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Cascade Initiation of Ring Opening Polymerization for Dynamic Covalent Poly(disulfide)s: One-Step Double Modification and Copoly(disulfide) Synthesis by Living Polymerization

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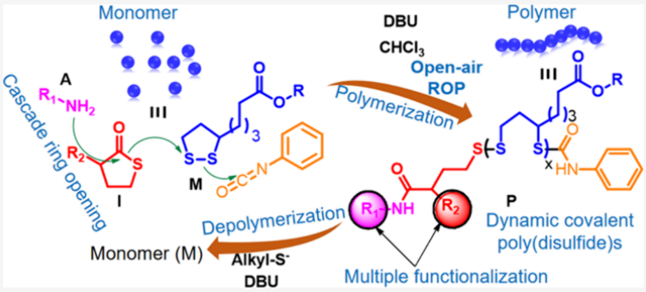
ABSTRACT: The dynamicity and recyclability of a material are the chemical bases of sustainable future smart materials. In this context, the poly(disulfide)s of 1,2-dithiolane are a very significant class of polymers due to the presence of dynamic covalent disulfide bonds in the main-chain polymer. Here we reported an amine-activated cascade initiation of thiolate-induced ring opening polymerization (ROP) of the 1,2-dithiolane ring to synthesize functional poly(disulfide)s at room temperature and under an open-air condition. In situ generation of the thiolate initiator by the reaction of the thiolactone ring and amine, stabilization, and use of the phenyl isocyanate terminator enable us to perform the polymerization in a controlled manner. Additionally, in situ, one-step, dual modification at the polymer chain end by varying amine and thiolate allowed us to access a variety of functional poly(disulfide)s. The primary amine is found to be a more effective activator compared to the secondary amine. We also demonstrated the living nature of the poly(disulfide)s and synthesized tailor-made copoly(disulfide)s. We believe that the ROP of poly(disulfide)s activated by amine is the first report in the literature where we can use a library of amines to functionalize poly(disulfide)s and access diverse structures of polymers. This methodology establishes a versatile platform and opens up enormous opportunities for the synthesis of a variety of dynamic polymers.



■ INTRODUCTION

In modern science, achieving a material with a dynamic behavior like living systems in nature has become a fascinating field as the dynamic feature projects the material as a future smart material.[1,2] We consider the dynamic and recyclable polymers as sustainable and environment friendly materials for the future.[3−5] Despite the existence of dynamic covalent chemistry or noncovalent chemistry for long time, there is a budding need to improve chemical methodology accessories for easy engineering and producing dynamic covalent materials.[6−16] To that end, the sulfur atom shows a very interesting role in creating various dynamic materials. A series of sulfur-containing polymers including thioesters,[17,18] thiocarbonate,[19] thiourethane,[20] thioamides,[21] thiourea,[22] disulfide,[23] and polysulfide[24] are individually important due to their unique applications in chemistry and in material and biological science. In particular, disulfide is a dynamic covalent bond, robust, and media-tolerant;[25,26] ties peptides; and thus determines dynamic properties of many macromolecular proteins in nature.[27,28] On the one hand, the disulfide bond can maintain molecular integrity being a moderately strong bond with a bond dissociation energy of 60 kcal mol^{-1};[29] on the other hand, with respect to dynamicity, the bond is easily cleavable and exchangeable in the presence of physical (heat, light, mechanical force, etc.)[30−33] or chemical (nucleophile, base, or oxidizing agent)[34−37] stimuli by overpowering the energy barrier. The disulfide bond can be easily cleaved and reformed on demand, thus suggesting the dynamic nature of this bond. Within the concept of dynamic covalent chemistry, disulfide-based dynamic chemistry has been widely studied in the last two decades.[6−16] For instance, disulfide bonds are introduced in the main-chain polymer to synthesize poly(disulfide)s or to cross-link polymer chains for enabling dynamic properties in the polymer such as self-healing, adaptability, stress-resistance, responsive degradability, etc.[38−42] Both linear and cyclic poly(disulfide)s are individually important, but the cyclic polymer shows a unique dynamic nature due to ring strain, which increases the reactivity of disulfide bonds.[43] On the recent progress in designing dynamic poly(disulfide)s by reversible polymerization, a library of linear or cyclic poly(disulfide)s has been prepared by ring opening

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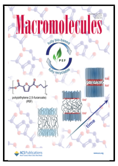

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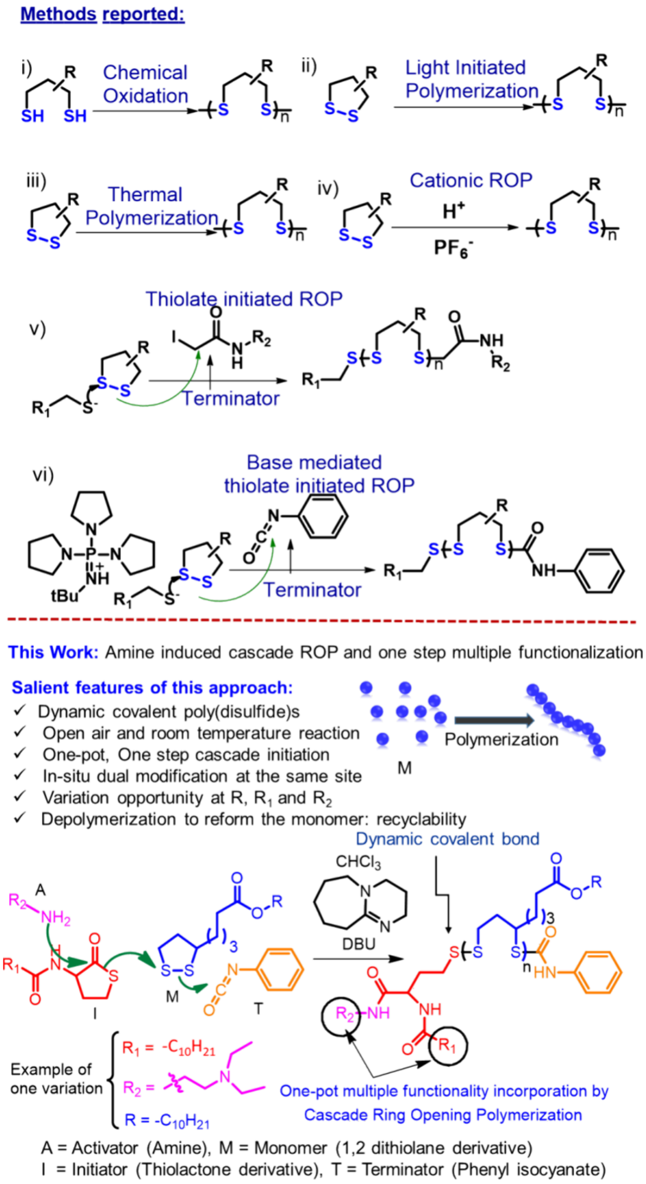
polymerization (ROP). The dynamic nature of disulfides in poly(disulfide)s imparts the unique nature of these polymers and made these polymers useful in various application areas such as gels,[44−46] self-healing materials,[47−50] elastomers,[51] adhesives,[48] polyelectrolytes,[52] and recyclable materials.[53,54]

