Fast and Selective Main-Chain Scission of Vinyl Polymers using the Domino Reaction in the Alternating Sequence for Transesterification

Yasuhiro Kohsaka[1,2*], Kaho Toyama[2], Moe Kawauchi[2]

[1] Research Initiative for Supra-Materials, Interdisciplinary Cluster for Cutting Edge Research, Shinshu University, 4-17-1 Wakasato, Nagano, Nagano 380-8553, Japan.
[2] Faculty of Textile Science and Technology, Shinshu University, 3-15-1 Tokida, Ueda, Nagano 386-8567, Japan.

ABSTRACT: This communication reports on vinyl polymers capable of selective and fast main-chain scission (MCS). The trick is the domino reaction in an alternating sequence of methyl 2-(trimethylsiloxymethyl)acrylate and 5,6-benzo-2-methylene-1,3-dioxepane, a cyclic ketene acetal for radical ring-opening polymerization. Removal of the trimethylsilyl group using $Bu_4N^+ \cdot F^-$ readily led to MCS via irreversible transesterification of the ester backbone, affording a five-membered lactone fragment. The molar mass decreased drastically within 5 min, and no side reactions were observed. Control experiments suggest that the formation of a five-membered ring via a domino reaction is critical for fast and selective MCS. The terpolymers with methyl methacrylate and styrene also exhibited a large decrease in molar mass within 5 min. In addition, MCS was also observed for the heterogeneous reaction system in acidic aqueous media; treatment of the binary copolymer in a 50 wt% acetic acid solution resulted in a significant decrease in molar mass after 30 min. These results suggest efficient construction of degradable sites using a binary monomer system corresponding to the pendant trigger and ester backbone. Because this molecular design, which uses a combination of simple monomers, is applicable to terpolymers containing other vinyl monomers, it can provide various degradable vinyl polymers.
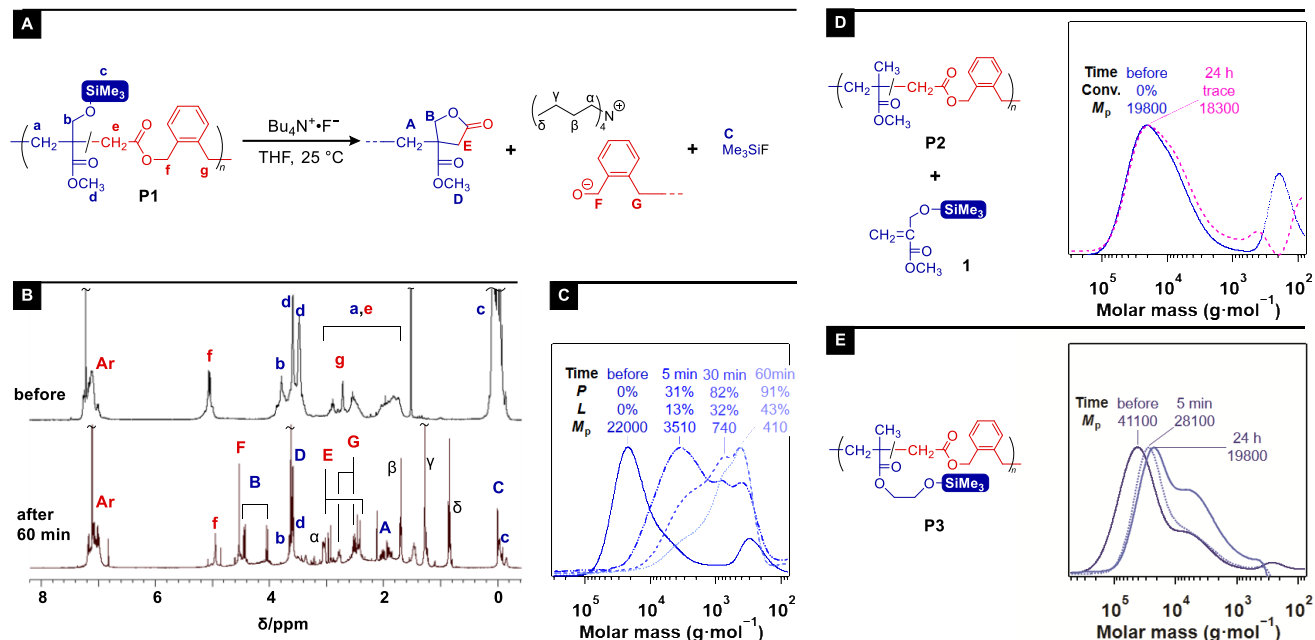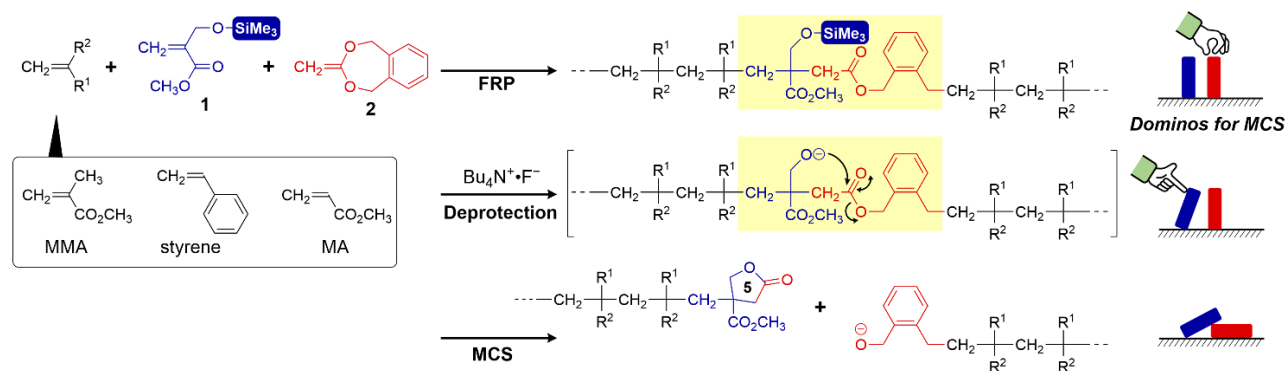
Domino reactions, also known as cascade and tandem reactions, are sequential reactions in which the moieties formed in the first reaction induce further intramolecular reactions.[1,2] In addition to the advantages of atom economy and eco-friendliness, domino reactions provide quantitative and regioselective modifications via intramolecular reactions. Therefore, domino reactions have also been applied to polymer synthesis.[3–12] We envisioned that a similar scheme would be effective for polymer degradation, particularly for fast and selective main-chain scission (MCS).

