Synthesis of Copolymers with Tailored Structure by Living Cationic Polymerization Using Selective Acetal Activation

A Doctoral Thesis

by

Norifumi Yokoyama

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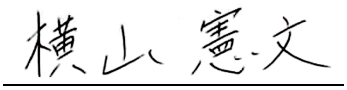


Norifumi Yokoyama
Department of Macromolecular Science
Graduate School of Science
Osaka University

Contents

Chapter 1

General Introduction

1. Background

1.1 Polymers with Special Architecture

Synthetic polymers with specially designed structures, such as block copolymers, graft copolymers, and star-shaped polymers, have attracted much attention in various fields, including electronics,[1] energy,[2,3] and biomedicine,[4,5] because their properties are completely different from those of linear homopolymers. For example, block copolymers with hydrophilic and hydrophobic segments exhibit unique behavior based on the self-assembling properties of each segment, which enables the formation of micelles or reverse-micelles in aqueous or organic media, respectively,[6] and microphase separation in the bulk state.[7,8] In addition, characteristics of branched polymers derived from the branched structure, such as low solution viscosity and unique phase diagram, are distinguishable from those of linear polymers.[9–11] The recent remarkable development of precise polymerization techniques have enabled the synthesis of polymers with such various architectures.[12] However, extremely precise control over polymer structures is needed for attaining sophisticated functions.

Stepwise synthesis using prepolymers, such as peptide synthesis via fragment condensation reactions and dendrimer synthesis via the convergent or divergent method, is a highly effective strategy for the synthesis of polymers with complicated structures. More specifically, the following three types of prepolymers (Figure 1)–macroinitiators,[13] macroterminators,[14–17] and macromonomers[18–24]–are mainly used

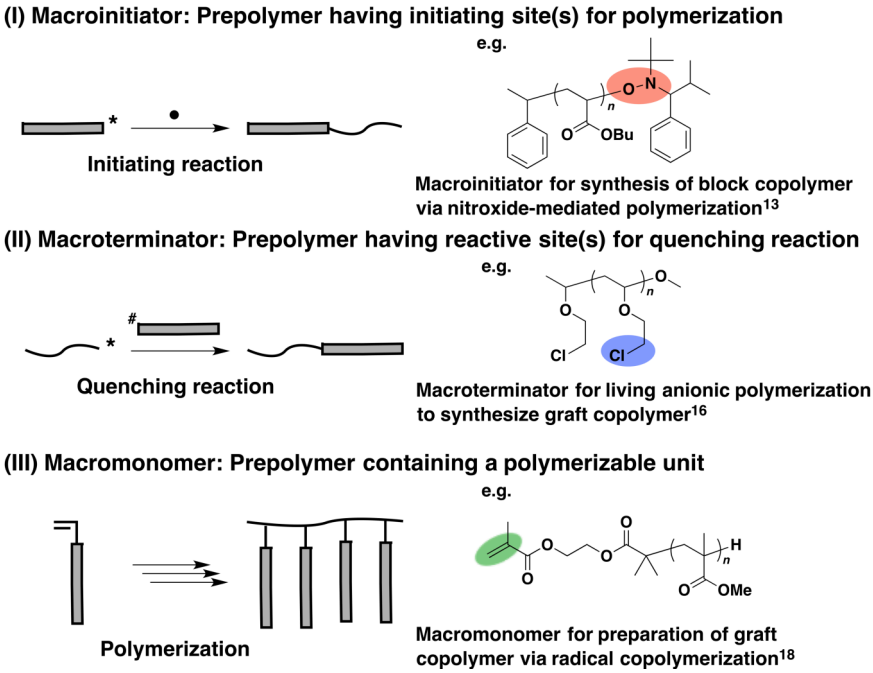
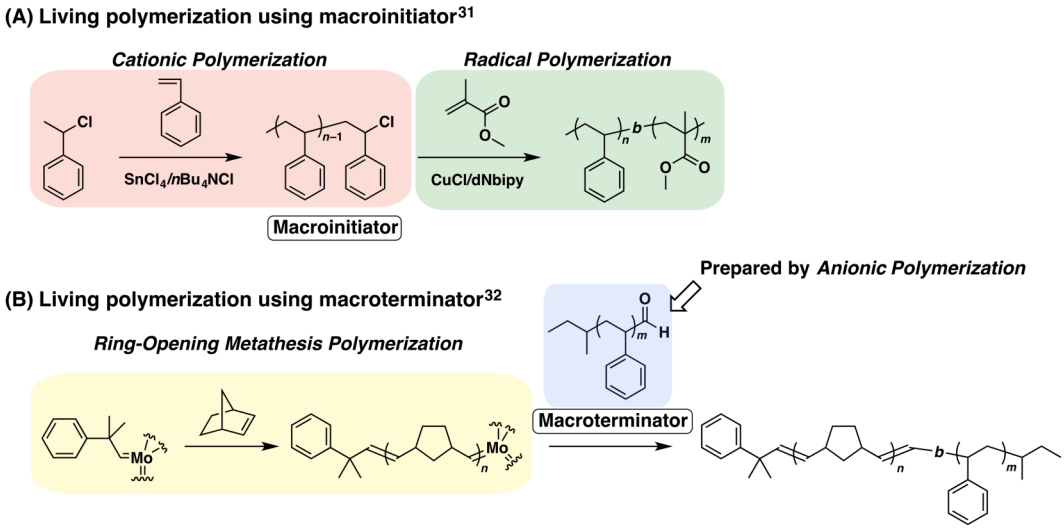


Figure 1. Features of prepolymers.

in stepwise synthesis of various polymers. Although polymer synthesis by means of prepolymers is more time-consuming than one-pot sequential copolymerization reactions due to the need for isolation and purification of prepolymers, a distinct advantage of this method is that each segment of copolymers can be prepared under the most appropriate conditions for the polymerization of each monomer. In particular, various copolymers were obtained from originally incompatible monomers through a combination of different polymerization mechanisms.[25–30] For instance, Coca and Matyjaszewski[31] reported the synthesis of block copolymers using a polystyrene with the terminal carbon–chlorine bond, synthesized by living cationic polymerization, as a macroinitiator for the living radical polymerization of methyl methacrylate [Scheme 1, (A)]. In addition, Register and co-workers[32] obtained block copolymers using a polystyrene with a formyl group at the chain end, which was synthesized via living anionic polymerization, as a macroterminator for ring-opening metathesis polymerization of norbornene [Scheme 1, (B)].

Scheme 1. Synthesis of Block Copolymers Using Prepolymers.



For the precision synthesis of polymers with specifically designed structures, prepolymers and the reactive sites of prepolymers are required to satisfy the following conditions: (1) a prepolymer has a controlled structure; (2) the reactive site has sufficiently high reactivity; (3) the reactive site is kept intact through isolation and purification procedures; and (4) the reactive sites are introduced quantitatively into a prepolymer. Although conditions (2) and (3) are contrary to each other, both are absolutely essential to accomplish the precision synthesis of polymers with precise structures.

1.2 Graft Copolymer

Graft copolymers have branched structures consisting of multiple branch chains and a backbone chain. Many researchers have investigated and synthesized graft copolymers as a model branched polymer.[33] For example, in most cases, the aggregation numbers of multimolecular micelles formed by graft copolymers were smaller than those of the micelles of linear block copolymers.[34,35] Moreover, some graft copolymers

form unimolecular micelles via single-chain folding, unlike multimolecular micelles formed via intermolecular association of linear block copolymers.[36–38] These characteristic phenomena stemmed from the efficient shielding of the backbone chain by the surrounding solvated graft chains. In addition, the morphology of graft copolymers is obviously different from that of block copolymers because of the topological constraints that hinder the polymer reptation motion.[39–44] Moreover, graft copolymers with a high density of branched chains are classified as "bottlebrush polymers". Bottlebrush polymers have rodlike structures derived from a nearly extended conformation due to the steric repulsion among the branched chains,[45–48] which is responsible for various unique properties of bottlebrush polymers.[49–52] These specific properties of graft copolymers have also been exploited for commercial uses as adhesives, emulsifiers, compatibilizing agents, and tough plastics.[53]

Three major methodologies, "grafting-from", "grafting-onto", and "grafting-through" methods, have been employed for the synthesis of graft copolymers with the use of appropriate prepolymers (Figure 2 upper).[12,33] The "grafting-from" method employs a macroinitiator, a polymer that contains initiating moieties at side chains, to initiate the polymerization of grafted chains. Graft polymers are obtained in high yield through this method due to the minimal steric hindrance of other graft chains. In the case of the "grafting-onto" method, the living propagating chains are attached to a backbone polymer through the reaction with reactive sites present along its main chain. Graft copolymers consisting of well-defined backbone and branch chains are prepared by the "grafting-onto" method because both chains are prepared via controlled polymerizations with high initiation efficiency. In the "grafting-through" method, polymers with a pendant polymerizable unit are (co)polymerized to synthesize graft copolymers. Graft copolymers with branched chains in high density can be synthesized by the "grafting-through" method.

A further precise design of graft copolymers was performed by Paraskeva and Hadjichristidis,[54] who synthesized a graft copolymer with a highly defined structure, or an "exact graft copolymer", by combining living anionic polymerization and repetitive polymer coupling reactions by means of 1,4-bis(phe-

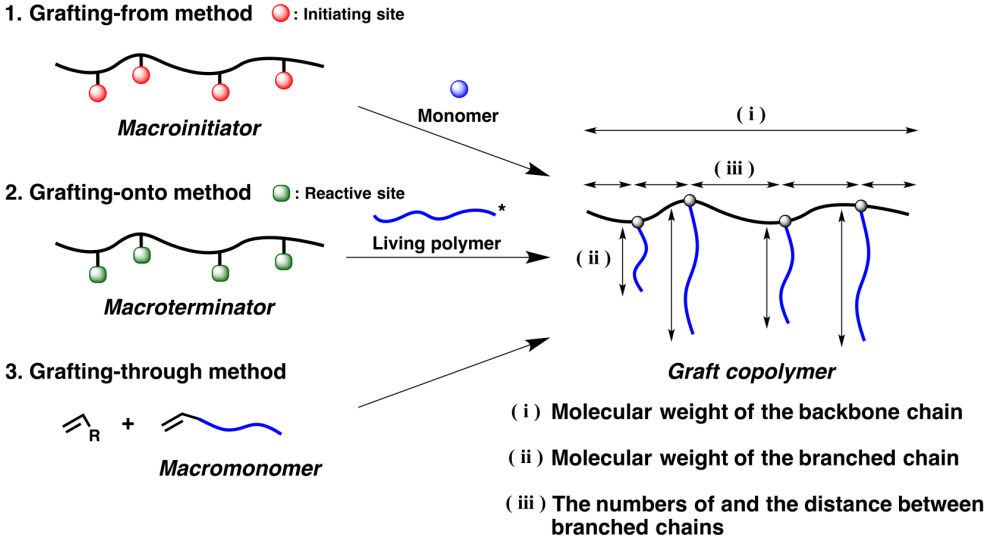
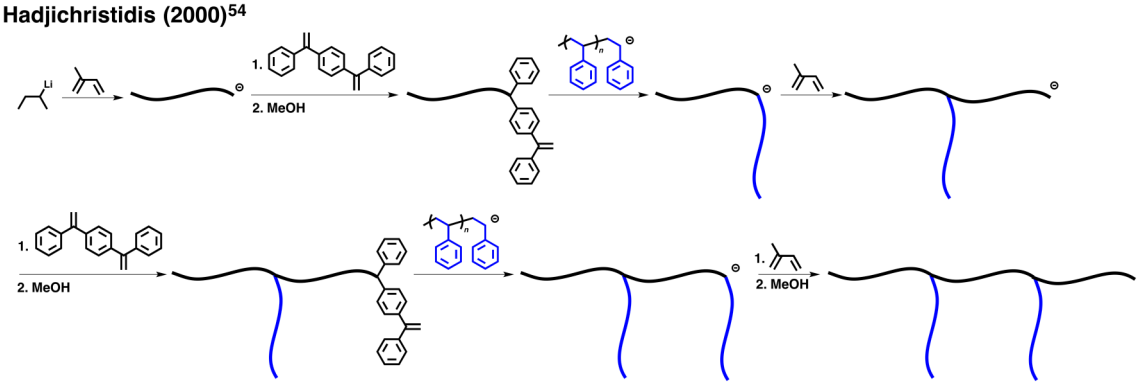


