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Polythioethers bearing side groups for efficient degradation by E1cB reaction: reaction design for polymerization and main-chain scission†

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We have previously reported the polycondensation by the tandem reactions of dithiols and α-(bromomethyl)acrylates, consisting of conjugate substitution (S_N2' reaction) and conjugate addition (Michael addition) reactions. The resulting polythioethers underwent a main-chain scission (MCS) by E1cB reaction, which is the reverse reaction of conjugate addition, although it was not quantitative due to the equilibrium. Herein, the modification of the structures of polythioethers led to irreversible MCS, whereby the β-positions of ester moieties were substituted with a phenyl group. This slight modification in the polymer structure influenced the monomer structures and polymerization mechanisms. The understanding of reaction mechanisms by model reactions was required to obtain high molecular weights of polythioethers. It was clarified that the consequent additions of 1,4-diazabicyclo[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and PBu$_3$ were effective to achieve high molecular weight. The resulting polythioethers decomposed by irreversible MCS *via* E1cB reaction with DBU.

Introduction

The main-chain scission (MCS) of polymers leads to a high decrease in molecular weight through a small number of reactions. As a result, the thermal properties, such as glass transition temperature (T_g) and melting temperature (T_m), mechanical properties, such as Young modulus and elasticity, and the solubility were drastically changed. The changes in physical properties by MCS have been applied to photoresists,[1] dismantling adhesions,[2] degradable crosslinked polymers,[3] and a prospective strategy for controlling and supporting biodegradation.[4–6] Therefore, the developments of polymers accepting MCS by specific stimuli are important issues.

Although the method to break a carbon–carbon (C–C) covalent bond is limited,[7–11] those of carbon–heteroatom (C–X) are often performed.[12–16] Recently, Hoye *et al.* applied the E1cB reaction (retro-oxa-Michael addition) to the MCS of polyester.[17] The polyester was prepared by ring-opening polymerization of a δ-lactone derivative bearing a carbonyl pendant at the γ-position, and the E1cB reaction by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) resulted in MCS producing an acrylate monomer at

a high yield (95%). This study suggests that the E1cB reaction is effective for quantitative and selective MCS.

Polythioethers are typically synthesized by the polyaddition of thiols with alkenes[18] or alkynes,[19] whereas the radical ring-opening polymerization of cyclic α-(thiomethyl)acrylates is another practical route.[20] The former, polyaddition, are based on thiol–ene and thiol–yne click reaction that progresses quantitatively even under ambient condition. Thiol–ene reactions include both radical and ionic mechanisms.[21] The latter is the so-called Michael addition reaction between thiols and α,β-unsaturated carbonyl compounds, such as acrylates, which is reverse of the E1cB reaction. Therefore, optimization of molecular and reaction designs would lead to both polymerizations by Michael addition and efficient MCS by E1cB reaction under suitable conditions.

We recently reported the polycondensation *via* a tandem reaction of conjugate substitution and addition reactions of α-(bromomethyl)acrylate **1a** and dithiol **2** (Scheme 1A).[16,22] The product, **4a**, underwent MCS *via* E1cB reaction in the presence of DBU.[15] However, since the E1cB reactions were not irreversible, the end-capping of formed thiol-end with monothiol was required to promote MCS. However, the MCS was not quantitative; for example, **4a** ($M_n = 10\,700$ and $Đ = 1.89$) decomposed to an oligomer ($M_n = 2100$ and $Đ = 1.83$) even in the presence of 5.0 equimolar monothiol.

Herein, new polythioethers **4b** and **4c**, bearing methyl and phenyl substituents next to the sulphur atom, respectively, were designed to achieve more efficient MCS (Scheme 1B). The allylic substituents were found as the key leading to the MCS by the irreversible E1cB reaction. On the other hand, substitution at

