

Dynamic Ring-chain Equilibrium of Nucleophilic Thiol-yne “Click” Polyaddition for Recyclable Poly(dithioacetal)s

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 Electronic Supplementary Information

Abstract We report a dynamic polymerization system based on the reversible nucleophilic Michael polyaddition of activated alkynes and dithiols. Four poly(dithioacetal)s (**P1–P4**) were prepared via the base-catalyzed thiol-yne “click” polyaddition of two dithiols (1,4-butanedithiol (**4S**) and 1,5-pentanedithiol (**5S**)) and two alkynones (3-butyne-2-one (**Y1**) and 1-phenyl-2-propyne-1-one (**Y2**)) at high concentrations. We systematically investigated the base-catalyzed polymerization of **4S** and **Y1** (for polymer **P1**) under different conditions, and found that this polymerization was a highly concentration-dependent dynamic system: polymer **P1** was formed at high concentration, while seven-membered dithioacetal, 1-(1,3-dithiepan-2-yl) propan-2-one (**C1**), was obtained at low concentration. The polymerization of **4S** and **Y2** (for polymer **P4**) displayed similar polymerization behavior, generating 2-(1,3-dithiepan-2-yl)-1-phenylethanone (**C4**) at low concentration. On the contrary, polymer **P2** (from **Y1** and **5S**) was exclusively obtained with no formation of eight-membered dithioacetal. The polymerizations of **Y1** with 1,2-ethanedithiol (**2S**) and 1,3-dimercaptopropane (**3S**) only afforded corresponding five- and six-membered dithioacetals, 1-(1,3-dithiolan-2-yl) propan-2-one (**C2**) and 1-(1,3-dithian-2-yl) propan-2-one (**C3**). This dynamic behavior of **P1** and **P4** was attributed to the concentration-dependent retro-Michael addition reaction between a thiol and a β -sulfinyl- α,β -unsaturated carbonyl compound catalyzed by bases. Furthermore, polymers **P1** and **P4** could be depolymerized into **C1** and **C4** in yields of 58% and 95%, respectively. The ring-opening polymerization of **C1** at high concentration could successfully regenerate polymer **P1**. Thus, a new type of closed-loop recyclable poly(dithioacetal)s was developed.

Keywords Poly(dithioacetal)s; Nucleophilic thiol-yne “click” polyaddition; Chemical recycling; Ring-chain equilibrium

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INTRODUCTION

Polysulfide is a very important kind of sulfur-containing polymers.^[1–3] Aromatic polysulfides such as poly(phenylene sulfide) have been used as high-performance engineering plastics, and aliphatic polysulfides have been used as redox carriers for drug delivery and biological detection.^[4] Since Sharpless *et al.* proposed the concept of “click chemistry” in 2001,^[5] a series of efficient organic reactions based on sulfhydryl groups have been widely used for the synthesis of polysulfides,^[6–10] greatly enriching the structural diversity and application scenarios of polysulfides. However, most of the polysulfides are difficult to degrade and recycle, which does not meet the requirements of current sustainable polymer development.^[11–16]

Common click reactions for the synthesis of polysulfides in-

clude thiol-based click reactions such as thiol-epoxy, thiol-ene, and thiol-yne *etc.* Among them, the thiol-yne reaction is more interesting, because two sulfhydryl groups can react with the triple bond twice, thus enabling construction of polymers with complex topological structures.^[8,10,17,18] There are two types of thiol-yne reactions: free radical addition and nucleophilic addition.^[19] The free radical reaction can be initiated by light or heat in the presence of an radical initiator, and it is tolerant to a variety of functional groups. It has been widely used in the preparation of linear functional polymers, cross-linking networks, dendrimers, hyperbranched molecules.^[8,20–24] However, the free radical species are very active and side reactions are, in most cases, difficult to avoid. In contrast, the nucleophilic addition of thiols to activated alkynes (aromatic and electron-deficient) in the presence of a suitable nucleophilic or basic catalyst can be fast, selective and clean. Studies have shown that the first Michael addition of a thiol to an activated alkyne is 10^3 times faster than the second one,^[25] and the second addition needs a strong basic catalyst.^[26] In a long period of time, the nucleophilic thiol-yne “click” addition has been focused on the first addition. For ex-

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ample, Tang's group has synthesized aryl poly(vinylene sulfide)s with high regio- and stereo-selectivity and excellent optical properties through the step-growth polymerization of a diyne ester and a dithiol.^[27,28] Dove's group systematically investigated the effect of catalyst and solvent on the reaction regio-selectivity of thiols and propionic acid esters, achieved good control over the stereo-structure of the formed poly(vinylene sulfide)s, and obtained high-molar-mass elastomers with high crystallinity and mechanical properties.^[29] They also extended the reactions to aqueous system and fabricated strong hydrogels for encapsulating cells.^[30,31]

In fact, the double Michael addition reaction of a thiol to an activated alkyne is also a powerful means for the simple synthesis of polymers with structural diversity and advanced functionality. By controlling the reaction conditions and the feed ratio of thiols to alkynes, two identical or different thiol groups can be selectively added to the triple bond. For example, Durmaz *et al.* used the double addition of sulfhydryl groups to modify the polyesters containing activated alkyne moieties in the backbone. Because the triple bond was activated at both sides by the ester group, double addition took place on two different carbon atoms.^[32] For a terminal activated alkyne, double addition of sulfhydryl groups occurred on the same carbon atom to form a dithioacetal.^[25,26] Dithioacetal is a commonly used protecting group for carbonyl compounds.^[33] Compared with similar acetal bonds, dithioacetals possess higher stability in both basic and acidic media. However, upon treatment with mercury ion and other soft metals or reactive oxygen species, dithioacetals can break into the corresponding carbonyl compounds and thiols. Therefore, dithioacetals are often introduced into polymers as cleavable sites to construct oxidation-responsive drug delivery systems.^[34,35] Besides, dithioacetal is also a special type of dynamic covalent bond. Under acidic conditions, dithioacetal can exchange with thiols, and this property of dithioacetal has been used to construct a dynamic combinatorial chemistry library for molecular recognition.^[36,37] Furthermore, dithioacetals bearing electron-withdrawing groups can undergo retro-Michael reaction under basic conditions to achieve an equilibrium of β -sulfido- α , β -unsaturated carbonyls, thiols, and dithianes, as demonstrated by Anslyn *et al.*^[38] Recently, these properties of dithioacetals have been used to prepare self-repairing inject-

able hydrogels and dynamic adaptive networks.^[39,40]

As early as 1997, Endo *et al.* reported the polymerization of ester-activated terminal alkynes with dithiols.^[41] Very recently, Durmaz *et al.* also investigated similar polymerization of activated internal alkynes and dithiols.^[42,43] The dynamic properties of the formed polysulfides were observed, but no detailed investigation was conducted. Another recent report demonstrated that the more activated alkynes led to more obvious dynamic property of the dithioacetals,^[40] but the degradation products were unable to be re-polymerized. On the basis of these previous reports, we intend to develop a method to fabricate a new kind of fully recyclable poly(dithioacetals) by the reactions of activated alkynes and dithiols. To this end, the base-catalyzed thiol-yne "click" polyaddition of four dithiols (**2S–5S**) to two activated alkynes (**Y1** and **Y2**) were systematically investigated. Two poly(dithioacetal)s (**P1** from **4S** and **Y1**, **P4** from **4S** and **Y2**) could be readily depolymerized into seven-membered cyclic dithioacetals, and they could be subsequently ring-opening polymerized at high concentrations in the presence of a strong base to regenerate the corresponding polymers (Scheme 1).