Figure 2. Three methods for syntheses graft copolymer and three parameters defining the structure of a graft copolymer.

nylethenyl)benzene (Scheme 2). Exact graft copolymers possess the following parameters that define their structures (Figure 2 lower): (i) molecular weight of the backbone chain, (ii) molecular weight of the branched chain, and (iii) the number of and the distance between the branched chains. Moreover, Hirao and co-workers[55–59] synthesized a variety of exact graft copolymers with more complicated structures by living anionic polymerization, which revealed the influence of minute differences of grafting positions on morphology.[60] To further investigate the effects of branched structures on the properties of graft copolymers, it is necessary to develop new strategies that allow for the synthesis of highly controlled graft copolymers.

Scheme 2. Synthetic Route of "Exact Graft Copolymer" via Living Anionic Polymerization.



1.3 Living Cationic Polymerization

Living polymerization, a chain-growth polymerization free from any side reactions, such as chain transfer and termination reactions, is a powerful tool for synthesizing polymers with well-defined structures. The first report of living polymerization was demonstrated by Szwarc[61] in 1956 for the living anionic polymerization of styrene. Since this discovery, controlled/living polymerization has been achieved through a variety of polymerization mechanisms, including ring-opening,[62] cationic,[63,64] group transfer,[65] radical,[66–73] ring-opening metathesis,[74] and coordination mechanisms.[75] These living polymerization systems produce polymers with predetermined molecular weights and narrow molecular weight distributions. Moreover, polymers with various architectures, such as block, gradient, graft, and star-shaped polymers, are obtained via living polymerization. In addition, polymers prepared by living polymerization have definite terminal structures derived from fragments of initiator or quencher due to the absence of side reactions (Figure 3).

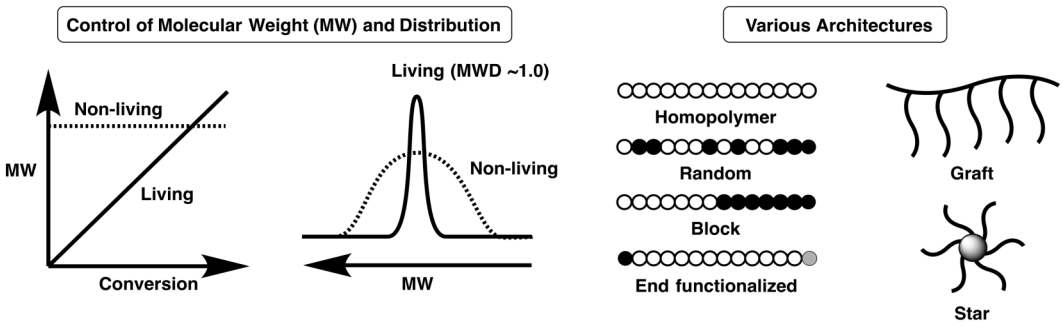


Figure 3. Control of structures by living polymerization.

Living cationic polymerization is the optimum method to prepare well-defined poly(vinyl ethers) [poly(VEs)], poly(styrene derivatives), and polyisobutene. The first achievements of living cationic polymerization were the polymerization of isobutyl VE (IBVE) using the HI/I_2 initiating system in 1984[76] and the polymerization of isobutene using the tertiary ester/BCl_3 system in 1986.[77] The prerequisite for living cationic polymerizations was the construction of a suitable equilibrium between the active and dormant species. After this breakthrough, diverse initiating systems for living cationic polymerization, such as the systems employing a weak Lewis acid in the absence of additives[78–80] or a strong Lewis acid in the presence of a weak Lewis base or an added salt,[81–84] have been developed to extend the scope of applicable monomers, tolerant functional groups, and constructible polymer structures.

Among the initiating systems developed, base-assisting living cationic polymerization, which employs a weak Lewis base as an additive, has been demonstrated to be highly efficient for the synthesis of functional polymers with well-defined structures from a wide variety of monomers. Aoshima and Higashimura[85–88] reported the living cationic polymerization of VEs via the stabilization of the growing carbocationic ends by means of weak Lewis bases, such as ester and ether. In this system, weak Lewis bases contribute to establishing an appropriate dormant–active equilibrium, stabilizing propagating ends, and adjusting the activity of Lewis acid catalysts. More recently, a wide variety of metal halides were demonstrated to function effectively as catalysts for base-assisting living cationic polymerization of isobutyl VE[89] and *p*-methoxystyrene[90] (Figure 4). In particular, the nature of the central metals of metal halides, such as chlorophilicity and oxophilicity, was highly responsible for the polymerization behavior.[91] Metal halides with suitable catalytic activities and tolerances to functional groups have also enabled the controlled polymerization of various monomers that were previously difficult to polymerize in a controlled manner.[92–95] Furthermore, polymers with precisely designed structures, such as block, gradient, and star-shaped polymers, have been synthesized through base-assisting living cationic polymerization.[96–99]

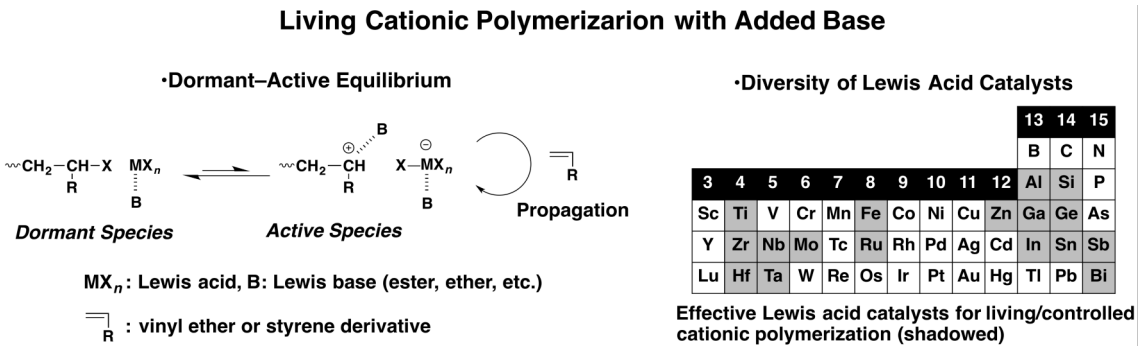


Figure 4. Features of the base-assisting living cationic polymerization.

Macroinitiators have been scarcely employed for the preparation of block, graft, or star-shaped copolymers by living cationic polymerization, in contrast to the remarkable development of the initiating systems for controlled polymerization reactions. The lability of initiating species, such as VE–hydrogen halide adducts, in air and/or at ambient temperature, is most likely responsible for the difficulty in employing

macroinitiators for living cationic polymerization. A few studies have reported using macroinitiators that required a specially prepared initiating site or a stepwise activation of latent initiating sites. Such examples include the syntheses of polymers through the initiation of a hemiacetal ester moiety, prepared using $SnBr_4$ as a catalyst, at the chain end of a poly(IBVE);[100] graft copolymers through the activation of cyclic acetal moieties at the side chains of poly(2-chloroethyl VE)-*block*-poly{2-[2-(1,3-dioxan-2-yl)ethoxy]ethyl VE} with trimethylsilyl iodide;[101] and star-shaped polymers through the generation of initiating sites by reacting hydrogen chloride and the residual vinyloxy groups in a microgel prepared from divinyl ethers.[102] Thus, the development of new initiating sites that possess high stability, reactivity, and accessibility is needed for the stepwise synthesis of polymers with more complicated structures by means of macroinitiators via living cationic polymerization.

1.4 Application of Acetal for Cationic Polymerization

Acetal is a common protective group widely used for the protection of carbonyl, diol, and hydroxy groups in organic synthesis.[103] Acetal is stable to aqueous and nonaqueous bases, and nucleophiles including organometallic reagents. On the other hand, acetal decomposes easily under acidic conditions. In addition, the stability of acetal moiety can be adjusted by changing its structure. When a methyl group is introduced into the acetal carbon of a non-substituted acyclic acetal, the hydrolysis rate of the acetal becomes 10^3 times faster.[104] Moreover, acyclic acetals are more labile to acid-catalyzed hydrolysis than cyclic acetals.[105] In the field of chain-growth polymerization, acetal moieties have been used to introduce aldehyde or hydroxy groups into polymers for avoiding undesirable reactions. Initiators or monomers with acetal moieties have been used for anionic polymerization[106–114] or radical polymerization[115–122] to yield polymers with acetal (or aldehyde) moieties.

In cationic polymerization, acetal compounds, which have structures of VE–alcohol adducts, were used as effective initiators for living polymerizations of VEs.[123–125] By contrast, the controlled cationic polymerizations of acetal-containing monomers have also been achieved without activating the acetal moieties present in the side chains.[101,126–131] Two conflicting situations arose from the selective activation of acetal moieties with suitable Lewis acid catalysts. In fact, Aoshima and co-workers[132] achieved Lewis acid-selective activation of acetal moieties in living cationic polymerization of VEs. These authors demonstrated that highly efficient activation of acetal compounds could be achieved with oxophilic metal chlorides, such as $TiCl_4$ and $ZrCl_4$. However, chlorophilic metal chlorides, such as $ZnCl_2$ and $SnCl_4$, were inert for activation of acetal compounds.

