosslinking and re-crosslinking.

1,2-Dithiolane is a five-membered ring structure with adjacent sulfur atoms. This chemical motif is inherent in naturally occurring α -lipoic acid (LA), also known as thioctic acid, which exhibits biological activities such as robust antioxidant properties (Fig. 1a).^{1,2} In addition, LA derivatives are recognized for various applications including the stabilization of quantum dots and metal nanoparticles.^{3–5} In recent years, considerable attention has been directed towards the utilization of 1,2-dithiolanes in polymer science as a pivotal motif for creating “circular” plastics with recyclability,^{6,7} and adaptable networks with functionalities like self-healing.^{8–11} These attributes are based on the reversible ring-opening reaction of 1,2-dithiolane and the resulting disulfide-containing chain which has the dynamic covalent bonding character (Fig. 1a). The development of methods for introducing the 1,2-dithiolane moiety into a polymer structure enables the creation of polymer materials with controllable crosslinking and the resulting material properties (Fig. 1b).

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† This paper is dedicated to Professor Atsuhiko Osuka on the occasion of his 70th birthday

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Passerini polymerization of α -lipoic acid for dynamically crosslinking 1,2-dithiolane-functionalized polymers†‡

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Due to its natural occurrence and abundance, LA is highly attractive as a source of the 1,2-dithiolane moiety, making it a sustainable raw material for functional polymers. Recently, methods employing LA for polymer synthesis have been extensively studied, with most of them utilizing the ring-opening reaction of 1,2-dithiolane to form the S-S backbone of poly(disulfide)s.^{12–15} On the other hand, the 1,2-dithiolane-functionalized (pendant) polymers have high material potential due to the broad range of polymer chain structure. The syntheses of such polymers were achieved through post-modification of polymers using LA, such as amide condensation between the CO₂H group in LA and NH₂ group in the polymer

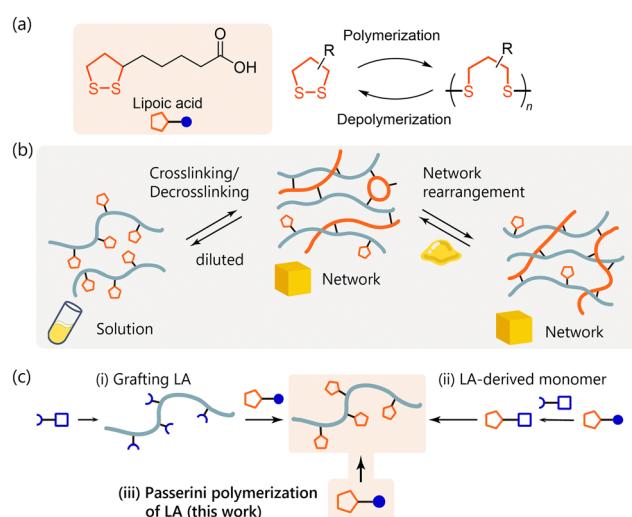


Fig. 1 (a) The chemical structure of α -lipoic acid (LA), and the reversible ring-opening polymerization of 1,2-dithiolane. (b) Schematic illustration of reversible polymer networks derived from 1,2-dithiolane functionalized polymers. (c) Synthetic routes for 1,2-dithiolane functionalized polymers: (i) grafting LA onto a functionalized precursor polymer, (ii) polymerization of LA-derived monomer, and (iii) one-step Passerini polymerization of LA (this work).



(Fig. 1c).^{3,10,16,17} LA-derived monomers with the polymerizable functional groups have also been developed.^{9,11,18–20} However, there has been a lack of simple methods for directly utilizing LA as a raw material for polymers possessing the 1,2-dithiolane moiety as a functional group.

