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Thiol-Dibromomaleimide Polymerization: A Simple Strategy for Easily Degradable and Modifiable Polythioether Synthesis

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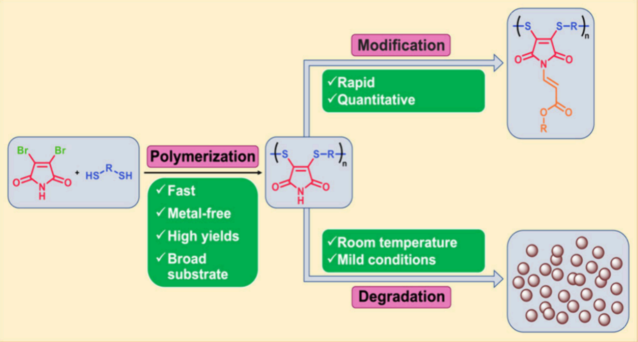

ABSTRACT: In this study, linear poly(maleimide thioether)s were prepared by thiol-dibromomaleimide (thiol-DBM) reaction using 2,3-dibromomaleimide (DBM) and dithiol monomers. Various parameters, such as solvent, reactant concentration, and time, were initially screened to reveal the optimum conditions for polymerization. A wide range of dithiols were then reacted with DBM under optimum conditions. The polymerizations proceed in a substitution mechanism, resulting in an unsaturated maleimide backbone along the main chain, accompanied by pendant imide N−H groups. Polymers were obtained in high yields with varying molecular weights ranging from 7.3 to 68.2 kDa. Postpolymerization modification of the pendant N−H groups was achieved via imide-yne click reaction with various propiolates using an organocatalyst 1,4-diazabicyclo[2.2.2]octane (DABCO). All synthesized polymers displayed a wide range of glass transition temperatures depending on the type of dithiols used. The obtained poly(maleimide thioether)s were found to be readily degradable in the presence of a monothiol; a degradation study was performed on a model polymer and a cross-linked structure using an excess amount of 1-propanethiol in the presence of triethylamine (TEA). We believe the presented chemistry is practical, offering a time- and energy-saving approach, and may pave the way for new developments in polymer synthesis, functionalization, and degradation.

■ INTRODUCTION

Maleimides are highly versatile compounds, distinguished by their unique reactivity and extensive applications in organic and polymer chemistry, material science, and bioconjugation.[1−4] The core structure of a maleimide consists of a five-membered imide ring fused to a conjugated electron-deficient double bond. This electron deficiency, imparted by the two carbonyl groups, renders them particularly reactive toward nucleophiles and dienes, enabling their comprehensive use in the Michael additions,[1,5−16] cycloaddition reactions,[17−30] radical and anionic polymerizations.[31−40] However, mono- and dihalomomaleimides exhibit entirely different behavior. At the beginning of the past decade, monobromo maleimide emerged as a versatile compound for selective reactions with cysteine, also facilitating thiol regeneration.[41] Instead of participating in typical addition, they undergo substitution reactions with thiol nucleophiles, retaining a double bond.[4,41−43] This contrasts with the saturated succinimide product that results from the addition of thiol to maleimide.

Caddick and Baker demonstrated that dihalomaleimides react rapidly and efficiently with two equivalents of thiol, following a mechanism similar to that of monobromo maleimide.[42] Among these, diiodomaleimide showed the fastest reaction, dichloromaleimide was the slowest, and 2,3-dibromomaleimide (DBM) exhibited an intermediate reactivity, depending on the effectiveness of the leaving group.[43] In their work, dibromo- and dithio-maleimides, in the presence of a reducing agent, were effectively utilized for bioconjugation, site-specific protein modification and rapid rebridging of disulfide linkages, addressing common challenges associated with disulfide reduction, such as protein unfolding, aggregation, and disulfide bond scrambling. Unlike the conventional irreversible Michael addition with maleimides, the substitution product can proceed through a thiol exchange by adding an excess of a competing thiol.[42,43]

DBM derivatives, recognized for their selective and efficient reactivity toward thiols, have been incorporated into polymer chemistry as RAFT agents,[44] ATRP initiators,[45,46] and monomer functionality,[47−49] largely due to the ease of postpolymerization modifications and disulfide rebridging. Although initial attempts to use them as ATRP initiators were unsuccessful either due to radical addition to the maleimide,[45] Haddleton and colleagues developed dithiophenol maleimides incorporating a bromoisobutyrate moiety,

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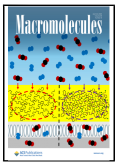

