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Disulfide-Mediated Reversible Polymerization toward Intrinsically Dynamic Smart Materials

Qi Zhang, Da-Hui Qu,* Ben L. Feringa, and He Tian*



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ABSTRACT: The development of a dynamic chemistry toolbox to endow materials dynamic behavior has been key to the rational design of future smart materials. The rise of supramolecular and dynamic covalent chemistry offers many approaches to the construction of dynamic polymers and materials that can adapt, respond, repair, and recycle. Within this toolbox, the building blocks based on 1,2-dithiolanes have become an important scaffold, featuring their reversible polymerization mediated by dynamic covalent disulfide bonds, which enables a unique class of dynamic materials at the intersection of supramolecular polymers and adaptable covalent networks. This Perspective aims to explore the dynamic chemistry of 1,2-dithiolanes as a versatile structural unit for the design of smart materials by summarizing the state of the art as well as providing an overview of the fundamental challenges involved in this research area and its potential future directions.

INTRODUCTION

Dynamic behavior as a signature feature of living systems has become a common goal in modern material research.^{1–3} Endowing synthetic materials with dynamic properties is not only the chemical basis for future smart materials,⁴ but it also facilitates the fundamental understanding of dynamic chemical systems in nature. Dynamic chemistry, including supramolecular noncovalent and dynamic covalent chemistry,^{5–8} offers a tremendous toolbox to fabricate dynamic materials from a “bottom-up” approach. These materials exhibit life-like architectures, functions, and motions at all scales,^{9–12} including responsive molecular units, supramolecular self-assembly, and macroscopic motions.^{13–15} During the past decades, increasing awareness of the importance and urgency of evolving traditional synthetic materials, such as plastics, toward dynamic, responsive, and recyclable materials, has pushed an exponential development of this area.^{16–22} Despite the many milestones attained by supramolecular and dynamic covalent chemistry,^{23–30} there is a growing need to expand the chemical toolbox for fabricating dynamic materials, especially those combining the features of dynamic covalent and noncovalent materials.

Among many dynamic chemical bonds, the disulfide bond, the bond that ties peptides,³¹ acts as a key player in determining the dynamic properties of many proteins.³² Disulfide bonds simultaneously combine the features of robustness and dynamicity.³³ The robustness stems from the covalent disulfide’s bond dissociation energy (60 kcal mol⁻¹).³⁴ With respect to dynamicity, the fast thiol–disulfide exchange reactions make these robust linkages reversible under mild conditions.³⁵ The structure–dynamicity relationships of a series of disulfides has been well established, including those found in cyclic disulfides activated by the ring strain.^{35–39} The introduction of disulfide bonds in a polymeric network as dynamic cross-links has become more prevalent,^{40–44} resulting

in dynamic covalent materials exhibiting repairability and stimuli-responsiveness.⁴⁵ These pioneering efforts represent the milestones of utilizing these nature-derived dynamic covalent bonds for capturing contemporary opportunities in designing dynamic smart materials.

This Perspective will focus, instead of providing a comprehensive review of dynamic covalent chemistry and related materials,^{46–50} on the recent progress of designing dynamic materials by the reversible polymerization of cyclic disulfides, especially five-membered 1,2-dithiolanes. As opposed to disulfide-cross-linked networks,^{40–45} the emphasis of this work is to combine disulfide-based dynamic chemistry with ring-opening polymerization (ROP) to enable mainchain-dynamic polymers and materials capable of performing distinctive assembling processes and functional applications. The objective of this Perspective is to give timely insights into the most promising directions and multidisciplinary applications associated with this dynamic chemistry toolbox. This Perspective will start with the discovery and development of the disulfide-mediated ROP, including polymerization methodologies and supramolecular assembly control. Then state-of-the-art multidisciplinary applications for dynamic smart materials are summarized. It concludes with an outlook of the current challenges and future opportunities for intrinsically dynamic smart materials. Due to limited space, only a small number of representative examples on this topic are highlighted.

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METHODOLOGY DEVELOPMENTS

The first chemical synthesis of poly(1,2-dithiolane)s was serendipitous. When exploring the chemical synthesis of thioctic acid (TA),^{51,52} a naturally occurring 1,2-thiolane, the observation of poly(TA) polymers was reported in 1956 by Thomas and Reed, and it was described as “sticky, colorless polymers are produced as by-products in the oxidation of DL-6,8-dithiolactanoic acid”.⁵³ At the very same time, Calvin et al. reported the photoinduced polymerization of 1,2-dithiolanes by spectroscopic methods (Figure 1),⁵⁴ showing disulfide bonds can be activated by the ring strain of five-membered rings. The bonds dissociate into diradicals upon irradiation with long-wavelength UV light, resulting in the formation of polymers/oligomers in diluted solutions. These two pioneering

studies at an early stage represent a milestone that initiates the exploration of poly(1,2-dithiolane) polymers.

A more detailed understanding of poly(1,2-dithiolane) based on unambiguous structural information started with the study by Endo et al. in 2006.^{55,56} In that study, high-molecule-weight homopolymers of 1,2-dithiolanes and copolymers with six-membered 1,2-dithianes were prepared by the one-pot melting polymerization method. The initiator-free polymers were found to be cyclic. Dynamic viscoelasticity measurements indicated a rubbery plateau region in the absence of covalent or noncovalent cross-linkers, and the region became smaller with decreased frequencies, suggesting mechanical entanglements among the resulting cyclic polymer chains. Combined with other structural evidence, it was concluded that the resulting poly(1,2-dithiolane)s feature a mechanically cross-linked poly(catenanes) network. This example was also recognized as one of the very few approaches to access mechanically interlocked poly[*n*]catenanes.^{57,58}