The Passerini reaction is a multicomponent reaction that affords a three-component adduct from a carboxylic acid, an aldehyde, and an isocyanide.^{21,22} Passerini polymerization, which extends the Passerini reaction to polymerization by using di-functional components, enables polymer synthesis with a versatile carboxylic acid when dialdehyde and diisocyanide are employed.^{23–26} 1,2-Dithiolane has rich reactivity, undergoing ring-opening reactions induced by temperature, light, and external radicals, nucleophiles, and electrophiles. These features are the origin of 1,2-dithiolane's chemistry and functions; however, they pose a challenge to polymerizing 1,2-dithiolane-containing monomers while retaining the 1,2-dithiolane moiety.^{27,28} To address this challenge, Passerini polymerization provides an opportunity for the direct polymerization of LA, owing to the mild reaction conditions and the reaction mechanism without radicals, strong nucleophilic or electrophilic species (Fig. 1c).

In this study, we demonstrated the synthesis of 1,2-dithiolane-functionalized polymers directly using LA as a raw material through Passerini polymerization, and the resulting polymer exhibited characteristics of a dynamically crosslinked polymer network.

First, we conducted the Passerini reaction using LA, butyraldehyde, and 1,6-diisocyanohexane to test the compatibility of the reaction condition for the 1,2-dithiolane moiety. The mixture of the three compounds afforded the adduct within 1 h at 40 °C, and the ¹H NMR analysis of the product confirmed the retention of 1,2-dithiolane moiety (Fig. S1 in ESI‡). Next, we conducted Passerini polymerization using LA, glutaraldehyde, and 1,6-diisocyanohexane (Fig. 2). The reaction in THF solvent afforded the polyamide **PA-LA** with a 1,2-dithiolane pendant group derived from LA, whose structure was characterized by IR

Table 1 Synthesis of **PA-LA** and **PA-LA/HA**^a

| Run | Carboxylic acid ^b | Solvent | Conversion: CHO, NC ^c (%) | <i>M_n</i> ^d | <i>D</i> ^d |
|-----|------------------------------|-------------------|--------------------------------------|-----------------------------------|-----------------------|
| 1 | LA | THF | 97, 100 | 6590 | 1.95 |
| 2 | LA | THF ^f | 88, 100 | 2980 | 2.29 |
| 3 | LA | THF ^g | 98, 100 | 8740 | 2.01 |
| 4 | LA | CHCl ₃ | — ^e | — | — |
| 5 | LA/HA (1/1) | THF | 99, 100 | 8860 | 1.98 |
| 6 | LA/HA (1/2) | THF | 98, 100 | 8750 | 2.02 |
| 7 | LA/HA (1/4) | THF | 98, 100 | 8920 | 2.00 |

^a [Carboxylic acid]:[glutaraldehyde]:[1,6-diisocyanohexane] = 2.2:1:1. [Carboxylic acid] = 2.0 M. For the detailed conditions, see ESI. ^b Molar ratio is given for lipoic acid (LA) and hexanoic acid (HA) mixture.

^c Conversions of aldehyde and isocyanide groups calculated by the ¹H NMR signal intensity of CHO in the starting dialdehyde. ^d Calculated against PMMA standards. ^e The reaction mixture became a gel during the reaction. ^f [Carboxylic acid] = 1.0 M. ^g [Carboxylic acid] = 2.5 M.

and NMR spectroscopies (Table 1 and ESI‡). ATR-IR measurement of the polyamide exhibited distinctive vibration signals of $\nu_{C=O, \text{amide}}$ of the main chain amide moiety at 1658 cm^{–1}. In addition, $\nu_{C=O, \text{ester}}$ at 1738 cm^{–1} indicated the presence of an ester group, which corresponds to the α -acyloxy polyamide structure (Fig. S2, ESI‡). These observations confirmed the incorporation of LA into the polymer main chain through the conversion of the CO₂H group. The ¹H NMR spectra of **PA-LA** confirmed proton signals of CH of α -carbonyloxy amide (5.05 ppm), amide NH (6.45 ppm), and those in LA-derived 1,2-dithiolane moiety, indicating the successful formation of polyamide with 1,2-dithiolane pendant group (Fig. 2). The signal observed at 9.76 ppm was assigned to the remaining CHO at the polymer chain end, while no peaks assigned to the remaining isocyanide group in the polymer were observed. This indicated that the chain end structure of the polymer would be CHO group derived from glutaraldehyde. GPC analysis of the **PA-LA** taken from the reaction mixture resulted in *M_n* = 6590 and *D* = 1.95 (Fig. 3a). From this result, the number of 1,2-dithiolane groups was roughly determined to be 20 in one **PA-LA** chain on average according to calculations based on the molecular weight of the repeating unit.