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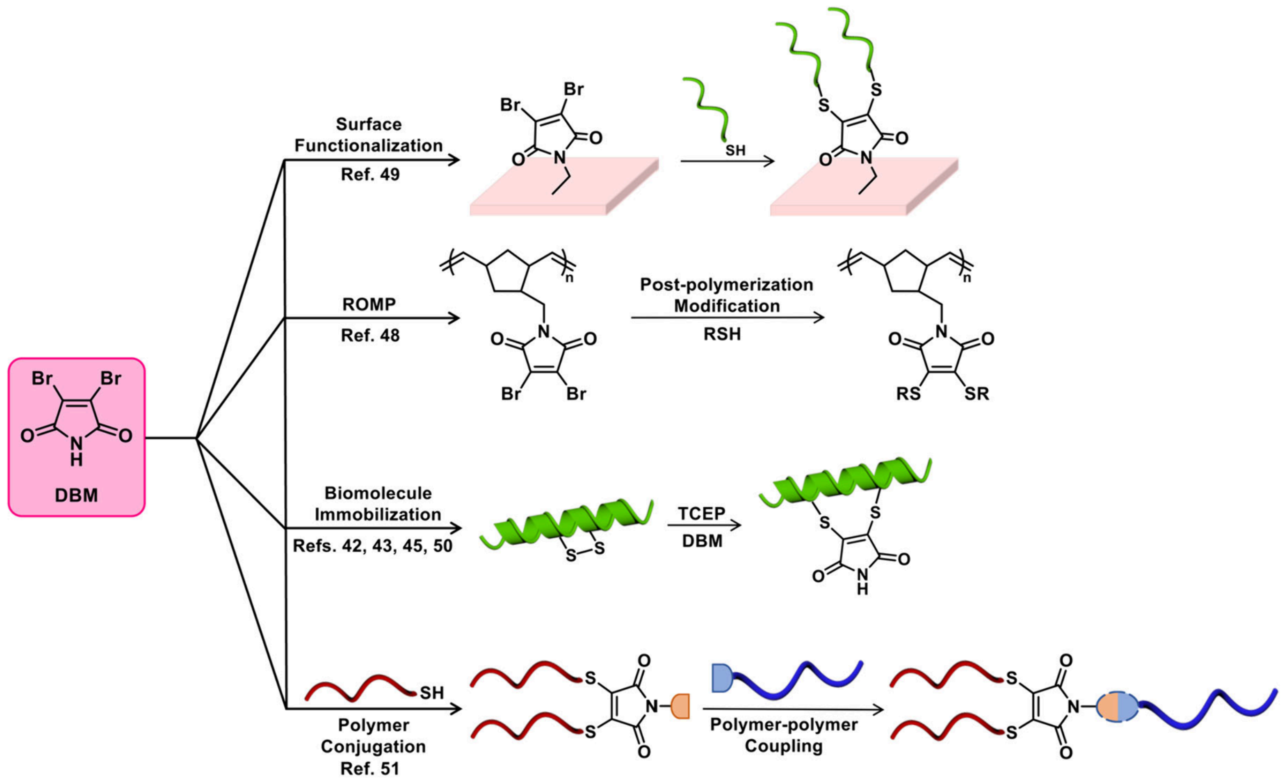
Scheme 1. Schematic Representation of DBM and Its Use in Various Applications in the Literature



which proved to be successful.[50] Jiang and co-workers synthesized norbornene monomers bearing the DBM group, which, upon polymerization via ring-opening metathesis polymerization (ROMP), generated two reactive sites per repeating unit, enabling postpolymerization modifications.[48] Ross et al., in their work, synthesized a DBM functional monomer, which was polymerized onto a surface using the chemical vapor deposition method. This approach yielded DBM-functional surfaces capable of immobilizing and releasing thiol-functionalized biomolecules from the coated surfaces.[49] Polymers with thiol end groups were also coupled with *N*-alkyl azide-functional DBM, following a copper-catalyzed azide−alkyne cycloaddition reaction gave an A_2B-type miktoarm star polymer.[51] Other distinct compounds following similar reaction mechanisms have also been reported in the literature. Baker and Chudasama demonstrated that 4,5-dibromopyridazine-3,6-dione derivatives could also bioconjugate with cysteine residues and aniline derivatives. In their work, thiol linkages were found to be cleavable with excess reactive thiols, whereas the C−N bonds remained stable.[52] Recently, Jennings and co-workers employed perfluorocyclopentene to synthesize perfluorinated polythioethers, demonstrating their facile synthesis and exceptional thermal stability.[53] The representative examples of the utility of DBM in the literature are summarized in Scheme 1.

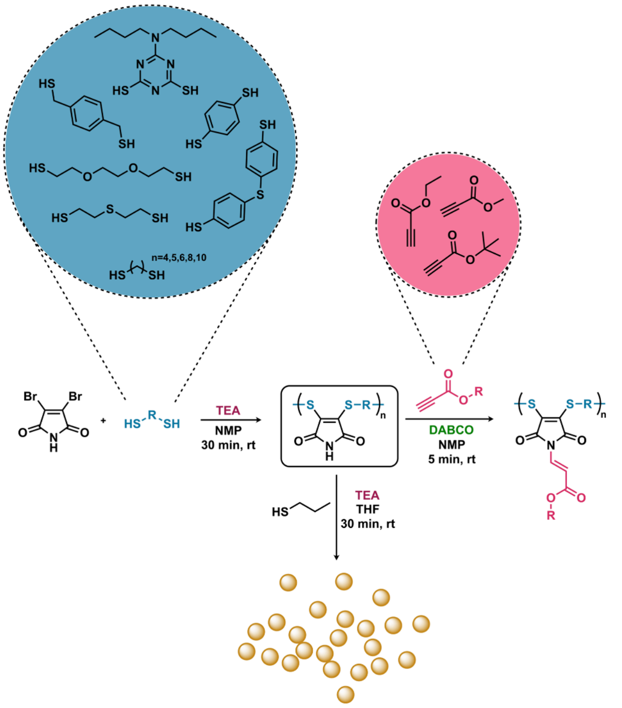
To our knowledge, DBM was utilized as a monomer to polymerize with dithiol in only one study. In 2013, the You group reported that sequence-controlled polymers could be synthesized via the formation of dithiols derived from a thiolactone compound and subsequent in situ addition of DBM to the prepared dithiol reaction mixture. This one-pot process produced a polymer having a molecular weight of 8.5 kDa.[54] The exceptional reactivity of DBM toward thiols prompted us to investigate this compound in detail to prepare linear polythioether synthesis. In this contribution, we employed DBM as a monomer and reacted it with various aliphatic and aromatic dithiol compounds to obtain poly(maleimide thioether)s (Scheme 2). Due to the easily cleavable Csp^2-S bond in the resulting polymers, a degradation study was performed in the presence of a competing thiol. Pendant imide N−H bonds were further utilized for postpolymerization modification (PPM) through imide-yne click reaction similar to our previous study.[55]