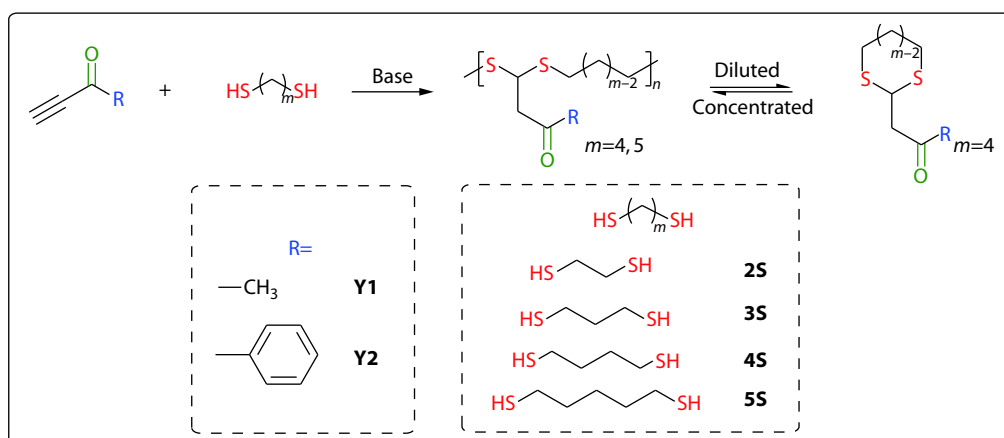
EXPERIMENTAL

Materials

The following chemicals were used as received: 1,2-ethanedithiol (**2S**, 98.5%, J&K), 1,3-dimercaptopropane (**3S**, 97%, Alfa Aesar), 1,4-butanedithiol (**4S**, 98%, J&K), 1,5-pentanedithiol (**5S**, 98%, J&K), 1-phenyl-2-propyn-1-one (**Y2**, >95%, Life), 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, 99%, J&K), triethylamine (TEA, 99%, Kemiou). 3-Butyn-2-one (**Y1**, 97%, Energy-Chemical) was purified by distillation prior to use. 1,8-Diazabicyclo[5.4.0]-undec-7-ene (DBU, 98%, J&K) was purified by distillation under reduced pressure prior to use. All the solvents were purchased from Beijing Tongguang Fine Chemical Company. Chloroform was distilled from P_2O_5 and dried with a 4Å molecular sieve.

Instrumentation

^1H -NMR (400 MHz) and ^{13}C -NMR (100 MHz) spectra were recorded on a Bruker Avance-400 spectrometer in $CDCl_3$ or $DMSO-d_6$. Chemical shifts are reported in ppm with tetramethylsilane (TMS) as the internal reference.



Scheme 1 Synthesis and recycling of poly(dithioacetal)s.

High resolution mass spectra (HRMS) were recorded on a Bruker Solarix XR Fourier transform mass spectrometer using electrospray ionization (ESI) source in the positive ion mode or electron ionization (EI) source.

Size exclusion chromatography (SEC) was performed on a Waters system equipped with a Waters 1525 binary HPLC pump, a Waters 2414 refractive index detector, and three Waters Styragel HT columns (HT2, HT3, HT4) thermostated at 35 °C. HPLC-THF was used as eluent at a flow rate of 1.0 mL/min. The calibration was made against linear polystyrene standards, and the data was collected and processed with Breeze 3.30 SPA software.

Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF-MS) was recorded on an AB Sciex 5800 spectrometer. The sample was mixed with 20 mg/mL 2,5-dihydroxybenzoic acid (DHB, Sigma Aldrich) in 50% acetonitrile/50% H₂O/0.2% trifluoroacetic acid (V/V/V) in 1/1 ratio (V/V). An aliquot of polymer solution (1 µL) was then spotted onto a MALDI plate, and analyzed using an AB SCIEX 5800 TOF/TOF (AB SCIEX, USA) in reflector mode for positive ion detection. MS spectra were acquired with *m/z* between 500 and 4000.

Thermal gravimetric analysis (TGA) was conducted on a Q600-SDT thermogravimetric analyzer (TA Co. Ltd.) from 50 °C to 600 °C at a heating rate of 10 °C/min under a nitrogen flow of 100 mL/min. Differential scanning calorimetry (DSC) test was performed on a TA Q100 differential scanning calorimeter under a nitrogen flow of 50 mL/min. The heating rate was 10 °C/min and cooling rate was 20 °C/min. Measurements were conducted from –60 °C to 120 °C. Data of the endothermic curves were acquired from the second heating scan for each polymer sample. TA Universal Analysis software was applied for data acquisition and processing in TGA and DSC measurements.

Synthesis of Polymers (P1–P4)

Polymers were prepared by the nucleophilic thiol-yne “click” polyadditions of the dithiols (**4S** and **5S**) to the alkynones (**Y1** and **Y2**) (Scheme 2).

Polymerization was carried out in a sealed Schlenk tube. Take the synthesis of **P1** as an example ([**Y1**]₀=[**4S**]₀=5.0 mol/L). To a 10 mL Schlenk tube charged with nitrogen was sequentially added 3-butyne-2-one (**Y1**, 408 mg, 6.0 mmol), CHCl₃ (900 µL) and 1,4-butanedithiol (**4S**, 732 mg, 6.0 mmol). The mixture was then frozen with liquid nitrogen, and TBD (300 µL, 0.4 mol/L, 0.12 mmol) was added quickly. The tube was then immersed into an oil bath thermostated at 50 °C. After 24 h, half of the above reaction mixture was taken out and quenched by adding excess benzoic acid (40 mg, 0.3 mmol). The polymer was subsequently recovered by precipitation into methanol for three times, and then it was dried under vacuum for 48 h to get polymer **P1** in 74% yield.

Acetic anhydride (60 mg, 0.6 mol) was added to the re-

maining reaction mixture, and the mixture was allowed to react for another 24 h to obtain the acetyl end-capped **Acet-P1** in 73% yield.

For the kinetics studies of the base-catalyzed polymerization of **Y1** and **4S**, aliquots (20 µL) of the reaction mixture were taken out at prescribed time, quenched with benzoic acid, and characterized by ¹H-NMR and SEC.

Similarly, polymer **P2** was synthesized in 88% yield from **Y1** and **5S** (Table 1, entry 2), polymer **P3** was obtained in 81% yield via the reaction of **Y1** with **4S** and **5S** (equal molar amount) (Table 1, entry 3), and polymer **P4** was obtained in 70% yield from **Y2** and **4S** (Table 1, entry 4).

Depolymerization of Polymers (P1–P4) in Dilute Solutions

Degradation of the polymers was carried out in a 20 mg/mL solution in a sealed Schlenk tube. Take the TBD-catalyzed degradation of **P1** catalyzed in CHCl₃ as an example. Polymer **P1** (80 mg) was dissolved in CHCl₃ (4 mL) and added into a 25 mL Schlenk tube charged with nitrogen. TBD (40 µL, 0.4 mol/L, 16 µmol) was subsequently added quickly. Then, the tube was placed in an oil bath set at 50 °C. Aliquots (500 µL) of the reaction mixture were taken out at prescribed time, quenched by benzoic acid, and characterized by ¹H-NMR and SEC.