The study of the polymerization progress found that both CHO and isocyanide groups were rapidly consumed in the early stage of polymerization, following third-order reaction kinetics (Fig. 3b). The molecular weight increased with the conversion of functional groups, and nearly reached a plateau after around 20–40 hours. The concentration of starting materials correlated to the molecular weight of polymers, with higher concentrations yielded longer polymers (run 2–3). However, excessively high concentrations led to gelation during the reaction, making the analysis difficult. Such gelation was also observed when CHCl₃ was used as a solvent (run 4).

After precipitating from a selective solvent (Et₂O), the isolated **PA-LA** was crosslinked and insoluble in the solvent used in the polymerization. Slow evaporation of sodium lipoate aqueous solution is reported to result in the concentration-induced formation of poly(disulfide) via ring-opening reaction of 1,2-dithiolane, which indicates that the reaction occurs even at room temperature.¹³ Thus, the isolation of **PA-LA** caused

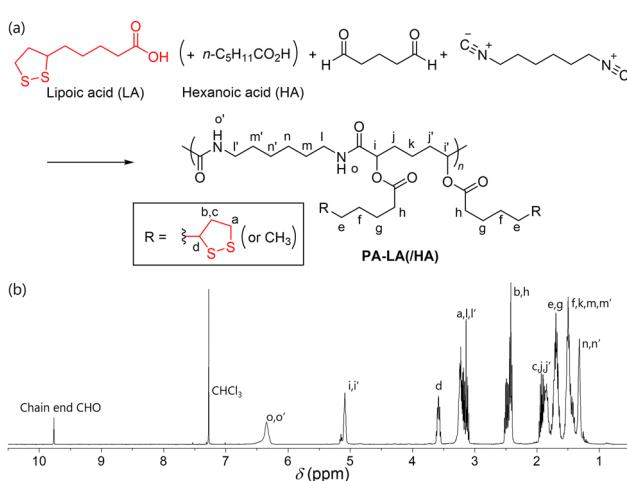


Fig. 2 Reaction scheme and ¹H NMR spectrum of **PA-LA** (sample of Table 1, run 3).



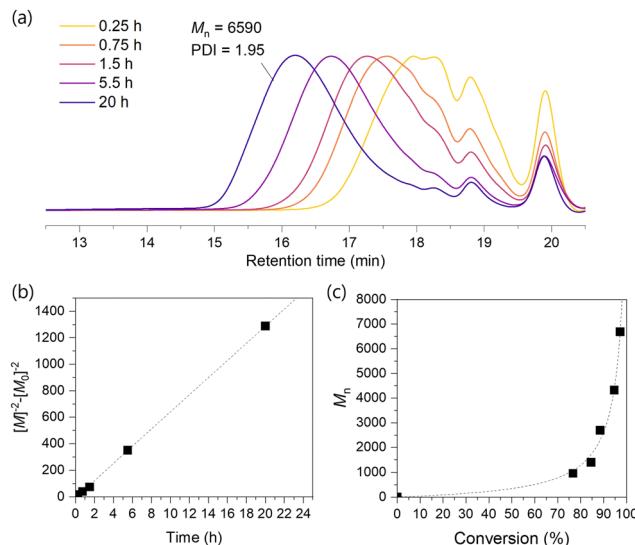


Fig. 3 (a) GPC profiles in the synthesis of **PA-LA**, (b) the kinetic curve, and (c) M_n evolution against the conversion of CHO group (Table 1, run 1).

such concentration-induced crosslinking. However, the cross-linked **PA-LA** could be applied for hot-press molding at 150 °C (Fig. 4a). This experiment indicated that the dynamic covalent bond nature of 1,2-dithiolane-derived disulfide bonds in cross-linked **PA-LA** (Fig. 4b).