Acetal moieties are possible candidates as reactive sites of prepolymers due to their stability and catalyst-selective reactivity. Most importantly, acetal moieties are introduced very easily into the chain end of a poly(VE) by quenching the living cationic polymerization reactions with alcohols. The labile carbon–halogen bonds at the propagating chain ends are quantitatively converted to acetal moieties through reactions with alcohols.[133] Acetal moieties have also been introduced into the side chains of polymers

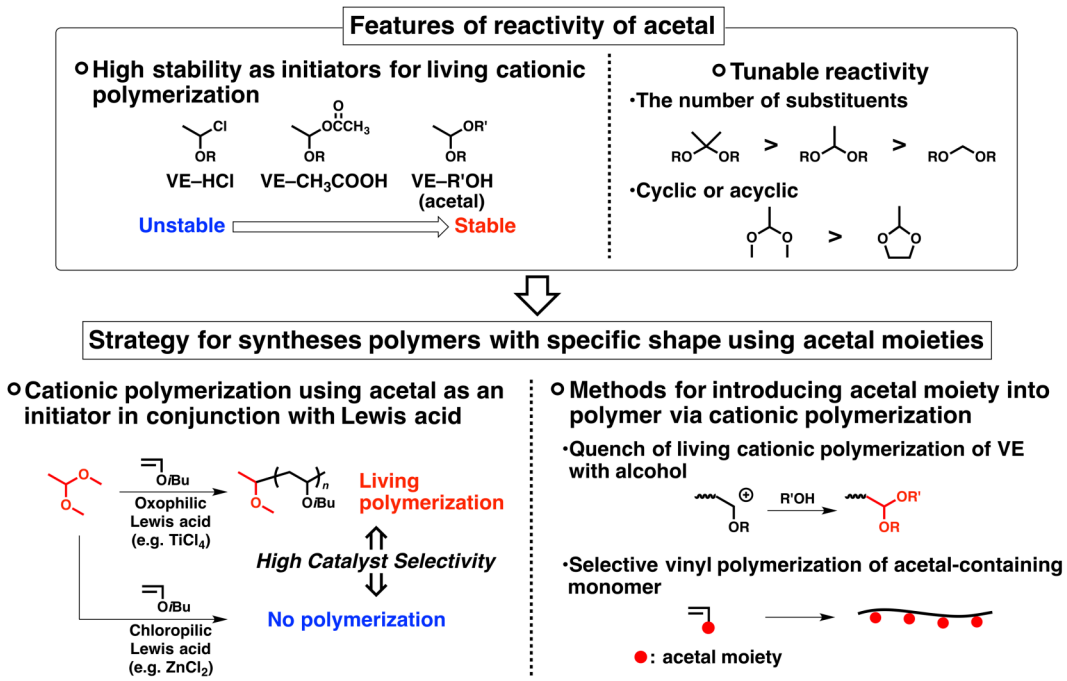


Figure 5. Features and strategy of acetal as a reactive site for syntheses polymers with special architecture.

through the cationic polymerization of acetal-containing VEs.[101,126–131,132] In addition, an aldehyde group in the polymer chains can be converted to an acetal moiety by reaction with alcohols (Figure 5).

2. Objective and Outline of This Thesis

The objective of this thesis is to precisely synthesize polymers with specific shape using acetal compounds or acetal moieties of prepolymers as reactive sites for base-assisting living cationic polymerization through stepwise synthesis (Chart 1). Although various polymers with special architectures have been prepared by living cationic polymerization, the high reactivity and lability of initiating sites prevented the development of stepwise synthesis via living cationic polymerization. Therefore, the author focused on acetal as a reactive site because the features of acetal, such as the catalyst selectivity and the stability, are suited for stepwise synthesis by means of prepolymers. First, the author examined the synthesis of branched copolymers using prepolymers with acetal moieties that were prepared by cationic polymerization. Next, VE macromonomers containing an acetal moiety at the ω-end were prepared with VE type of alcohols as quenchers for living cationic polymerization of VEs. The obtained macromonomers were polymerized via the cationic mechanism without reaction of the acetal moieties. The author also examined the use of acetal compounds as the "two-staged latent initiators". The α-ends derived from the several acetal compounds after the first-stage living cationic polymerization were successfully used as the initiating sites for the subsequent living polymerization reaction, yielding block copolymers in high yield. Moreover, a novel synthetic method for highly defined graft copolymers was designed with cyclic acetal moieties as two-staged initiating sites.

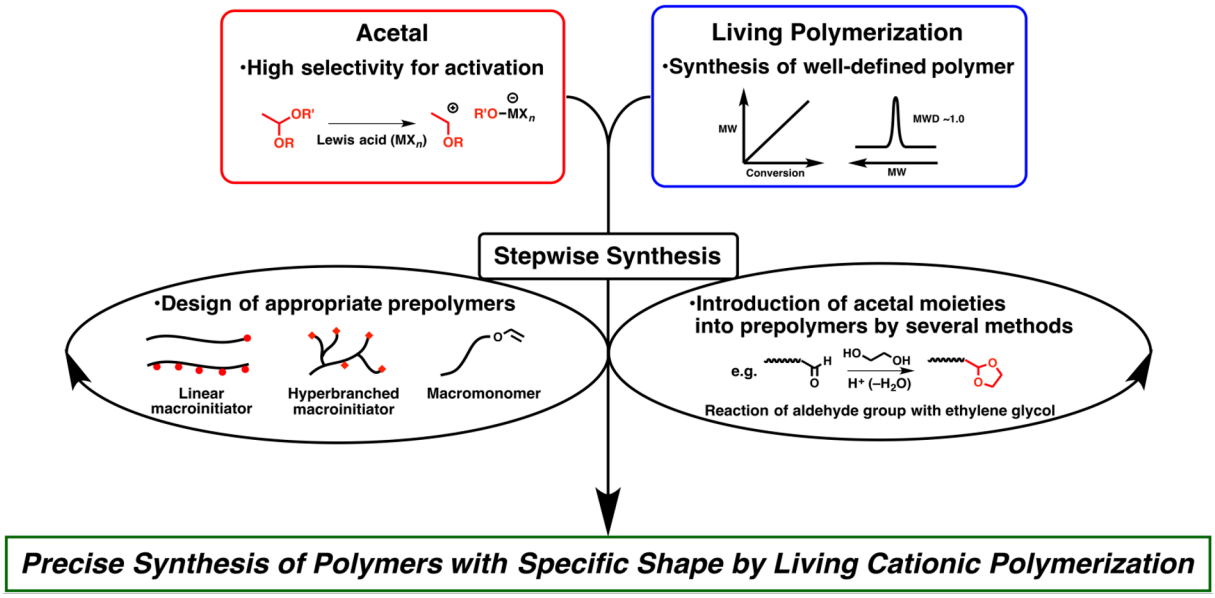
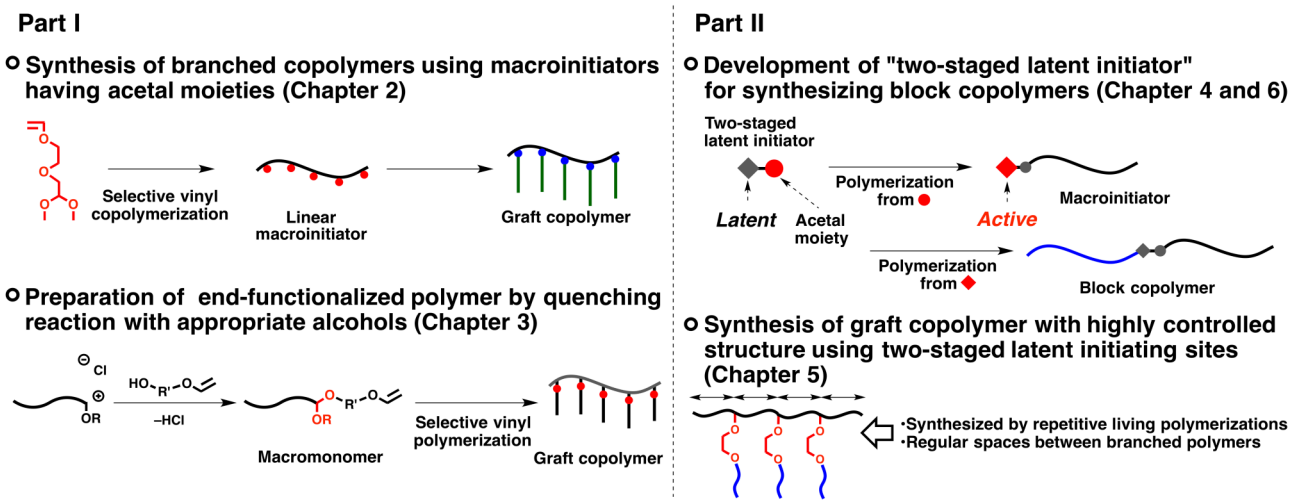


Chart 1. Objective of this thesis.

This thesis consists of two parts (Scheme 3). Part I (Chapters 2 and 3) describes the introduction of acetal moieties into polymers and the synthesis of various polymers by adjusting the reactivities of acetal moieties. In Part II (Chapters 4–6), acetals were used as two-staged latent initiators for the synthesis of block and graft copolymers with highly precise structures.

Scheme 3. Outline of This Thesis.



Chapter 2 addresses the precision synthesis of block and graft copolymers containing poly(*p*-methylstyrene) [poly(pMeSt)] segments with the use of acetal-containing poly(alkyl VE)s as macroinitiators (Figure 6). The living cationic polymerization of pMeSt from the acetal moiety introduced at the chain end (Macroinitiator 1) or the side chains (Macroinitiator 2) of poly(VE)s is achieved with quantitative initiation efficiency under optimized conditions, yielding well-controlled block or graft copolymers in 100 % yield. The precision synthesis of block and graft copolymers using alkoxystyrenes, styrene derivatives that are more reactive than pMeSt, is also successfully achieved in a similar manner.

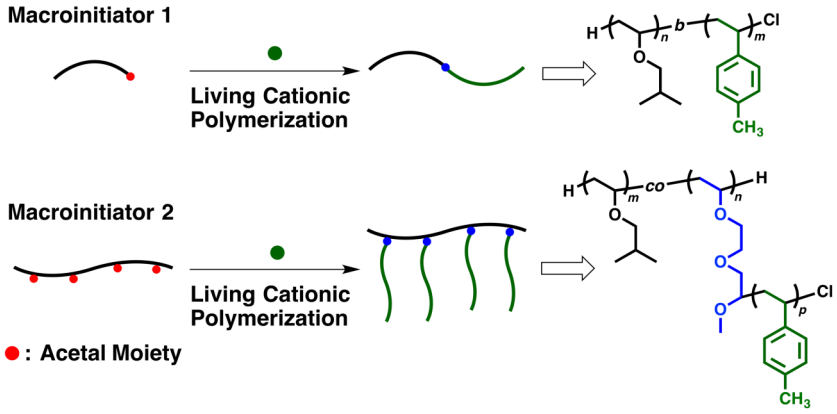


Figure 6. Synthesis of block and graft copolymers containing poly(pMeSt) segments.