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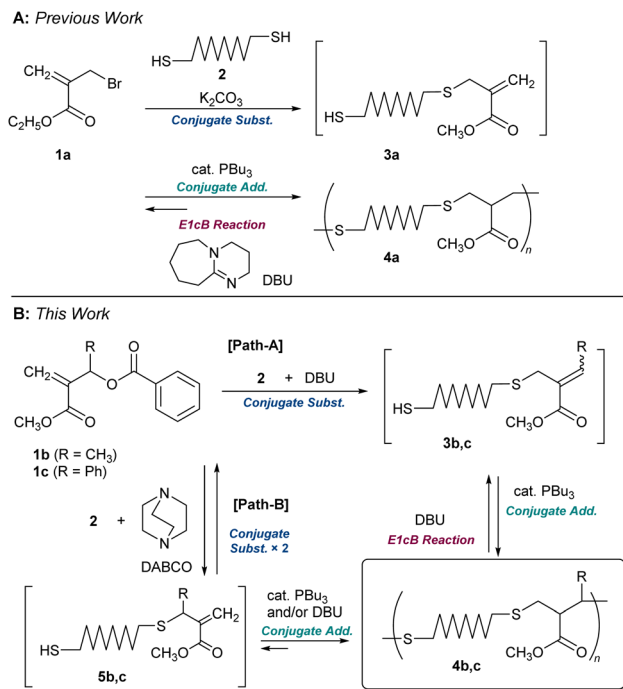
Scheme 1 Synthesis and MCS of polythioethers. (A) Our previous report.[22] (B) This report.

Scheme 2 A model reaction of **1b** and **c** with **6** (A) and the proposed reaction mechanisms (B) and (C).
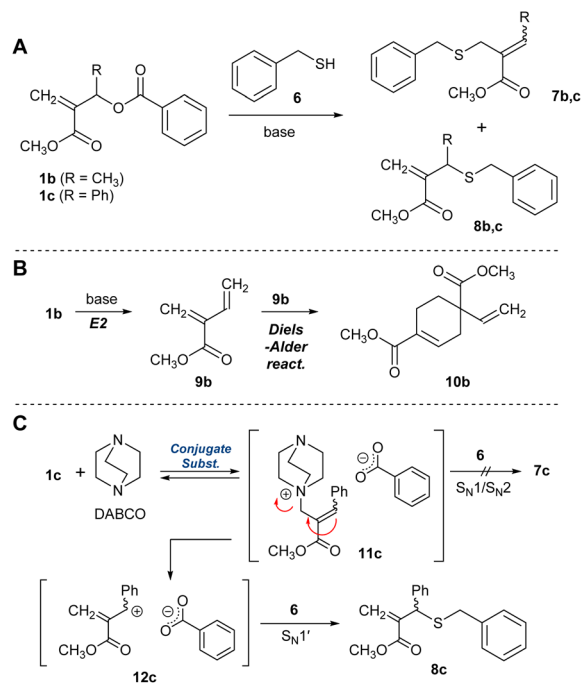
the allylic position complicated the polymerization. An understanding of the reaction mechanism and careful examination of the conditions were required to achieve a high degree of polymerization.

Results and discussion

Molecular design and model reactions

For the difficulty in synthesis, **1b** and **1c**, which have no halogen atom but a benzoyloxy group as a leaving group for conjugate substitution, were prepared. Two routes are possible to access **4b**:[23] one is a direct conjugate substitution with **2**, and the subsequent conjugate addition (Scheme 1B, path A). As this is a reversible reaction, the reaction condition is expected to be the key to achieving a high degree of polymerization. The other is the conjugate addition reaction of **5b**, which seems more reactive than **3b** due to the *exo*-olefin structure (path B). Thus, we initially planned the polymerization *via* path B. For this strategy, the issue of how **5b** can be prepared from **1b** must be addressed.

Yu *et al.* have reported the synthesis of an *exo*-methylene product by the nucleophilic substitution reaction of the analogue of **1b** and a phenol catalysed by Et$_3$N,[24] which was a hint to prepare **5b** from **1b**, although the product yield was not quantitative. As is well known, quantitative and selective conversion is necessary for polycondensation. Therefore, a model experiment with benzyl mercaptan (**6**) was conducted in CDCl$_3$ to optimize the reaction condition for the selective and quantitative synthesis of an *exo*-olefin **8b** (Scheme 2A). Without a base, no reaction occurred (Table 1, entry 1). Then, **6** was added to a mixture of DABCO and **1b**, but an E2 reaction and the