Ring-opening Polymerization of C1

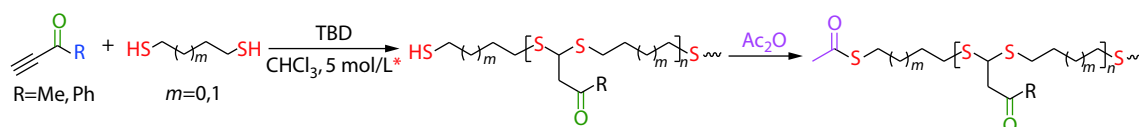
Compound **C1** (190 mg, 1.0 mmol) was dissolved in 150 µL of CHCl₃ ([**C1**]₀=5.0 mol/L) and added into a 10 mL Schlenk tube charged with nitrogen. The mixture was frozen with liquid nitrogen, and TBD (50 µL, 0.4 mol/L, 0.02 mmol) was added quickly. The tube was then immersed into an oil bath thermostated at 50 °C. After being stirred for 24 h, the reaction mixture was quenched by adding excess benzoic acid. The polymer (**P1**) was recovered in 75% yield by precipitating into methanol for three times.

Synthesis of Small Cyclic Molecules

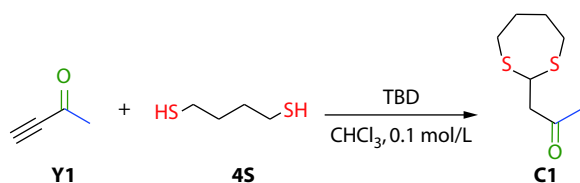
1-(1,3-Dithiepan-2-yl) propan-2-one (**C1**) (Scheme 3)

To a 50 mL Schlenk tube charged with nitrogen was sequentially added **Y1** (272 mg, 4.0 mmol), CHCl₃ (40 mL), **4S** (488 mg, 4.0 mmol), and TBD (28 mg, 0.2 mmol) ([**Y1**]₀=[**4S**]₀=0.1 mol/L). After being stirred for 48 h at 50 °C, the mixture was quenched by adding excess benzoic acid. The solvent was removed by rotary evaporation, and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 16/1, V/V). Pure **C1** was obtained as a colorless oil (at 30 °C) in 59% yield.

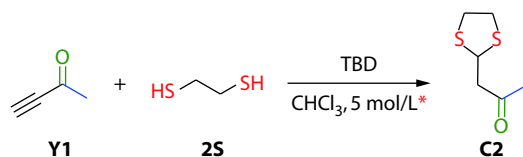
¹H-NMR (400 MHz, CDCl₃, δ, ppm): 4.61 (t, *J*=6.9 Hz, 1H), 2.97 (ddd, *J*=10.0, 6.1, 2.4 Hz, 2H), 2.90 (d, *J*=7.0 Hz, 2H), 2.79–2.67 (m, 2H), 2.18 (s, 3H), 2.06–1.90 (m, 4H). ¹³C-NMR (101 MHz, CDCl₃, δ, ppm): 204.6(1C), 50.3 (1C), 46.5 (1C), 31.7 (2C), 31.3 (2C), 30.6 (1C). ESI-HRMS (*m/z*): Calcd. for C₈H₁₄OS₂: 190.04861; Found: 191.05562 [M+H]⁺, 208.08215 [M+NH₄]⁺, 213.03755 [M+Na]⁺.



Scheme 2 Synthesis and end-capping of polymers (**P1–P4**).

Scheme 3 Synthesis of **C1** at 0.1 mol/L.1-(1,3-Dithiolan-2-yl)propan-2-one (**C2**) (Scheme 4)

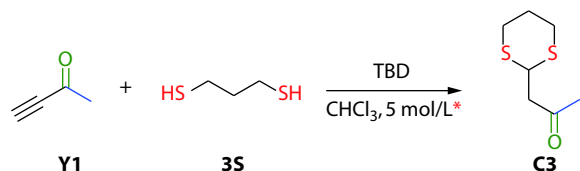
Pure **C2** was obtained as a colorless oil in 63% yield from **Y1** and **2S** in solution (5.0 mol/L in CHCl_3) after being purified on a silica column (petroleum ether/ethyl acetate, 10/1, V/V).

Scheme 4 Synthesis of **C2** at 5.0 mol/L.

$^1\text{H-NMR}$ (400 MHz, CDCl_3 , δ , ppm): 4.81 (t, $J=6.9$ Hz, 1H), 3.30–3.14 (m, 4H), 3.02 (d, $J=7.0$ Hz, 2H), 2.17 (s, 3H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3 , δ , ppm): 205.80 (1C), 53.42 (1C), 46.77 (1C), 38.54 (2C), 30.10 (1C). EI-HRMS (m/z): $[\text{M}^+]$ Calcd. for $\text{C}_6\text{H}_{10}\text{OS}_2$: 162.01676; Found: 162.01688.

1-(1,3-Dithian-2-yl)propan-2-one (**C3**) (Scheme 5)

Pure **C3** (melting point: 70 °C by DSC) was obtained as a light-yellow crystal in 81% yield from **Y1** and **3S** in solution (5.0 mol/L in CHCl_3) after being purified on a silica column (petroleum ether/ethyl acetate, 10/1, V/V).

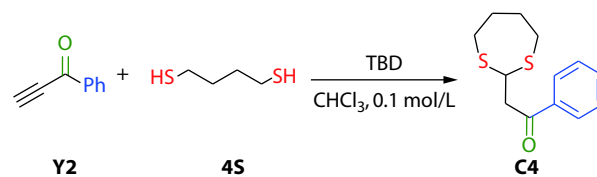
Scheme 5 Synthesis of **C3** at 5.0 mol/L.

$^1\text{H-NMR}$ (400 MHz, CDCl_3 , δ , ppm): 4.49 (t, $J=6.9$ Hz, 1H), 2.95 (ddd, $J=14.1$, 8.9, 3.2 Hz, 2H), 2.88–2.79 (m, 4H), 2.21 (s, 3H), 2.12 (dt, $J=16.0$, 5.3, 2.6 Hz, 1H), 1.87 (dt, $J=14.5$, 11.4, 3.2 Hz, 1H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3 , δ , ppm): 203.90 (1C), 48.70 (1C), 41.01 (1C), 30.62 (1C), 30.20 (2C), 25.25 (1C). EI-HRMS (m/z): $[\text{M}^+]$ Calcd. for $\text{C}_7\text{H}_{12}\text{OS}_2$: 176.03241; Found: 176.03243.

2-(1,3-Dithiepan-2-yl)-1-phenylethanone (**C4**) (Scheme 6)

Pure **C4** (melting point: 79 °C by DSC) was obtained as a white flocculent solid in 85% yield from **Y2** and **4S** in solution (0.1 mol/L in CHCl_3) after being purified on a silica column (petroleum ether/ethyl acetate, 20/1, V/V).

$^1\text{H-NMR}$ (400 MHz, CDCl_3 , δ , ppm): 7.96 (d, $J=7.4$ Hz, 2H), 7.58 (t, $J=7.3$ Hz, 1H), 7.47 (t, $J=7.6$ Hz, 2H), 4.84 (t, $J=6.8$ Hz, 1H), 3.46 (d, $J=6.8$ Hz, 2H), 3.06–2.92 (m, 2H), 2.84–2.71 (m, 2H), 2.01 (d, $J=3.4$ Hz, 4H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3 , δ , ppm): 196.24 (1C), 136.61 (1C), 133.40 (1C), 128.69 (2C), 128.23 (2C), 46.92 (1C), 45.64 (1C), 31.77 (2C), 31.42 (1C). EI-HRMS (m/z): $[\text{M}^+]$ Calcd. for $\text{C}_{13}\text{H}_{16}\text{OS}_2$: 252.06371; Found: 252.06391.