Chapter 3 describes the preparation of end-functionalized polymers with an acetal moiety at the ω-end by quenching the living cationic polymerization of isobutyl VE (IBVE) with several alcohols (Figure 7). The use of alcohols with suitable structures for the quenching reaction yields a block copolymer and macromonomers in high yield. The cationic copolymerization reactions of the obtained macromonomers are investigated by selected metal halide catalysts to synthesize graft copolymers via the grafting-through method.

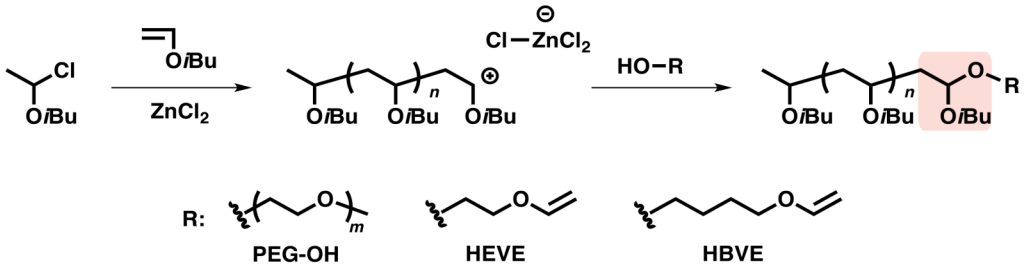


Figure 7. Synthesis of block copolymers and macromonomers by quenching reaction of living cationic polymerization of IBVE with various alcohols.

In Chapter 4, a cyclic acetal is demonstrated to function as a two-staged latent initiator for the synthesis of block copolymers (Figure 8). The initiation reaction quantitatively occurs through the ring-opening reaction of a cyclic acetal with the use of a suitable Lewis acid catalyst, resulting in the successful living cationic polymerization of VEs. The structure of cyclic acetals is also highly responsible for the quantitative initiation reactions of the living cationic polymerization. The hydroxy group generated as a result of the ring-opening reaction of the cyclic acetal is employed as an initiating site for the subsequent ring-opening anionic polymerization of L-lactide (LLA). Notably, the VE prepolymer is used as a macroinitiator without post-polymerization modification reactions.

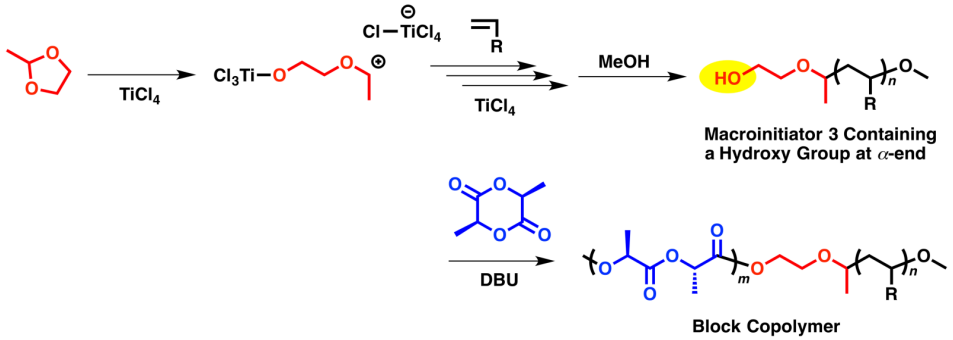


Figure 8. Synthesis of block copolymers using a cyclic acetal as a two-staged latent initiator (DBU: 1,8-diazabicyclo-[5.4.0]-7-undecene).

Chapter 5 presents the synthesis of well-defined graft copolymers with regular spaces between branches by the use of cyclic acetal moieties as two-staged latent initiating sites (Figure 9). Five-membered cyclic acetal moieties introduced at the chain end of poly(VE)s through the reaction between the aldehyde group and ethylene glycol are employed as the initiating sites for the living cationic polymerization of VEs. The repetitive operation of the polymerization and the acetalization generates a macroinitiator with several hydroxy groups in the side chain of a poly(VE) backbone. Graft copolymers having branches with narrow MWDs and regular spaces between the branches are synthesized by the ring-opening polymerization of LLA using this macroinitiator.

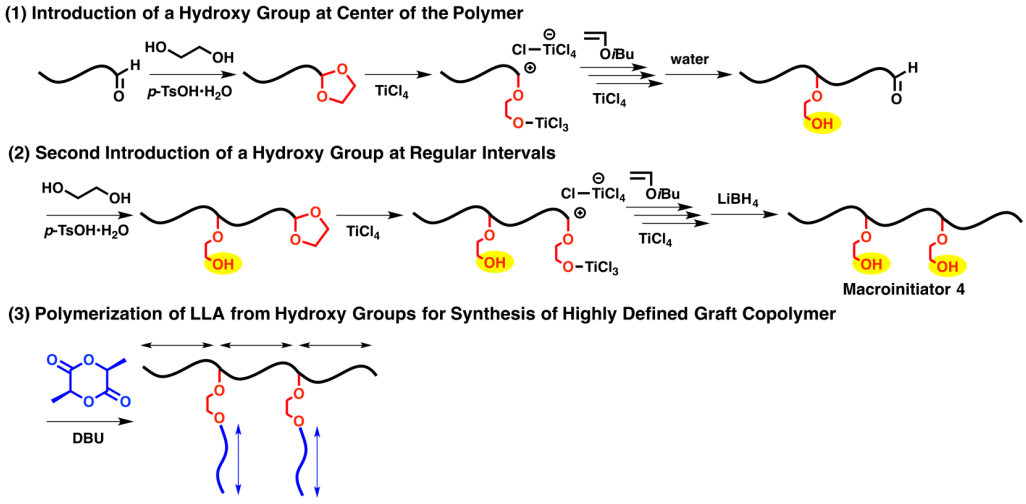


Figure 9. Synthesis of graft copolymers with highly defined structures using cyclic acetal moieties as two-staged latent initiating sites (*p*-TsOH·H_2O: *p*-toluenesulfonic acid monohydrate).

In Chapter 6, to prepare another type of macroinitiators, the author investigates cationic polymerization using an aromatic acetal as a two-staged latent initiator (Figure 10). When isopropyl VE is polymerized by means of the aromatic acetal/$TiCl_4$ initiating system at low temperature, a polymer with a benzyl ether moiety at the α-end is obtained quantitatively (Macroinitiator 5). The benzyl ether unit is activated through the abstraction of the alkoxy group under optimized conditions using a suitable Lewis acid catalyst, which results in an efficient initiating reaction for the subsequent cationic polymerization of vinyl monomers to yield block copolymers.

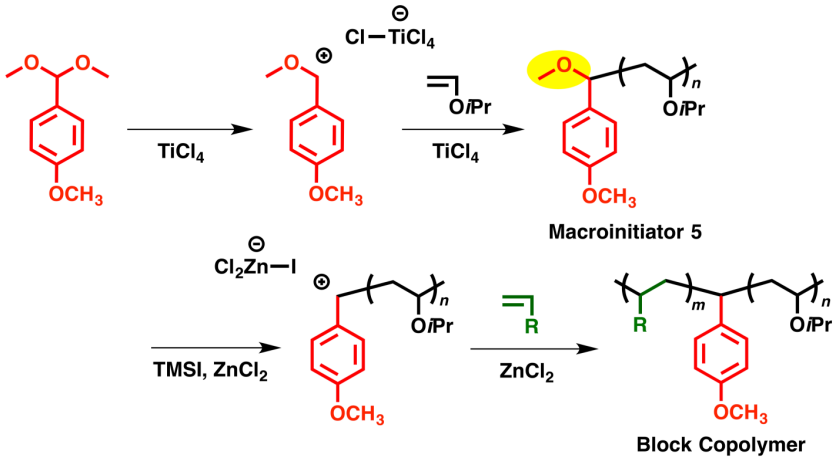


Figure 10. Cationic polymerization using an aromatic acetal as a two-staged latent initiator (TMSI: trimethylsilyl iodide).

References

1. Nie, Z.; Kumacheva, E. *Nat. Mater.* **2008**, *7*, 277–290.
2. Orilall, M. C.; Wiesner, U. *Chem. Soc. Rev.* **2011**, *40*, 520–535.
3. Niitani, T.; Amaike, M.; Nakano, H.; Dokko, K.; Kanamura, K. *J. Electrochem. Soc.* **2009**, *156*, A577–A583.
4. Kataoka, K.; Harada, A.; Nagasaki, Y. *Adv. Drug Delivery Rev.* **2001**, *47*, 113–131.
5. Qiu, L. Y.; Bae, Y. H. *Pharm. Res.* **2006**, *23*, 1–30.
6. Riess, G. *Prog. Polym. Sci.* **2003**, *28*, 1107–1170.
7. Leibler, L. *Macromolecules* **1980**, *13*, 1602–1617.
8. Bates, F. S.; Fredrickson, G. H. *Phys. Today* **1999**, *52*, 32–38.
9. Graessley, W. W. *Acc. Chem. Res.* **1977**, *10*, 332–339.
10. Kajiura, H.; Ushiyama, Y.; Fujimoto, T.; Nagasawa, M. *Macromolecules* **1978**, *11*, 894–899.
11. Milner, S. T. *Macromolecules* **1994**, *27*, 2333–2335.
12. Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Mays, J. *Prog. Polym. Sci.* **2006**, *31*, 1068–1132.
13. Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904–3920.
14. Allcock, H. R.; Powell, E. S.; Chang, Y.; Kim, C. *Macromolecules* **2004**, *37*, 7163–7167.
15. Olsen, B. D.; Segalman, R. A. *Macromolecules* **2005**, *38*, 10127–10137.