To study the effect of the number of crosslinking 1,2-dithiolane groups in the polymer chain, copolymerization using another carboxylic acid was examined. We conducted Passerini polymerization using LA and hexanoic acid (HA) in 1:1 ratio, and glutaraldehyde and 1,6-diisocyanohexane (Table 1, run 5). The polymerization successfully afforded **PA-LA/HA** with high monomer conversion. Polymerization monitoring by ^1H NMR measurements indicated a random incorporation of LA and HA units into the polymer chain. The structure of **PA-LA/HA** was further identified, as well as **PA-LA** (Fig. S3, ESI‡). The $M_n = 8860$ of **PA-LA/HA** corresponded to twelve 1,2-dithiolane groups, which is half of the dithiolane

density compared to **PA-LA**. Similarly, **PA-LA/HA** from different feeding ratios of LA and HA were synthesized in the same manner (Table 1, runs 6 and 7).

PA-LA and **PA-LA/HA** (LA/HA = 1/1) exhibited a swelling property with a swelling ratio of 120% for **PA-LA** and 308% for **PA-LA/HA** using CHCl_3 (Fig. 4a). The higher swelling ratio for **PA-LA/HA** is attributed to the lower crosslink density in the network. These swelling behaviours without dissolution indicates the presence of covalent crosslinks in the material. Thermal gravimetry analysis (TGA) of these polymers exhibited the 5% thermal decomposition temperatures ($T_{\text{deg},5\%}$) above 278 °C, showing their thermal robustness (Fig. S4, ESI‡). Differential scanning calorimetry (DSC) measurements revealed the glass transition temperature (T_g) at 29 °C and 24 °C for crosslinked **PA-LA** and **PA-LA/HA**, respectively (Fig. S5, ESI‡). The lower T_g of **PA-LA/HA** is likely due to the incorporation of a less sterically bulky C5-alkyl chain instead of a tetramethylene 1,2-dithiolane chain.

The viscoelastic properties of the crosslinked **PA-LA** and **PA-LA/HA** (LA/HA = 1/1) were characterized by rheology measurements. These materials exhibited typical curves of crosslinked polymers in temperature ramp measurements, with a notable modulus at low temperature and a rubbery plateau at high temperature (Fig. S6 and S7, ESI‡). While both materials showed almost identical moduli (approximately 100 MPa) at the temperature below their respective T_g , **PA-LA/HA** exhibited an order of magnitude lower modulus (0.3 MPa) compared to that of **PA-LA** (2.3 MPa) at the temperature above their respective T_g . These experiments suggest the potential for tuning viscoelastic properties of these materials using additional carboxylic acid. The mechanical property of the material was further examined by a uniaxial tensile test, and **PA-LA/HA** (1/1) exhibited a stretch ratio of over 500% (Fig. S10, ESI‡).

The dynamic covalent bonding nature of S-S bonds in **PA-LA/HA** imparted the characteristics of healable elastomers (Fig. S11, ESI‡) and recyclable adhesives. These polymers had almost no tackiness and lacked adhesive strength when they were simply sandwiched between stainless steel plates under pressure. On the other hand, when these specimens were heated at 180 °C under pressure for 10–20 min, they displayed significant adhesive properties with a shear strength of 10.8 MPa for **PA-LA/HA** (LA/HA = 1/1, Fig. 5). After the break of the specimen, the polymer was collected and used for a new

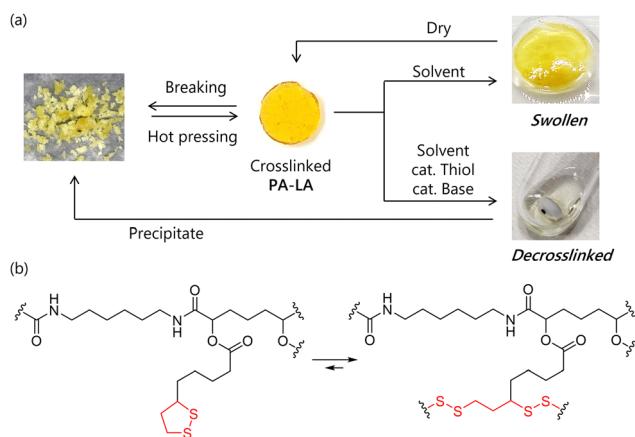


Fig. 4 (a) Cycle of crosslinked **PA-LA**: molding, swelling, decrosslinking, and recovery. (b) A plausible mechanism of bond exchanging.