Scheme 6 Synthesis of **C4** at 0.1 mol/L.

RESULTS AND DISCUSSION

Preparation and Properties of Polymers **P1**–**P4**

Y1 was first used as the activated alkyne to evaluate its reactivity with different dithiols (**2S**, **3S**, **4S** and **5S**) at 50 °C at high concentration (5.0 mol/L) in CHCl_3 using 2 mol% TBD as the catalyst.^[26] The $^1\text{H-NMR}$ spectra of the reaction mixtures after 24 h were recorded as shown in Fig. 1. All the spectra are well-resolved and can be assigned unambiguously, suggesting that the reaction was clean with no side reactions. In all the systems, the starting material **Y1** completely disappeared, and the peaks assigned to the characteristic methine protons of dithioacetal appeared at 4.0–5.0 ppm, suggesting successful double additions of the four dithiols to **Y1**. For **Y1/2S** and **Y1/3S**, the reaction products were confirmed to be pure five- and six-membered dithioacetals (**C2**, Scheme 4 and Fig. S3 in the electronic supplementary information, ESI; **C3**, Scheme 5 and Fig. S4 in ESI), respectively, no any polymer was formed. For **Y1/4S** and **Y1/5S**, however, the increase of solution viscosity was observed during the reaction, indicating the formation of polymers in these two systems. The *in situ* NMR spectrum of **Y1/4S** indicated the coexistence of polymer (**P1**) and a small amount of seven-membered compound **C1** (Scheme 3, Figs. S1 and S2 in ESI) formed by the 1:1 adduct of **Y1/4S**, suggesting that a ring-chain equilibrium existed in the polymerization system of **Y1** and **4S**, while **Y1/5S** formed exclusively polymer **P2**.

Polymer **P1** (from **Y1/4S**) was recovered in 74% yield by precipitation of the reaction mixture into methanol (Fig. S6 in ESI). The structure of **P1** was characterized by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, MALDI-TOF-MS and SEC (Fig. 2). In the $^1\text{H-NMR}$ spectrum (Fig. 2A), the characteristic signal of dithioacetal was observed at 4.27 ppm. The weak signals (x and h/i) represented the sulfhydryl and olefinic protons as the polymer ends, and the *cis/trans* ratio for the alkene was 1/3. There are three series of peaks in the MALDI-TOF-MS spectrum (Fig. 2B), each spaced by intervals of 190 Da, corresponding to the molar mass of the repeating unit of **P1**. These three series of peaks can be assigned to linear **P1** with three different kinds of end groups, which is rational for the common “A₂+B₂” step-growth polymerization. The SEC trace of **P1** is unimodal (Fig. 2D), the molar mass (M_n) and dispersity ($\mathcal{D}$) are 6.5 kDa and 1.59, respectively. Polymer **P1** was further end-capped with acetyl anhydride to block the active thiol-end groups. $^1\text{H-NMR}$ spectrum proved the successive end-capping reaction and polymer **Acet-P1** was obtained and used as a control polymer for the next depolymerization studies (Scheme 2 and Fig. S7 in ESI).

Changing **Y1** to **Y2**, polymer **P4** (Fig. S8 in ESI) and a small amount of seven-membered compound **C4** (Scheme 6 and Fig. S5 in ESI) were obtained and identified, further testifying the ring-chain equilibrium in the polymerization of **4S** and al-

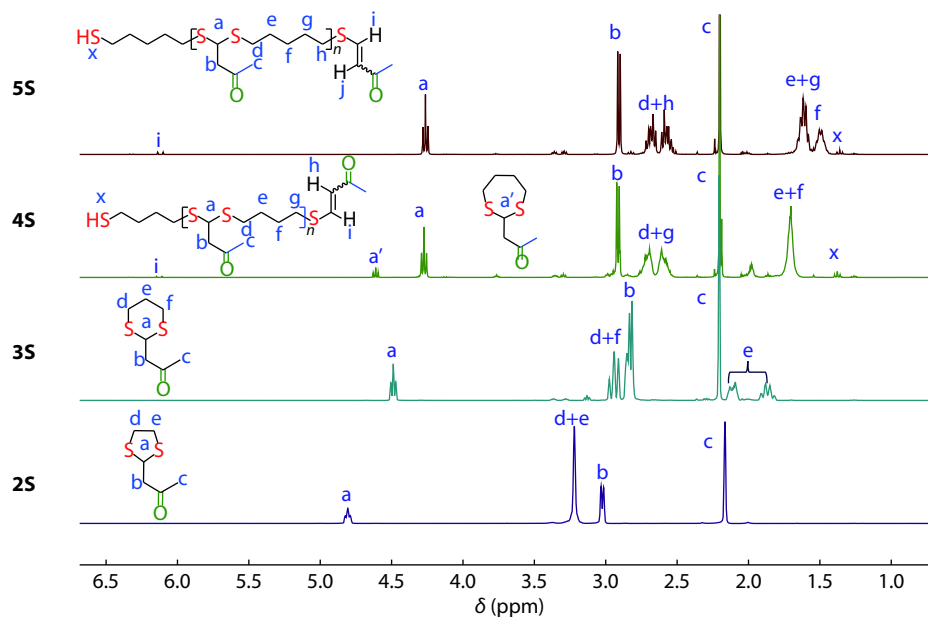


Fig. 1 *In situ* ^1H -NMR spectra of reactions between **Y1** and dithiols after 24 h (5.0 mol/L).