16. Schappacher, M.; Deffieux, A. *Macromol. Chem. Phys.* **1997**, *198*, 3953–3961.
17. Ryu, S. W.; Hirao, A. *Macromolecules* **2000**, *33*, 4765–4771.
18. Ross, S. G.; Müller, A. H. E.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 8331–8335.
19. Shinoda, H.; Matyjaszewski, K.; Okrasa, L.; Mierzwa, M.; Pakula, T. *Macromolecules* **2003**, *36*, 4772–4778.
20. Muehlebach, A.; Rime, F. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3425–3439.
21. Ederle, Y.; Isel, F.; Grutke, S.; Lutz, P. J. *Macromol. Symp.* **1998**, *132*, 197–206.
22. Christodoulou, S.; Iatrou, H.; Lohse, D. J.; Hadjichristidis, N. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4030–4039.
23. Hilf, S.; Kilbinger, A. F. M. *Macromol. Rapid Commun.* **2007**, *28*, 1225–1230.
24. Shiono, T.; Azad, S. M.; Ikeda, T. *Macromolecules* **1999**, *32*, 5723–5727.
25. Keszler, B.; Fenyvesi, Gy.; Kennedy, J. P. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 706–714.
26. Bernaerts, K. V.; Du Prez, F. E. *Polymer* **2005**, *46*, 8469–8482.
27. Feldthusen, J.; Iván, B.; Müller, A. H. E. *Macromolecules* **1998**, *31*, 578–585.
28. Higashihara, T.; Feng, D.; Faust, R. *Macromolecules* **2006**, *39*, 5275–5279.
29. Risse, W.; Grubbs, R. H.; *Macromolecules* **1989**, *22*, 1558–1562.
30. Kwon, Y.; Faust, R. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **2005**, *42*, 385–401.
31. Coca, S.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 3425–3439.
32. Notestein, J. M.; Lee, L.-B. W.; Register, R. A. *Macromolecules* **2002**, *35*, 1985–1987.
33. Lutz, P. J.; Peruch, F. in *Polymer Science: A Comprehensive Reference*, 1st ed.; Matyjaszewski, K.; Möller, M. Eds.; Elsevier Science: Amsterdam, 2012; Chapter 6.14, 511–542.
34. Pispas, S.; Hadjichristidis, N.; Mays, J. W. *Macromolecules* **1996**, *29*, 7378–7385.
35. Pitsikalis, M.; Woodward, J.; Mays, J. W.; Hadjichristidis, N. *Macromolecules* **1997**, *30*, 5384–5389.
36. Price, C.; Woods, D. *Polymer* **1973**, *14*, 82–86.
37. Selb, J.; Gallot, Y. *Makromol. Chem.* **1980**, *181*, 809–822.
38. Kikuchi, A.; Nose, T. *Polymer* **1996**, *26*, 5889–5896.
39. Hadjichristidis, N.; Iatrou, H. *Macromolecules* **1993**, *26*, 5812–5815.
40. Xenidou, M.; Beyer, F. L.; Hadjichristidis, N.; Gido, S. P.; Tan, N. B. *Macromolecules* **1998**, *31*, 7659–7667.
41. Lee, C.; Gido, S. P.; Poulos, Y.; Hadjichristidis, N.; Tan, N. B.; Trevino, S. F.; Mays, J. W. *Polymer* **1998**, *39*, 4631–4638.
42. Bayer, F. L.; Gido, S. P.; Büschl, C.; Iatrou, H.; Uhrig, D.; Mays, J. W.; Chang, M. Y.; Garetz, B. A.; Balsara, N. P.; Tan, N. B.; Hadjichristidis, N. *Macromolecules* **2000**, *33*, 2039–2048.
43. Matsushita, Y. *Macromol. Symp.* **2000**, *160*, 151–158.
44. Matsushita, Y.; Takano, A.; Torikai, N.; Watanabe, J.; Yoshida, Y.; Momose, H.; Suzuki, J. *Koubunshi Ronbunshu* **2000**, *57*, 803–809.

45. Wintermantel, M.; Gerle, M.; Fischer, K.; Schmidt, M.; Wataoka, I.; Urakawa, H.; Kajiwara, K.; Tsukahara, Y. *Macromolecules* **1996**, *29*, 978–983.
46. Lecommandoux, S.; Chécot, F.; Borsali, R.; Schappacher, M.; Deffieux, A.; Brûlet, A.; Cotton, J. P. *Macromolecules* **2002**, *35*, 8878–8881.
47. Rathgebar, S.; Pakula, T.; Wilk, A.; Matyjaszewski, K.; Beers, K. L. *J. Chem. Phys.* **2005**, *122*, 124904–124916.
48. Zhang, B.; Gröhn, F.; Pedersen, J. S.; Fischer, K.; Schmidt, M. *Macromolecules* **2006**, *39*, 8440–8450.
49. Terao, K.; Nakamura, Y.; Norisue, T. *Macromolecules* **1999**, *32*, 711–716.
50. Inoue, Y.; Matsuo, K.; Watanabe, H.; Nakamura, Y. *Macromolecules* **2006**, *39*, 7601–7606.
51. Xia, Y.; Olsen, B. D.; Kornfield, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2009**, *131*, 18525–18532.
52. Rzayev, J. *ACS Macro. Lett.* **2012**, *1*, 1146–1149.
53. Uhrig, D.; Mays, J. *Polym. Chem.* **2011**, *2*, 69–76.
54. Paraskeva, S.; Hadjichristidis, N. *J. Polym. Sci. Part A: Polym. Chem.* **2000**, *38*, 931–935.
55. Hirao, A.; Watanabe, T.; Kurokawa, R. *Macromolecules* **2009**, *42*, 3973–3981.
56. Hirao, A.; Murano, K.; Kurokawa, R.; Watanabe, T.; Sugiyama. K. *Macromolecules* **2009**, *42*, 7820–7827.
57. Hirao, A.; Murano, K.; Abouelmagd A.; Uematsu, M.; Ito, S.; Goseki, R.; Ishizone, T. *Macromolecules* **2011**, *44*, 3302–3311.
58. Hirao, A.; Uematsu, M.; Kurokawa, R.; Ishizone, T.; Sugiyama, K. *Macromolecules* **2011**, *44*, 5638–5649.
59. Ito, S.; Ishizone, T.; Hirao, A. *Macromolecules* **2015**, *48*, 8307–8314.
60. Takano, A.; Kondo, K.; Ueno, M.; Ito, K.; Kawahara, S.; Isono, Y.; Suzuki, J.; Matsushita, Y. *Polym. J.* **2001**, *33*, 732–740.
61. Szwarc, M. *Nature* **1956**, *178*, 1168–1169.
62. Penczek, S.; Cypryk, M.; Duca, A.; Kubisa, P.; Slomkowski, S. *Prog. Polym. Sci.* **2007**, *32*, 30–92.
63. Kennedy, J. P.; Iván, B. *Designed Polymers by Carbocationic Macromolecular Engineering: Theory and Practice*; Henser: Munich, 1992.
64. Aoshima, S.; Kanaoka, S. *Chem. Rev.* **2009**, *129*, 5245–5287.
65. Webster, O. W. *Adv. Polym. Sci.* **2004**, *167*, 1–34.
66. Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661–3688.
67. Ouchi, M.; Terashima, T.; Sawamoto, M. *Chem. Rev.* **2009**, *109*, 4963–5050.
68. Tsarevsky, N. V.; Matyjaszewski, K. *Chem. Rev.* **2007**, *107*, 2270–2299.
69. Moad, G.; Rizzardo, E.; Thang, S. H. *Polymer* **2008**, *49*, 1079–1131.
70. Otsu, T. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 2121–2136.
71. Rosen, B. M.; Percec, V. *Chem. Rev.* **2009**, *109*, 5069–5119.
72. Yamago, S. *Chem. Rev.* **2009**, *109*, 5051–5068.

73. Goto, A.; Tsujii, Y.; Fukuda, T. *Polymer* **2008**, *49*, 5177–5185.
74. Bielawski, C. W.; Grubbs, R. H. *Prog. Polym. Sci.* **2007**, *32*, 1–29.
75. Domski, G. J.; Rose, J. M.; Coates, G. W.; Boling, A. D.; Brookhart, M. *Prog. Polym. Sci.* **2007**, *32*, 30–92.
76. Miyamoto, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1984**, *17*, 265–268.
77. Faust, R.; Kennedy, J. P. *Polym. Bull.* **1986**, *15*, 317–323.
78. Sawamoto, M.; Okamoto, C.; Higashimura, T. *Macromolecules* **1987**, *20*, 2693–2697.
79. Kojima, K.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1989**, *22*, 1552–1557.
80. Schappacher, M.; Deffieux, A. *Macromolecules* **1991**, *24*, 2140–2142.
81. Ishihama, Y.; Sawamoto, M.; Higashimura, T. *Polym. Bull.* **1990**, *24*, 201–206.
82. Balogh, L.; Faust, R. *Polym. Bull.* **1992**, *28*, 367–374.
83. Pernecker, T.; Kennedy, J. P.; Iván, B. *Macromolecules* **1992**, *25*, 1642–1647.
84. Kamigaito, M.; Maeda, Y.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1993**, *26*, 1643–1649.
85. Aoshima, S.; Higashimura, T. *Polym. Bull.* **1986**, *15*, 417–423.
86. Higashimura, T.; Kishimoto, Y.; Aoshima, S. *Polym. Bull.* **1987**, *18*, 111–115.
87. Aoshima, S.; Higashimura, T. *Macromolecules* **1989**, *22*, 1009–1013.
88. Kishimoto, Y.; Aoshima, S.; Higashimura, T. *Macromolecules* **1989**, *22*, 3877–3882.
89. Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2009**, *42*, 3965–3972.
90. Kanazawa, A.; Shibutani, S.; Yoshinari, N.; Konnno, T.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2012**, *45*, 7749–7757.
91. Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2010**, *43*, 2739–2747.
92. Yonezumi, M.; Takaku, R.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 2202–2211.
93. Oda, Y.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 1207–1213.
94. Ishido, Y.; Aburaki, R.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2010**, *43*, 2739–2747.
95. Shinke, Y.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2013**, *51*, 4828–4834.
96. Seno, K.; Tsujimoto, I.; Kikuchi, T.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 6151–6164.
97. Shimomoto, H.; Fukami, D.; Irita, T.; Katsukawa, K.; Nagai, T.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 1547–1555.
98. Yoshimitsu, H.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2012**, *45*, 9427–9434.
99. Kanaoka, S.; Yamada, M.; Ashida, J.; Kanazawa, A.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 4594–4598.
100. Hashimoto, T.; Iwata, T.; Minami, A.; Kodaira, T. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 3173–3185.