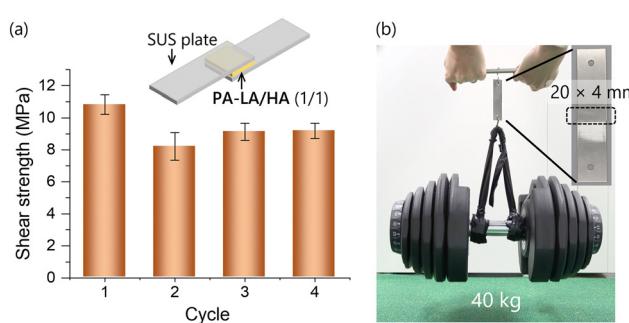


Fig. 5 Adhesion cyclic test of **PA-LA/HA** (1/1) (a) and a demonstrating loading test (b). The standard errors are shown on the bars.



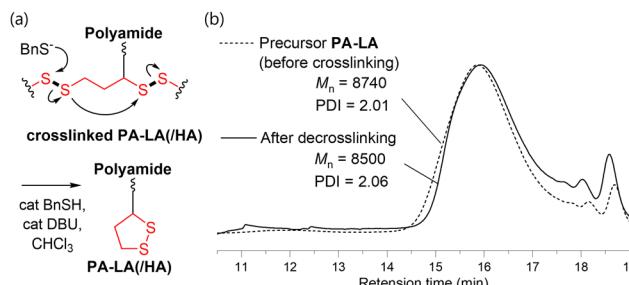


Fig. 6 Decrosslinking of crosslinked **PA-LA(HA)**: (a) a plausible mechanism of bond exchanging, and (b) GPC profiles of **PA-LA** before the crosslinking and after the decrosslinking. The GPC profile of precursor was obtained at the time of polymer synthesis.

specimen under the same preparation procedure. The specimen exhibited adhesion strength again, and this recycling process could be repeated (Fig. 5). This strong adhesion can be attributed to the polar and flexible main chain of polyamide that enhances the interaction at the interface, the flexible alkyl side chain derived from LA and HA, and dynamic and robust disulfide crosslinks that reconstruct the network structure enabling a large and optimal contact area.

Finally, we studied the solubilization and recovery of these crosslinked polymers *via* catalytic decrosslinking of disulfide bonding. The crosslinked **PA-LA** was immersed in CHCl₃ and added a catalytic amount of benzyl sulfide (BnSH) and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU).¹⁷ The crosslinked polymer underwent dissolution in CHCl₃, yielding a homogeneous solution. GPC analysis of the resulting polymer solution revealed a profile consistent with that of the precursor **PA-LA** before crosslinking, showing successful decrosslinking (Fig. 6). The recovered **PA-LA** were crosslinked again by concentrating the solution or precipitating the polymer using Et₂O. Similarly, the decrosslinking of crosslinked **PA-LA(HA)** was achieved in the same manner (Fig. S12, ESI†). These experiments suggest that the 1,2-dithiolane pendant group allowed facile manipulation of the crosslinked and non-crosslinked structure of the polymers, highlighting the recyclability of these polymers.

In conclusion, we have developed a synthesis of 1,2-dithiolane-functionalized polymer directly using naturally abundant LA as a raw material by Passerini polymerization. The resulting dynamically crosslinked polymer exhibited characteristics of adaptable elastomers, such as re-processability and recyclable adhesion. This work provides easy access to a variety of polymers with 1,2-dithiolane functionalities, which encompass not only dynamic crosslinking presented in this study but also inherent features of 1,2-dithiolane, such as antioxidant activity and applications in nanomaterials.

Y. N., Y.-S. H. and C.-F. H. designed and conceived the experiments; Y. N., Y.-S. H., and S. S. conducted the experiments.

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Conflicts of interest

There are no conflicts to declare.

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