Scheme 1. Top: Summary of the Reported Synthetic Methodologies of Poly(disulfide)s from the 1,2-Dithiolane Monomer; Bottom: the Method Presented in This Work and Its Salient Features



Although there are various well-established methodologies for the controlled synthesis of poly(disulfide)s using a naturally occurring 1,2-dithiolane ring, a robust methodology with diversity in easily preparing functional dynamic polymers has yet to be established. The conventional methods for the synthesis of poly(disulfide)s cover oxidative polymerization by chemicals,[55,56] radical polymerization by light,[37,49,57,58] thermally induced polymerization,[59,60] and thiolate-initiated living polymerization.[61−64] Here, the last method of thiolate-initiated ROP has emerged as an encouraging method for controlled poly(disulfide) synthesis.[63] This strategy involves initiating polymerization by ring opening with a thiolate anion and growth by cascade ring opening. Matile et al. pioneered the synthesis of cell penetrating poly(disulfide)s initiated by anionic thiolate.[64] The same group extended the idea of the synthesis of poly(disulfide)s on the surface for extensive use of the polymers in biological applications. Zhang and Waymouth showed the thermodynamic aspect of monomer−polymer equilibrium by synthesizing a thiol-initiated poly(disulfide) network in a micellar core.[44] Along the same line, we also reported the reducing-agent-induced formation of a micelle with a 1,2-dithiolane based cross-linked poly(disulfide) core for use in the drug delivery applications.[65] Liu and Moore reported the architecture (linear and cyclic topology)-controlled synthesis of poly(disulfide)s based on the structure of the thiolate initiator (alkyl or aryl thiolate) and organic base.[62] Liu et al. recently reported the anion binding approach to control the high reactivity of thiolate anion and synthesizing poly(disulfide)s with narrow dispersity and high regioregularity by the living ring opening polymerization technique.[66] However, there are some limitations of the anionic polymerization that need to be addressed to make the synthesis of poly(disulfide)s more robust. The limitations are as follows: (i) the thiolates can easily be oxidized, and thus, the reaction condition should be inert; (ii) monomers with active protons are not allowed to be used in anionic polymerization. Therefore, a new methodology that can address those limitations and introduce more benefit from the perspective of material property and functional diversity is necessary. Here, instead of a direct thiolate anion, we generated a thiolate anion in situ in a controlled manner using amine as an activator and the thiolactone ring as a source of the thiolate anion (Scheme 1). We believe that this is the first report of 1,2-ditholane based poly(disulfide) synthesis using a cascade ring opening reaction activated by amine. Here, as soon as thiolate is generated in the reaction medium by amine-induced opening of the thiolactone ring, it initiates the ROP by opening the 1,2-dithiolane ring, thus avoiding the possibility of the oxidation of thiolate. Therefore, there is no requirement of inert conditions, and the reaction happens at room temperature and in an open-air condition. The variation of amines and thiolactone derivatives enables access to diverse dynamic materials. To increase the number of different chemical functionalities at the same site of a polymer chain, introduction of multiple functional groups in a one-pot and one-step fashion can be an attractive feature of a polymerization methodology. Here, we introduced the one-step method of dual modification at the polymer chain end using the thiolactone ring and chain propagation in a cascade manner. Additionally, using the living nature of the polymer chain end, copoly(disulfide)s are synthesized in a controlled manner. Therefore, the idea of complex catalyst free cascade initiation of ROP of the 1,2-dithiolane ring by using amine as an activator in an open-air condition and sequential addition of various 1,2-dithiolane monomers to prepare copoly(disulfide)s might bring many opportunities for the design and synthesis of a library of diverse dynamic homo- and copoly(disulfide)s.

■ RESULT AND DISCUSSION

Poly(disulfide) Synthesis by Cascade Ring Opening Using Thiolactone Chemistry. The motivation for the discovery of a new methodology for poly(disulfide) synthesis came from our long-term interest in the synthesis of a dynamic covalent polymer of the 1,2-ditholane ring. Here, a naturally occurring lipoic acid derivative is used as a source of the 1,2-dithiolane ring, which acts as a monomer. Because it is known that the thiolate anion triggers the ring opening reactions of 1,2-dithiolane,[64] we aimed for the in situ generation of the thiolate anion using the amine activator. The advantage of using amine is the privilege of introducing a variety of new functionalities at the polymer chain end due to the availability of the expanded library of primary and secondary amines. One can easily control the polymerization rate by varying the nature of the amine. The in situ generation of the thiolate anion by amine might minimize the oxidation of thiolate in the solution. Additionally, it is also possible to tune the molecular weight of the polymer by monitoring the terminator addition time. Here, to prepare the 1,2-dithiolane based monomers (M1 or M2), commercially available lipoic acid was condensed with decanol or tetraethylene glycol monomethyl ether (Scheme S1), and for the synthesis of the thiolactone derivative based initiator (I), D/L-homocysteine thiolactone was reacted with acid chloride in the presence of an organic base (see Scheme S2 for the synthesis). The polymerization did not proceed when monomer and initiator were mixed in the presence of an organic base (DBU) in the organic solvent $CHCl_3$. The polymer is obtained successfully after the addition of amine (A) (activator) to the reaction mixture containing the monomer (M), initiator (I), and base (B). The resulting product appeared as a free-standing gel as shown in the inset of Figure 1a. Here the amine opens up the thiolactone ring and generates the thiolate anion, which triggers the 1,2-ditholane ring and initiates the disulfide exchange ring opening polymerization (Scheme 1, right). This is a remarkable example of one-pot cascade ring opening (thiolactone ring opening followed by 1,2 dithiolane) mediated initiation of ROP to synthesize functional poly(disulfide)s. Here, we used time-dependent UV/vis spectroscopy to monitor the progress of polymerization as the monomer has a distinct characteristic band at 335 nm. Initially, the mixture of the monomer and initiator did not show any change in the UV/vis band as the initiator is inactive in the absence of amine. After the addition of amine to the reaction mixture, the band at 335 nm corresponding to the monomer gradually decreased and almost vanished after 100−120 min of reaction, suggesting the consumption of the monomers and growth of the polymer. After 120 min, the spectrum shows no change, which clearly indicates the quantitative consumption of the monomers and the formation of the poly(disulfide)s of 1,2-dithiolane (Figure 1a). Here, for checking the complete polymerization time, we did not stop the polymerization by adding any terminator, but the terminator addition is feasible to stop the growth of the polymer in any estimated time to achieve the desired molecular weight of the polymer, which we performed and represented in Table 1. The polymer is characterized by ^1H NMR (Figure 1b,c) and size exclusion chromatography (SEC) (Figure S1). As shown in Figure 1b, for the monomer M1, the $-CH_2$ protons as indicated by “g” showed the resonance at δ3.20 ppm, and the “f” protons appeared at δ1.90 and δ2.46 ppm, suggesting the existence of a dithiolane ring. In the ^1H NMR of the polymer, we showed the partial disappearance of the peaks of $-CH_2$ as indicated by “f” and “g” in the monomer and appearance of new peaks at δ2.80 and δ1.98 ppm for “g” and “f” protons, respectively. This suggests a decrease of chemical bond tension as the monomeric ring opened up due to polymerization and formation of poly(disulfide)s. The calculation of the percentage of conversion made from the NMR data shows ∼71% conversion (Figure 1c for calculation). The SEC profile showed a unimodal distribution with a dispersity ($Đ$) of 1.43 and molecular weight (Mn) of 23,700 g/mol (Figure S1).