subsequent Diels–Alder reaction to yield **9b** and **10b**, respectively, were observed (Scheme 2B, entry 2, Fig. S3†). To avoid these side reactions, **1b** and **6** were mixed in advance, and DABCO was added (entry 3, Fig. S4†). The main product was *exo*-olefin **8b**, with some slight side reactions. To reduce the side reactions, the feed of DABCO was decreased to a catalytic amount, but selectivity was unchanged, thus slowing down the process (entry 4, Fig. S5†). Weak bases, such as Et$_3$N (entry 5) and iPr$_2$NEt (entry 6), resulted in low conversion and selectivity,

Table 1 Model experiments with benzyl mercaptan (**6**) using various bases

Entry[a]	**1**	Base[b] (equimol.)	Time [h]	Conv.[c] [%]	Composition[c] [%]			
					7	8	9	10
1	**1b**	—	1	0				
2[d]	**1b**	DABCO (1.2)	1	86			85	15
3	**1b**	DABCO (1.2)	1	>99	1	95	1	2
4	**1b**	DABCO (0.33)	15	81	1	94	3	2
5	**1b**	Et$_3$N (1.2)	24	26	58	38	0	4
6	**1b**	iPr$_2$NEt (1.2)	24	Trace				
7	**1b**	DBU (1.2)	3	>99	96	2	1	1
8	**1b**	DBU (0.33)	36	27	95	1	0	4
9	**1c**	—	1	0				
10	**1c**	DABCO (1.2)	1	97	<1	>99	0	0
11	**1c**	Et$_3$N (1.2)	24	35	61	31	0	0
12	**1c**	iPr$_2$NEt (1.2)	24	18	>99	<1	0	0
13	**1c**	DBU (1.2)	1	97	97	3	0	0

[a] **1**: 60 μmol, [**1**]/[**6**] = 1/1.2, CDCl$_3$: 0.70 mL, 25 °C. A base was added after mixing **1** and **6**. [b] Equimolar to **1**. [c] Determined by ^{1}H NMR spectra. [d] **1b** and DABCO were mixed before adding **6**.

while a stronger base, DBU, yielded **7b** as the main product (entry 7). The side reactions are not desirable for polycondensation as they lead to a low degree of polymerization. Thus, **1c**, which has a phenyl group instead of methyl group at the allylic substituent, was prepared as a substrate free from the possibility of an E2 reaction.[24] As expected, the selective formation of **8c** was achieved with DABCO (entry 10, Fig. S6†). Thus, the combination of **1c** and DABCO seemed suitable for path B in Scheme 1B. Notably, bases with low nucleophilicity, such as iPr$_2$NEt (entry 12) and DBU (entry 13), were effective in preparing **7c**. Since iPrNEt$_2$ resulted in decreased conversion, a combination of **1c** and DBU seemed suitable for the preparation of **7c** and path A in Scheme 1B.

The experiments suggested the following reaction mechanism. A poor nucleophilic base, *e.g.* DBU, led to the deprotonation of **6** and the subsequent conjugate substitution reaction to yield **7c**. In contrast, a nucleophilic base, such as DABCO, preferred the conjugate substitution to **1c** than the deprotonation of **6** (Scheme 2C). Then, the *endo*-olefin intermediate, **11c** was formed. Since the product **8c** involved an S_N1' mechanism, *i.e.*, the elimination–substitution mechanism, was considered reasonable rather than S_N1 and S_N2 reaction[25] toward **7c**. In this context, the phenyl substituent might have a decisive effect on promoting the formation of **8c**, as the resonance effect stabilizes the intermediate **12c**.

Polymerization

Since DBU was expected to yield the intermediate **3c** selectively and quantitatively (Scheme 1B), the polycondensations of **1c** and **2** through path A were conducted in the presence of DBU (Table 2, entries 1–3). Polymerization conditions were referred from our previous papers[22] to compare polymerization behaviors with **4a** ($M_n = 10\,700$ and $Đ = 1.89$). However, lower molecular weight polymers were obtained (Table 2, entry 1, $M_n = 5600$ and $Đ = 2.10$). The polymerization was further monitored by size-exclusion chromatograms (SECs, Fig. S9†). The molecular weight increased after 7 h but decreased after 24 h, suggesting MCS by E1cB reaction after the propagating reaction. Therefore, the reaction system seemed to have reached equilibrium. The addition of PBu$_3$ to promote the conjugate addition (propagating reaction) resulted in a slight increase in molecular weight (entries 4 and 5, Fig. S10†).