Because MCS significantly reduces the molar mass in a small number of reactions,[13–16] it causes drastic changes in polymer materials, such as the size, topology, mobility, and entanglement of polymer chains at the microscopic level, [17] as well as solubility,[18] solution viscosity,[19] and self-assembly[20–23] at the macroscopic level. Owing to this feature, MCS has been applied to photoresists,[18,24,25] dismountable adhesives,[26] degradable gels,[27] and drug delivery systems.[28] Vinyl polymers are attractive for applications in material engineering because of their facile synthesis by free radical polymerization (FRP) and property tunability by copolymerization. However, the MCS of vinyl polymers requires harsh conditions because the carbon backbones are thermodynamically stable.[29–33] Therefore, the incorporation of ester bonds via radical ring-opening polymerization (rROP),[34] typically using cyclic ketene acetals (CKAs),[35–39] has gained attention. Nevertheless, this strategy is not always optimal, particularly for polymers bearing ester pendants such as poly(meth)acrylates. The MCS of such polymers requires excess reagents[37,39] and long reaction times,[36,37] because the ester bonds in both the main chains and pendants are hydrolyzed. For application in material engineering, a selective MCS that rapidly reduces molar mass using weak stimuli is desirable.

To address these demands, we noticed a domino reaction consisting of pendant modification and subsequent MCS. Such reactions have already been reported for some polyesters that undergo MCS via the amination of pendant groups.[40,41] To apply this concept to vinyl polymers, copolymerization of **1**[42] and CKA **2**[43] was proposed (**Scheme 1**). **1** and **2** were expected to form statistically alternating sequences,[37,39] as predicted by the classical Alfrey–Price *Q-e* scheme.[38,44] In the alternating sequence, the removal of silyl protection readily led to MCS via transesterification, affording a five-membered lactone. Importantly, because five-membered lactones have few ring strains,[45] MCS is expected to become irreversible with increasing entropy. Note that the protection of the hydroxy group with a trimethylsilyl (TMS) group was necessary; otherwise, electrophilic addition of the hydroxyl group of **1** to **2** occurred before polymerization (**Figure S1**).

The concept was first examined using **P1**, a binary copolymer of **1** and **2** (**Table 1**). **P1** was treated with $Bu_4N^+F^-$ in tetrahydrofuran (THF) at 0 °C for 30 min (**Figure 1A**). In the ^{1}H NMR spectrum after 60 min (**Figure 1B**), signals A, B, and E indicate the five-membered lactone fragment, whereas signal F indicates the benzyloxy fragment. The

Scheme 1. Design of degradable vinyl polymers via domino reaction.

Figure 1. MCS of **P1** using $Bu_4N^+\cdot F^-$ in THF (**A**) and the changes in ^{1}H NMR spectra (**B**: 400 MHz, CDCl$_3$, 25 °C) and SECs (**C**: THF, 40 °C, PMMA standards). The SEC changes during the reaction of **P2** and **1** with $Bu_4N^+\cdot F$ (**D**) and during that of **P3** and $Bu_4N^+\cdot F^-$ (**E**).