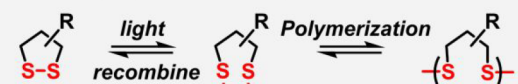
The living polymerization of poly(1,2-dithiolane)s has been developed in the last decades toward more precise control over capping groups, polymer length, and molecular weight distribution.^{59–63} A general strategy involves initiating the polymerization with thiolates capable of easily targeting and breaking disulfide bonds to induce the growth of polymer chains by cascaded ROP. The reversible nature of the thiolate-disulfide exchange enables the ROP process of 1,2-dithiolanes to be thermodynamically controlled like many other ROP.⁶⁴ Matile et al. pioneered the anionic ROP of 1,2-dithiolanes in 2011 (Figure 1).⁵⁹ They utilized asparagusic acid (AA) units, a symmetric 1,2-dithiolane, as the terminal polymerizable groups of a building block that can perform typical H-type supramolecular self-assembly through aromatic stacking and H-bonds. Initiated by reactive thiolates liberated from (S,S)-dithiothreitol in situ on a substrate, surface-supported polymer brushes of poly(1,2-dithiolane)s can be formed by the synergy of dynamic covalent disulfide-mediated polymerization and supramolecular self-assembly, resulting in well-controlled polymeric materials on surfaces. Then the same group extended the concept to poly(disulfides)-assisted cell penetration by replacing the substrate of thiolate initiators with drugs and probes incapable of penetrating cells without assistance (Figure 1).⁶⁰ The inherent depolymerization ability of the poly(1,2-dithiolane)s further enables the on-demand release of substrates. This creative concept inspired the biological application of poly(disulfides), as detailed in a separate perspective.⁶⁵

The ring strain of 1,2-dithiolanes plays a key role in determining the thermodynamics of the monomer–polymer equilibrium. Widely used 1,2-dithiolanes include TA, AA, and their derivatives, which due to the ring strain enable high conversion to the polymer at the equilibrium state. Waymouth et al. compared the thermodynamic aspects of the monomer–polymer equilibrium of monosubstituted 1,2-dithiolanes,⁶¹ (e.g., TA methyl ester) and disubstituted 1,2-dithiolanes, (e.g., methyl-substituted AA (MAA) methyl ester). The equilibrium constant, K_{eq} , of TA methyl ester was approximately 3 times higher than the equilibrium constant for MAA methyl ester. The mechanism and structural basis for the differences caused by the substitution effect is attributed as a typical example of the Thorp–Ingold effect.⁶⁶ In other words, the additional methyl substitution can facilitate the ring-closing reaction (i.e., the depolymerization reaction).

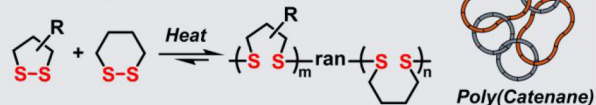
i) Chemical oxidation (from thiols) (Reed et al.)^{52,53}



ii) Photo-polymerization (Calvin et al.)⁵⁴



iii) Thermal polymerization (Endo et al.)^{55,56}

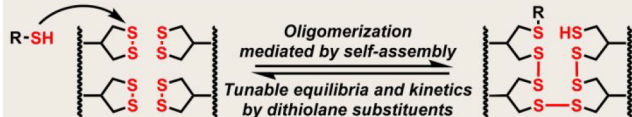


iv) Thiolate-initiated ROP

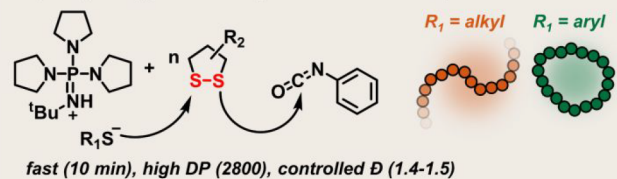
a) On surfaces/interfaces (Matile et al.)^{59,60}



b) In confined micelles (Waymouth et al.)⁶¹



c) Topology control (Liu, Moore et al.)⁶²



d) Cryo-polymerization (Lu et al.)⁶³

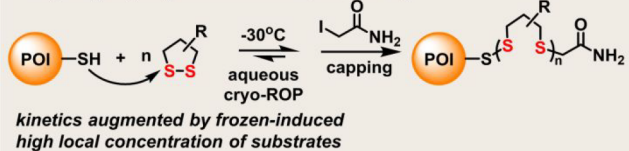


Figure 1. Synthetic methodology development of poly(1,2-dithiolane)s, from discovery to well-controlled living ROP. The milestones are listed following the time sequence.

Topological control endows polymer property tunability via spatially geometrical architectures.⁶⁷ For the topology of poly(1,2-thiolanes), in general, the polymers made from solvent-free melting methods result in cyclic structures.^{55,56} The photopolymerized products are cyclic in the solvent-free state,⁶⁸ but become linear when proton-donor solvents, such as water and alcohols, protonate the sulfur radicals to form relatively inactive thiol end groups.⁶⁹ Living polymerization initiated by thiolates shows a high dependency on the initiator type. Liu and Moore et al. reported alkyl thiolates led to linear poly(1,2-dithiolane)s,⁶² while aryl thiolates produced cyclic species (Figure 1), because of the different nucleophilicity of initiators. Using organic bases with high steric hindrance and benzyl mercaptan or benzenethiol as the initiators enables the fast polymerization of large polymers (630 kDa) with a low dispersity and precise architecture control. This approach represents the state-of-the-art polymerization methodology for the synthesis of poly(1,2-dithiolane)s.

The disulfide-rich backbone of poly(1,2-dithiolane)s brings inherent redox responsiveness and the reduction-degraded products are small-molecule monomers with biocompatibility.⁷⁰ This feature makes poly(1,2-dithiolane)s potentially useful as biodegradable polymers for biomaterials. A necessary step in achieving this goal requires the application of aqueous polymerization to poly(1,2-dithiolane)s, which depends upon high water solubility of the monomers and general aqueous polymerization methodologies. Several water-soluble 1,2-dithiolanes have been synthesized by modifying the monomeric side chain with water-soluble groups.^{60,63,71,72} Taking advantage of these building blocks, water-soluble initiators can be used to trigger the aqueous ROP of 1,2-dithiolanes capped by water-soluble reactants.⁶⁰ However, the limited water solubility of monomers results in a low yield of polymers in aqueous solutions. To overcome this issue, Lu and co-workers recently reported how a frozen environment can assist the ROP of 1,2-dithiolanes in aqueous solutions with both favorable thermodynamics and augmented kinetics, due to local concentration of monomers induced by freezing.⁶³ This method enables high conversion for preparation of protein-poly(1,2-dithiolane) conjugates. The inherent existence of thiol groups in many proteins avoids the tedious chemical installation of initiator groups for polymers. Meanwhile, the glutathione-induced depolymerization of poly(1,2-dithiolane)s also enables an effective degrafting reaction on demand and *in vivo*. This work represents a substantial progress for poly(1,2-dithiolane)s as cleavable polymers for dynamic protein modification.