■ EXPERIMENTAL SECTION

Materials. 2,3-Dibromomaleimide (DBM, 97%), 1,6-hexanedithiol (HDT, 97%), 1,8-octanedithiol (97%), 1,5-pentanedithiol (96%), 1,4-butanedithiol (97%), 2,2′-(ethylenedioxy)diethanethiol (95%), 2,2′-thiodiethanethiol (90%, technical grade), benzene-1,4-dithiol (99%), 1,4-benzenedimethanethiol (98%), 4,4′-thiobisbenzenethiol (98%), trimethylolpropane tris(3-mercaptopropionate) (95%), triethylamine (TEA, 99.5%), *N*,*N*-diisopropylethylamine (DIPEA, 99%), 1,4-diazabicyclo[2.2.2]octane (DABCO, 98%), 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU, 98%), 1,1,3,3-tetramethylguanidine (TMG, 99%), methyl propiolate (99%), ethyl propiolate (99%), *tert*-butyl propiolate (98%), 1-propanethiol (99%), tetrahydrofuran (THF, 99%), and chloroform ($CHCl_3$, 99.8%, amylene stabilized) were all purchased from Aldrich and used as received. 1,10-Decanedithiol (95%) and 6-(dibutylamino)-1,3,5-triazine-2,4-dithiol (98%) were purchased from Fisher Scientific and used as received. Dimethyl sulfoxide (DMSO, 99.9%, Aldrich), *N*,*N*-dimethylacetamide (DMAc, 99.8%, Aldrich), *N*,*N*-dimethylformamide (DMF, 99.8%, Aldrich), and *N*-methyl-2-pyrrolidone (NMP, 99.5%, Aldrich) were anhydrous and used without further purification. Methanol was of reagent grade and used as received.

Instrumentation. ^1H (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded using an Agilent VNMRS 500 instrument in $CDCl_3$ and DMSO-d_6. Gel permeation chromatography (GPC) measurements were carried out with an Agilent instrument (model 1100) with a pump, refractive index and UV detectors, and four

Scheme 2. Outline of the Study: Polymerization of DBM with Various Dithiols, Post-Polymerization Modification (PPM) of a Model Polythioether through Imide-Yne Click Reaction with Various Propiolates, and Degradation of the Same Model Polythioether in the Presence of Excess 1-Propanethiol



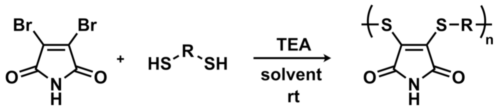
Waters Styragel columns (HR 5E, HR 4E, HR 3, HR 2) (4.6 mm internal diameter, 300 mm length, packed with 5 μm particles). The effective molecular weight ranges of the columns were 2000–4000000, 50–100000, 500–30000, and 500–20000 g/mol, respectively. THF was used as an eluent at a flow rate of 0.3 mL/min at 30 °C, and 2,6-di-*tert*-butyl-4-methylphenol (BHT) was used as an internal standard. The weight-average molecular weights (M_w) and dispersities ($Đ$) of the polymers were calculated based on linear polystyrene (PS) standards (Polymer Laboratories). Differential scanning calorimetry (DSC) measurements were performed under a nitrogen atmosphere using a TA Q1000 DSC apparatus. For the synthesized polymers, two different temperature procedures were applied based on their physical properties. **P1–P6** polymer samples were first heated to 100 °C with a heating rate of 10 °C/min. The samples were kept at this temperature for 2 min, then cooled to −60 °C with a cooling rate of 10 °C/min and kept at this temperature for 2 min. Finally, they were reheated to 100 °C with a heating rate of 10 °C/min. **P7–P11** polymer samples were first heated to 150 °C with a heating rate of 10 °C/min. The samples were kept at this temperature for 2 min, then cooled to −60 °C with a cooling rate of 10 °C/min and kept at this temperature for 2 min. Finally, they were reheated to 150 °C with a heating rate of 10 °C/min. In both cases, the data from the second heating cycle were reported. Fourier transform infrared (FTIR) spectra were recorded on a Shimadzu IRSpirit-T (Shimadzu, Japan) instrument in the 4000–650 cm^{-1} range.

General Procedure for Thiol-Dibromomaleimide Polymerization. To a 10 mL round-bottom flask equipped with a magnetic stir bar was added DBM (200 mg, 0.785 mmol, 1 equiv) and dissolved in NMP (785 μL). Dithiol monomer (0.785 mmol, 1 equiv) was then added, and upon complete dissolution, TEA (328.3 μL, 2.355 mmol, 3 equiv) was finally added to the flask. Upon the addition of TEA, an exothermic reaction occurred, accompanied by a color change and turbidity (salt formation). The reaction was allowed to stir at room temperature for 30 min. After the specified time, the reaction mixture was precipitated into acidified methanol and the supernatant was decanted, except for polymers **P8** and **P10**, which were directly filtered. The dissolution–precipitation procedure (THF-acidified methanol) was repeated two times. The resultant polymers were dried *in vacuo*. The synthetic procedures and characterization details of the obtained linear polymers can be found in the Supporting Information.

Postpolymerization Modification of P1 via Imide-yne Click reaction. To a 10 mL round-bottom flask equipped with a magnetic stir bar was added **P1** (100 mg, 0.411 mmol, based on repeating unit, 1 equiv) and dissolved in 1 mL of NMP. Then, a propiolate ester compound (0.616 mmol, 1.5 equiv) and DABCO (4.59 mg, 0.0411 mmol, 0.1 equiv) were added to the reaction medium, respectively. Upon the addition of DABCO, the bright yellow solution instantly turned dark brown. The mixture was allowed to stir at room temperature for 5 min and then precipitated into acidified methanol, and the supernatant was decanted. The dissolution–precipitation procedure ($CHCl_3$-acidified methanol) was repeated two times. The resultant polymers were dried *in vacuo*. The synthetic procedures and characterization details of the modified polymers can be found in the Supporting Information.

Degradation Study of P1. To a 10 mL round-bottom flask equipped with a magnetic stir bar was added **P1** (100 mg, 0.411 mmol, based on repeating unit, 1 equiv) and dissolved in 3 mL of THF. Then, 1-propanethiol (114.5 μL, 1.233 mmol, 3 equiv) and TEA (171.8 μL, 1.233 mmol, 3 equiv) were added to the reaction medium, respectively. Aliquots of 25 μL were withdrawn from the reaction medium at different time intervals and characterized by GPC.