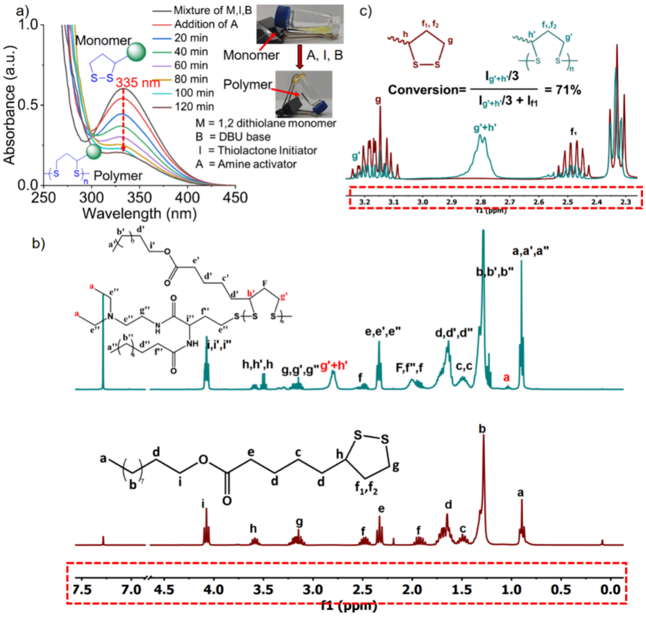


Figure 1. (a) Monitoring polymerization by time-dependent UV/vis spectroscopy. Inset shows that the liquid monomer converts to a gel-like polymer. (b) Comparison of ^1H NMR of the 1,2-dithiolane monomer and corresponding poly(disulfide)s. (c) Calculation of % of conversion and zoomed image of the distinct band for the polymer.

Tunability in Polymer Molecular Weight. Using this approach, we were able to produce a high-molecular-weight polymer in about 2 h. The beauty of this technique is that we may tailor the molecular weight by adding a terminator at a certain moment. The addition of a terminator can stop the growth of the polymer chain at the desired molecular weight. The kinetics of the polymerization is monitored by UV/vis spectroscopy and ^1H NMR after the addition of the phenyl isocyanate terminator in the course of polymerization in a specific time interval. In the polymerization reaction, the terminator was added at 20 min intervals, and the total course of the reaction was set for 120 min. All the parameters including the percentage of conversion (calculated from ^1H NMR), degree of polymerization, and molecular weight (calculated from ^1H NMR and SEC) systematically increased with the increase of terminator addition time (20 to 100 min). According to SEC data, the molecular weight increased from 5400 to 13,000 g/mol (Figure 2a,e), the % of conversion started from 41% and ended up at 64% (Figure 2d), and the degree of polymerization (DP) varied from 14 to 36 (Figure 2f) due to the time-dependent addition of the terminator within the studied time frame. In a parallel reaction, without the terminator, the molecular weight and DP were found to be 23,700 g/mol and 67, respectively, after 120 min of the reaction. Hence, the molecular weight of the polymer is highly controllable in this method. The calculated molecular weight from the SEC data corroborated well with the NMR results, thus indicating good acceptance of the data (Table 1). The comparison of the UV/vis plot for terminator addition at 20, 40, 60, 80, and 100 min clearly demonstrates a higher concentration of monomer at 20 min and a lower concentration at 80 min, therefore reflecting less conversion at 20 min and greater conversion at 100 min (Figure 2b,c and Figure S2). The plots corresponding to 20 and 80 min are presented in Figure 2a,b, and the rest are presented in Figure S2. The saturation in the UV/vis plot is reached as soon as the terminator is added at

Table 1. Comparison of Molecular Weight and DP by SEC and ^{1}H NMR[a]

terminator addition time (min)	molecular weight from SEC (g/mol)	DP from SEC result	molecular weight from NMR data (g/mol)	DP from NMR result	% conversion	dispersity ($Đ$)
T = 20	5400	14	6750	18	41	1.20
T = 40	7050	19	7450	20	45	1.28
T = 60	9800	27	8850	24	51	1.42
T = 80	10,200	28	9900	27	56	1.39
T = 100	13,000	36	11,800	34	64	1.48
T = no addition	23,700	67	24,100	68	71	1.43

[a] The % conversion was calculated from NMR data.

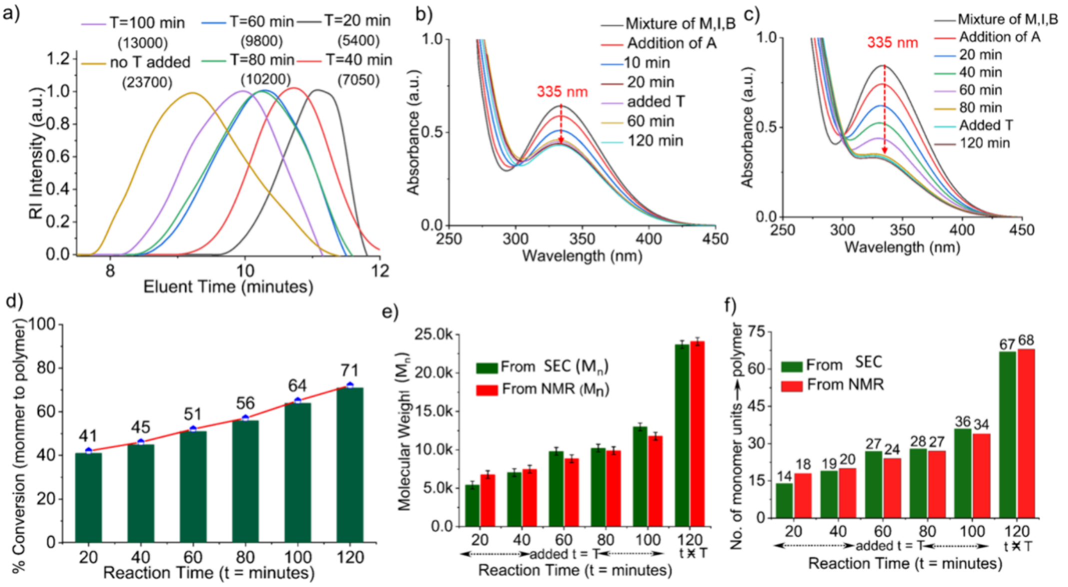


Figure 2. (a) Controlling the molecular weight of the polymer by time-dependent addition of the terminator as represented by the size exclusion chromatography profile. The reaction kinetics for the control of the molecular weight was probed by UV/vis spectroscopy by monitoring the absorption intensity of the monomer at 335 nm. (b, c) Plot for the terminator addition at 20 and 80 min, respectively. M= monomer, I = initiator, B = base, A = amine, and T = terminator. (d) Plot of % conversion vs reaction time. Comparison of the (e) molecular weight and (f) degree of polymerization of poly(disulfide)s by SEC (size exclusion chromatography) and ^{1}H NMR spectroscopy.