101. Ariura, F.; Schappacher, M.; Borsali, R.; Deffieux, A. *React. Funct. Polym.* **2009**, *69*, 402–408.
102. Suzuki, T.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Polym. Prepr. Jpn.* **2014**, *63(2)*, 4082–4083.
103. Wuts, P. G. M.; Greene, T. W. in *Greene's protective groups in organic synthesis*, 4th ed.; Wiley-Interscience: New York, 2007; Chapters 2 and 4.
104. Satchell, D. P. N.; Satchell, R. S. *Chem. Soc. Rev.* **1990**, *19*, 55–81.
105. Vollhardt, K. P. C.; Schore, N. E. in *Organic Chemistry: Structure and Function*, 6th ed.; Freeman: New York, 2010; Chapter 17.
106. Schulz, D. N.; Halasa, A. F.; Oberster, A. E. *J. Polym. Sci.: Polym. Chem. Ed.* **1974**, *12*, 153–166.
107. Hayashi, M.; Loykulnant, S.; Hirao, A.; Nakahama, S. *Macromolecules* **1998**, *31*, 2057–2063.
108. Ishizone, T.; Mochizuki, A.; Hirao, A.; Nakahama, S. *Macromolecules* **1995**, *28*, 3787–3793.
109. Ishizone, T.; Tominaga, T.; Kitamura, K.; Hirao, A.; Nakahama, S. *Macromolecules* **1995**, *28*, 4829–4836.
110. Loykulnant, S.; Yamashiro, M.; Hirao, A. *Macromol. Chem. Phys.* **2001**, *202*, 1791–1798.
111. Lee, J.; Hogen-Esch, T. E. *Macromolecules* **2001**, *34*, 2805–2811.
112. Natalello, A.; Tonhauser, C.; Frey, H. *ACS Macro. Lett.* **2013**, *2*, 409–413.
113. Sweat, D. P.; Kim, M.; Schmitt, A. K.; Perroni, D. V.; Fry, C. G.; Mahanthappa, M. K.; Gopalan, P. *Macromolecules* **2014**, *47*, 6302–6310.
114. Sweat, D. P.; Yu, X.; Kim, M.; Gopalan, P. *J. Polym. Sci., Part A: Polym. Chem.* **2014**, *52*, 1458–1468.
115. Bes, L.; Angot, S.; Limer, A.; Haddleton, D. M. *Macromolecules* **2003**, *36*, 2493–2499.
116. Tao, L.; Mantovani, G.; Lecolley, F.; Haddleton, D. M. *J. Am. Chem. Soc.* **2004**, *126*, 13220–13221.
117. Bernaerts, K. V.; Prez, F. E. D. *Polymer* **2005**, *46*, 8469–8482.
118. Zhang, Z.; Liu, G.; Bell, S. *Macromolecules* **2000**, *33*, 7877–7883.
119. Camp, W. V.; Prez, F. E. D. *Macromolecules* **2004**, *37*, 6673–6675.
120. Zhen, Y.; Wan, S.; Liu, Y.; Yan, H.; Shi, R.; Wang, C. *Macromol. Chem. Phys.* **2005**, *206*, 607–612.
121. Li, R. C.; Broyer, R. M.; Maynard, H. D. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5004–5013.
122. Zhao, J.; Wang, H.; Liu, J.; Deng, L.; Liu, J.; Dong, A.; Zhang, J. *Biomacromolecules* **2013**, *14*, 3973–3984.
123. Meirvenne, D. V.; Haucourt, N.; Goethals, E. J. *Polym. Bull.* **1990**, *23*, 185–190.
124. Haucourt, N.; Goethals, E. J.; Schappacher, M.; Deffieux, A. *Macromol. Chem., Rapid Commun.* **1992**, *13*, 329–336.
125. Satoh, K.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **2000**, *33*, 748–753.
126. Minoda, M.; Yamaoka, K.; Yamada, K.; Takaragi, A.; Miyamoto, T. *Macromol. Symp.* **1995**, *99*, 169–177.
127. Yamada, K.; Yamaoka, K.; Minoda, M.; Miyamoto, T. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 256–261.
128. Yamada, K.; Minoda, M.; Miyamoto, T. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 751–757.

129. Yamada, K.; Yamaoka, K.; Minoda, M.; Miyamoto, T. *Polym. Int.* **2001**, *50*, 531–537.
130. D'Agosto, F.; Charreyre, M.-T.; Delolme, F.; Dessalces, G.; Cramail, H.; Deffieux, A.; Pichot, C. *Macromolecules* **2002**, *35*, 7911–7918.
131. Namikoshi, T.; Hashimoto, T.; Urushisaki, M. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 4855–4866.
132. Shimomoto, H.; Yoshida, H.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3703–3709.
133. Sawamoto, M.; Higashimura, T. *Makromol. Chem., Macromol. Symp.* **1990**, *32*, 131–144.

Part I

Precision Synthesis of Multibranched Copolymers Using Catalyst-Selectivity of Acetal Moieties

Chapter 2

Synthesis of Block or Graft Copolymers Containing Poly(Styrene Derivatives) Segments by Living Cationic Polymerization Using Acetal Moieties as Latent Initiating Sites

Introduction

Polymer synthesis using prepolymers containing initiating, terminating, and polymerizable units—i.e., macroinitiators, macroterminators, and macromonomers, respectively—is a powerful tool for the production of copolymers with well-defined structures from different types of monomers. In peptide synthesis via fragment condensation, the use of prepolymers can be crucial to the synthesis of polymers with complicated structures. For a prepolymer in chain polymerization, a macroinitiator, a macroterminator, or a macromonomer is used: macroinitiator-initiated polymerization or the termination reaction of living polymerization by a macroterminator yields block or graft copolymers;[1–3] the controlled polymerization of a macromonomer produces graft copolymers with branched chains of a regular length.[4]

A distinct advantage of the use of prepolymers over one-pot sequential copolymerization is that each segment can be prepared under appropriate conditions for each monomer, enabling the synthesis of copolymers from monomers with completely different reactivities. In particular, an unusual combination of monomers that polymerize via different mechanisms, such as radically or cationically polymerizable monomers, can be employed for copolymer synthesis.[5–7] The development of living polymerization has expanded the scope of macroinitiators, macroterminators, and macromonomers.

Aoshima and co-workers[8] recently achieved Lewis acid-selective activation of acetal functional groups for controlled cationic polymerization of vinyl ethers (VEs), leading to the facile synthesis of block or graft copolymers using only the cationic mechanism without post polymerization transformation of functional groups. Systematic investigation revealed that highly efficient acetal activation for the initiation of VE polymerization was achieved using an oxophilic metal chloride, such as $TiCl_4$ and $ZrCl_4$, whereas chlorophilic metal chlorides, such as $ZnCl_2$ and $SnCl_4$, were inert. Thus, an acetal-inert Lewis acid was used to prepare a macroinitiator with acetal moieties in the side chains via living cationic copolymerization of an acetal-containing VE monomer. The quantitative activation of the pendant acetals with a catalyst active in acetal-initiated living polymerization of another VE produced a graft copolymer. The macroinitiator method should be applicable to the synthesis of copolymers derived from comonomers that are cationically polymerizable but have very different reactivities. Although cationic polymerizations using acetals as a cationogen have been employed in several studies by other groups (e.g., aliphatic acetals treated with trimethylsilyl iodide[9,10] or aromatic acetals coupled with $AlCl_3$[11]), catalyst-selective synthesis has never been reported.

In this chapter, the author examines the synthesis of block and graft copolymers containing poly(alkyl VE) and poly(styrene derivatives) segments via living cationic polymerization of styrene derivatives using acetal-containing macroinitiators (Chart 1). Prior to the macroinitiator synthesis, a low-molecular-weight acetal compound is first examined as a model cationogen for the polymerization of *p*-methylstyrene, a monomer that is much less reactive than alkyl VEs. The synthesis of block and graft copolymers containing poly(alkyl VE) and poly(pMeSt) segments are then examined using the initiating system designed based on the results of the model reaction. Block and graft copolymers containing poly(VE) and poly(alkoxystyrene) segments are synthesized in a similar manner.

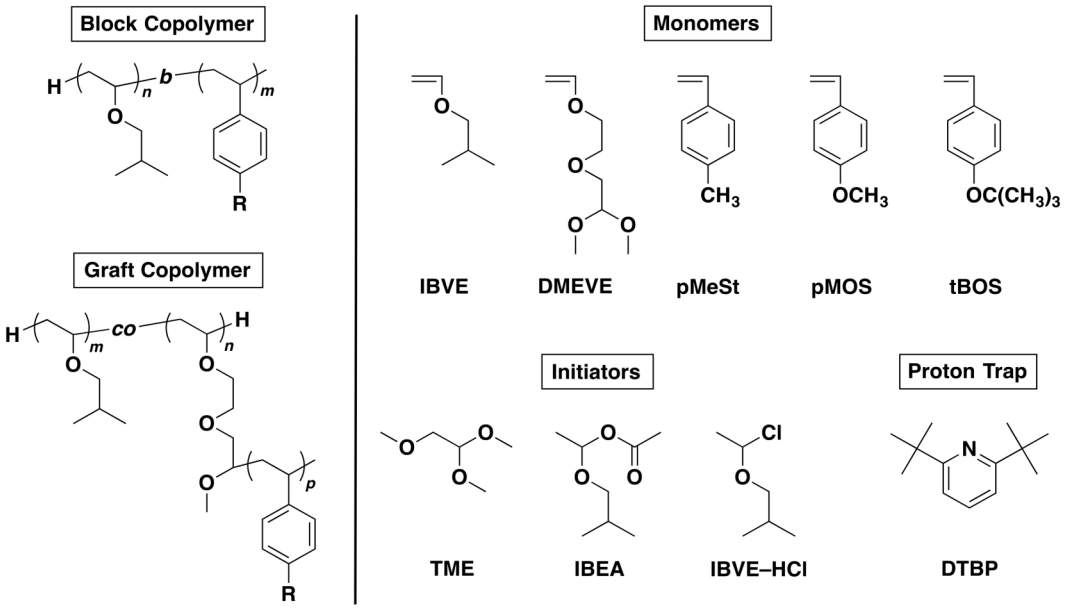


Chart 1. Structures of polymers and reagents related to this chapter.

Experimental

Materials

Isobutyl VE (IBVE; TCI; >99%) and 1,1-dimethoxyethane (DME; TCI; >98.0%) were distilled twice over calcium hydride. *p*-Methylstyrene (pMeSt; TCI; >98%), *p*-*tert*-butoxystyrene (tBOS; Wako; >98%), *p*-methoxystyrene (pMOS; TCI; >95%), 1,1,2-trimethoxyethane (TME; TCI; >98.0%) and 2,6-di-*tert*-butylpyridine (DTBP; Aldrich; 97%) were distilled twice over calcium hydride under reduced pressure. Ethyl acetate (Wako; >99.5%) was dried overnight over molecular sieves 3A and 4A and distilled twice over calcium hydride. Toluene (Wako; >99.5%), dichloromethane (CH_2Cl_2; Wako; >99.0%), and hexane (Wako; 96.0%) were dried using solvent purification columns (Glass Contour; Solvent Dispensing System). The acetal-containing VE 2-(2,2-dimethoxy)ethoxyethyl VE (DMEVE) was prepared from addition reaction of 2-hydroxyethyl VE (TCI; >98.0%) with bromoacetaldehyde dimethyl acetal (Aldrich; 97%) according to the procedure by Aoshima and co-worekers.[8] and distilled three times over calcium hydride. The adducts of IBVE with HCl [IBVE–HCl; $CH_3CH(O\mathit{i}Bu)Cl$] or acetic acid [IBEA; $CH_3CH(O\mathit{i}Bu)OCOCH_3$] were prepared from addition reaction of IBVE with HCl or acetic acid according to

the literature method,[12] respectively. $LiBH_4$ (Aldrich; 2.0 M solution in tetrahydrofuran) was used as received. $TiCl_4$ (Aldrich; 1.0 M solution in toluene), $ZnCl_2$ (Aldrich; 1.0 M solution in diethyl ether), $SnCl_4$ (Aldrich; 1.0 M solution in CH_2Cl_2), $Et_{1.5}AlCl_{1.5}$ (Nippon Aluminum Alkyls; 1.0 M solution in toluene), and $EtAlCl_2$ (Wako; 1.0 M solution in hexane) were used without further purification. A stock solution of $ZrCl_4$ in ethyl acetate was prepared from anhydrous $ZrCl_4$ (Aldrich; 99.99%). All chemicals, except for toluene, dichloromethane, and hexane, were stored in brown ampules under dry nitrogen.