Table 1. Solvent Optimization for Thiol-DBM Polymerization[a]



		M_w (kDa)[b]/$Đ$[b]						
entry	solvent	5 min	30 min	1 h	2 h	4 h	6 h	8 h
1	NMP	14.6/2.0	15.7/2.1	15.8/2.2	16.2/2.2	16.3/2.1	16.7/2.1	17.6/2.0
2	DMSO	13.5/1.7	14.6/2.2	15.4/2.1	15.1/2.1	15.1/2.1	15.3/2.2	15.4/2.3
3	DMAc	9.6/1.9	10.4/1.9	10.5/2.1	10.4/2.0	10.5/1.9	11.7/2.2	11.8/2.1
4	DMF	13.1/2.1	13.1/2.1	13.3/2.0	13.6/2.1	14.2/2.1	14.7/2.2	14.9/2.2
5[c]	NMP	19.1/2.2	22.3/2.0	22.3/2.4	22.9/2.3	23.4/2.0	24.3/2.4	24.3/2.0
6[d]	NMP	21.6/2.0	25.2/2.0	25.5/1.9	25.8/2.3	25.9/2.2	26.1/2.4	26.7/2.3

[a] Reaction conditions: 0.785 mmol of DBM, 0.785 mmol of HDT, and 2.355 mmol of TEA in 1.57 mL of solvent at room temperature. [b] Determined by GPC calibrated based on linear PS standards in THF. [c] Reaction was carried out using monomer concentrations of 0.75 M. [d] Reaction was carried out using monomer concentrations of 1 M.

Table 2. Determination of Suitable Base for Thiol-DBM Polymerization[a]

entry	base	M_w (kDa)[b]/$Đ$[b]						
		5 min	30 min	1 h	2 h	4 h	6 h	8 h
1	TEA	14.6/2.0	15.7/2.1	15.8/2.2	16.2/2.2	16.3/2.1	16.7/2.1	17.6/2.0
2	DBU	16.6/2.3	15.9/2.5	13.6/2.3	11.5/2.2	9.4/2.0	8.6/2.1	8.0/2.0
3	DIPEA	9.1/1.8	10.5/1.9	10.5/1.9	10.7/1.9	10.9/1.9	10.7/1.9	11.0/1.9
4	TMG	12.7/2.2	13.0/2.4	13.3/2.1	13.7/2.2	13.6/2.3	14.2/2.4	14.4/2.4

[a]Reaction conditions: 0.785 mmol of DBM, 0.785 mmol of HDT, and 2.355 mmol of base in 1.57 mL of NMP at room temperature. [b]Determined by GPC calibrated based on linear PS standards in THF.

Table 3. Optimization of TEA Equivalent for Thiol-DBM Polymerization[a]

entry	equivalent	M_w (kDa)[b]/$Đ$[b]						
		5 min	30 min	1 h	2 h	4 h	6 h	8 h
1	2	15.4/1.6	17.8/1.6	17.8/1.6	17.7/1.7	19.1/2.2	18.9/2.1	19.0/2.0
2	3	21.6/2.0	25.2/2.0	25.5/1.9	25.8/2.3	25.9/2.2	26.1/2.4	26.7/2.3
3	4	22.5/2.1	26.3/2.3	27.1/2.0	27.2/2.0	27.9/2.1	28.1/2.2	28.7/2.3
4[c]	3	11.0/1.5	11.6/1.6	11.7/1.6	11.9/1.7	12.0/1.7	12.4/1.8	12.5/1.9

[a]Reaction conditions: 0.785 mmol of DBM and 0.785 mmol of HDT in 0.785 mL of NMP at room temperature. [b]Determined by GPC calibrated based on linear PS standards in THF. [c]Reaction was carried out at 0 °C.

The GPC traces of degradation products with respect to reaction time are shown in Figure 4.

Synthesis of Cross-Linked Polymer. To a 10 mL round-bottom flask equipped with a magnetic stir bar was added DBM (200 mg, 0.785 mmol, 1.5 equiv) and dissolved in NMP (1.570 mL). Trimethylolpropane tris(3-mercaptopropionate) (172.3 μL, 0.523 mmol, 1 equiv) was then added, and upon complete dissolution, TEA (218.8 μL, 1.570 mmol, 3 equiv) was finally added to the flask. Upon the addition of TEA, an exothermic reaction and gel formation occurred simultaneously.

Degradation of Cross-Linked Polymer. To the same round-bottom flask with the cross-linked polymer, 3 mL of THF was added, followed by 1-propanethiol (145.8 μL, 1.570 mmol, 3 equiv relative to the used trimethylolpropane tris(3-mercaptopropionate)) and TEA (218.8 μL, 1.570 mmol, 3 equiv), respectively. During degradation, the salts trapped within the gel were released and mixed with the solution. After 30 min, stirring was stopped, and the solid, insoluble salts settled to the bottom. Then, the reaction solution was filtered to give a clear solution. Figure 5 illustrates the degradation process of the cross-linked polymer through visual representations.

■ RESULTS AND DISCUSSION

First, we examined the optimization conditions for polymerization. To this end, HDT was chosen as the model dithiol and reacted with DBM in equimolar amounts. Both monomers were dissolved in various polar solvents at a concentration of 0.5 M, ensuring the full solubility of both DBM and the resulting polymer **P1** (Table 1). Since the substitution reaction generates HBr, TEA was initially used in 3-fold molar excess to maintain a basic environment during polymerization. It is worth mentioning here that upon the addition of TEA to the reaction medium, an exothermic reaction occurred, producing an excess of salt (triethylammonium bromide), and the polymerization medium became viscous. Polymerizations were monitored by GPC for up to 8 h. Among the solvents tested, NMP produced polymers with slightly higher molecular weights when compared to DMSO, DMAc, and DMF, making it the most suitable solvent for polymerization (Table 1, entries 1−4). An increase in molecular weights was observed when the concentration of monomers was increased to 0.75 and 1 M (Table 1, entries 5 and 6). Further increases in monomer concentrations did not allow proper stirring of the reaction medium. However, due to the increased viscosity of the reaction mixture, maintaining a homogeneous solution became challenging. Therefore, the type of the base and its equivalent were systematically tested at 0.5 M concentration.