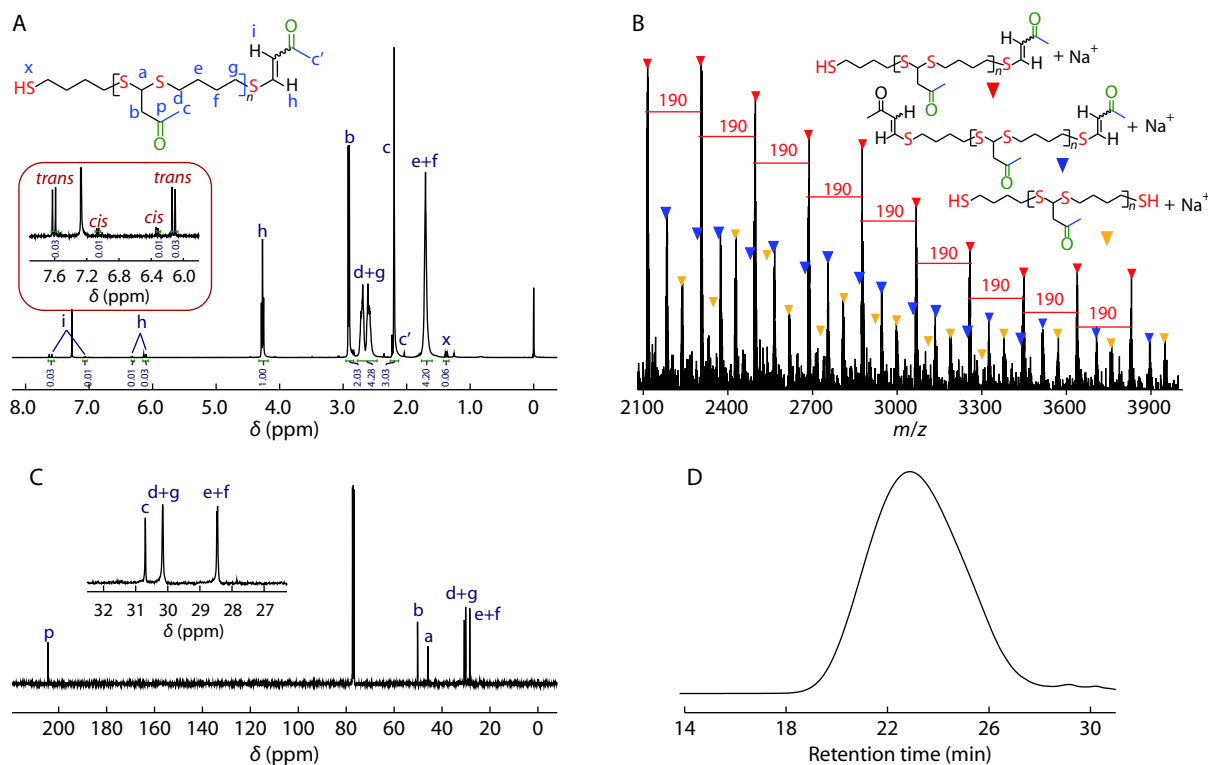


Fig. 2 Characterization of **P1**: (A) ^1H -NMR and (B) ^{13}C -NMR spectra in CDCl_3 ; (C) MALDI-TOF-MS spectrum; (D) SEC trace ($M_n=6.5$ kDa, $D=1.59$).

kynones. By contrast, changing **4S** to **5S**, **P2** was exclusively generated (Fig. S9 in ESI) in 88% yield ($M_n=7.8$ kDa and $D=1.63$), and no any small ring molecules were obtained.

The above results clearly demonstrated that the double thia-Michael addition reactions between alkynones and dithiols under strong basic conditions could efficiently occur to generate poly(dithioacetal)s. Depending on the chain length

of the dithiols, the behavior of the polymerization was different: **Y1** with **2S** and **3S** formed exclusively stable five- or six-membered small molecules (**C2** and **C3**); **Y1** with **5S** formed exclusively polymer **P2** with no contamination of eight-membered dithioacetal; while **Y1** (**Y2**) with **4S** formed mainly polymers (**P1** and **P4**) plus a small amount of seven-membered dithioacetals (**C1** and **C4**). These results revealed

the order of thermodynamic stability of cyclic dithioacetals ($8 < 7 < 5, 6$), which is consistent with that of cycloalkanes.^[44] Since non-homopolymerizable lactones such as γ -butyrolactone could be copolymerized with other monomers,^[45,46] we also conducted three copolymerizations of **Y1** with equimolar mixture of two different dithiols (Table S1 in ESI). Clearly, **Y1/4S/2S** and **Y1/4S/3S** only generated polymer **P1** and the corresponding **C2** and **C3**, while **Y1/4S/5S** formed a new polymer **P3** ($M_n=7.8$ kDa, $\bar{D}=1.54$) in 81% yield, whose structure consisted of two repeating units (Fig. S10 in ESI).

The thermal properties of polymer **P1–P4** were characterized (Fig. 3, Table 1). These polymers are thermally stable up to 188–217 °C, and polymer **P4** is the least thermal stable with a $T_{d,5\%}$ of 188 °C, which might be caused by the aromatic dithioacetal structure. DSC thermograms show that the four polymers are all amorphous with glass transition temperatures ranging from –47 °C to –16 °C.

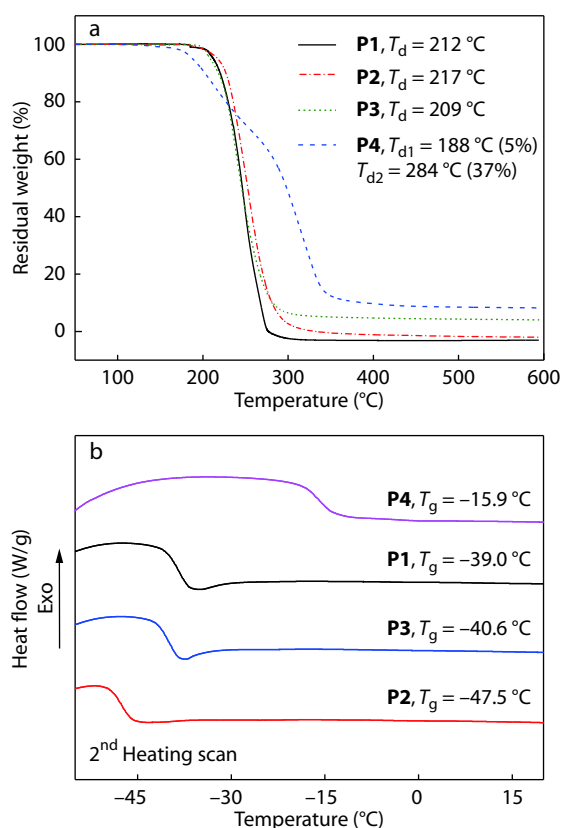


Fig. 3 TGA (a) and DSC thermograms (b) of polymers **P1–P4**.

Optimization of Polymerization Conditions

As aforementioned, the TBD-catalyzed double additions of dithiols to alkynes can be carried out in high efficiency. Whether polymers or small cyclic compounds are obtained depending on the stability of the small cyclic dithioacetals related to the dithiols. The polymerization of **Y1** (**Y2**) and **4S** shows interesting ring-chain equilibrium in the polymerization solution. To better understand this type of polymerization, we systematically investigated the polymerization of **Y1** and **4S** (Table S2 in ESI).

First, the catalytic activities of three bases TBD, DBU, and

Table 1 Results of thiol-yne “click” polyaddition.^a

Polymer	Monomer	Yield ^b (%)	Molar mass ^c (kg·mol ⁻¹)	$\bar{D}$ ^c (M_w/M_n)	T_g ^d (°C)	T_d ^e (°C)
P1	Y1+4S	74	6.5	1.59	–39.0	212
P2	Y1+5S	88	7.8	1.63	–47.5	217
P3	Y1+4S/5S	81	7.8	1.54	–40.6	209
P4	Y2+4S	80	5.6	1.66	–15.9	188

^a Polymerizations were performed in CHCl_3 at 50 °C for 24 h, $[\text{Y}]_0/[\text{NS}]_0=1/1$, $[\text{Y}]_0=5.0$ mol/L; ^b Determined after precipitation in methanol and vacuum dryness (48 h); ^c Determined by SEC in THF using PS standards; ^d Determined by DSC, 10 °C/min scan rate. Values were recorded from the second scan. ^e Determined by TGA, 10 °C/min scan rate. T_d is defined as the temperature when 5% weight loss occurs.

TEA were investigated. Though they could all catalyze the polymerization and generate polymer **P1**, TBD was demonstrated to be the most active (Table S2, entries 2, 6, and 8, in ESI), affording **P1** in short time and high molar mass under similar conditions. To be noted, in the reactions of thiols with ethyl propanoate^[26] and ester-activated diyne,^[32] only TBD can catalyze the second addition reaction. This difference may imply the higher reactivities of the terminal alkynes than those of the other activated alkynes, which will be the subject of a future study.

We followed the kinetics of the TEA-catalyzed polyaddition (Table S2, entries 1–5, in ESI) by time-dependent ¹H-NMR and SEC (Fig. S11 in ESI) at 30 °C. Complete disappearance of the alkyne signals can be observed within 5 min, indicating that the first addition was much faster. As the polymerization time was prolonged, the intensity of the thiol signals and alkene signals gradually weakened, while the dithioacetal signals strengthened simultaneously. After 5 days, polymer **P1** ($M_n=4.8$ kDa) was formed. DBU could also catalyze similar polymerization at 30 °C, and **P1** was obtained after 1 h ($M_n=2.7$ kDa), and a high-molar-mass polymer was obtained after 24 h (Table S2, entries 6 and 7, in ESI).