any time within 120 min. This signifies that polymerization can be halted at any moment to attain the appropriate molecular weight, rendering the molecular weight very adjustable in this polymerization technique. The progress of the polymerization is shown by the time-dependent ^{1}H NMR data as represented by the stack plot in Figure S3. For the monomer (bottom spectrum), there is no peak at 2.8 corresponding to the polymer. Upon the addition of amine, a new peak emerged at 2.8 ppm, and its intensity progressively increased over time, signifying the advancement of polymerization.

The reactivity of amine plays a very crucial role in controlling the rate of the polymerization. As we know, secondary amine is less nucleophilic than primary amine. We compared the polymerization rate of a specific monomer (M1) by using primary and secondary amines.[67] Here, *N*,*N*-diethylethylenediamine (primary amine (A1)) and 1-methylpiperazine (secondary amine (A2)) were used as activator, and interestingly, it was found that for A1, the reaction was completed in 120 min (spectra saturated at 120 min), but for A2, it was completed in 300 min (spectra saturated at 300 min) (Figure 3a,b). In the case of A2, after 120 min, the reaction was completed to the extent of ∼60% (Figure 3c). On the one hand, the polymerization rate is directly dependent on the availability of the thiolate anion; on the other hand, the rate of generation of thiolate anion is dependent on the reactivity of amine. Therefore, by varying the reactivity of amine, we can monitor the rate of the polymerization.

Probing the One-Pot Cascade Nature of the Polymerization. Further, to test the one-pot cascade nature of the polymerization reaction, we have performed a few control reactions where we excluded one of the components in each case and checked the polymerization by monitoring UV/vis spectroscopy data. Interestingly, we observed no polymer formation if one of the component is absent (Figure S4a,b). The polymerization happens if all four components (monomer, initiator, activator, and base) are present in the mixture. Figure S5a shows the formation of polymer after the addition of activator in the mixture of monomer, initiator, and base as the peak intensity at 335 nm decreases over time. In the absence of a base, the ROP reaction did not proceed as shown by no change in the 335 nm band intensity, which can be attributed to the protonation-mediated quenching of the active thiolate anion generated by the amine-induced opening of the thiolactone ring (Figure S5b). Here the base plays an important role to scavenge the protons and stop the quenching of the thiolate anion. The one-pot presence of four components and therefore thiolactone ring opening by amine is necessary for the polymer formation, which was also probed by the ^{1}H NMR experiment. Figure S4c shows no polymer peak in the absence of either the initiator or activator, but in the presence of all the components, a new peak

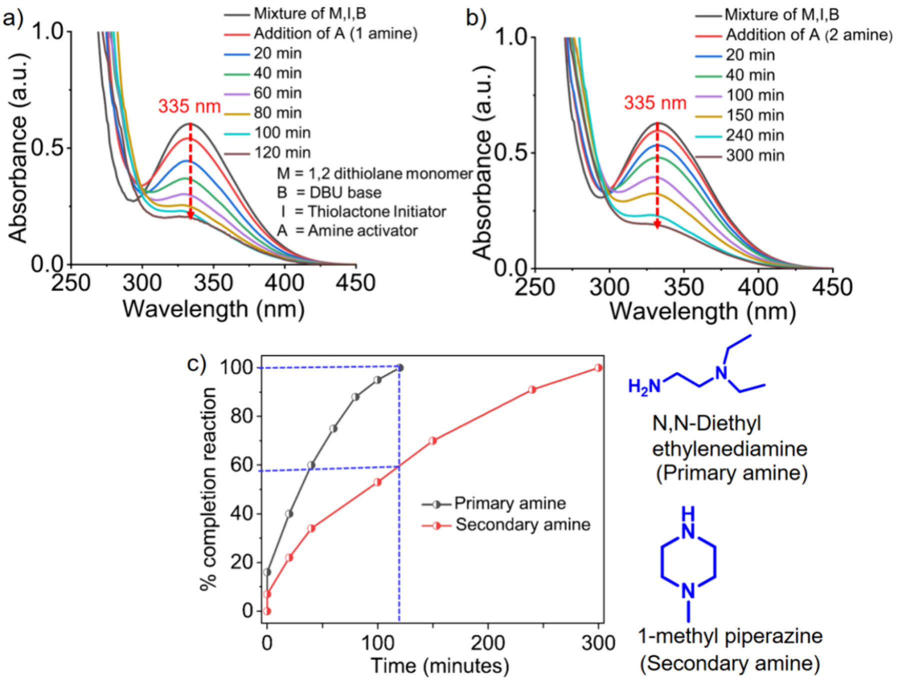


Figure 3. Polymerization kinetics monitored by UV/vis spectroscopy after the addition of (a) primary amine *N,N*-diethyl ethylenediamine (1 amine) and (b) secondary amine 1-methyl piperazine (2 amine). (c) Comparison of the % of completion of reaction vs time.