Table 1. Copolymers for degradation tests.

Code	M1	M2	M3	Composition[a] (%) M1	M2	M3	M_n[b] (g·mol^{-1})	Đ[b]	T_g[c] (°C)	T_{d5}[c] (°C)
P1	**1**	**2**	–	73	27	–	18900	1.59	34	328
P2	MMA	**2**	–	66	34	–	11000	2.00	35	307
P3	**3**	**2**	–	74	26	–	16100	2.72	−5	312
P4	**1**	**2**	MMA	57	18	25	31100	1.54	48	307
P5	**1**	**2**	MMA	41	28	36	20600	1.90	40	308
P6	**1**	**2**	MMA	28	25	47	18700	1.93	50	320
P7	**1**	**2**	MMA	10	12	78	13500	2.83	50	242
P8	**1**	**2**	styrene	45	9	46	15200	1.76	58	302
P9	**1**	**2**	MA	7	8	85	19100	2.32	31	332

[a]Determined by ^{1}H NMR spectroscopy (**Figure S6–11**). [b]Determined by SEC (THF, 40 °C, PMMA standard). [c]Determined using TG-DTA and DSC curves (**Figure S12–27**).

peak-top molar mass (M_p) observed in the size-exclusion chromatograms (SECs; **Figure 1C**) shifted from 22000 to 3510 g·mol^{-1} after 5 min and outside of the calibration curve (< 830 g mol^{-1}) after 30 min, suggesting the progress of the MCS. The extension of the reaction at 25 °C resulted in a shift of M_p to an even lower molar mass region after 30 min, that is, 1 h after the start of the reaction, but no changes were observed thereafter. The degree of deprotection (P) at each reaction time was estimated from the intensity of ^{1}H NMR signals c and C, while those of lactonization (L) were estimated from the intensity of signals f and B. P and L after 5 min were 31% and 13%, respectively, and the expected peak-top molar mass (M_e) was 3470 g·mol^{-1}, which is in agreement with the M_p of 3510 g·mol^{-1}. Therefore, we concluded that MCS is induced by a domino reaction triggered by the removal of the TMS group.

To evaluate the importance of five-membered lactone formation, **P2**, a copolymer of methyl methacrylate (MMA) and **2**, was treated with $Bu_4N^+\cdot F^-$ in the presence of **1** as an external alkoxide source. No significant changes were observed in the SECs (**Figure 1D**) or ^{1}H NMR spectra after 24 h (**Figure S28**), suggesting the absence of MCS. A similar experiment was conducted using **P3**, a copolymer of 2-

trimethylsiloxyethtyl methacrylate (**3**) and **2**. If MCS by the domino reaction occurs for **P3**, the fragment should be an eight-membered lactone (**Figure S29A**). M_p decreased from 41100 to 28100 g·mol^{-1} (**Figure 1E**), whereas that expected for complete deprotection was 29600 g·mol^{-1}. Therefore, the decrease in M_p was mainly attributed to deprotection. The shoulder of the SEC in the lower molar mass region became larger after 24 h and precipitation was observed. Apparently, these changes were not caused by MCS. A possible scenario is loop formation by intramolecular transesterification between ester pendants (**Figure S29A**). In fact, ^{1}H NMR signal Q, assignable to ethylene glycol, a byproduct of transesterification, was observed (**Figure S29B**). These experiments using **P2** and **P3** suggest that the formation of a five-membered lactone is significant for efficient and fast MCS.

P1, prepared from an equimolar mixture of **1** and **2**, contained more **1** units (**Table S1**), and not all **1** units functioned as triggers for MCS. To reduce such 'useless investment,' terpolymer **P4**, containing MMA at 25 mol%, was prepared. Treatment of **P4** with Bu$_4$N$^+$·F$^-$ resulted in lactone formation (**Figure 2A**), as indicated by the ^{1}H NMR spectrum (**Figure 2B**), whereas M_p decreased from 39300 to 4890 g·mol^{-1} after 5 min and to 1370 g·mol^{-1} after 7 h (**Figure 2C**). M_p agreed with M_e (**Table S2**), suggesting MCS via a domino reaction. Therefore, molecular design using **1** and

2 was also effective for the terpolymer. **Figure 2D** shows the relationship between MMA content and M_p reduction in various terpolymers. Notably, the decrease in M_p after 5 min was not significantly different, regardless of the MMA content. In other words, the rate of MCS at the early stage was not affected by the content of degradable sites. Terpolymers **P8** and **P9**, containing styrene and methyl acrylate (MA) units, respectively, were also examined. **P8** exhibited degradability (**Figure S31**), whereas the SEC of **P9** was barely changed (**Figure S32**). M_p after 7 h was 24600 g·mol^{-1}, which is close to M_e in the absence of MCS (30300 g·mol^{-1}). The poor degradability of **P9** was attributed to the low content of the alternating sequence of **1**–**2** due to the low copolymerizability of MA.