After obtaining preliminary results with TEA, various organobases were evaluated to identify the most effective one. Among them, DBU demonstrated exceptional performance, producing relatively high molecular weight polymers within just 5 min (Table 2, entry 2). However, extended reaction times with DBU led to depolymerization. It should be noted here that DBU is the most basic and nucleophilic compound among the organobases tested in this study.[56−59] Therefore, it is thought that the combination of these two properties accelerates depolymerization over time. In contrast, both DIPEA and TMG yielded polymers with lower molecular weights than TEA over an 8-h period (Table 2, entries 3 and 4). Thus, TEA was selected as the most suitable base for the polymerization and used in the rest of the study.

Lastly, we examined the effect of TEA equivalent on polymerization. As stated previously, 3 equiv of TEA were initially employed to maintain a basic environment for polymerizations. Reducing the TEA to 2 equiv resulted in polymers with lower molecular weights (Table 3, entry 1). Increasing the TEA concentration to 4 equiv slightly enhanced the molecular weight of the polymers (Table 3, entry 3). Lower molecular weight polymers were obtained when the polymerization was conducted at 0 °C, indicating the necessity of exothermicity to promote polymerization (Table 3, entry 4).

Based on the results obtained from the optimization studies, it was found that NMP was the appropriate solvent, and TEA was identified as the most suitable base. To achieve high molecular weight polymers, molar ratios of dithiol:DBM:TEA were set to 1:1:3, and a 1 M monomer concentration was used throughout the diversification studies. It is also worth noting that optimization studies revealed that a reaction time of 30 min was sufficient for the proposed polymerization; no distinct change was observed after this time, indicating a time-saving polymerization process (Table 1, entry 6).

Before diversification studies, the model polymer, **P1**, was first analyzed using NMR spectroscopy. The ^{1}H NMR spectrum exhibited four distinct peaks that can be attributed to the polymer structure (Figure 1a). The imide N*H* proton was observed at δ 11.08 ppm, while S−CH_2 protons appeared at δ 3.19 ppm. The remaining linear alkyl main chain protons SCH$_2$CH_2 and SCH$_2$CH$_2$CH_2 were observed at 1.55 and 1.34 ppm, respectively. The structure of **P1** was further confirmed through ^{13}C NMR analysis (Figure 1b). The imide carbonyl carbons and double bond carbons were observed at δ 167.84 and 136.27 ppm, respectively. Peaks corresponding to HDT main chain carbons appeared at δ 31.29, 30.34, and 27.77 ppm. The FTIR spectrum of **P1** (Figure S3) also indicated that the peaks associated with C═O (symmetric and asymmetric), C—N, and C—S stretching vibrations at 1770, 1702, 1321, 1192, and 735 cm^{-1}, respectively. All these results validate the successful synthesis of the expected product, **P1**, and indicate that the thiol-DBM polymerization proceeded smoothly.

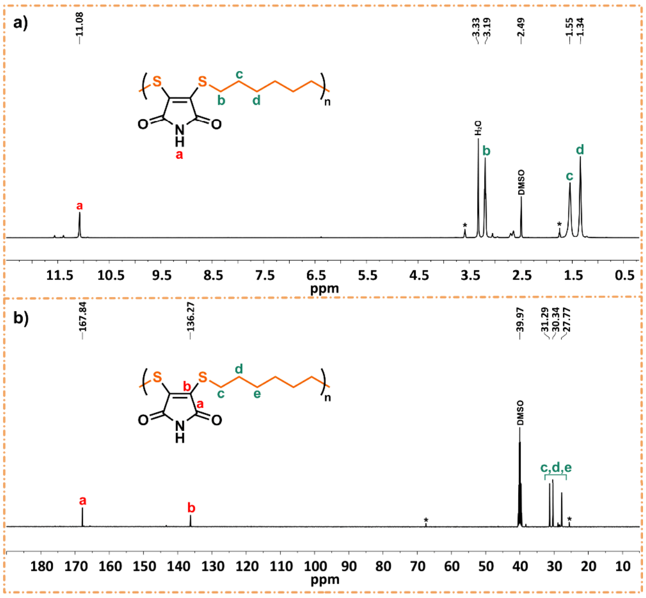


Figure 1. ^{1}H NMR spectrum (a) and ^{13}C NMR spectrum (b) of **P1** in DMSO-d_6 (500 MHz). Residual THF peaks are marked with an asterisk (*).

Various dithiols, ranging from aliphatic to aromatic, were reacted with DBM under the optimum conditions, and the results obtained are presented in Table 4. Aliphatic dithiols (**P1**−**P5**), including HDT, produced polymers with moderate molecular weights, ranging from 7.3 to 26.3 kDa. Among them, **P5** derived from 1,4-butanedithiol yielded the lowest molecular weight (M_w = 7.3 kDa), which might be attributed to possible side reactions such as cyclization during polymerization, which suppressed the growth of the polymer. Heteroatom-containing dithiols, namely 2,2′-(ethylenedioxy)diethanethiol (**P6**) and 2,2′-thiodiethanethiol (**P7**), also yielded moderate molecular weight polymers in good yields. Aromatic dithiols were next examined. Although benzene-1,4-dithiol (**P8**) and 4,4′-thiobisbenzenethiol (**P10**) are assumed to be sterically more congested compared to 1,4-benzenedimethanethiol (**P9**), these polymers produced moderate molecular weights, while 1,4-benzenedimethanethiol yielded low molecular weight. These results indicate that in a highly basic medium, thiophenol structures can easily lose their acidic protons and transform into thiophenolates that are highly nucleophilic to react with DBM; however, 1,4-benzenedimethanethiol, which contains a methylene spacer between SH and the benzene ring, becomes less nucleophilic under the same conditions, producing lower molecular weight polymer. Surprisingly, the highest molecular weight polymer (**P11**, M_w = 68.2 kDa) in this study was obtained by the reaction of 6-(dibutylamino)-1,3,5-triazine-2,4-dithiol with DBM. Indeed, considering the sterically hindered structure of 6-(dibutylamino)-1,3,5-triazine-2,4-dithiol, this result is not expected. However, since **P11** has a rigid backbone, its poor folding could likely result in a large hydrodynamic volume and hence a high molecular weight polymer. Figure 2 shows overlaid ^{1}H NMR spectra of representative polymers. As shown in this figure, the expected main backbone signals are clearly detectable, indicating smooth polymerization in all cases. The NMR spectra of all polymers are provided in the Supporting Information.