Since their discovery in 1950s, the synthetic methodologies applied to poly(1,2-dithiolane) polymers have ranged from the less controllable oxidation of dithiols to topology-tunable anionic ROP with high homogeneity (Figure 1). Despite these improvements in controllability, many fundamental challenges hinder further applications of this polymer. For example, current strategies for controlled polymerization of 1,2-dithiolanes rely on thiolate-initiated anionic ROP, which requires the bases and thiolates to remain inert (i.e., limiting the diversity of substrates). As previously stated, realizing chemoselective polymerization of asymmetric 1,2-dithiolanes remains unknown.^{73,74} Sequence-specific copolymerization of different 1,2-dithiolanes still presents a significant challenge. A polymer system standing at the interface of dynamic covalent chemistry and ROP requires further exploration. In addition to advancing synthetic methods, the next steps involve exploring

the fundamental approaches to control the assembly as well as practical applications in dynamic functional materials, which will be discussed in the next two sections.

■ SUPRAMOLECULAR CONTROL

Supramolecular control over polymers enables dynamic modulation of self-assembly, topological transition, and long-range order of polymer chains.^{75–78} Considering the dynamic covalent mainchain of poly(1,2-dithiolane)s, it is intriguing to engineer the side chain taking advantage of the versatile supramolecular (noncovalent) toolbox, which can serve as a unique scaffold to explore many fundamental questions. For example, could two or more types of dynamic covalent and supramolecular systems be orthogonalized in a single chemical network?^{79,80} How do they affect, cooperate, or even communicate with each other? In the case of poly(1,2-dithiolane)s, supramolecular side chain engineering may not only control the interchain cross-links, but it may tune the dynamic polymerization equilibrium of 1,2-dithiolanes by controlling the cross-links' spatiotemporal distribution. Moreover, the simultaneous presence of dynamic covalent and noncovalent bonds may also improve material performances through synergistic effects.

For example, using natural 1,2-dithiolane TA as a starting material, our group explored a series of dynamic supramolecular materials exhibiting tunable mechanical properties and dynamic functions (Figure 2).^{81–84} TA was selected because of its low cost, biocompatibility, and the carboxyl group that can be a versatile noncovalent site. The low melting point of TA allows poly(TA) to be easily formed by melting TA solids at 70 °C. Further, a free-standing network can be formed by continuing to cross-link the polymer with 1,3-diisopropenylbenzene (DIB) and iron(III) ions.⁸¹ The resulting materials exhibited a low Young's modulus of 81 KPa and highly stretchable mechanics because of the weak H-bond cross-linking of carboxyl groups. The supramolecular cross-linking also endowed the material with a fast self-healing ability at room temperature. Freshly cut materials can be completely repaired within 5 min. Meanwhile, the dynamic covalent mainchain should also contribute to the self-healing process because the self-healing ability is not hindered by interface aging or immersion in water, which usually inhibits H-bond-enabled self-healing processes. Moreover, this supramolecular material readily made from small-molecule TA can be used as a novel reusable hot-melt adhesive, exhibiting a strong and repeatable adhesive ability for many surfaces.

By further investigating the role of iron(III) ions in the poly(TA-DIB-Fe) network, we found adding iron(III) ions substantially strengthens materials due to the formation of strong iron(III)–carboxylate complexes.⁸² Unexpectedly, iron(III)–carboxylate complexes at higher concentrations in the solvent-free network can lead to further aggregation into secondary ionic clusters through Coulombic forces, which is usually hindered in a solvated network (i.e., gels) because the solvation effect of solvents inhibits the secondary ionic interactions.⁸⁵ Thus, the resulting ionic clusters remarkably strengthened the materials (Young's modulus increased from 81 KPa to 5.1 MPa) without compromising the stretchability or the room-temperature self-healing capability. Due to the simplicity of the material preparation and starting materials,⁸⁶ this multifunctional dynamic supramolecular material has been widely used as a polymer platform in many emerging

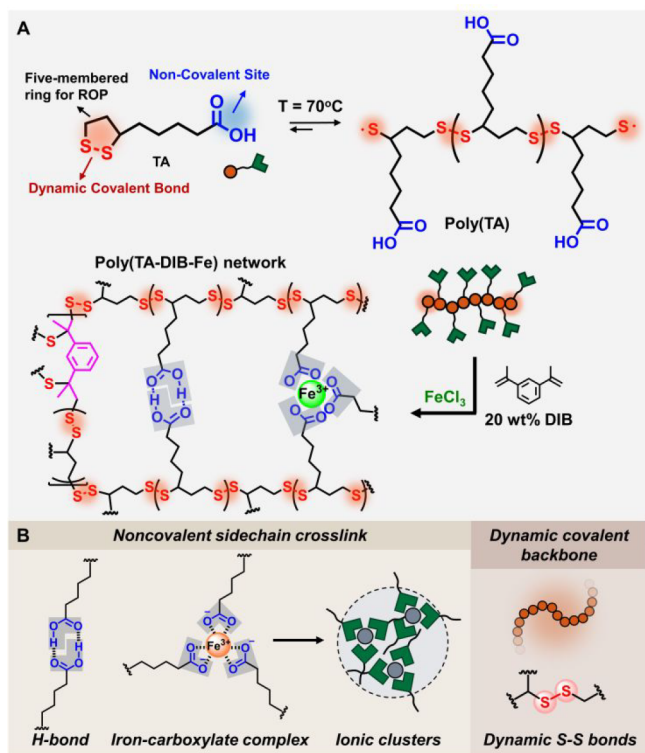


Figure 2. Supramolecular side chain cross-linking strategy to enable simultaneous noncovalent and dynamic covalent network. (A) Molecular illustration of the one-pot solvent-free ROP of TA followed by cross-linking by DIB and iron(III) ions. For clarity, only one possible regio- and stereochemical structure of the random polymers is presented. (B) Schematic representation of the dynamic chemical bonds in the network. Ionic clusters of iron–carboxylate complexes are observed in the network when the concentration of iron(III) ions is up to 1% molar ratio of TA.