Although the reaction in THF led to efficient and fast MCS, the reaction in a homogeneous system is impractical in material engineering. Therefore, MCS in aqueous media was investigated. **P7**, a terpolymer containing 78 mol% MMA, was suspended in 70 wt% Bu$_4$N$^+$·F$^-$ aq. at 25 °C, although no changes were observed in SEC (**Figure S33**). A similar experiment at 65 °C resulted in a decrease in M_p from 29900 to 2470 g·mol^{-1} (**Figure S34**), whereas the ^{1}H NMR spectrum did not clearly show lactone signals (**Figure S35**). To observe the details, the binary copolymer **P1** was treated under similar conditions. Although the SEC after the reaction exhibited no polymer peaks, no polymer fragments were observed in the ^{1}H NMR spectrum (**Figure S36**). This suggests that the products were water-soluble and could not be extracted using chloroform. Thus, side reactions, such as the hydrolysis of ester pendants, may have occurred because of the basic conditions.

To achieve selective MCS, other stimuli were investigated. **P1** was suspended in 50 wt% acetic acid aq at 25 °C (**Figure 3A, B**). M_p decreased from 24000 to 3510 g·mol^{-1} after 3 h, whereas SEC exhibited a shoulder in the higher molar mass region (**Figure S37a**). SEC became unimodal after 24 h. The ^{1}H NMR spectrum (**Figure 3C-c**) was similar to that obtained after degradation by Bu$_4$N$^+$·F$^-$ in THF (**Figure 3C-b**), suggesting lactone formation. Therefore, the domino reaction was effective even under heterogeneous conditions. Note that a control experiment using **P2**, a copolymer of MMA and **2**, did not show any changes in the SEC (**Figure S38**). Next, the acceleration of the MCS by heating was investigated. **Figure 3D** shows the change in M_p over time during the reaction at each temperature. The reaction became much faster above 60 °C, which is sufficiently higher than the glass transition point (T_g = 34 °C). MCS became faster with increasing acetic acid concentration (**Figure 3E**). To understand this phenomenon, similar experiments were conducted using different aqueous solutions. The oxalic acid buffer solution (pH 1.6) resulted in a decrease in M_p (**Figure S40b**), although the reaction was slower than that using 30 wt% acetic acid (pH 1.4; **Figure s40a**). The ^{1}H NMR spectrum (**Figure S41**) also suggests MCS via a domino reaction. In contrast, diluted sulfonic acid (pH 1.4) did not induce MCS even after 24 h (**Figure S42, S43A**), suggesting that pH was not the key to accelerating MCS. However, the dilution of this sulfonic acid solution with an equal volume of THF, a good solvent for **P2**, resulted in a decrease in M_p (**Figure S42B**), while the ^{1}H NMR spectrum suggested the deprotection and formation of the lactone (**Figure S44**).
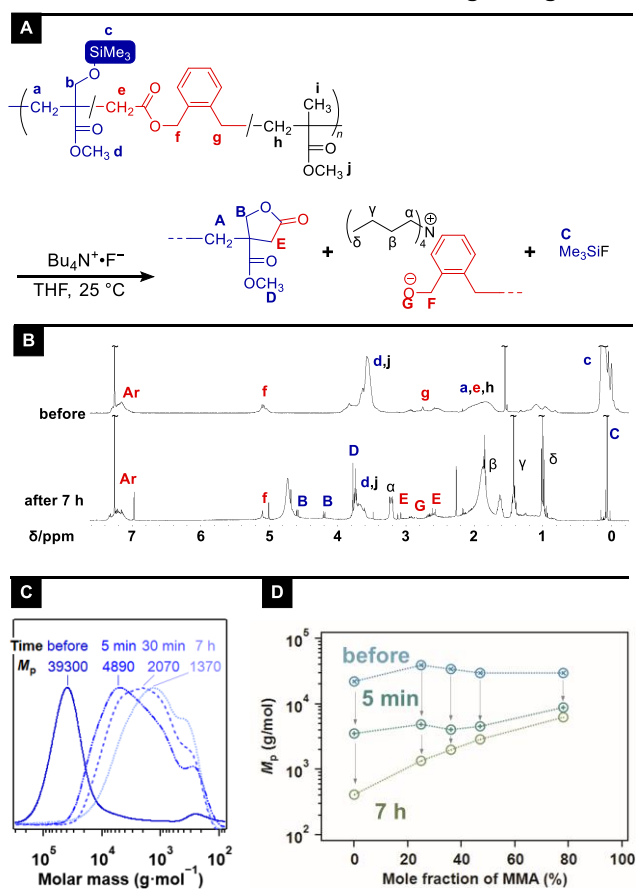
Figure 2. MCS of the terpolymers using Bu$_4$N$^+$·F$^-$ in THF (**A**). Changes in ^{1}H NMR spectra (**B**: 400 MHz, CDCl$_3$, 25 °C) and SECs (**C**: THF, 40 °C, PMMA standards) during the reaction of **P4**. The relationship between the mole fraction of MMA and M_p during MCS (**D**); the raw SECs are shown in **Figure S30**.
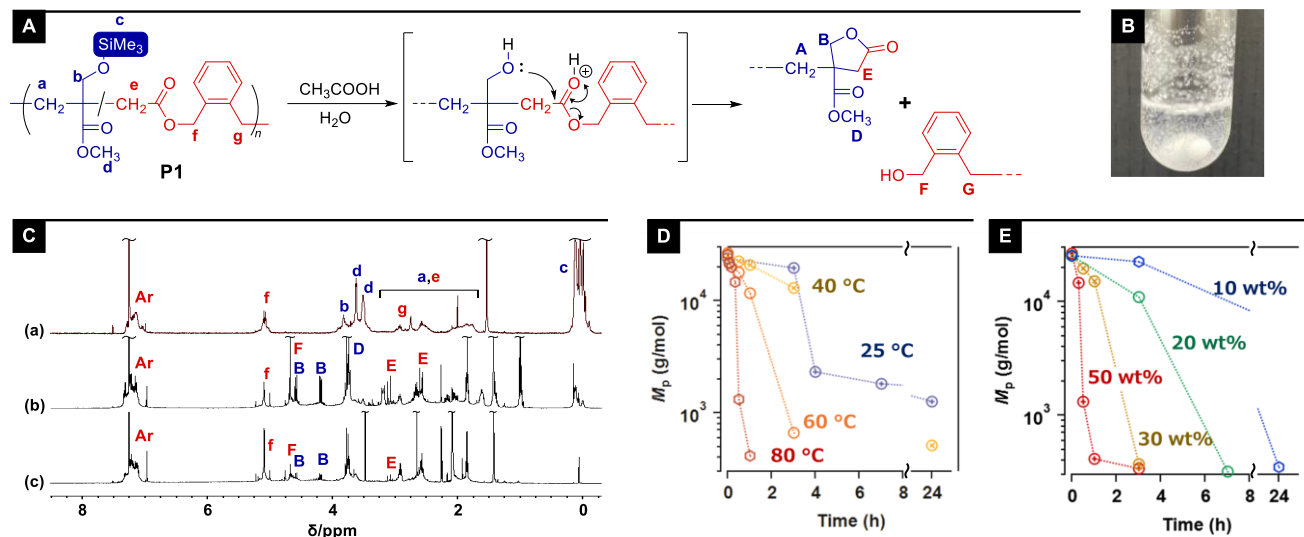
Figure 3. A: MCS of **P1** in 50 wt% aq. **B**: Photograph of the reaction mixture at the initiation. **C**: ^{1}H NMR spectra (400 MHz, CDCl$_3$, 25 °C) of **P1** (a), reaction products of **P1** and Bu$_4$N$^+$·F$^-$ in THF (b), and reaction products of **P1** and acetic acid in water (c). **D**: Decrease in M_p over time during reactions using 50 wt% of acetic acid aq. at various temperatures. The raw SECs are shown in **Figure S37**. **D**: Decrease in M_p over time during reactions using various concentrations of aqueous acetic acid at 80 °C. The raw SECs are shown in **Figure S39**.