Table 4. Results of Synthesized Polymers[a]

polymer	dithiol	M_w[b] (kDa)	$Đ$[b]	T_g (°C)[c]	isolated yield (%)[d]
P1[e]	1,6-hexanedithiol	26.3	2.3	−19.9	86
P2	1,8-octanedithiol	23.4	2.0	−26.2	87
P3	1,10-decanedithiol	16.7	1.7	−45.9	72
P4	1,5-pentanedithiol	12.7	1.6	−18.6	70
P5	1,4-butanedithiol	7.3	1.3	−2.3	50
P6	2,2′-(ethylenedioxy) diethanethiol	24.0	1.8	−6.9	86
P7	2,2′-thiodiethanethiol	26.0	2.0	36.3	90
P8	benzene-1,4-dithiol	18.9	1.9	43.1	85
P9	1,4-benzenedimethanethiol	7.4	1.5	41.3	75
P10	4,4′-thiobisbenzenethiol	14.7	1.8	104.4	72
P11	6-(dibutylamino)-1,3,5-triazine-2,4-dithiol	68.2	2.7	57.8	88

[a] Reaction conditions: 0.785 mmol of DBM, 0.785 mmol of dithiol monomer, and 2.355 mmol of TEA in 0.785 mL of NMP at room temperature for 30 min. [b] Determined by GPC calibrated based on linear PS standards in THF. [c] Determined by DSC from the second heating cycle. [d] Gravimetric yield obtained after first precipitation. [e] Freshly prepared on a large scale.

The synthesized polymers exhibited T_gs ranging from −45.9 to 104.4 °C, as summarized in Table 4. For polymers **P1** to **P5**, dithiols with varying linear alkyl chain lengths ranging from 4 to 10 carbons were incorporated in the following order: **P5** (shortest chain) < **P4** < **P1** < **P2** < **P3** (longest chain). A clear decreasing trend in T_g values was observed as the chain length increased, indicating that chain flexibility increased with increasing main chain methylene units. Among the polymers derived from aromatic dithiols, **P10** exhibited the highest T_g, which can be attributed to its highly rigid aromatic backbone. **P11**, derived from 6-(dibutylamino)-1,3,5-triazine-2,4-dithiol, showed a moderate T_g of 57.8 °C. **P8**, where thiol groups are directly attached to the benzene ring, exhibited a T_g of 43.1 °C. In contrast, **P9** displayed a slightly lower T_g of 41.3 °C compared to **P8**, likely due to the increased flexibility introduced by the additional methylene groups. Moreover, **P6** and **P2** are synthesized from dithiol compounds having chains containing an equal number of atoms and similar lengths. **P2** is made from 1,8-octanedithiol, whereas **P6** (derived from 2,2′-(ethylenedioxy)diethanethiol) contains a similar dithiol in which two carbon atoms are replaced with oxygen atoms. Both **P6** and **P2** yielded similar molecular weights; however, the T_g of **P6** was 19.3 degrees higher than that of **P2**. This situation was attributed to the increased intermolecular forces, i.e., dipole−dipole interactions (polar-

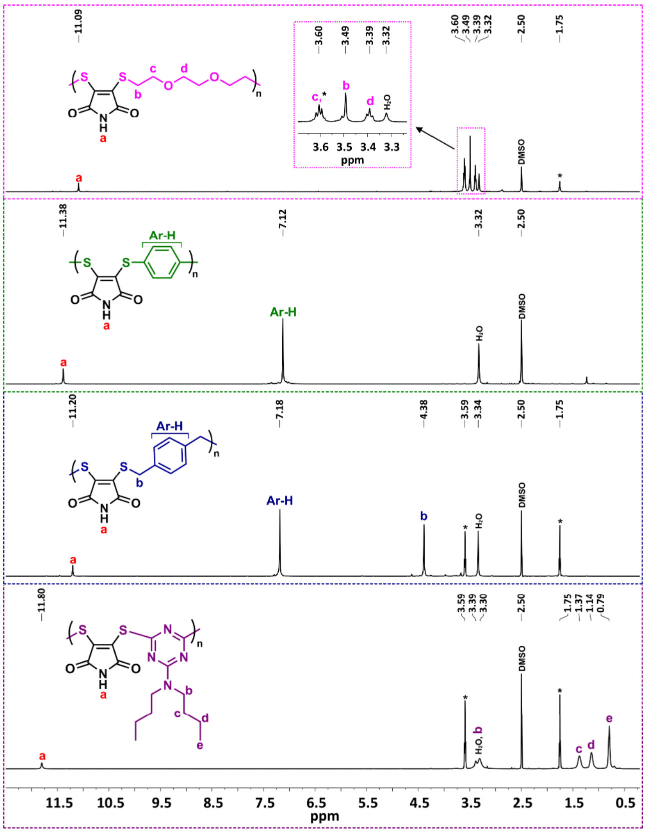


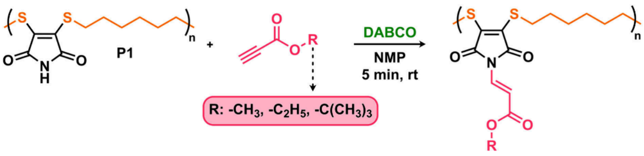
Figure 2. ^{1}H NMR spectra of **P6**, **P8**, **P9**, and **P11** (from top to bottom) in DMSO-d_6 (500 MHz). Residual THF peaks are marked with an asterisk (*).

ity) in **P6** due to the presence of oxygen atoms. The relatively higher T_g of **P7** compared to its structural analogue, **P4**, could be ascribed to the higher molecular weight of **P7**. Furthermore, it is believed that the flexible 2,2′-thiodiethanethiol-containing chains of **P7** facilitated the ordering and molecular packing of the poly(thioether) chains rather than leading to increased free volume.