Since TBD was the most active, we also examined the effects of temperature. By increasing the reaction temperature from 30 °C to 50 °C and 80 °C (Table S2, entries 10–12, in ESI), we found that **P1** with the highest molar mass was obtained at 50 °C. We also regulated the stoichiometric ratios of **Y1** to **4S** at 50 °C and as expected, only when they were in strict stoichiometry that the highest molar-mass **P1** could be obtained (Fig. S12 in ESI). Therefore, this type of polyaddition followed the classical step-growth polymerization mechanism of double additions of dithiols to alkynes.

Finally, we evaluated the concentration-dependent ring-chain dynamic equilibrium of this system.^[47] The polymerization was carried out at four different monomer concentrations (0.1, 0.2, 0.4 and 5.0 mol/L), and the ¹H-NMR spectra of the mixture are shown in Fig. 4. The relative ratio of compound **C1** to polymer **P1** was evaluated by comparing the intensities of the dithioacetal methine protons (4.61 ppm in **C1**, and 4.27 ppm in **P1**). Clearly, high concentration favored the formation of polymer **P1**, while low concentration favored formation of compound **C1**.

Chemical Recycling of P1 and P4 in Dilute Basic Solution

The particular concentration-dependent ring-chain equilibrium existing in the polymerization of **Y1/Y2+4S** motivated us to

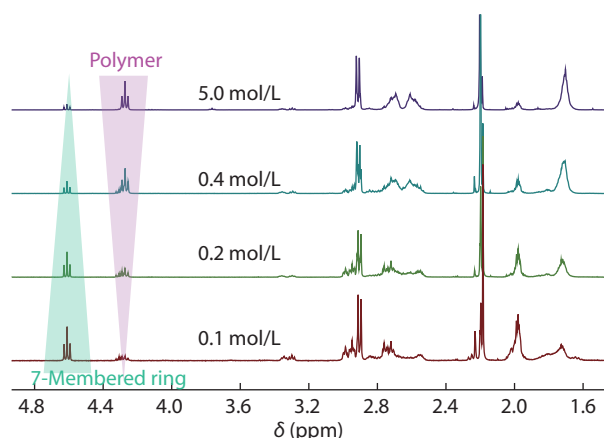


Fig. 4 *In situ* ^1H -NMR spectra of the reaction mixture of **Y1** and **4S** at different initial concentrations (24 h).

investigate the recycling of **P1** and **P4** into **C1** and **C4** at low concentration. Thus, a polymer **P1** sample was dissolved in CHCl_3 at a concentration of 20 mg/mL in the presence of TBD. The depolymerization was followed by SEC and ^1H -NMR (Fig. 5). As can be seen from the SEC traces (Fig. 5a), after 2 days, **P1** completely disappeared. In the ^1H -NMR spectra shown in Fig. 5(b), the signals of the methine protons of dithioacetal at 4.27 ppm (**P1**) became very weak, while those of compound **C1** (4.61 ppm) were intensified, demonstrating the shift of the equilibrium from chain (**P1**) to ring (**C1**). Because of the concentration limit, the recovery yield of **C1** was 58%, and other products were oligomers. Excitingly, the TBD-catalyzed ROP polymerization of **C1** at a high concentration of 5.0 mol/L could afford identical **P1** with an even higher molar mass of 8.4 kDa, compared with the virgin **P1** (Fig. 5). However, due to the dynamic ring-chain equilibrium, the molar mass of the regenerated **P1** was limited below 11.1 kDa (Table S3 in ESI). Whatever, a closed-loop recycling of **P1** could be achieved via concentration regulations. Similarly, polymer **P4** could also be

depolymerized into **C4** (Fig. S14 in ESI) under identical conditions as for polymer **P1**. The recovery yield of **C4** was 95%, higher than that of **C1** (58%), which could be attributed to different stabilities of these two cyclic dithioacetals caused by substituents.

Mechanism of Ring-chain Equilibrium and Depolymerization

The next question is the mechanism of depolymerization, random cleavage or head-to-tail unzipping. Gillies *et al.* reported a polymer based on *N,N'*-dimethylethylenediamine and 2-mercaptoethanol linked by carbamates and thiocarbamates which underwent a cascade of head-to-tail degradation by cyclization reaction initiated from the attack of terminal thiol group to the adjacent carbamates upon removal of the end-capping agents.^[48] We wondered whether the above concentration-dependent ring-chain equilibrium and polymer recycling mechanism was similar to this. To this end, we blocked the terminal thiol groups of **P1** by reaction with acetic anhydride. The acetyl end-capped **Acet-P1** (Fig. S7 in ESI) was subjected to depolymerization under identical conditions as for **P1**. We found that this polymer also degraded into **C1** (Fig. S15 in ESI), thus excluding the mechanism of head-to-tail unzipping. We then rationalized that retro-Michael addition reaction of β -dithiane carbonyl compounds under basic conditions may account for it.^[38] As shown in Fig. 5(c), dithioacetal linkages in the backbone of **P1** were randomly cleaved into β -sulfido- α,β -unsaturated carbonyls and thiol groups, forming an intermediate (compound **M**), which probably be probed during the polymerization of **C1** catalyzed by TEA (Fig. S13 in ESI). This compound, which can be considered as an AB monomer, at high concentration, is polymerized into polymers via the intermolecular thiol-ene Michael addition reaction; while at low concentration, it cyclized into **C1**. The ROP mechanism of **C1** followed similar mechanism, and it can be considered as “ring-opening polyaddition”. To further confirm this mechanism, degradation

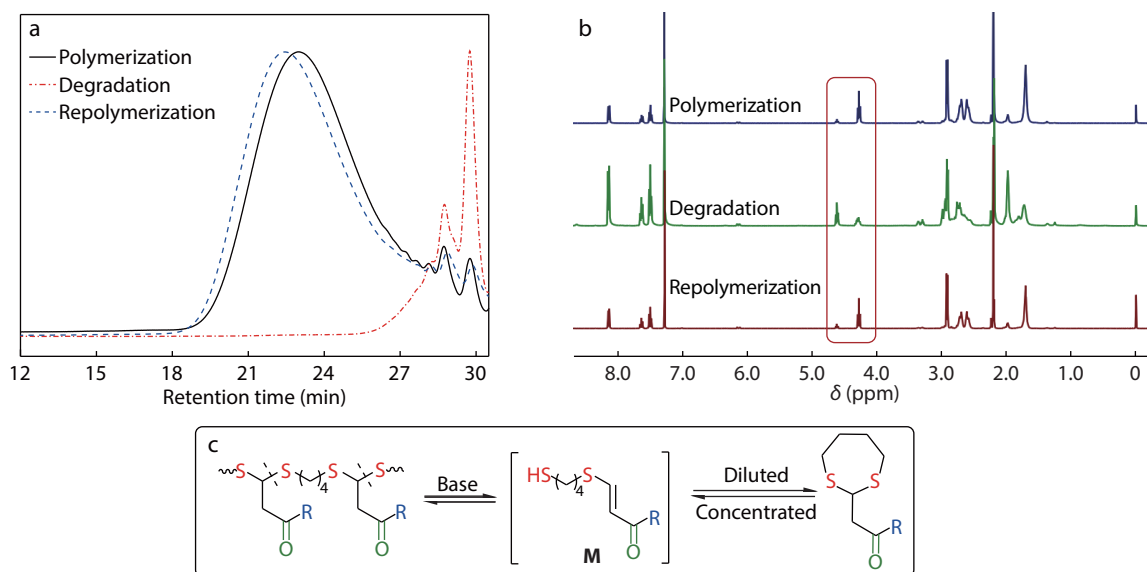


Fig. 5 Recycling of **P1** by the TBD-catalyzed thiol-yne “click” polyaddition and concentration-dependent ring-chain equilibrium: (a) SEC traces; (b) ^1H -NMR spectra in CDCl_3 ; (c) Proposed mechanism.