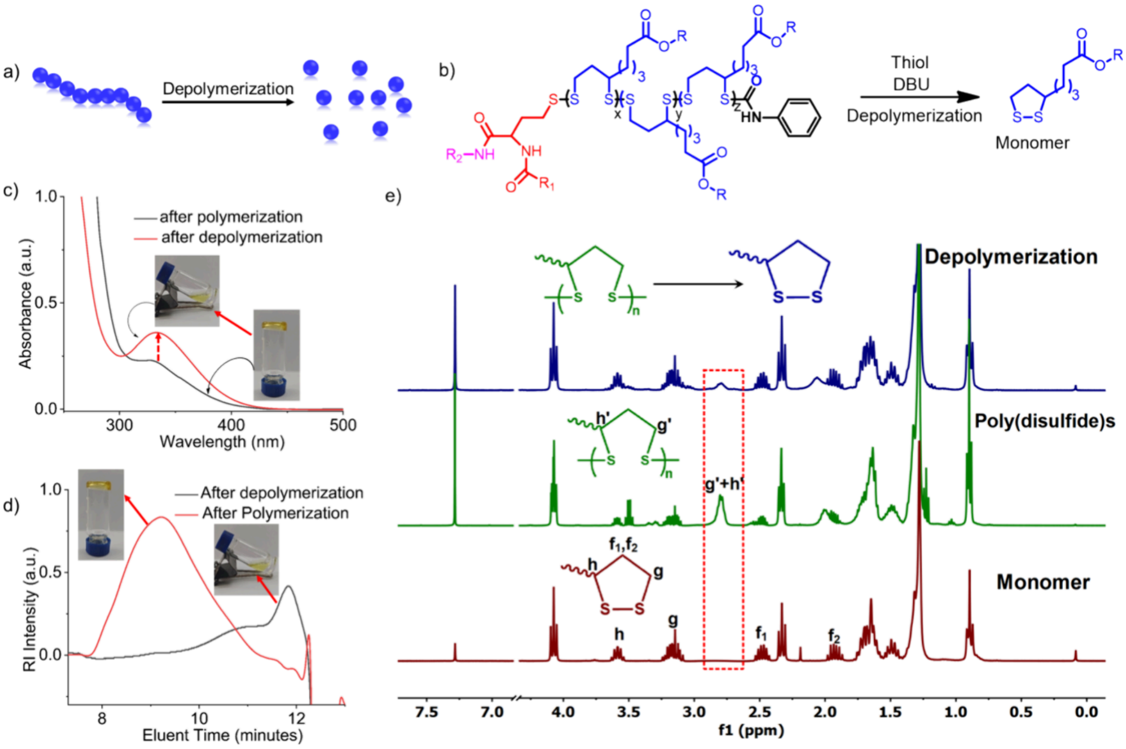


Figure 4. (a) Cartoon presentation of the depolymerization of a polymer chain. (b) Structural representation of the thiolate-mediated depolymerization of poly(disulfide)s. Probing the depolymerization and regeneration of the monomer by (c) UV/vis spectroscopy and (d) size exclusion chromatography. (e) Comparison of ^1H NMR of monomer, polymer, and depolymerized sample.

appeared at $\delta 2.80$ ppm, thus suggesting the formation of polymer.

Reversibility and Recyclability of the Poly(disulfide)s. Finally, we also demonstrated the reversibility and recyclability of the polymer to the ring-closed monomeric form due to the dynamic covalent nature of the disulfide bonds. It is reported in the literature that the linear polymer goes back to the monomeric form in the presence of a chemical initiator, e.g., external thiolate anion (Figure 4a,b).[68] In a typical reaction, 1 mol % of butanethiol was dissolved in $CHCl_3$ in the presence of the DBU base, which makes thiolate anion. Then, a measured amount of poly(disulfide)s was added to the solution and stirred for some time at room temperature. Interestingly, a yellow and clear solution appeared due to the reformation of the 1,2-dithiolane ring as indicated by the distinctive absorption band at 335 nm in UV/vis spectroscopy (Figure 4c). This suggests the successful recovery of the five-membered disulfide ring monomer by the thiolate-initiated depolymerization of poly(disulfide)s. The size exclusion chromatography profile further supports the depolymerization as the polymer band disappeared after treatment with thiolate anion (Figure 4d). For a more profound support of the depolymerization, we performed ^{1}H NMR of the depolymerized product and observed the disappearance of the distinctive broad polymer peak at δ2.80 ppm, and the whole spectrum looks very similar to the spectrum of the pure monomer (Figure 4e). Further, we performed another very interesting quantitative supporting experiment, liquid chromatography−mass spectrometry (LC−MS) (Figure S6), which revealed a prominent peak at 347.21 corresponding to the mass of the lipoic acid monomer (M1), thus suggesting the reversibility and reformation of the monomer. These experiments showed thiolate-mediated depolymerization, thus demonstrating the advantage of the dynamic covalent polymer toward the chemically recyclable polymer. In a control experiment, we treated the polymer with only DBU in the absence of butanethiol and found no change in the absorption band at 335 nm. In ^{1}H NMR, there was no change in the polymer peak at δ2.80 after treatment with only a base (Figure S7). Hence, the depolymerization indeed happened due to the reaction with thiol in the presence of a base.

One-Step Dual Modification at the Polymer Chain End. Next, the introduction of more than one functionality at the same site of a polymer chain is highly demanding to create a library of functional polymers. Prof. Du Prez and Prof. Espeel showed the double modification at the telechelic polymers,[68] but so far, there is no such report in the literature for the incorporation of multiple functional groups at the same site of the poly(disulfide)s chain. As poly(disulfide)s are considered a significant class of polymers, developing a new method for functionalization of poly(disulfide)s and accessing a library of functional polymers would be highly appreciable in the field of dynamic covalent polymer chemistry. In this article, we focused on the thiolactone ring opening mediated one-step double modification at the poly(disulfide) chain end in the process of polymer synthesis. The functional amine opens the thiolactone ring, releasing the thiolate anion that initiates the ring opening disulfide exchange polymerization by opening the 1,2-dithiolane monomer present in the same medium, enabling the quantitative introduction of two different functionalities (one from amine, i.e., R2, and another from the thiolactone derivative, i.e., R1) at the polymer chain end (Figure 5a,b). To expand the scope and versatility of this methodology, we have used one dithiolane monomer, four different amines, and three different thiolactone derivatives to synthesize (1 × 4 × 3= 12, P1 to P12) 12 functional dynamic poly(disulfide)s (Figure 6). The variation in monomer substitution, amine, and thiolactone would lead to the formation of a library of functional poly(disulfide)s. The detection of functional group present at the chain end of a relatively high-molecular-weight polymer is always a tricky job, and to overcome this problem, we have used a few amines with π-conjugated chromophore so that the functionalization can be traced by spectroscopic and NMR studies. Therefore, the in situ, one-step, dual modification provides access to poly(disulfide)s exhibiting a wide variety of functional polymers. Here, the corresponding amine introduces a variety of functionality, including *N*,*N*-diethyl, naphthalene, pyrene, and polyethylene glycol, at the end of the polymer chain, while the thiolactone derivatives incorporate pentafluorobenzene, a long hydrophobic chain and unsaturated chains. All of these functionalities in the polymers were detected by ^{1}H NMR spectroscopy. The change in SEC profile after the functionalization further confirms the successful functionalization (Figure S8). The ^{1}H NMR of P1, P5, and P9 revealed characteristic triplet peak at 0.95 ppm for six methyl protons (Ha) of the amine and peak at 2.8 ppm for g' and h' protons of the poly(disulfide)s (Figures S9, S13, and S17). This indicates the incorporation of amine functionality and formation of polymer. Similarly, the ^{1}H NMR of P2, P6, and P10 showed characteristics peaks in the aromatic region for naphthyl protons and peak at 2.8 ppm for g' and h' protons of the poly(disulfide)s, which suggest the incorporation of a naphthyl group and formation of a polymer structure (Figures S10, S14, and S18). In another set of polymers (P3, P7, and P11), the incorporation of the pyrene moiety was established by ^{1}H NMR peaks in the region of 8.0−8.5 ppm (S11, S15, and S19). For P4, P8, and P12 polymers, the conjugation of another hydrophilic polymer, i.e., polyethylene glycol, was successfully carried out as shown by the ^{1}H NMR peaks in the region of 3.3 ppm for $-OCH_3$ and 3.6 ppm for $-O-CH_2-$ (Figures S12, S16, and S20). For polymers P1 to P4, the presence of unsaturation contributed by the thiolactone derivative at the polymer chain end was shown by the ^{1}H NMR peak at 5.4 ppm (Figures S9, S10, S11, and S12). The incorporation of the pentafluoro phenol moiety at polymers P9−P12 was probed by the ^{19}F NMR data, which show peaks at −166, −156, and −147 ppm corresponding to the pentafluorobenzene (Figure S21). In polymers P5 to P8 (Figures S13, S14, S15, and S16), the long hydrophobic chain is incorporated by the thiolactone derivative, and successful incorporation was shown by the ^{1}H NMR peak at 0.9 ppm and 1.3−2.0 ppm corresponding to methyl and $-CH_2$ protons, respectively.