Polymerization Procedure

Synthesis of the Linear Macroinitiator Containing Acetal Moieties in the Side Chains

The polymerization was performed under a dry nitrogen atmosphere in a glass tube with a three-way stopcock. The glass tube was baked using a heat gun (Ishizaki; PJ-206A; blow temperature ~450 °C) under dry nitrogen for 10 min before use. The statistical copolymerization of DMEVE and IBVE in toluene at 0 °C is described as a representative example. The reaction was initiated by the addition of a prechilled $Et_{1.5}AlCl_{1.5}$ solution in toluene (0.20 mL; 200 mM) to a mixture of DMEVE, IBVE, ethyl acetate, and the cationogen (IBVE–HCl) (3.80 mL) at 0 °C using a dry syringe. After a certain period, the polymerization was terminated using a solution of $LiBH_4$ in tetrahydrofuran[13] (0.20 mL; 2.0 M). The quenched reaction mixture was diluted with CH_2Cl_2 and washed with water to remove the initiator residues. The volatile substances were then removed under reduced pressure. The monomer conversion was determined by a gravimetric method.

Synthesis of the Block Copolymer by Sequential Copolymerization

The first-stage polymerization of IBVE was started by addition of an $SnCl_4$ solution (0.30 mL in toluene; 100 mM) to a solution (2.40 mL) containing toluene, IBVE, ethyl acetate, the cationogen (IBEA), and $Et_{1.5}AlCl_{1.5}$ using dry syringes. To this solution, pMeSt (0.30 mL) was added to start the second-stage polymerization. After a certain period, the polymerization was terminated using chilled methanol containing a small amount (0.1%) of an aqueous ammonia solution (3.0 mL). The quenched reaction mixture was diluted with CH_2Cl_2 and then washed with water to remove the initiator residues. The volatiles were then removed under reduced pressure at 50 °C, and the residue was vacuum-dried for > 3 h at 60 °C. The conversion of IBVE and pMeSt were determined by a gravimetric method.

Synthesis of the Graft Copolymer

For the graft copolymerization of pMeSt, a solution (2.10 mL) of predried poly(IBVE-*co*-DMEVE), ethyl acetate, DTBP solution in CH_2Cl_2, and a solution of $TiCl_4$ in CH_2Cl_2 (0.30 mL; 50 mM) were successively added to the tube using dry syringes. To this solution, pMeSt (0.30 mL) and $SnCl_4$ in CH_2Cl_2 (0.30 mL; 200 mM) were successively added to start the pMeSt polymerization. After a certain period, the polymerization was terminated using chilled methanol containing a small amount (0.1%)

of an aqueous ammonia solution (3.0 mL). The monomer conversion was determined by a gravimetric method.

Characterization

The molecular weight distribution (MWD) of the polymers was measured by gel permeation chromatography (GPC) in chloroform at 40 ºC with polystyrene gel columns [Tosoh; TSKgel G-4000H_{XL}, G-3000H_{XL}, and G-2000H_{XL} (exclusion limit molecular weight = 4×10^5, 6×10^4, and 1×10^4, respectively; bead size = 5 μm; column size = 7.8 mm i.d. × 300 mm), TSKgel MultiporeH_{XL}-M × 3 (exclusion limit molecular weight = 2×10^6; bead size = 5 μm; column size = 7.8 mm i.d. × 300 mm), or TSKgel GMH_{HR}-M × 3 or 2 (exclusion limit molecular weight = 4×10^6; bead size = 5 μm; column size = 7.8 mm i.d. × 300 mm) flow rate = 1.0 mL/min] connected to a Tosoh DP-8020 pump, a CO-8020 column oven, a UV-8020 ultraviolet detector, and an RI-8020 refractive index detector. The number-average molecular weight (M_n) and polydispersity ratio [weight-average molecular weight/number-average molecular weight (M_w/M_n)] were calculated from the chromatographs with respect to 16 polystyrene standards (Tosoh; M_n = 577−1.09 × 10^6, $M_w/M_n \leq 1.1$). The absolute weight-average molecular weight and the exponent *a* of the Mark–Houwink–Sakurada equation were determined using the GPC system comprised of a pump (Viscotek VE 1122), two polystyrene gel columns [TSKgel GMH_{HR}-M × 2 (exclusion limit molecular weight = 4×10^6; bead size = 5 μm; column size = 7.8 mm i.d. × 300 mm) flow rate = 0.7 mL/min], and a Viscotek TDA 305 triple detector [refractive index, laser light scattering (λ = 670 nm, 90º and 7º; RALS and LALS), and differential pressure viscometer]. NMR spectra were recorded using a JEOL JNM-ECA 500 spectrometer (500.16 MHz for ^{1}H). Differential scanning calorimetry (DSC; DSC-6220, Hitachi High-Tech Science) was used to determine the glass transition temperature (T_g) of product copolymers. The heating and cooling rates were 10 ºC/min. The T_g of the copolymers was defined as the temperature of the midpoint of a heat capacity change on the second heating scan.

Results and Discussion

Catalyst Survey for Acetal-Initiated Living Cationic Polymerization of *p*-Methylstyrene

To identify a suitable catalyst for the acetal-initiated living cationic polymerization of *p*-methylstyrene (pMeSt), various metal chlorides were examined for the polymerization of pMeSt using 1,1,2-trimethoxyehane (TME) as the cationogen. The reactions were conducted in CH_2Cl_2 at 0 °C in the presence of ethyl acetate as an added base and 2,6-di-*tert*-butylpyridine (DTBP) as a proton trap reagent (Table 1). The catalyst concentration was similar to that used for the living polymerization of pMeSt with a hydrogen chloride adduct of a styrene derivative or a VE as the cationogen.[14,15] However, the Lewis acid catalysts used ($ZnCl_2$, $SnCl_4$, $Et_{1.5}AlCl_{1.5}$, and $TiCl_4$) induced almost no polymerization (entries 1–4 in Table 1). The most unexpected outcome was the lack of polymerization in the presence of $TiCl_4$, which induces the living polymerization of IBVE using TME.[8] One of the main roles of $TiCl_4$ is the generation of the real

Table 1. Cationic Polymerization of pMeSt by TME/Lewis Acid Initiating Systems[a]

entry	solvent	Lewis acid	additive	conv. (%)	$M_n \times 10^{-4}$ (GPC)[b]	$M_n \times 10^{-4}$ (calcd)	M_w/M_n (GPC)[b]
1	CH_2Cl_2	$ZnCl_2$	ethyl acetate, DTBP	0	–	–	–
2		$SnCl_4$		2	0.42	0.04	2.02
3		$Et_{1.5}AlCl_{1.5}$		1	0.73	0.02	2.40
4		$TiCl_4$		1	0.06	0.02	1.41
5		$TiCl_4/SnCl_4$		98	2.00	2.20	1.15
6			none	97	0.91	2.19	2.05
7			ethyl acetate	99	0.66	2.22	1.24
8	toluene		ethyl acetate, DTBP	4	0.11	0.09	1.22

[a] $[pMeSt]_0 = 0.76$ M, $[TME]_0 = 4.0$ mM, $[Lewis\ acid]_0 = 20$ mM (entries 1, 3 and 4) or 10 mM (entry 2) or 5.0/10 mM (entries 5–8), [DTBP] = 10 mM (except for entries 6 and 7), [ethyl acetate] = 50 mM (except for entry 6), at 0 ºC. [b] Determined by GPC with polystyrene calibration.

initiating species, i.e., a *β*-methoxy methyl VE–hydrogen chloride adduct, via the exchange reaction between the methoxy group of TME and the chloride anion of $TiCl_4$. This type of exchange reaction was confirmed by ^{1}H NMR analysis of the reactions of 1,1-dimethoxyethane (DME) and $TiCl_4$ in the presence of ethyl acetate [Figure 1 (E)]. Thus, the inability of $TiCl_4$ in the presence of ethyl acetate to polymerize pMeSt may reflect insufficient Lewis acidity for the propagation of the polymerization of the much less reactive pMeSt. $SnCl_4$, a stronger Lewis acid that enables living cationic polymerization of pMeSt with a different cationogen,[14,15] did not induce polymerization due to the limited exchange reaction between the methoxy group of TME and the chloride anion of $SnCl_4$ [*cf*. Figure 1 (C)].

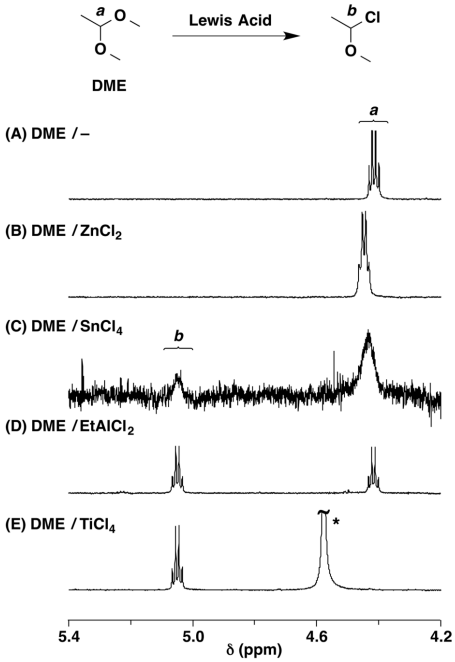
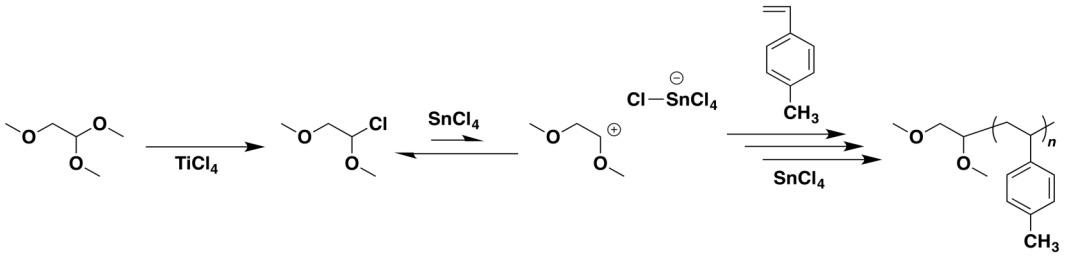


Figure 1. ^{1}H NMR spectra of (A) DME in toluene-d_8 and the mixtures of DME, ethyl acetate, and (B) $ZnCl_2$, (C) $SnCl_4$, (D) $EtAlCl_2$, and (E) $TiCl_4$ in toluene-d_8 at 0 ºC: $[DME]_0 = 10$ mM, [ethyl acetate] = 100 mM, $[Lewis\ acid]_0 = 10$ mM. *The methoxy group that coordinated with Ti.