Next, polymerizations through path B were investigated using DABCO and PBu$_3$ in CHCl$_3$ (Table 3, entry 1). However,

Table 3 Polycondensation of **1c** and **2** using DABCO and catalysts

Entry[a]	Catalyst	Solvent	Temp. [°C]	Yield [%]	M_n[b]	$Đ$[b]
1	PBu$_3$	CHCl$_3$	25	10	1000	2.25
2	PBu$_3$	CH$_3$CN	25	27	1600	2.09
3	PBu$_3$	CH$_3$CN	50	66	1100	2.02
4	Et$_3$N[c]	CH$_3$CN	25	51	1900	1.78
5	iPr$_2$NEt[c]	CH$_3$CN	25	49	1800	2.31
6	DBU[c]	CH$_3$CN	25	83	5400	2.16
7[d]	DBU + PBu$_3$	CH$_3$CN	25	29	5600	2.05
8[e]	DBU/PBu$_3$	CH$_3$CN	25	57	13 000	1.63

[a] **1c**: 0.750 mmol, [**1c**]/[**2**]/[base]/[catalyst] = 1/1.0/1.2/0.2. Solvent: 0.75 mL. [b] Determined by SEC (THF, 40 °C, polystyrene standards). [c] **1c**: 0.500 mmol, [**1c**]/[**2**]/[base]/[catalyst] = 1/1.0/1.2/0.2. Solvent: 0.50 mL. Catalysts were added after 1 h and the reaction was conducted for more than 22 h. [d] **1c**: 0.500 mmol, [**1c**]/[**2**]/[base]/[catalyst] = 1/1.0/1.2/0.2. Solvent: 0.50 mL DBU and PBu$_3$ were added after 1 h, at the same time, and the reaction was conducted for more than 22 h. [e] **1c**: 0.500 mmol, [**1c**]/[**2**]/[base]/[catalyst] = 1/1.0/1.2/0.2. Solvent: 0.50 mL DBU and PBu$_3$ were added after 1 h and 2 h, respectively, and the reaction was conducted for more than 22 h.

the resulting product was a polymer with a low degree of polymerization ($M_n = 1000$ and $Đ = 2.25$). Similar results were obtained in CH$_3$CN (entries 2 and 3). To investigate the reason of unsuccessful polycondensation, the reaction was monitored in CD$_3$CN by ^{1}H NMR spectra (Fig. S11†). After 1 h, **5c** was observed as the main product, indicating reaction proceeding through path B as expected. However, signal X assigned to the *endo*-olefin proton was observed around 7.7 ppm, which became more pronounced after 16 h, suggesting an unexpected reaction that inhibited further propagation. A possible mechanism of the side reaction is described in Scheme 3. The conjugate addition proceeds through the addition of PBu$_3$ to an acrylate skeleton to form enolate intermediate **3-I**.[21] The subsequent proton transfer forms thiolate anion **3-II**, and the conjugate addition follows. Herein, the elimination from the phosphonium end of **3-III** to the chain end **3-IV** is possible. A basic catalyst, such as Et$_3$N, that directly deprotonates thiols was also effective in promoting conjugate substitution,[25] and the weak base was expected to decrease the side reaction. Thus, Et$_3$N (entry 4) and iPr$_2$NEt (entry 5) were analysed but found ineffective in increasing the molecular weight, probably due to the low activity. A stronger base, DBU, was more effective (entry 6, $M_n = 5400$, and $Đ = 2.16$), although the molecular weight was still lower than polymers obtained in entry 5 in Table 2. Stronger bases than DBU were expected to be ineffective in increasing the