applications such as wearable devices, electronic skins, and flexible sensors.^{87–94}

Another feature of TA molecule is its amphiphilic structure, offering supramolecular pathways to confine the dynamic covalent ROP of 1,2-dithiolanes within the hydrophobic microenvironments of micelles and vesicles.^{61,95–99} For example, Zhang et al.⁹⁶ reported the use of TA-ammonium salts as building blocks for preparing micelles and vesicles by amphiphilic self-assembly in aqueous media. These can be further covalently cross-linked by light-induced ROP of the hydrophobic 1,2-dithiolanes. The resulting polymersomes can act as carriers for capturing specific molecules, such as drugs and probes, and then release them upon chemical reduction by glutathione, a small molecule related to many human diseases.¹⁰⁰

Controlling polymer crystallinity (i.e., assembling order) can maximize interchain supramolecular interactions, including van der Waals forces and H-bonds, and usually enables the formation of high-performance materials.^{101,102} Generally, polymer crystallization occurs in polymer melts that simultaneously exhibit a high tacticity and an ordered backbone sequence.¹⁰³ However, the lack of a chemoselective polymerization method forces poly(1,2-dithiolane)s to exist as an amorphous material. Introducing strong supramolecular interactions like Coulombic forces and templating strategies using physical forces may lead to self-assembly with high ordering.¹⁰⁴

Recently, our group discovered a simple approach for assembling ordered layered architectures by combining amphiphilic organization, dynamic covalent ROP, and evaporation-induced interfacial self-assembly (Figure 3).⁸²

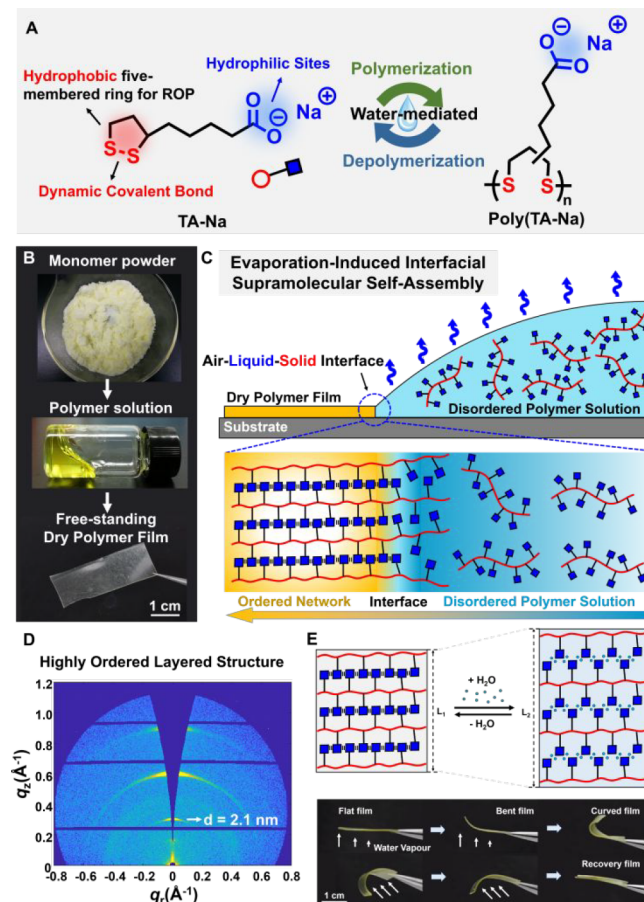


Figure 3. Reversible polymerization of TA-Na in aqueous solution. (A) Molecular illustration of the amphiphilic structure of TA-Na and the polymer structure. (B) Photographs of the monomers and the resulting polymeric film. (C) Schematic representation of the evaporation-induced interfacial supramolecular self-assembly of TA-Na aqueous solution on a substrate. The movement of the air–liquid–solid interface drives the local concentration and ordered polymerization of TA-Na. (D) Two-dimensional SAXS pattern of the resulting dry poly(TA-Na) film. The sharp scattering peaks indicate the highly ordered layered architecture. (E) Schematic representation and photographs of the humidity-responsive actuation ability of the resulting poly(TA-Na) film with ordered layered structure. The absorbed water molecules are present in the hydrophilic side chain carboxylate region as water channels. Reproduced with permission from ref 82. Copyright 2019 American Chemical Society.

Based on the natural amphiphilic structure of TA molecule, we deprotonated the carboxyl groups of TA and obtained sodium thioctate (TA-Na) with a high water solubility (Figure 3A). A free-standing film of poly(TA-Na) was easily formed by slowly evaporating the aqueous solution of TA-Na monomers on surfaces (Figure 3B,C). X-ray small-angle scattering (SAXS) indicated the polymer films formed a highly ordered layered structure with an interlayer distance of 2.1 nm (Figure 3D). The high degree of ordering was induced by the interfacial effect that spatially confined the dynamic covalent polymer growth and the supramolecular ionic cross-linking. The resulting ordered layered architectures promoted the materials