These results suggest that the affinity of the aqueous solution for the polymer is an important factor in MCS. This tendency is in agreement with our recent report on MCS of unsaturated polyesters in aqueous suspensions.[46]

In conclusion, the domino reaction between alternating sequences of **1** and **2** was effective in inducing fast and selective MCS in both homogeneous and heterogeneous systems. This molecular design is applicable to terpolymers that contain MMA and styrene. For MCS in aqueous suspensions, an increase in temperature above T_g significantly increases the reaction rate. However, MCS was also observed at temperatures lower than T_g. Consequently, the strategy in which the trigger reaction is initiated at pendant groups with high mobility to induce the subsequent local intramolecular reaction enables the MCS in polymers in the glass state. We believe that the strategy proposed in this study will contribute to material engineering by providing a variety of degradable vinyl polymers with tunable properties through copolymerization.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures, ^{1}H and ^{13}C NMR spectra, TG–DTA and DSC curves, SECs. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

Yasuhiro Kohsaka - Research Initiative for Supra-Materials (RISM), Interdisciplinary Cluster for Cutting Edge Research (ICCER), Shinshu University, 4-17-1 Wakasato, Nagano, Nagano 380-8553, Japan; Faculty of Textile Science and Technology, Shinshu University, 3-15-1 Tokida, Ueda, Nagano 386-8567, Japan; https://orcid.org/0000-0001-9833-0929; Email: kohsaka@shinshu-u.ac.jp