Table 2 Polycondensation of **1c** and **2** using DBU and PBu$_3$

Entry[a]	Base (equimol.)	Solvent	Temp. [°C]	Time [h]	Yield [%]	M_n[b]	$Đ$[b]
1	1.2	CHCl$_3$	25	24	>99	5600	2.10
2	1.2	CH$_3$CN	25	24	>99	4900	2.32
3	1.2	CH$_3$CN	50	24	>99	4700	1.91
4	1.2	CH$_3$CN	25	24 + 5[c]	37	6600	1.60
5	2.2	CH$_3$CN	25	24 + 5[c]	28	7300	1.74

[a] **1c**: 0.750 mmol, [**1c**]/[**2**]/[base]/[catalyst] = 1/1.0/1.2/0.2. Base: DBU, catalyst: PBu$_3$, solvent: 0.75 mL. [b] Determined by SEC (THF, 40 °C, polystyrene standards). [c] Polycondensation for 24 h with DBU, and then, PBu$_3$ was added.
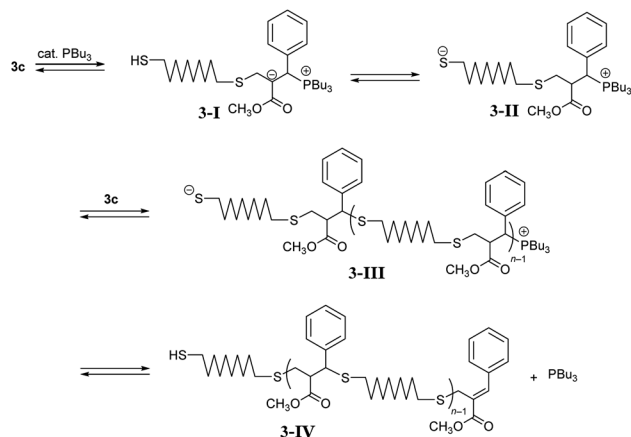
Scheme 3 A proposed side reaction in the polycondensation of **3c** catalyzed by PBu₃.

molecular weight because they promoted to MCS by E1cB reaction. So in the place of such stronger bases, PBu₃, a catalyst which promote the Michael addition, was used with DBU to enhance the propagation. However, the polymerization, initiated with DABCO and promoted by adding DBU and PBu₃ simultaneously, resulted in a similar molecular weight (entry 7). In entry 8, the reaction of **1c** and **2**, initiated with DABCO, was monitored by SEC (Fig. S12†). After 1 h, DBU was added to promote conjugate addition. As a result, M_n increased from 510 to 7100 after a further 1 h. Then, PBu₃ was added and the reaction was allowed to proceed for 22 h at which point the M_n

had increased to 13 000. Thus, the addition of PBu₃ at the early stage of reaction was ineffective because of the side reaction of elimination from the phosphonium intermediate **3-III**. However, the addition of PBu₃ after the almost complete consumption of the acrylate chain end promoted further propagation. In this stage, the elimination from the chain end to prevent further propagation was not a fatal problem.