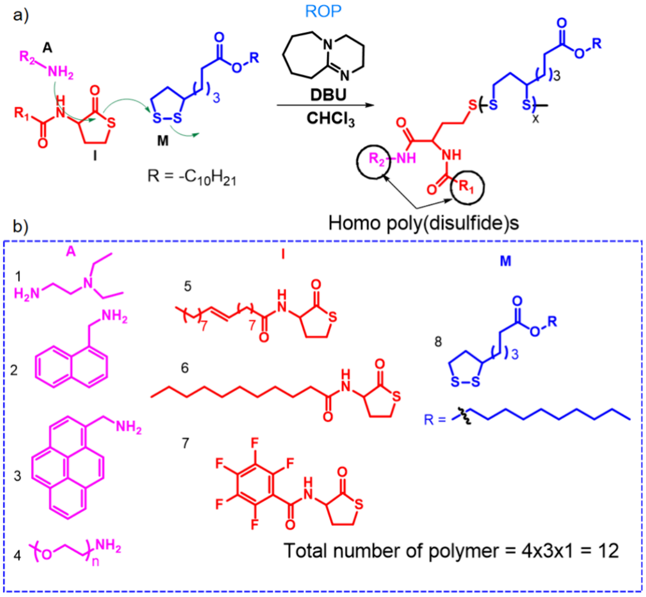


Figure 5. (a) General polymerization reaction scheme. (b) Structure of activators, initiator, and monomer used to make a library of poly(disulfide)s.

Probing the Living Nature of the Poly(disulfide) Synthesis and Preparation of Copoly(disulfide)s. Further, using this cascade ring opening method, we demonstrated the

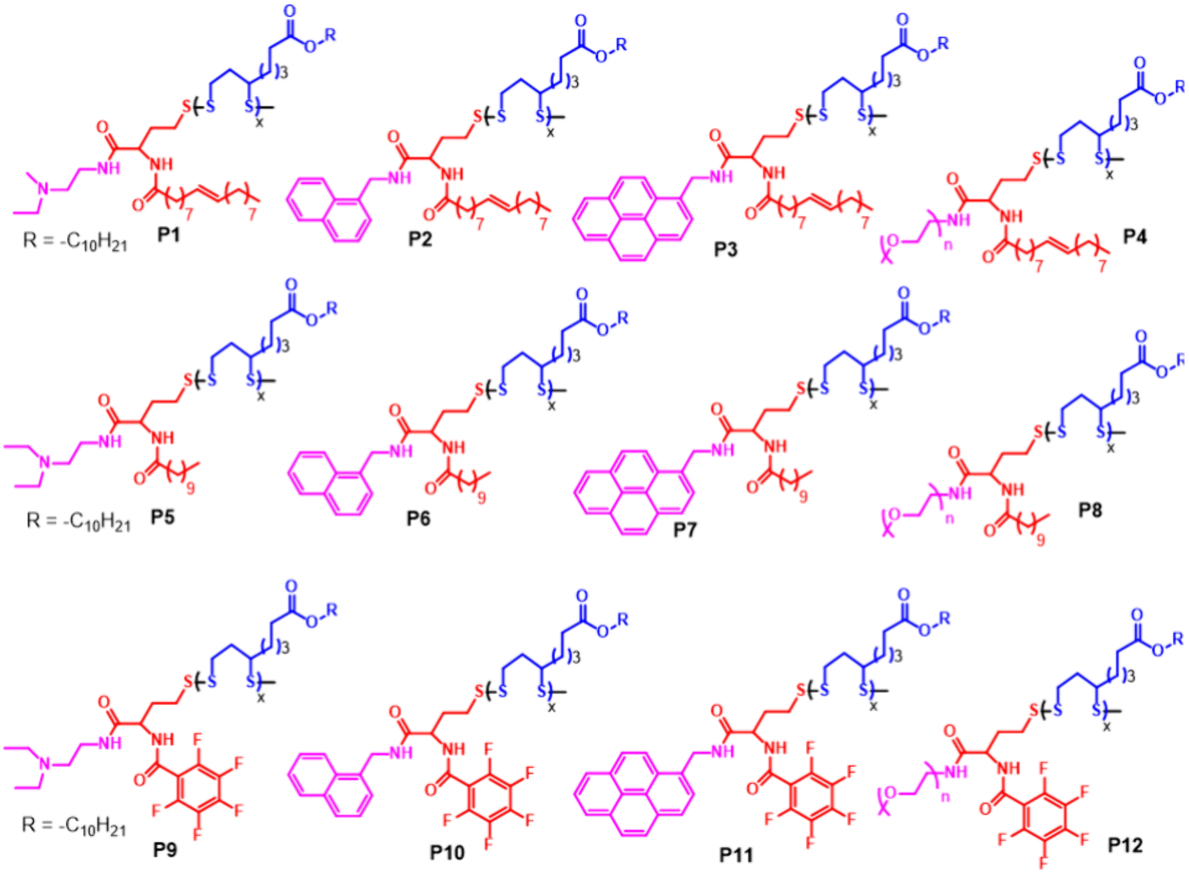


Figure 6. Chemical structure of the library of functional poly(disulfide)s synthesized by varying the activator and initiator.