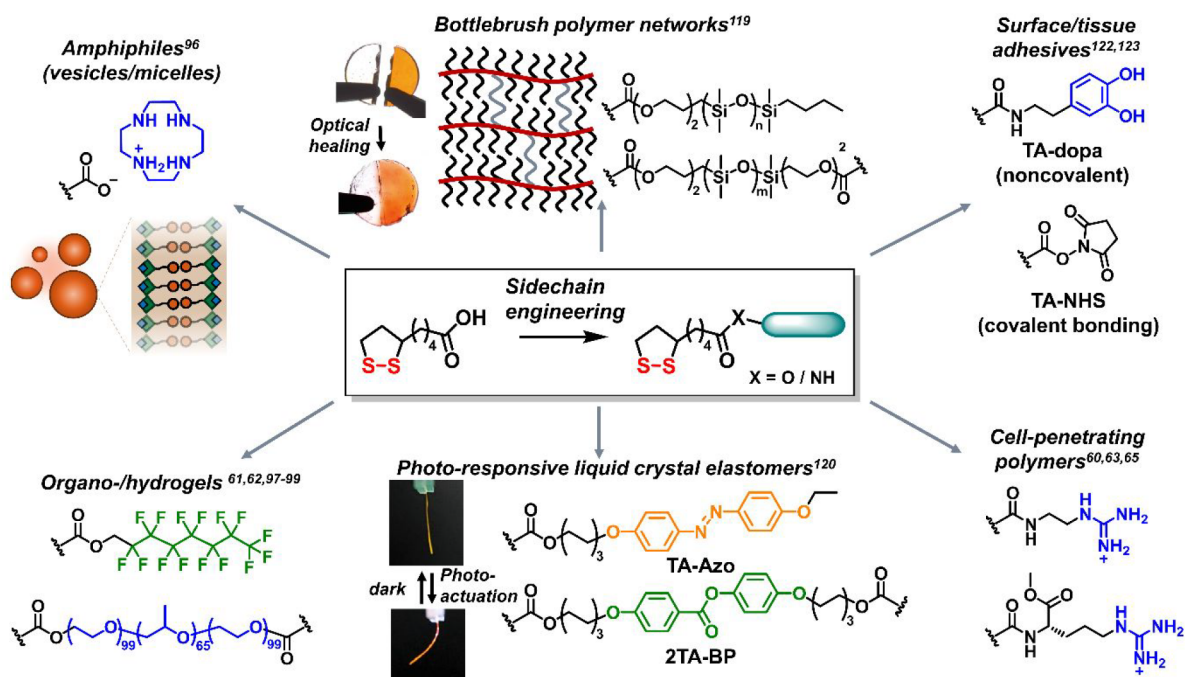


Figure 4. Side chain engineering strategy diversifies the multidisciplinary applications of poly(1,2-dithiolane) polymers. Reproduced with permission from refs 119 and 120. Copyright 2021 American Chemical Society.

mechanical robustness and humidity responsiveness (Figure 3E). In addition, the poly(1,2-dithiolane) backbones endowed the resulting materials with the ability to self-repair cracks in humid environments and depolymerize into monomers after dissolving in water by taking advantage of its dynamic functions. This general method of evaporation-induced ROP of ST has been used to prepare polymer-nanoclay composite materials that exhibit robustness and dynamic recyclability.¹⁰⁵ Due to the layered nature of materials with highly ordered water channels, the materials may possess proton transporting properties if larger-scale long-range order can be realized by more continuous physical fields, such as flow,¹⁰⁴ magnetic field,¹⁰⁶ and mechanical shearing.¹⁰⁷

TRENDS IN APPLICATIONS

Dynamic polymeric materials are used in a number of fields and attract increasing attention due to the quest for future plastics with intrinsic recycling properties.^{16–22,108,109} The signature dynamicity of poly(1,2-dithiolane)s comes from their disulfide-rich mainchain backbone. Compared with other dynamic chemistry opportunities, such as macrocycle-based host–guest systems,¹¹⁰ 1,2-dithiolanes feature structural simplicity and compatibility with many chemical environments. The disulfide bond is intrinsically dynamic, and the dynamicity is extrinsically controllable.¹¹¹ As such, the disulfide-linked mainchain can be readily switched between dynamicity (i.e., fast dissociable exchange) and stability (i.e., robust covalent bonding). This feature makes poly(1,2-dithiolane)s fundamentally intriguing because they combine the robustness of covalent polymers and the intrinsic dynamicity of supramolecular polymers in a single molecular system.

The structural simplicity of the 1,2-dithiolanes allows a large chemical space to explore tunability and diversity with respect to chemistry and materials. Generally, the building blocks of 1,2-dithiolanes can be molecularly engineered via two pathways: mainchain engineering and side chain engineering.

The former can be realized by modulating the ring strain of 1,2-dithiolanes using a substituent effect, such as the Thorpe–Ingold effect. Some recent studies on synthesis and modification methodologies expanded the building block library of 1,2-dithiolanes.^{112–114} Six-membered disulfide rings are also polymerizable,^{55,115} despite the fact that their lower ring strain contributes a lower enthalpic force for the ROP when compared to five-membered 1,2-dithiolanes. The diselenium bond is an emerging type of dynamic covalent bond.^{116–118} Replacing the two sulfur atoms with selenium atoms can produce diselenium-mediated materials with unique dynamic properties. Fundamental studies on poly(diselenium)s are still very rare, and more attention should be given to such systems in the future.

However, side chain engineering strategies can significantly expand the application scope of poly(1,2-dithiolane)s. Similar to well-established polyacrylates, the side chain, especially one with carboxyl groups, offers modification sites for diverse applications. A series of TA-derived 1,2-dithiolanes was synthesized, and these polymers were successfully utilized as functional materials in diverse areas, such as stimuli-responsive vesicles, bottlebrush polymer networks,¹¹⁹ gels,^{97–99} photo-responsive liquid crystal elastomers,¹²⁰ adhesives,^{68,81,121–123} and biomaterials^{60,63} (Figure 4).