Authors

Kaho Toyama - Faculty of Textile Science and Technology, Shinshu University, 3-15-1 Tokida, Ueda, Nagano 386-8567, Japan

Moe Kawauchi - Faculty of Textile Science and Technology, Shinshu University, 3-15-1 Tokida, Ueda, Nagano 386-8567, Japan

Funding Sources

ACKNOWLEDGMENT

ABBREVIATIONS

MCS, main-chain scission; SEC, size exclusion chromatography; TG–DTA, thermogravimetry–differential thermal analysis; DSC, differential scanning calorimetry; PMMA, poly(methyl methacrylate); MMA, methyl methacrylate; MA, methyl acrylate; THF, tetrahydrofuran

REFERENCES

(1)   Parsons, P. J.; Penkett, C. S.; Shell, A. J. Tandem Reactions in Organic Synthesis: Novel Strategies for Natural Product Elaboration and the Development of New Synthetic Methodology. *Chem. Rev.* **1996**, *96* (1), 195–206.

(2)   Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. Tandem Reactions, Cascade Sequences, and Biomimetic Strategies in Total Synthesis. *Chem. Commun.* **2003**, 551–564.

(3)   Hu, R.; Li, W.; Tang, B. Z. Recent Advances in Alkyne-Based Multicomponent Polymerizations. *Macromol. Chem. Phys.* **2016**, *217* (2), 213–224.

(4)   Matsumoto, S.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. Tandem Reaction of Cationic Copolymerization and Concertedly Induced Hetero-Diels-Alder Reaction Preparing Sequence-Regulated Polymers. *J. Am. Chem. Soc.* **2017**, *139* (23), 7713–7716.

(5) Naito, T.; Kanazawa, A.; Aoshima, S. Tandem Polymerization Consisting of Cyclotrimerization and the Tishchenko Reaction: Synthesis of Acid- and Alkali-Degradable Polymers with Cyclic Acetal and Ester Structures in the Main Chain. *Polym. Chem.* **2022**, *13* (40), 5757–5768.

(6) Peterson, G. I.; Choi, T.-L. Cascade Polymerizations: Recent Developments in the Formation of Polymer Repeat Units by Cascade Reactions. *Chem. Sci.* **2020**, *11* (19), 4843–4854.

(7) Yuan, J.; Wang, W.; Zhou, Z.; Niu, J. Cascade Reactions in Chain-Growth Polymerization. *Macromolecules* **2020**, *53* (14), 5655–5673.

(8) Zhu, N.; Chiou, M.-F.; Xiong, H.; Su, M.; Su, M.; Li, Y.; Wan, W.-M.; Bao, H. The Introduction of the Radical Cascade Reaction into Polymer Chemistry: A One-Step Strategy for Synchronized Polymerization and Modification. *iScience* **2020**, *23* (3), 100902.

(9) Kakuchi, R. The Dawn of Polymer Chemistry Based on Multicomponent Reactions. *Polym. J.* **2019**, *51* (10), 945–953.

(10) Hagiwara, K.; Kohsaka, Y. Divergence of Polycondensation by a Tandem Reaction Based on Sequential Conjugate Substitutions. *Polym. Chem.* **2020**, *11* (32), 5128–5132.

(11) Kohsaka, Y.; Hagiwara, K.; Ito, K. Polymerization of Alpha-(Halomethyl)Acrylates through Sequential Nucleophilic Attack of Dithiols Using a Combination of Addition-Elimination and Click Reactions. *Polym. Chem.* **2017**, *8* (6), 976–979.

(12) Kawatani, R.; Hagiwara, K.; Tanaka, A.; Kohsaka, Y. Polythioethers Bearing Side Groups for Efficient Degradation by E1cB Reaction: Reaction Design for Polymerization and Main-Chain Scission. *RSC Adv.* **2023**, *13* (30), 20782–20786.

(13) Yoon, J.-S.; Chin, I.-J.; Kim, M.-N.; Kim, C. Degradation of Microbial Polyesters: A Theoretical Prediction of Molecular Weight and Polydispersity. *Macromolecules* **1996**, *29* (9), 3303‑3307.

(14) Basedow, A. M.; Ebert, K. H.; Ederer, H. J. Kinetic Studies on the Acid Hydrolysis of Dextran. *Macromolecules* **1978**, *11* (4), 774–781.

(15) Ziff, R. M.; McGrady, E. D. Kinetics of Polymer Degradation. *Macromolecules* **1986**, *19* (10), 2513–2519.