very interesting living synthesis of functional copoly(disulfide)s (Figure 7a,b). Because there might be a possibility of chain transfer, we designated it as a copolymer instead of block copolymer. Here, we did not use any chain terminator after the completion of the synthesis of the homopolymer of the M1 monomer to keep the terminal thiol group as a free living thiolate anion for further extending the polymer chain in the presence of another 1,2-dithiolane monomer. To probe whether the free thiolate anion is indeed present at the polymer chain end, the very well-known Ellman's test was carried out using Ellman's reagent (Figure S22).[69] In a typical reaction, after complete consumption of the M1 monomer, an aliquot of the polymer solution was added to the Ellman's reagent, which showed a distinct band at 470 nm as indication of a positive Ellman's test result (see the SI for detail description). Hence, the polymer chain end with free thiolate shows a living nature, which can be utilized for further growth of the polymer chain. Next, to the original polymer solution, another hydrophilic 1,2-dithiolane monomer, M2, was added and allowed to polymerize for 120 min. After the polymerization, similar to the homopolymer synthesis, the Ellman's reagent shows a positive test result, i.e., the existence of a living nature of the polymer chain end (Figure S22). Further, for the attachment of another monomer, the hydrophobic monomer M1 was added again to the original polymer solution, and the polymerization was carried out for another 120 min. Lastly, the chain terminator was added to protect the thiolate anion; otherwise, it will let the polymer depolymerize over time in the absence of any new monomer. In this case, Ellman's test showed a negative result as the free thiol was already reacted with the chain terminator phenyl isocyanate (Figure S22). In a control experiment, by Ellman's test, we also showed further the existence of a living thiolate anion in the absence of a chain terminator (Figure S22). This suggests the probability of further connecting another type of monomer. The copolymer synthesis was monitored by UV/vis spectroscopy (Figure 7d−f) and the SEC profile (Figure 7c). The peak at 335 nm corresponding to the M1 monomer gradually reduced after the consumption of all the monomers, and then the addition of monomer M2 again shows a peak for monomer, which gradually reduced when all the M2 monomer was consumed. A similar observation is true for the synthesis of the last block by the addition of monomer M1 (Figure 7d−f). Here, we synthesized a copoly(disulfide) of three monomers (PM1-PM2-PM1'). The SEC profile clearly indicates a gradual increase of the molecular weight after the incorporation of each type of monomer. The molecular weight of the PM1 homopolymer was found to be 66,550 g/mol, and it increased to 95,660 g/mol after the addition of the next monomer, i.e., PM2 polymer, which further increased to 198,270 g/mol after the addition of the third monomer, i.e., PM1' (Figure 7c).

Thermal Property of the Poly(disulfide)s. Finally, we have checked the thermal properties of these copolymers by thermogravimetric analysis (TGA) to get an insight into the change in material properties after synthesizing the copolymer from the homopolymer following living polymerization. The TGA thermogram revealed a loss of 50 wt % of their original mass at 288 °C for the homopolymer (PM1), 305 °C for the copolymer (PM1-PM2), and 325 °C for the tricopolymer (PM1-PM2-PM1). The complete degradation of the homopolymer was achieved at 410 °C, whereas for the di- and

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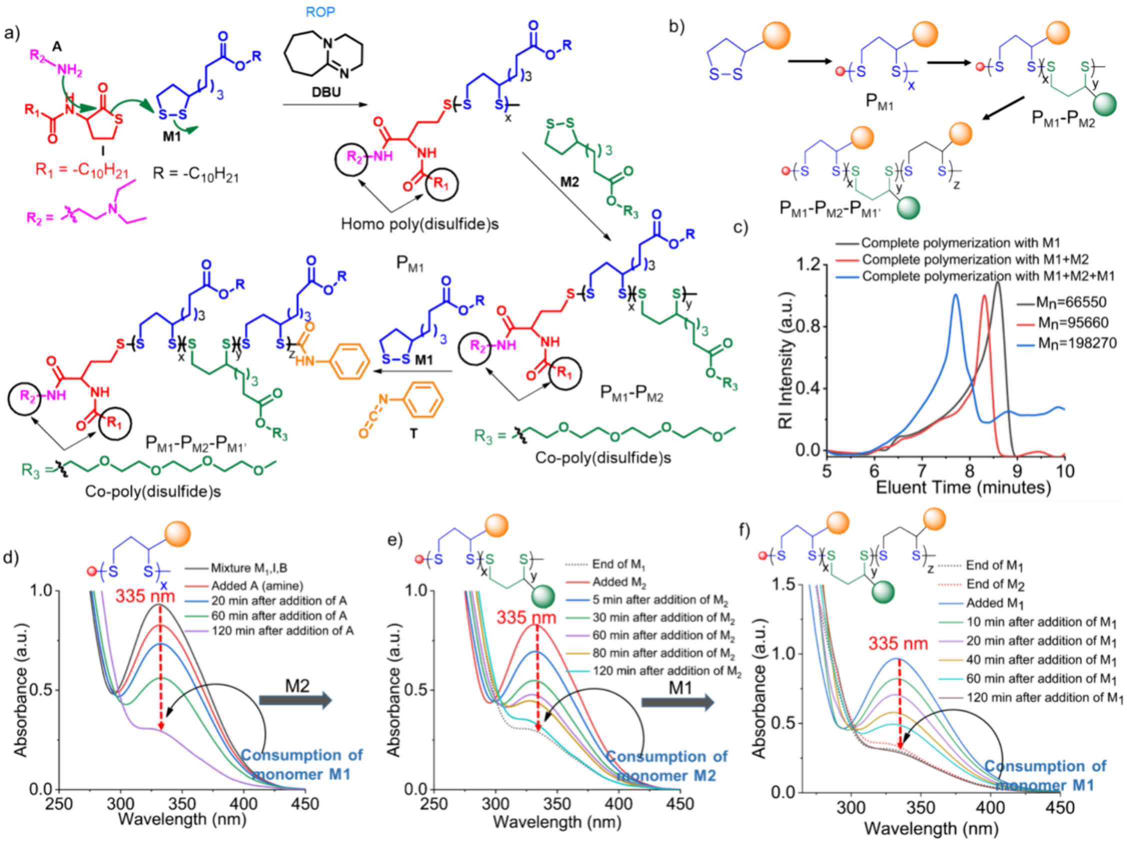

Figure 7. (a, b) Schematic representation of copoly(disulfide) synthesis. (c) SEC profile of the polymers. Monitoring the consumption of monomer (d) M1, (e) M2, and (f) M1 again by the absorption band of the monomer at 335 nm in UV/vis spectroscopy.