The replacement of traditional polymeric backbones with poly(1,2-dithiolane)s can additionally provide dynamic functions. For example, by taking advantage of the inherent photoresponsive ability of 1,2-dithiolanes, Bates and Read de Alaniz et al. reported the readily photo-cross-linked bottlebrush network created by using TA as the terminal group of PDMS polymers.¹¹⁹ The PDMS-TA precursor can be completely cured by UV light irradiation (365 nm) in 100 s. The resulting cross-linked network exhibited fast repairability under UV light irradiation (Figure 4), which occurred due to the photoexcited disulfide exchange. The disulfide-cross-linked network can also degrade into oligomeric species after heating

to 180 °C or adding basic or reducing reagents. Instead of using TA as the terminal groups, our group reported the side chain TA-grafting strategy to endow PDMS linear polymers with photo-cross-linking ability as well as increasing chemical dissociation initiated by thiolates.¹²⁴ These efforts reveal a potential direction for designing dynamic photocuring materials based on 1,2-dithiolanes for various applications including 3D printing, coatings, and other soft materials.

The reversible polymerization ability of 1,2-dithiolanes is a key feature desired by future sustainable plastics. Chemical recycling of synthetic polymers, especially those exhibiting recyclability in a closed-loop manner,^{16–21} has become a major goal for chemists due to the pressing need for society to address environmental, energy, and health concerns associated with plastics. The depolymerization process of poly(1,2-dithiolane)s can be triggered by the simultaneous presence of a dilute solution and the conditions required for activation of the open-chain disulfide bonds, such as heat (>150 °C),⁶⁸ nucleophiles (e.g., thiolates, hydroxyl ions, and sulfur radicals),¹¹¹ and short-wavelength UV light.⁵⁵ The concept of depolymerizing poly(1,2-dithiolane)s has been the focus of several studies.^{53,60–63} However, with regards to cost-effective chemical recycling, the recycling conditions of polymers should be scalable, environmentally friendly, and cost efficient. In addition, an important feature for the recycling involves how high-quality monomers can be readily separated from the depolymerized mixtures.^{17,20}

Our study recently demonstrated chemical recycling of poly(TA) polymers in a dually closed-loop manner (Figure 5).⁸⁴ By using a dilute aqueous solution of sodium hydroxide (0.5 M), both poly(TA-M) (M = Fe³⁺, Cu²⁺, Zn²⁺, Ca²⁺) elastomers and poly(TA-Na) ionic networks can be readily depolymerized into monomers due to a base-catalyzed cascade depolymerization. The degraded mixture can be purified first

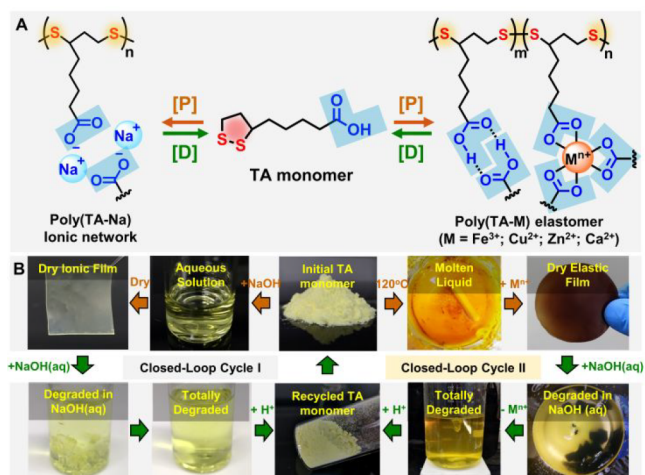


Figure 5. Dual closed-loop chemical recycling system of TA-based polymers. (A) Molecular structures of TA monomer and the resulting polymers. [P] refers to polymerization and [D] refers to depolymerization. For clarity, only one possible regio- and stereochemical structure of the random polymers is presented. (B) Procedures of the circular system being initiated from TA monomers, involving two kinds of polymers, and recycling back to the same monomer. The depolymerization step is performed in 0.5 M NaOH aqueous solution, and the monomer recovery is realized by acidification-induced precipitation. Reproduced with permission from ref 84. Copyright 2021 Elsevier.

by filtration (to remove metal precipitates), followed by acidification (to precipitate TA monomers from the water), and concluded with a second filtration (to collect the TA monomers as yellow crystalline solids). The recycled TA monomers are of virgin quality and can be used for regenerating polymeric materials capable of exhibiting identical mechanical properties as the original materials. Moreover, owing to the self-healing and reprocessability of the supramolecular network, poly(TA) materials can be both physically and chemically recycled (i.e., possessing a long life cycle and multipath recycling characteristics). Although these materials are still in the proof-of-concept stage, the principle of dynamic covalent and noncovalent materials with chemical recyclability can be expanded to many other materials with diverse applications.

For example, a recent example reported by Li et al. detailed a chemically recyclable liquid crystal elastomer based on a poly(1,2-dithiolane) backbone.¹²⁰ The resulting cross-linked network maintained the long-range order of a liquid crystal elastomer, so it could perform photoinduced actuation. The poly(1,2-dithiolane) network can be degraded into soluble monomers and oligomers by external addition of thiolates, and similar polymeric materials can be recovered from these degraded species. This work represents a significant step toward introducing the dynamic chemistry of poly(1,2-dithiolane)s into the field of liquid crystal elastomers.

The capability of reversible polymerization of poly(1,2-dithiolane)s can also be extended to surface modification (i.e., chemically recyclable surfaces), as shown in Figure 6. The binding of polymers to surfaces can be realized via covalent or noncovalent approaches. As demonstrated above, Matile et al. pioneered the surface-initiated ROP of 1,2-dithiolanes since 2011 by introducing thiolates on surfaces followed by the covalent growth of poly(1,2-dithiolane)s on the surfaces.⁵⁹ Supramolecular bonding via H-bonds,⁸¹ metal–ligand com-