(16) Sato, T.; Nalepa, D. E. Shear Degradation of Cellulose Derivatives. *J. Appl. Polym. Sci.* **1978**, *22* (3), 865–867.

(17) Messmer, D.; Bertran, O.; Kissner, R.; Alemán, C.; Schlüter, A. D. Main-Chain Scission of Individual Macromolecules Induced by Solvent Swelling. *Chem. Sci.* **2019**, *10* (24), 6125–6139.

(18) Rathore, A.; Pollentier, I.; Singh, H.; Fallica, R.; De Simone, D.; De Gendt, S. Effect of Molecular Weight on the EUV-Printability of Main Chain Scission Type Polymers. *J. Mater. Chem.* **2020**, *8* (17), 5958‑5966.

(19) Tayal, A.; Khan, S. A. Degradation of a Water-Soluble Polymer: Molecular Weight Changes and Chain Scission Characteristics. *Macromolecules* **2000**, *33* (26), 9488–9493.

(20) Men, Y.; Brevé, T. G.; Liu, H.; Denkova, A. G.; Eelkema, R. Photo Cleavable Thioacetal Block Copolymers for Controlled Release. *Polym. Chem.* **2021**, *12* (25), 3612–3618.

(21) Wang, L.; Zhu, K.; Cao, W.; Sun, C.; Lu, C.; Xu, H. ROS-Triggered Degradation of Selenide-Containing Polymers Based on Selenoxide Elimination. *Polym. Chem.* **2019**, *10* (16), 2039–2046.

(22) Pasparakis, G.; Manouras, T.; Vamvakaki, M.; Argitis, P. Harnessing Photochemical Internalization with Dual Degradable Nanoparticles for Combinatorial Photo–Chemotherapy. *Nat. Commun.* **2014**, *5* (1), 3623.

(23) Muratov, A.; Baulin, V. A. Degradation versus Self-Assembly of Block Co-Polymer Micelles. *Langmuir* **2012**, *28* (6), 3071–3076.

(24) Konda, A.; Yamamoto, H.; Yoshitake, S.; Kozawa, T. Dependence of Dissolution Kinetics of Main-Chain Scission Type Resists on Molecular Weight. *J. Photopolym. Sci. Technol.* **2022**, *35* (1), 1–7.

(25) Hosaka, Y.; Oyama, T. G.; Oshima, A.; Enomoto, S.; Washio, M.; Tagawa, S. Pulse Radiolysis Study on a Highly Sensitive Chlorinated Resist ZEP520A. *J. Photopolym. Sci. Technol.* **2013**, *26* (6), 745–750.

(26) Sato, E.; Omori, C.; Yuri, M.; Koda, Y.; Horibe, H. Thermal Latent Reductants for Controlled Degradation of Polyperoxides and Their Application to High Performance Dismantlable Adhesives. *ACS Applied Polymer Materials* **2019**, *1* (8), 2140–2148.

(27) Hakuto, N.; Saito, K.; Kirihara, M.; Kotsuchibashi, Y. Preparation of Cross-Linked Poly(Vinyl Alcohol) Films from Copolymers with Benzoxaborole and Carboxylic Acid Groups, and Their Degradability in an Oxidizing Environment. *Polym. Chem.* **2020**, *11* (14), 2469–2474.

(28) Kamaly, N.; Yameen, B.; Wu, J.; Farokhzad, O. C. Degradable Controlled-Release Polymers and Polymeric Nanoparticles: Mechanisms of Controlling Drug Release. *Chem. Rev.* **2016**, *116* (4), 2602–2663.

(29) Young, J. B.; Hughes, R. W.; Tamura, A. M.; Bailey, L. S.; Stewart, K. A.; Sumerlin, B. S. Bulk Depolymerization of Poly(Methyl Methacrylate) via Chain-End Initiation for Catalyst-Free Reversion to Monomer. *Chem* **2023**, *9* (9), 2669–2682.

(30) Lohmann, V.; Jones, G. R.; Truong, N. P.; Anastasaki, A. The Thermodynamics and Kinetics of Depolymerization: What Makes Vinyl Monomer Regeneration Feasible? *Chem. Sci.* **2024**, *15* (3), 832–853.

(31) Chiba, Y.; Kawatani, R.; Kohsaka, Y. Chemically Recyclable Vinyl Polymers by Free Radical Polymerization of Cyclic Styrene Derivatives. *ACS Macro Lett.* **2023**, *12* (12), 1672–1676.

(32) Kazama, A.; Kohsaka, Y. Radical Polymerization of "dehydroaspirin" with the Formation of a Hemiacetal Ester Skeleton: A Hint for Recyclable Vinyl Polymers. *Polym. Chem.* **2019**, *10* (22), 2764–2768.