of polymer **P2** was examined under identical conditions. **P2** could be degraded in dilute solutions into oligomers via similar retro-Michael addition reaction (Fig. S16A in ESI), but no eight-membered dithioacetal was formed (Fig. S16B in ESI). These results revealed that an appropriate length of the dithiol was critical to achieve recycling of poly(dithioacetal)s. Finally, as expected, polymer **P3** could also degraded into compound **C1** in 30% yield (Fig. S17 in ESI).

CONCLUSIONS

We presented a simple approach to recyclable poly(dithioacetal)s via the base-catalyzed polyadditions of alkynones with suitable dithiols. We systematically investigated the polymerization of 3-butyne-2-one (**Y1**) with four dithiols (**2S–5S**), and found that the length of dithiols and concentration played vital roles in the formation and depolymerization of poly(dithioacetal)s. Reactions of **Y1** and **2S** and **3S** generated only corresponding five- and six-membered cyclic dithioacetals. The polymerization of **Y1/Y2** and **4S** had a dynamic ring-chain equilibrium, the mechanism of which was elucidated to be the base-catalyzed retro-Michael addition reactions between a thiol and a β -sulfido- α,β -unsaturated carbonyl. The ring-chain equilibrium process is concentration-dependent and base-sensitive. Strong base such as TBD and high concentration favored polymer formation. On the basis of these findings, **P1** and **P4** from **Y1+4S** and **Y2+4S** could be depolymerized into the corresponding seven-membered cyclic dithioacetals **C1** and **C4** in basic dilute solutions. The ring-opening polymerization of **C1** at high concentration could successfully regenerate polymer **P1** via the "ring-opening-stepwise" polymerization route. As far as we know, this is the first example of closed-loop recyclable poly(dithioacetal) through reversible thia-Michael reactions. Studies are in progress to expand the substrate scopes and explore the practical applications.

Electronic Supplementary Information

Electronic supplementary information (ESI) is available free of charge in the online version of this article at <http://doi.org/10.1007/s10118-021-2587-y>.

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REFERENCES

- Mutlu, H.; Ceper, E. B.; Li, X.; Yang, J.; Dong, W.; Ozmen, M. M.; Theato, P. Sulfur chemistry in polymer and materials science. *Macromol. Rapid Commun.* **2019**, *40*, e1800650.
- Zhang, C. J.; Zhang, X. H. Recent progress on COS-derived polymers. *Chinese J. Polym. Sci.* **2019**, *37*, 951–958.
- Wang, Y.; Yang, J. L.; Zhang, C. J.; Zhang, X. H. Organocatalytic polymerization of sulfur-containing one-carbon monomer and epoxides. *Acta Polymerica Sinica* (in Chinese) **2020**, *51*, 1092–1103.
- Napoli, A.; Valentini, M.; Tirelli, N.; Müller, M.; Hubbell, J. A. Oxidation-responsive polymeric vesicles. *Nat. Mater.* **2004**, *3*, 183–189.
- Kolb, H. C.; Finn, M. G.; Sharpless, K. B. Click chemistry: diverse chemical function from a few good reactions. *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021.
- Lowe, A. B. Thiol-ene "click" reactions and recent applications in polymer and materials synthesis. *Polym. Chem.* **2010**, *1*, 17–36.
- Hoyle, C. E.; Lowe, A. B.; Bowman, C. N. Thiol-click chemistry: a multifaceted toolbox for small molecule and polymer synthesis. *Chem. Soc. Rev.* **2010**, *39*, 1355–1387.
- Lowe, A. B. Thiol-yne 'click'/coupling chemistry and recent applications in polymer and materials synthesis and modification. *Polymer* **2014**, *55*, 5517–5549.
- Lowe, A. B. Thiol-ene "click" reactions and recent applications in polymer and materials synthesis: a first update. *Polym. Chem.* **2014**, *5*, 4820–4870.
- Nair, D. P.; Podgorski, M.; Chatani, S.; Gong, T.; Xi, W. X.; Fenoli, C. R.; Bowman, C. N. The thiol-Michael addition click reaction: a powerful and widely used tool in materials chemistry. *Chem. Mater.* **2014**, *26*, 727–744.
- Schneiderman, D. K.; Hillmyer, M. A. 50th Anniversary perspective: there is a great future in sustainable polymers. *Macromolecules* **2017**, *50*, 3733–3750.
- Hong, M.; Chen, E. Y. X. Chemically recyclable polymers: a circular economy approach to sustainability. *Green Chem.* **2017**, *19*, 3692–3706.
- Fortman, D. J.; Brutman, J. P.; De Hoe, G. X.; Snyder, R. L.; Dichtel, W. R.; Hillmyer, M. A. Approaches to sustainable and continually recyclable cross-linked polymers. *ACS Sustain. Chem. Eng.* **2018**, *6*, 11145–11159.
- Zhang, X.; Fevre, M.; Jones, G. O.; Waymouth, R. M. Catalysis as an enabling science for sustainable polymers. *Chem. Rev.* **2018**, *118*, 839–885.
- Tang, X. Y.; Chen, E. Y. X. Toward infinitely recyclable plastics derived from renewable cyclic esters. *Chem* **2019**, *5*, 284–312.
- Coates, G. W.; Getzler, Y. Chemical recycling to monomer for an ideal, circular polymer economy. *Nat. Rev. Mater.* **2020**, *5*, 501–516.
- Huang, D.; Liu, Y.; Qin, A.; Tang, B. Z. Recent advances in alkyne-based click polymerizations. *Polym. Chem.* **2018**, *9*, 2853–2867.
- Huang, D.; Liu, Y.; Guo, S.; Li, B. X.; Wang, J.; Yao, B. C.; Qin, A. J.; Tang, B. Z. Transition metal-free thiol-yne click polymerization toward Z-stereoregular poly(vinylene sulfide)s. *Polym. Chem.* **2019**, *10*, 3088–3096.
- Daglar, O.; Luleburgaz, S.; Baysak, E.; Gunay, U. S.; Hizal, G.; Tunca, U.; Durmaz, H. Nucleophilic thiol-yne reaction in macromolecular engineering: from synthesis to applications. *Eur. Polym. J.* **2020**, *137*, 109926.
- Han, J.; Zheng, Y.; Zhao, B.; Li, S.; Zhang, Y.; Gao, C. Sequentially hetero-functional, topological polymers by step-growth thiol-yne approach. *Scientif. Rep.* **2014**, *4*, 4387.
- Fairbanks, B. D.; Scott, T. F.; Kloxin, C. J.; Anseth, K. S.; Bowman, C. N. Thiol-yne photopolymerizations: novel mechanism, kinetics, and step-growth formation of highly cross-linked networks. *Macromolecules* **2009**, *42*, 211–217.
- Chen, G.; Kumar, J.; Gregory, A.; Stenzel, M. H. Efficient synthesis of dendrimers via a thiol-yne and esterification process and their potential application in the delivery of platinum anti-cancer drugs. *Chem. Commun.* **2009**, 6291–6293.
- Konkolewicz, D.; Gray-Weale, A.; Perrier, S. Hyperbranched polymers by thiol-yne chemistry: from small molecules to functional polymers. *J. Am. Chem. Soc.* **2009**, *131*, 18075–18077.
- Yao, B.; Hu, T.; Zhang, H.; Li, J.; Sun, J. Z.; Qin, A.; Tang, B. Z. Multi-