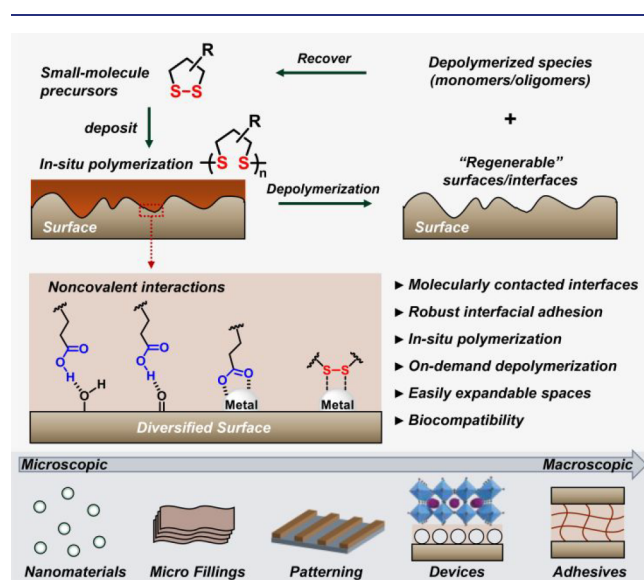


Figure 6. Applications of poly(1,2-dithiolane)s in surface-functionalized dynamic polymeric materials. The 1,2-dithiolane monomers (precursors) can penetrate the surfaces due to their small-molecule nature. Then in situ polymerization produces robustly adhered interfaces supported by noncovalent interactions or covalent bonds. The intrinsically dynamic backbone of poly(1,2-dithiolane)s enables the subsequent depolymerization.

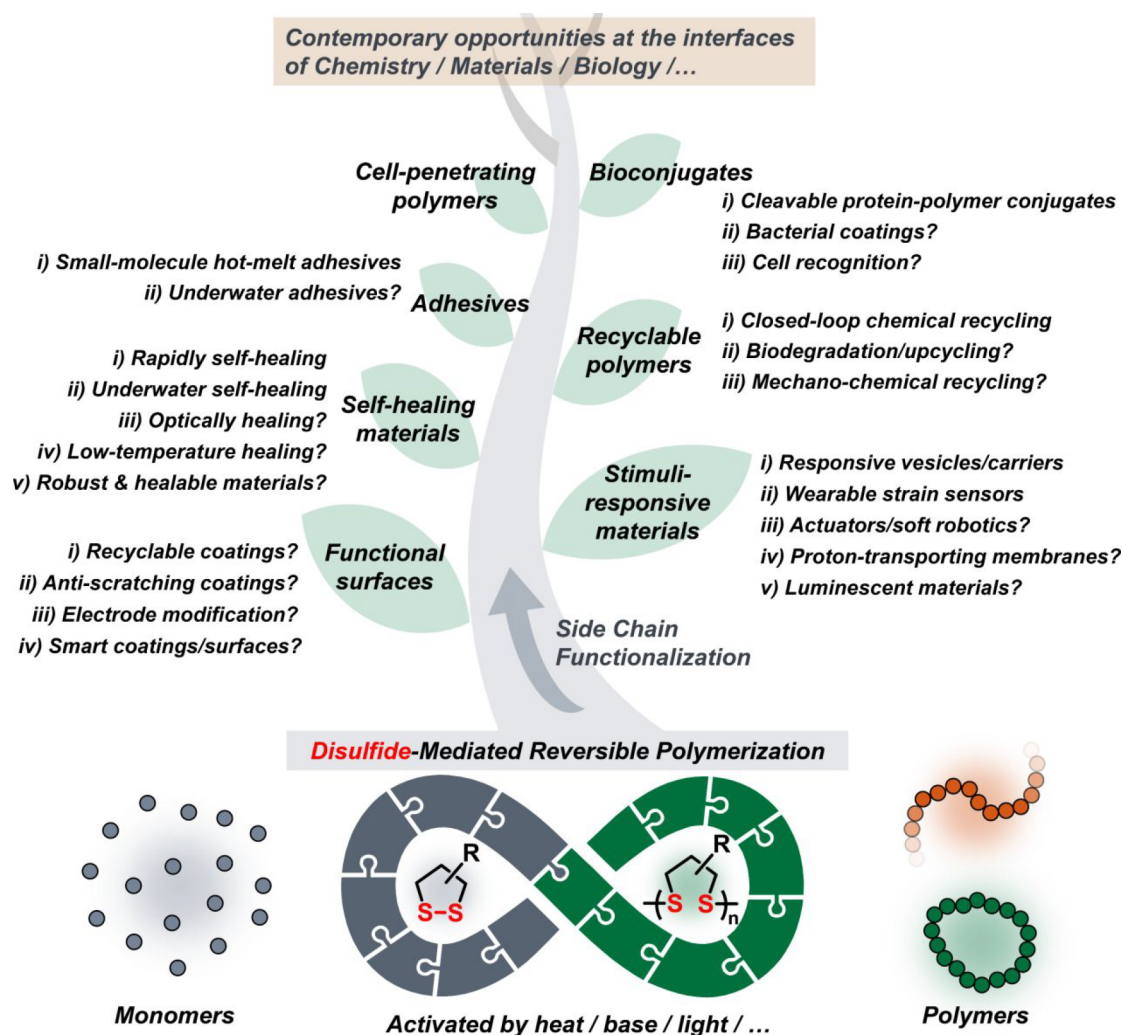


Figure 7. Overview for the likely future evolution of disulfide-mediated reversible polymerization in terms of contemporary opportunities at the interfaces of chemistry, material sciences, and biology. Proved concepts and remaining challenges and questions are exposed and summarized for the open exploration of the whole community. One “tree” is outlined as rooted from the building blocks of 1,2-dithiolanes, but one should realize that more “trees” will emerge and grow via the mainchain engineering strategy.

plexes,⁸³ and metal–sulfide interactions¹²¹ to surfaces is another approach to form a robust polymer–surface composite. This approach can be easily extended from the microscopic level of nanomaterials, microfillings, and micropatterns to macroscopic devices and adhesives.