(33) Kazama, A.; Kohsaka, Y. Diverse Chemically Recyclable Polymers Obtained by Cationic Vinyl and Ring-Opening Polymerizations of the Cyclic Ketene Acetal Ester "Dehydroaspirin." *Polym. Chem.* https://doi.org/10.1039/d2py01181f.

(34) Tardy, A.; Nicolas, J.; Gigmes, D.; Lefay, C.; Guillaneuf, Y. Radical Ring-Opening Polymerization: Scope, Limitations, and Application to (Bio)Degradable Materials. *Chem. Rev.* **2017**, *117* (3), 1319–1406.

(35) Agarwal, S. Chemistry, Chances and Limitations of the Radical Ring-Opening Polymerization of Cyclic Ketene Acetals for the Synthesis of Degradable Polyesters. *Polym. Chem.* **2010**, *1* (7), 953–964.

(36) Folini, J.; Murad, W.; Mehner, F.; Meier, W.; Gaitzsch, J. Updating Radical Ring-Opening Polymerisation of Cyclic Ketene Acetals from Synthesis to Degradation. *Eur. Polym. J.* **2020**, *134*, 109851.

(37) Lai, H.; Ouchi, M. Backbone-Degradable Polymers via Radical Copolymerizations of Pentafluorophenyl Methacrylate with Cyclic Ketene Acetal: Pendant Modification and Efficient Degradation by Alternating-Rich Sequence. *ACS Macro Lett.* **2021**, *10* (10), 1223–1228.

(38) Lena, J.-B.; Van Herk, A. M. Toward Biodegradable Chain-Growth Polymers and Polymer Particles: Re-Evaluation of Reactivity Ratios in Copolymerization of Vinyl Monomers with Cyclic Ketene Acetal Using Nonlinear Regression with Proper Error Analysis. *Ind. Eng. Chem. Res.* **2019**, *58* (46), 20923–20931.

(39) Hill, M. R.; Kubo, T.; Goodrich, S. L.; Figg, C. A.; Sumerlin, B. S. Alternating Radical Ring-Opening Polymerization of Cyclic Ketene Acetals: Access to Tunable and Functional Polyester Copolymers. *Macromolecules* **2018**, *51* (14), 5079–5084.

(40) Mizutani, M.; Palermo, E. F.; Thoma, L. M.; Satoh, K.; Kamigaito, M.; Kuroda, K. Design and Synthesis of Self-Degradable Antibacterial Polymers by Simultaneous Chain- and Step-Growth Radical Copolymerization. *Biomacromolecules* **2012**, *13* (5), 1554–1563.

(41) Lv, A.; Li, Z.-L.; Du, F.-S.; Li, Z.-C. Synthesis, Functionalization, and Controlled Degradation of High Molecular Weight Polyester from Itaconic Acid via ADMET Polymerization. *Macromolecules* **2014**, *47* (22), 7707–7716.

(42) Kohsaka, Y.; Yamamoto, K.; Suzawa, K.; Kitayama, T. Synthesis of Isotactic Poly Alpha-(Hydroxymethyl)Acrylate by

Anionic Polymerization of the Protected Monomer. *Polym. Bull.* **2017**, *74* (5), 1935–1948.

(43)   Bailey, W. J.; Ni, Z.; Wu, S. R. Free Radical Ring-Opening Polymerization of 4,7-Dimethyl-2-Methylene-1,3-Dioxepane and 5,6-Benzo-2-Methylene-1,3-Dioxepane. *Macromolecules* **1982**, *15* (3), 711–714.

(44)   Kress, A. O.; Mathias, L. J.; Cei, G. Copolymers of Styrene and Methyl .Alpha.-(Hydroxymethyl)Acrylate: Reactivity Ratios, Physical Behavior, and Spectral Properties. *Macromolecules* **1989**, *22* (2), 537–546.

(45)   Tang, X. Y.; Hong, M.; Falivene, L.; Caporaso, L.; Cavallo, L.; Chen, E. Y. X. The Quest for Converting Biorenewable Bifunctional Alpha-Methylene-Gamma-Butyrolactone into Degradable and Recyclable Polyester: Controlling Vinyl-Addition/Ring-Opening/Cross-Linking Pathways. *J. Am. Chem. Soc.* **2016**, *138* (43), 14326–14337.

(46)   Noda, T.; Kitagawa, T.; Kohsaka, Y. Degradation of Poly(Conjugated Ester)s Using a Conjugate Substitution Reaction with Various Amines and Amino Acids in Aqueous Media. *Polym. J.* **2024**, *56* (5), 343–351.

Authors are required to submit a graphic entry for the Table of Contents (TOC) that, in conjunction with the manuscript title, should give the reader a representative idea of one of the following: A key structure, reaction, equation, concept, or theorem, etc., that is discussed in the manuscript. Consult the journal's Instructions for Authors for TOC graphic specifications.

Insert Table of Contents artwork here

Domino for Chain Scission

1–9.