Main-chain scission

The polythioether **4c** obtained in Table 3 (entry 6) was treated with DBU (1.2 equimolar to the repeating unit) in various solvents for 17 h (Fig. 1A). It was noted that the isolated **4c** used in the MCS experiments were not completely soluble in these solvents even though the polymerization reactions in CH₃CN reported above proceeded in a homogeneous system. As the polymer was not completely dissolved in CH₃CN and DMSO, the MCS in these solvents resulted in incomplete degradation (Fig. 1B). On the other hand, the reaction in DMF proceeded in a homogeneous system, leading to efficient MCS to small molecules. Fig. 1C shows the ¹H NMR spectra before and after the reaction. The signals k–m assigned to the main-chain structure were scarcely observed after the reaction, while the signals x–z specific to the chain-end structure were observed at a high intensity. These changes suggest the MCS by E1cB reaction. In this reaction, not only the change from *exo*-olefin to *endo*-olefin but also the extension of a conjugated system to cover the cinnamate-like moieties is the driving forces to shift the equilibrium from polymerization to MCS. Furthermore, the amount of effective DBU in the polymerization system should
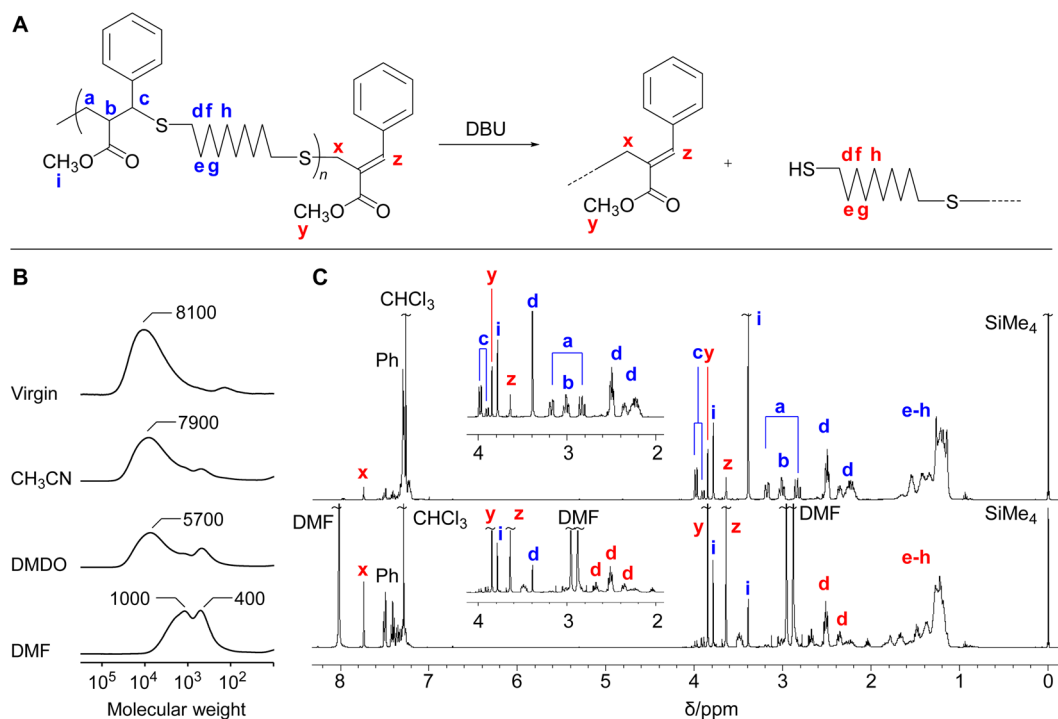

Fig. 1 (A) MCS of **4c** by E1cB reaction. (B) SECs before and after MCS in various solvents. The labels associated with peaks indicate the peak-top molecular weight (M_p). (C) ¹H NMR spectra of **4c** (entry 6) and after MCS in DMF.

be lower than that of MCS experiment, even if equal amount of DBU was used; in polymerization system, the acetic acid was formed as a byproduct in the conjugate substitution reaction, which played to deactivate the DBU. In addition, PBu₃ contributed equilibrium shift to the propagation side. In other words, the MCS reaction of the obtained polymers, employed using higher effective concentration of DBU and in the absence of PBu3, resulted in effective degradation.

Conclusions

In short, the designed polythioether, **4c**, underwent efficient MCS by E1cB reaction. The incorporation of a phenyl substituent was significant both in the polymerization and MCS: in polymerization, the phenyl substituent led to the formation of an inactive *endo*-olefin chain-end, while it was a key to achieving efficient MCS. In conventional polymer chemistry, the modification of the backbone structure has been the typical strategy to realize MCS, and the introduction of a 'weak' or 'dynamic' covalent bond is always in discussion.[26,27] In contrast, the above results cast a spotlight on the design of the side group. In this study, polymerization (path A) and MCS were based on the same equilibrium system. However, the polymerization through a different route (path B) enabled a high molecular weight ($M_n >$ 10^4). Therefore, the molecular weight increased compared to a complete equilibrium system. From the above points discussed, our conclusion is that 'side-group design' and 'backbone design' are important for both polymerization and MCS.

Author contributions

K. H. proposed the plan and employed experiments except those for Fig. S10–S12,† which were conducted by A. T., R. K. repeated the model experiments and proposed the reaction mechanism by S_N1' reaction. The draft of this article was written by R. K. and Y. K. Y. K. supervised the research project.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

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