One of the important outcomes of this study is the formation of pendant imide N−H groups, which can be utilized for postpolymerization modification (PPM). More recently, our group demonstrated that imide N−H groups could readily attack reactive triple bonds via imide−yne reaction to form linear polymeric structures.[55] Thus, an attempt was made to further functionalize this group via imide−yne click reaction after the successful synthesis of maleimide main chain polymers. Three different propiolate esters were utilized in the PPM reactions with **P1** (Table 4) polymer (Scheme 3).

The imide-yne reactions proceeded rapidly at room temperature using nucleophilic organocatalyst DABCO. Quantitative modification efficiencies were obtained from all reactions, and the products obtained were only in the *E*-isomer form, as confirmed by ^{1}H NMR. Here, the ^{1}H NMR spectrum of the polymer resulting from the reaction between **P1** and ethyl propiolate was examined in detail; NMR and FTIR spectra of all modified polymers are provided in the Supporting Information (Figures S50−S57). The ^{1}H NMR spectrum showed that the imide NH peak at δ 11.08 ppm completely disappeared, and N-vinyl proton signals appeared at δ 7.68 and 6.66 ppm. Furthermore, methylene protons (OCH_2CH_3) and (OCH_2CH_3) of the ethyl group were observed at δ 4.21 ppm and δ 1.30 ppm, respectively (Figure 3). From ^{13}C NMR analysis, the carbonyl carbons of imide and the ester were detected at δ 167.09 and 163.20 ppm, respectively. Also, the vinyl carbon of maleimide next to S appears at δ 136.67, while the carbons of the pendant vinyl units resulting from the imide-yne reaction appear at δ 130.07 and 107.00 ppm (Figure S50). Both ^{1}H and ^{13}C analyses confirm the successful PPM.

Scheme 3. Post-Polymerization Modification of P1 with Propiolate Esters via an Imide-yne Click Reaction



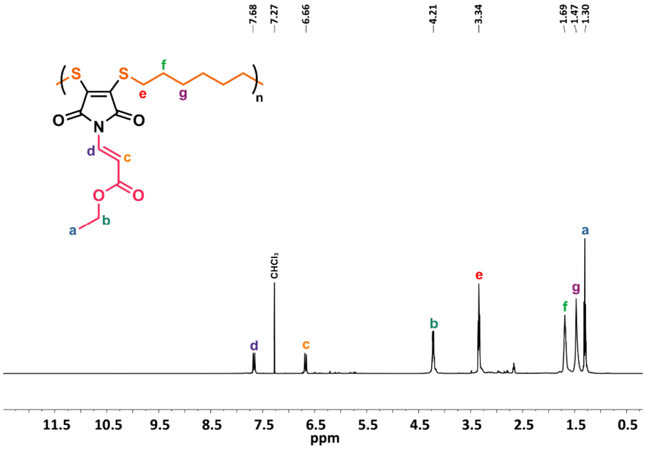
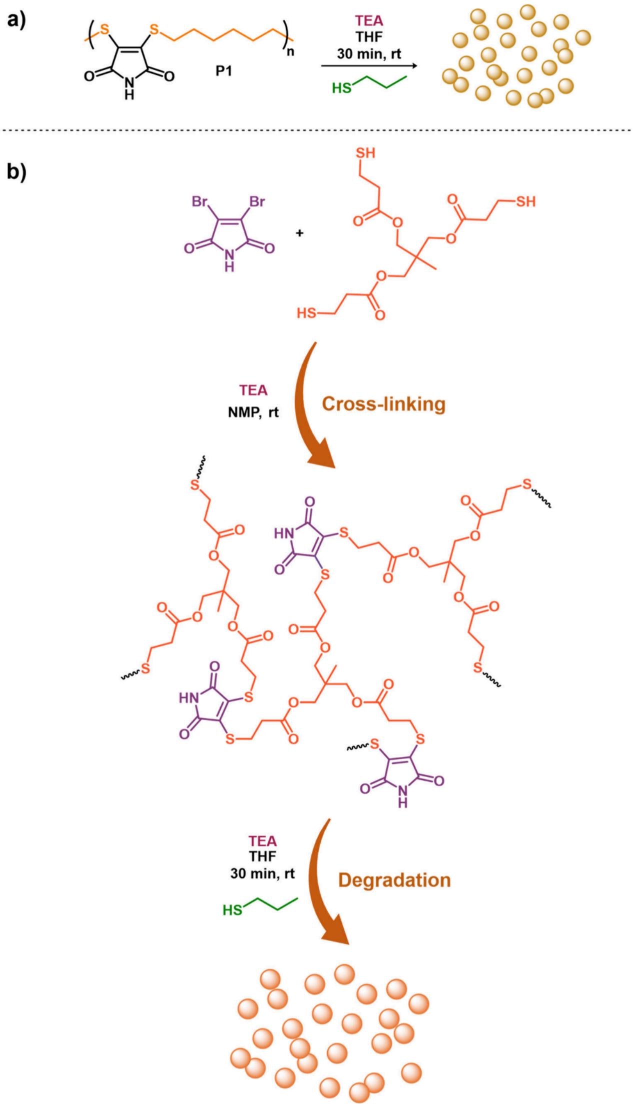


Figure 3. ^{1}H NMR spectrum of ethyl propiolate modified **P1** in $CDCl_3$ (500 MHz).

It is known that the Csp^2-S bond in the thiol-DBM products can easily undergo a thiol exchange reaction in the presence of excess thiol or can be easily cleaved using a reducing agent.[42] It is thought that employing one of these strategies in the resulting poly(maleimide thioether) polymers may lead to chain scission and, thus, degradation of the polymers. To examine this phenomenon, we reacted **P1** (Table 4) with a 3-fold excess (with respect to the polymer repeating unit) of 1-propanethiol and TEA at room temperature (Scheme 4a). The progress of the reaction was monitored by GPC by taking samples from the reaction medium at different time intervals. As shown in Figure 4, the polymer started to degrade within 5 min and its molecular weight decreased to 14.3 kDa. This decline continued for up to 1 h and remained constant thereafter. This result indicates that the polymer main chain undergoes a thiol exchange reaction with the monothiol, resulting in the cleavage of the polymer chain into low molecular weight oligomeric fractions.