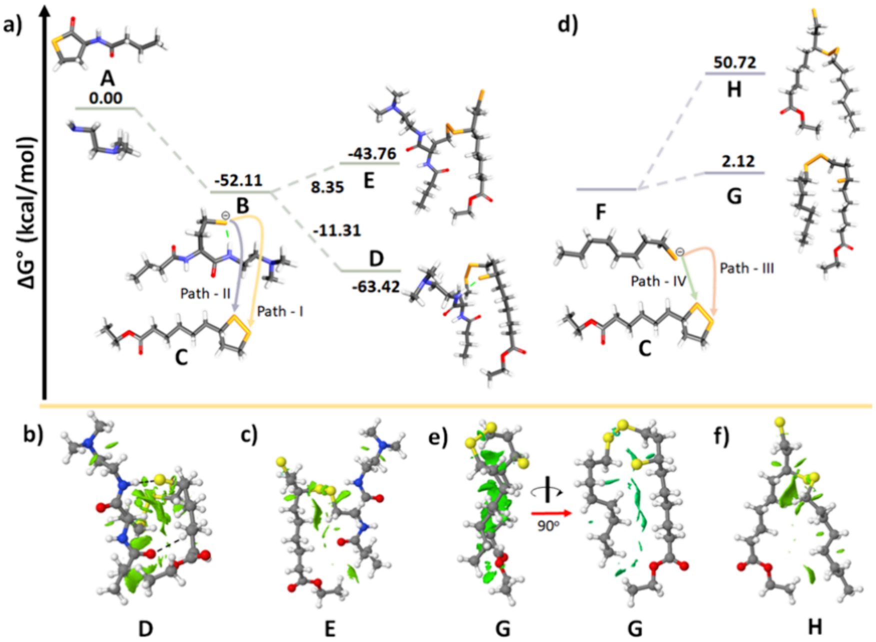

Figure 8. (a) Energy profile diagram of the cascade reaction using thiolactone as a source of *in situ* generated thiolate anion initiator. NCI plot of compounds (b) D and (c) E. (d) Energy profile diagram of the conventional reaction by thiolate anion. NCI plot of compounds (e) G and (f) H.

tricopolymer, the value was 450 °C (Figure S23a). Therefore, the improvement of thermal stability was observed with increasing molecular weight from homo- to tricopolymer. The analysis of differential scanning calorimetry (DSC) data of these polymers allowed the determination of the glass transition temperature (Tg). Interestingly, the Tg gradually increases from homopolymer to di- to tricopolymer (−44 to −39 to −21 °C) (Figure S23b−d). This can be attributed to the increasing molecular weight from the homopolymer to copolymer, which decreases polymer chain end concentration, resulting in less free volume at the end group region and hence higher Tg of tricopolymer.

Theoretical Calculation to Probe the Regioselectivity of the ROP and Feasibility of Thiolactone Ring Opening in ROP. To comprehend the polymerization reactions mentioned above, we utilized a combination of density functional theory (DFT) and noncovalent interaction (NCI) calculation. Initially, we observed that the nucleophilic attack by the amine on thiolactone A, resulting in the production of thiolate B, is a highly favorable and exothermic process with a free energy change of −52.11 kcal/mol (Figure 8a). The formation of the H-bond stabilized thiolate ion, and the amide bond from thiolactone played a crucial role in the stabilization of B, making the step feasible. The stable thiolate B can then initiate a polymerization reaction by attacking the 1,2-dithiolane ring (C). Interestingly, the two S atoms of the 1,2-dithiolane ring are attached to the primary and secondary carbon of the ring, allowing a choosable attack of thiolate B on the 1,2-dithiolane ring sulfur atoms (designated as paths I and II). When thiolate B attacks the S atom attached with primary carbon in the 1,2-dithiolane ring, a secondary thiolate D forms (path I); on the other hand, when it attacks the S atom attached with the secondary carbon, a primary thiolate E forms (path II) through the 1,2-dithiolane ring opening. Thermodynamically, the enthalpy changes for the S−S bond formation by thiolate attack and the S−S bond breaking by the opening of 1,2-dithiolane ring are nil for both the attacks. Additionally, the DFT results indicate that the formation of D is energy-releasing, producing 11.31 kcal/mol for this step, whereas the second type of attack (path II) is energy-demanding, requiring 8.35 kcal/mol. As a result, the formation of the D diastereomer (path I) is highly selective over the formation of E. To explore the reason for this selective attack, we performed NCI plots. The calculation indicates that the in situ generated thiolate anion from the thiolactone ring established a hydrogen bond with the amide N−H, which favors hydrophobic interactions between alkyl chains of D, as evident from the green isosurface in its NCI plot (Figure 8b). Meanwhile, due to the lack of proper molecular arrangement, such hydrogen bonds and hydrophobic interactions are less pronounced in E (Figure 8c). To assess the viability of this approach compared with the conventional method, we analyzed the energy dynamics of a similar reaction involving alkyl thiolate F (Figure 8d). The initial thiolate F attacks the sulfur atom attached with the primary carbon and yields the product G, which is a secondary thiolate anion (path III), requiring only 2.12 kcal/mol. However, an alternate attack occurs when thiolate F targets the sulfur atom attached with the secondary carbon of the 1,2-dithiolane ring, which results in primary thiolate (H) (path IV). This process is significantly energy-intensive, demanding 50.72 kcal/mol of energy. NCI plots of G (Figure 8e) and H (Figure 8f) further emphasize the critical role of hydrophobic interactions between the alkyl chains in their stability. The greater green isosurface of G compared to H indicates the superior stabilization of G. Therefore, it is important to note that the high-energy release during the formation of B, followed by the formation of D, establishes the superiority of this approach over the traditional method.

CONCLUSIONS

In conclusion, we report the controlled synthesis of dynamic covalent poly(disulfide)s by a new strategy of amine-activated one-pot cascade initiation of ring opening polymerization (ROP) at room temperature under an open-air condition. The cascade ring opening activated by amine leads to polymerization by the in situ-generated thiolate anion initiator. Here, the source of the thiolate anion is a thiolactone derivative, and the advantages of the thiolactone derivative and amine activator are as follows: (a) the amine mediated in situ generation of thiolate anion and (b) the incorporation of multiple functionalities via amine at the polymer chain end in the course of polymerization. The in situ, one-step, dual modification at the same site of the polymer by amine and thiolactone is considered to be a very attractive feature of this methodology of poly(disulfide) synthesis. The thiolate anion generated after the ring opening of 1,2-dithiolane is responsible as the living site for polymerization elongation and incorporation of different monomers as well. The cascade initiation of the polymerization by primary amine at room temperature and open-air condition and the absence of a complex catalyst made the reaction simple and versatile and enabled very fast polymerization. The depolymerization to monomer, i.e., recyclability, also was completed within a very short time and probed by various spectroscopic and SEC techniques. We demonstrated the living nature of the polymer and stitching of various monomers to synthesize copoly(disulfide)s in a very controlled manner. We anticipate that this work not only represents the first example of amine-activated cascade polymerization of the 1,2-dithiolane ring but also provides the opportunity of accessing a library of functional dynamic covalent poly(disulfide)s. This might be an easy gateway of incorporating multiple functionalities in the poly(disulfide) chain end and synthesizing functional recyclable polymers.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.macromol.4c02361.

> The synthesis of monomer, initiator, and controlled and functional poly(disulfide)s polymer scheme and procedure; ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra; LC−MS data; time-dependent UV/vis plot for the kinetics of polymerization and some controlled experiments; Ellman's profile diagram during poly(disulfide) polymerization; size exclusion chromatography (SEC) profile for the library of synthesized functional poly(disulfide)s polymers; and thermal properties like TGA and DSC of synthesized copolymers (PDF)

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Notes

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