Several advantages make poly(1,2-dithiolane)s attractive for surface functionalization. With regards to TA as an example, the small-molecule nature of the precursors allows molecular-level penetration for effective interfacial bonding. In addition, the integration of a nonpolar backbone and polar carboxyl groups enables an affinity for a range of distinct surfaces. A few reports also indicate how the disulfide-rich backbones may interact with some specific metal surfaces by forming metal–sulfur complexes.¹²¹ This is intriguing considering complexation usually provides opportunities for the modulation of the optical/electrical properties of inorganic surfaces such as quantum dots, plasmonic materials, and perovskites.

Several efforts have been made to realize cell-penetrating polymers,^{60,65} protein–polymer conjugates,⁶³ and stimuli-responsive drug carriers⁹⁶ by introducing the concept of disulfide-mediated reversible polymerization. The intriguing feature is how the polymer backbones can be on-demand

depolymerized into small-molecule monomers originally present in the biological systems, resulting in minimizing waste and potential hazards. In addition, some 1,2-dithiolanes, such as TA, naturally function as small-molecule modulators in biological systems.⁷³ Other opportunities arise if the disulfide-mediated reversible polymerization within the chemical network of physiological metabolism can be clarified to realize the regulation of a global metabolism network.

■ CHALLENGES AND FUTURE PERSPECTIVES

Throughout this Perspective, we have summarized the discovery and recent developments related to dynamic polymers and smart materials based on disulfide-mediated reversible polymerization. Taking naturally occurring disulfide-containing five-membered rings (i.e., 1,2-dithiolanes) as a versatile structural unit, considerable effort has been made, especially in the past decade, with regards to the design and fabrication of mainchain-dynamic polymeric materials with enhanced performances and applications. Despite this exciting progress, the emerging dynamic chemistry toolbox and various materials based on it still hold many opportunities, challenges, and a large space to be explored. Hence, this Perspective

finishes by discussing current key challenges and presents future directions in terms of applications beyond those demonstrated in the previous sections (Figure 7).

One of the promising applications of polymeric materials based on 1,2-dithiolanes involves next-generation sustainable plastics that can be recycled and show self-repair capability. However, major challenges remain with regard to enhancing the durability of polymers with disulfide-rich backbones. Due to the heat-labile nature of disulfide bonds, enhancing the melting or decomposition temperature by molecular engineering strategies may prove difficult. However, the temperature window of these polymers may still be further expanded in an opposite direction (e.g., exploring material applications at low temperature regions), such as antifreezing elastomers or anti-icing materials. In the future, poly(1,2-dithiolane) materials, especially those with noncovalent cross-links, may prove useful for those applications because some relevant efforts on antifreezing materials^{125–127} have demonstrated the capabilities of a supramolecular noncovalent network.

In addition, mechanical robustness is crucial for engineering materials. Currently, the supramolecular materials made from poly(1,2-dithiolane)s mostly exhibit soft (Young's moduli <10 MPa) and ductile properties,^{55,56,68,81,83,87–94} due to the relatively weak cross-link strength of noncovalent bonds. In order to overcome this issue and expand the applications of poly(1,2-dithiolane)s for engineering plastics, three approaches can be followed: (i) make recyclable vitrimers by enhancing covalent cross-linking density; (ii) elaborate noncovalent cross-linking chemistry by introducing cooperative interactions to enable high bonding affinity; and (iii) promote chain crystallization to maximize interchain interactions. This is challenging because mechanical robustness seems contradictory with dynamicity (chain mobility) in the case of a polymer network. However, a few solutions have been presented in recent studies.^{128–131}

Besides the durability and dynamicity of the material itself, another important step toward replacing industrial plastics involves developing the processing technologies associated with scalability and reproducibility production as well as environmentally benign recycling routes. This is still a major challenge considering the trade-off between profit and cost. Some emerging futuristic material technologies, such as 3D/4D printing, metamaterials, and biomimetic materials, should be considered and applied with respect to these intrinsically dynamic polymers in order to develop cutting-edge smart materials with dynamic behavior at all length scales.

Current efforts exploring the dynamicity of disulfide bonds in polymers are mainly driven by chemical approaches (i.e., thiolate-initiated reversible polymerization and depolymerization) or photochemical methods. Considering the many ways to sever disulfide bonds,¹¹¹ several alternatives remain to be explored. For example, recent literature has shown how disulfide bonds can be mechanically dissociated so that they can be considered as a type of mechanophore.¹³² Depolymerizing poly(1,2-dithiolane)s by mechanical forces is a worthwhile concept to explore. Disulfide bonds bear inherent and dynamic stereochemistry, which determines the folding architectures and functions of many natural proteins. Can one control the stereochemistry and amplify chirality through the poly(1,2-dithiolane) backbones in a biomimetic way? It is also promising and exciting from a fundamental perspective when one can realize the inherent nonplanar twisting structure of disulfide bonds.¹³³ The creation of the resulting chiral and

dynamic polymers is of great interest for applications in chiral materials and devices.^{134–136}

Among the examples we have summarized so far, the dynamic nature of the materials, such as self-healing ability, stimuli-responsive ability, adaptiveness, and recyclability, is under thermodynamic equilibrium control. The challenge is to establish how to modify this disulfide-mediated polymerization from equilibrium control to operate in nonequilibrium systems.¹³⁷ Answering this question may lead to dynamic chemical self-assembly, system chemistry, and alternative supramolecular polymers. For example, dissipative supramolecular systems mediated by dynamic covalent exchange have emerged because they can produce oscillations, waves, and motions in a fuelled and autonomous manner.^{138,139} These mechanical behaviors may be crucial for the design of smart materials. The dynamic chemistry toolbox of 1,2-dithiolanes, especially those orthogonalized with noncovalent chemistry, is extremely attractive and promising to address these challenges due to the interplay of the dynamic covalent and noncovalent chemistry in a single molecular system.

We envision that, in the years to follow, the exploration for dynamic smart materials will show an exponential increase. Intrinsically dynamic polymers based on disulfide-mediated reversible polymerization will inspire numerous application-oriented designs, new materials discovery, and other frontier areas. By further optimizing building blocks and exploring the chemical space via diverse modifications, we believe this unique dynamic chemistry toolbox can bring a bright future to intrinsically dynamic smart materials.

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Notes

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