Nowadays, one of the important topics in chemistry is the degradation of a cross-linked material by simple reactions under mild conditions. In line with this goal, we next aimed to prepare a cross-linked material through the thiol-DBM reaction and degrade the prepared network using the aforementioned thiol-exchange reaction. A cross-linked poly-

Scheme 4. Degradation of the Linear Polymer P1 (a) and the Synthesis and Following Degradation of the Cross-Linked Material (b)



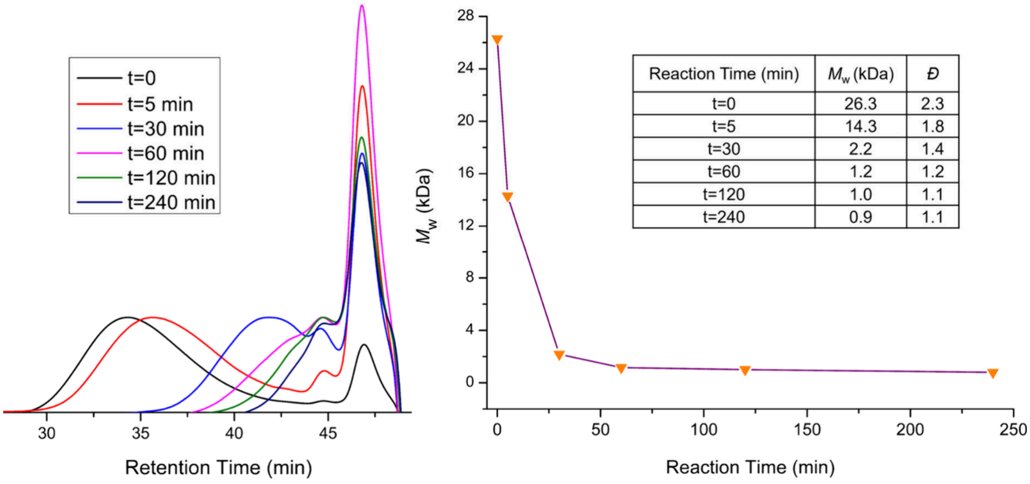
mer was prepared using DBM and a trifunctional thiol (i.e., trimethylolpropane tris(3-mercaptopropionate)) (Scheme 4b).

Following the same degradation mechanism, we were able to break down the cross-linked network. In our example, salts formed during gelation were entrapped within the gel matrix. These salts could be removed through multiple swelling and deswelling cycles; however, in our demonstration, the gel was used as is. As a result, the initially insoluble gel transformed into a soluble mixture containing insoluble salts within 30 min, demonstrating the efficiency of the degradation process (Figure 5). Degradation studies in both linear and cross-linked polymers highlight the great potential of the proposed chemistry for further applications.

■ CONCLUSIONS

In summary, thiol-DBM chemistry has been demonstrated as a practical method for preparing linear polymers with a maleimide backbone. Optimization studies showed that NMP and TEA are ideal solvents and bases for polymerization. The polymerization reactions proceeded at room temperature, and 30 min reaction time was found to be sufficient to reach high molecular weights. Various poly(maleimide thioether)s with different chemical backbones and varying molecular weights were found to be accessible in good to high yields using the optimum conditions. The resulting polymers exhibited a wide range of glass transition temperatures parallel to the thiol type used. The resulting polymers could also be readily functionalized via imide-yne click reaction between the N−H bonds in the polymers and the propiolate esters, highlighting another useful feature of the proposed chemistry. Due to the easily cleavable nature of the Csp^2-S bond in the resulting polymeric structure, **P1**, as a model polymer, was subjected to degradation via a thiol-exchange mechanism using an excess of 1-propanethiol; the kinetic experiment indicated that the polymer was rapidly degraded within a short time. The versatility of the proposed thiol-DBM chemistry was also utilized to create a network structure, and its degradation was subsequently demonstrated by employing the same thiol-exchange reactions.

The presented polymer synthesis strategy is believed to offer several advantages, such as mild conditions, metal-free, and readily available starting materials. Additionally, the obtained polymers can be easily functionalized and degraded, meeting



Reaction Time (min)	M_w (kDa)	$Đ$
t=0	26.3	2.3
t=5	14.3	1.8
t=30	2.2	1.4
t=60	1.2	1.2
t=120	1.0	1.1
t=240	0.9	1.1

Figure 4. Overlaid GPC traces of **P1** over time in the presence of TEA and 1-propanethiol.

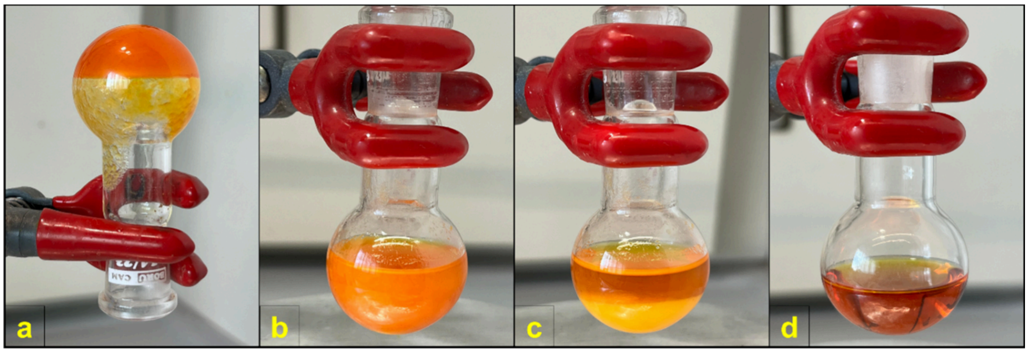


Figure 5. Images of (a) the cross-linked polymer, (b) liberation of entrapped salts from the gel during degradation, (c) phase separation of salt and solution after stirring was stopped, and (d) the clear reaction solution after filtration.

many demands of today's polymer science. As such, we believe the findings of this study will draw considerable attention from the literature and will be a strong tool in the hands of polymer and material chemists.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.macromol.5c00445.

Full experimental section, list of all polymers with GPC traces, NMR, FTIR, and DSC spectra (PDF)

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Notes

The authors declare no competing financial interest.

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