- functional hyperbranched poly(vinylene sulfide)s constructed via spontaneous thiol-yne click polymerization. *Macromolecules* **2015**, *48*, 7782–7791.
- 25 Kuroda, H.; Tomita, I.; Endo, T. Facile synthetic method for the preparation of dithioacetals by the double conjugate addition of acetylenes bearing electron-withdrawing groups with thiols. *Synthetic. Commun.* **1996**, *26*, 1539–1543.
 - 26 Truong, V. X.; Dove, A. P. Organocatalytic, regioselective nucleophilic "click" addition of thiols to propiolic acid esters for polymer-polymer coupling. *Angew. Chem. Int. Ed.* **2013**, *52*, 4132–4136.
 - 27 Jim, C. K. W.; Qin, A.; Lam, J. W. Y.; Mahtab, F.; Yu, Y.; Tang, B. Z. Metal-free alkyne polyhydrothiolation: synthesis of functional poly(vinylenesulfide)s with high stereoregularity by regioselective thiolclick polymerization. *Adv. Funct. Mater.* **2010**, *20*, 1319–1328.
 - 28 Du, J.; Huang, D.; Li, H.; Qin, A.; Tang, B. Z.; Li, Y. Catalyst-free click polymerization of thiol and activated internal alkynes: a facile strategy toward functional poly(β -thioacrylate)s. *Macromolecules* **2020**, *53*, 4932–4941.
 - 29 Bell, C. A.; Yu, J.; Barker, I. A.; Truong, V. X.; Cao, Z.; Dobrinyin, A. V.; Becker, M. L.; Dove, A. P. Independent control of elastomer properties through stereocontrolled synthesis. *Angew. Chem. Int. Ed.* **2016**, *55*, 13076–13080.
 - 30 Truong, V. X.; Ablett, M. P.; Richardson, S. M.; Hoyland, J. A.; Dove, A. P. Simultaneous orthogonal dual-click approach to tough, in-situ-forming hydrogels for cell encapsulation. *J. Am. Chem. Soc.* **2015**, *137*, 1618–1622.
 - 31 Macdougall, L. J.; Truong, V. X.; Dove, A. P. Efficient *in situ* nucleophilic thiol-yne click chemistry for the synthesis of strong hydrogel materials with tunable properties. *ACS Macro Lett.* **2017**, *6*, 93–97.
 - 32 Gunay, U. S.; Cetin, M.; Daglar, O.; Hizal, G.; Tunca, U.; Durmaz, H. Ultrafast and efficient aza- and thiol-michael reactions on a polyester scaffold with internal electron deficient triple bonds. *Polym. Chem.* **2018**, *9*, 3037–3054.
 - 33 Perin, G.; Mello, L. G.; Radatz, C. S.; Savegnago, L.; Alves, D.; Jacob, R. G.; Lenardao, E. J. Green, catalyst-free thioacetalization of carbonyl compounds using glycerol as recyclable solvent. *Tetrahedron Lett.* **2010**, *51*, 4354–4356.
 - 34 Fatona, A.; Moran-Mirabal, J.; Brook, M. A. Controlling silicone networks using dithioacetal crosslinks. *Polym. Chem.* **2019**, *10*, 219–227.
 - 35 Xu, L.; Zhao, M.; Zhang, H.; Gao, W.; Guo, Z.; Zhang, X.; Zhang, J.; Cao, J.; Pu, Y.; He, B. Cinnamaldehyde-based poly(ester-thioacetal) to generate reactive oxygen species for fabricating reactive oxygen species-responsive nanoparticles. *Biomacromolecules* **2018**, *19*, 4658–4667.
 - 36 Gaston Orrillo, A.; Escalante, A. M.; Furlan, R. L. E. Dithioacetal exchange: a new reversible reaction for dynamic combinatorial chemistry. *Chem. Eur. J.* **2016**, *22*, 6746–6749.
 - 37 Orrillo, A. G.; Escalante, A. M.; Furlan, R. L. E. Host amplification in a dithioacetal-based dynamic covalent library. *Org. Lett.* **2017**, *19*, 1446–1449.
 - 38 Joshi, G.; Anslyn, E. V. Dynamic thiol exchange with β -sulfido- α,β -unsaturated carbonyl compounds and dithianes. *Org. Lett.* **2012**, *14*, 4714–4717.
 - 39 Fan, B.; Zhang, K.; Liu, Q.; Eelkema, R. Self-healing injectable polymer hydrogel via dynamic thiol-alkynone double addition cross-links. *ACS Macro Lett.* **2020**, *9*, 776–780.
 - 40 van herck, N.; Maes, D.; Unal, K.; Guerre, M.; Winne, J. M.; Du Prez, F. E. Covalent adaptable networks with tunable exchange rates based on reversible thiol-yne cross-linking. *Angew. Chem. Int. Ed.* **2020**, *59*, 3609–3617.
 - 41 Kuroda, H.; Tomita, I.; Endo, T. A novel phosphine-catalysed polyaddition of terminal acetylenes bearing electron-withdrawing groups with dithiols. Synthesis of polymers having dithioacetal moieties in the main chain. *Polymer* **1997**, *38*, 6049–6054.
 - 42 Daglar, O.; Cakmakci, E.; Gunay, U. S.; Hizal, G.; Tunca, U.; Durmaz, H. A straightforward method for fluorinated polythioether synthesis. *Macromolecules* **2020**, *53*, 2965–2975.
 - 43 Daglar, O.; Gunay, U. S.; Hizal, G.; Tunca, U.; Durmaz, H. Extremely rapid polythioether synthesis in the presence of TBD. *Macromolecules* **2019**, *52*, 3558–3572.
 - 44 Andrzej, D.; Adam, K.; Jan, L.; Stanislaw, P. Thermodynamic and kinetic polymerizability of cyclic esters. *Macromol. Symp.* **2005**, *224*, 71–84.
 - 45 Hong, M.; Tang, X.; Newell, B. S.; Chen, E. Y. X. "Nonstrained" γ -butyrolactone-based copolyesters: copolymerization characteristics and composition-dependent (thermal, eutectic, cocrystallization, and degradation) properties. *Macromolecules* **2017**, *50*, 8469–8479.
 - 46 Shen, Y.; Li, Z. B. Ring-opening polymerization of cyclic esters by utilizing organophosphazene bases toward biodegradable polyesters. *Acta Polymerica Sinica (in Chinese)* **2020**, *51*, 777–790.
 - 47 Musgrave, R. A.; Russell, A. D.; Hayward, D. W.; Whittell, G. R.; Lawrence, P. G.; Gates, P. J.; Green, J. C.; Manners, I. Main-chain metallocopolymers at the static-dynamic boundary based on nickelocene. *Nat. Chem.* **2017**, *9*, 743–750.
 - 48 Dewit, M. A.; Beaton, A.; Gillies, E. R. A reduction sensitive cascade biodegradable linear polymer. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 3977–3985.