Scheme 1. Living Cationic Polymerization of pMeSt Using TME-$TiCl_4$/$SnCl_4$ System.



Based on the results above, the polymerization of pMeSt was conducted with an initiating system comprising both $TiCl_4$ and $SnCl_4$, which respectively induced the quantitative generation of the real initiating species through the exchange reaction between the methoxy group and the chloride anion [Figure 1 (E)], and catalyzed the efficient propagation reaction as a real activator (Scheme 1). Polymerization using the $TiCl_4$/$SnCl_4$ dual catalysts in conjunction with TME proceeded smoothly, with near quantitative conversion in 24 h. Furthermore, the product polymer had a narrow MWD (M_w/M_n = 1.15) and an M_n value consistent with that calculated from the monomer-to-initiator ratio (entry 5 in Table 1; Figure 2). The linear increase in the M_n values is consistent with the theoretical value and indicates that the living polymerization proceeded under these conditions.

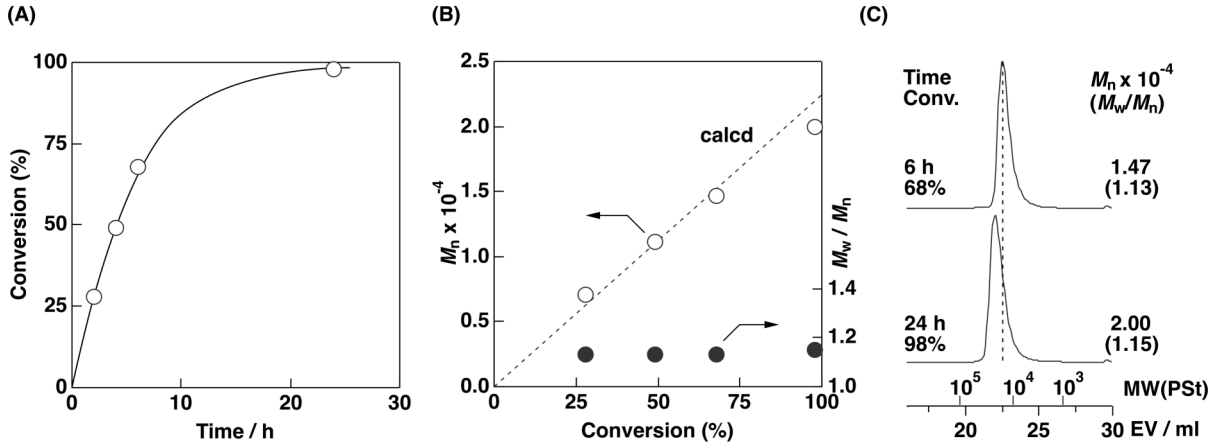


Figure 2. (A) Time–conversion curve, (B) M_n and M_w/M_n–conversion plots, and (C) MWD curves of the poly(pMeSt)s obtained using the TME-$TiCl_4$/$SnCl_4$ system: $[pMeSt]_0$ = 0.76 M, $[TME]_0$ = 4.0 mM, $[TiCl_4]_0$ = 5.0 mM, $[SnCl_4]_0$ = 10 mM, [DTBP] = 10 mM, [ethyl acetate] = 50 mM, in CH_2Cl_2 at 0 ºC.

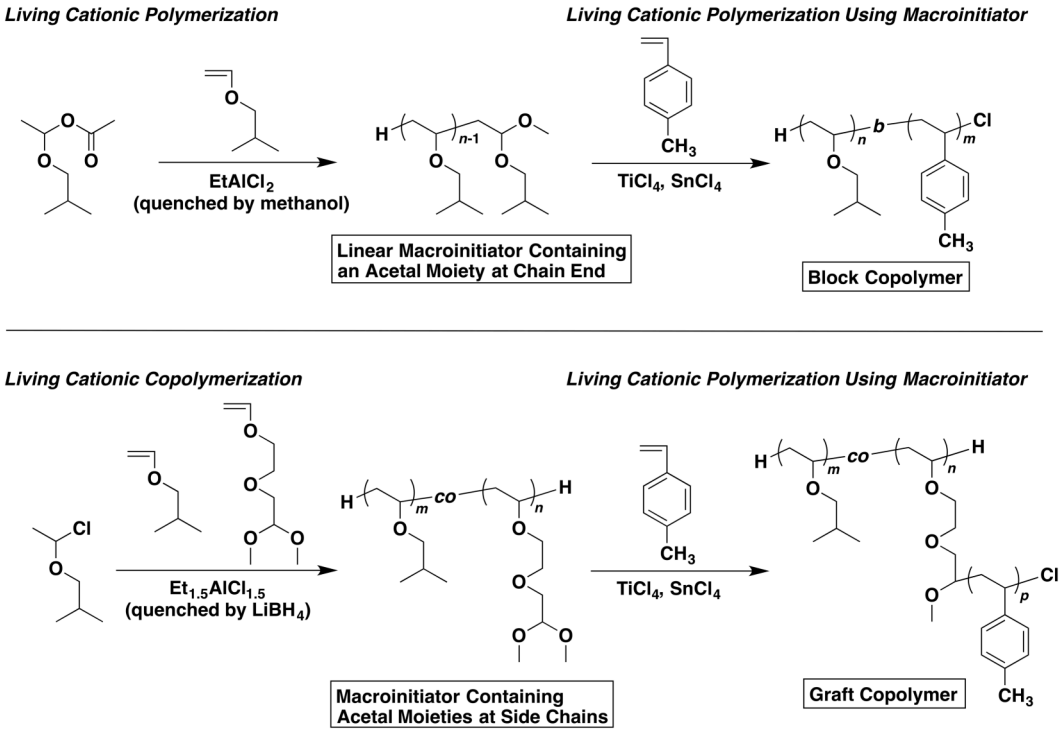
The use of appropriate additives was very important for the living polymerization of pMeSt using TME as a cationogen. When the polymerization using the $TiCl_4$/$SnCl_4$ initiating system was performed in the absence of additives, the reaction was uncontrolled and yielded poly(pMeSt) with a broad MWD (M_w/M_n = 2.05), most likely because the Lewis acidity of the catalysts was not moderated and/or the propagating carbocation was not stabilized in the absence of a weak Lewis base (entry 6 in Table 1). The polymerization using ethyl acetate alone as an additive was controlled, but the molecular weight of the resulting polymer was lower than the calculated value, likely due to the occurrence of initiation reactions from protic impurities other than TME, such as adventitious water (entry 7 in Table 1). A proton trap reagent, DTBP, was essential

for the suppression of such undesired initiation reactions. In addition, a lower polarity solvent was not suitable for the polymerization. Almost no polymerization of pMeSt occurred when toluene was used as the polymerization medium instead of CH_2Cl_2 (entry 8 in Table 1). Thus, the use of the $TiCl_4/SnCl_4$ initiating system in CH_2Cl_2 with an added base and a proton trap reagent was indispensable for the living cationic polymerization of pMeSt using acetal as a cationogen.

Macroinitiator-Initiated Block Copolymerization of pMeSt

The synthesis of a block copolymer composed of poly(IBVE) and poly(pMeSt) segments using a poly(IBVE) macroinitiator with an acetal moiety at the chain end was examined (Scheme 2). The macroinitiator with the methoxy- and isobutoxy-containing acetal moiety was prepared simply by quenching the living cationic polymerization of IBVE with methanol.[16] This macroinitiator quantitatively initiated the polymerization of pMeSt using the $TiCl_4/SnCl_4$ initiating system in a manner similar to the reaction using TME as the cationogen. The reaction yielded a block copolymer with a very narrow MWD (M_w/M_n = 1.08) without unreacted macroinitiator, suggesting that the terminal acetal moiety was quantitatively activated to function as an initiating site for the polymerization [Figure 3 (A)].

Scheme 2. Synthetic Routes of the Block and Graft Copolymers via Living Cationic Polymerization Using Macroinitiator.



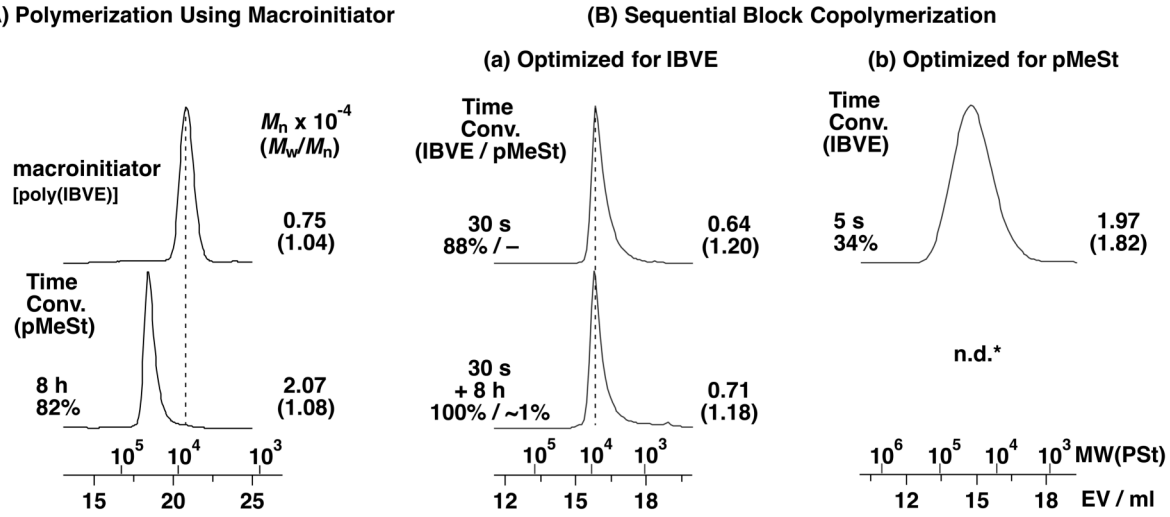


Figure 3. MWD curves for the synthesis of poly(IBVE)-*block*-poly(pMeSt) (A) using poly(IBVE) as a macroinitiator or (B) through sequential block copolymerization: (A) $[pMeSt]_0$ = 0.76 M, $[poly(IBVE)]_0$ = 4.0 mM, $[TiCl_4]_0$ = 5.0 mM, $[SnCl_4]_0$ = 10 mM, [DTBP] = 10 mM, [ethyl acetate] = 50 mM, in CH_2Cl_2 at 0 ºC (B) (a) $[IBVE]_0$ = 0.46 M, $[IBEA]_0$ = 4.0 mM, $[Et_{1.5}AlCl_{1.5}]_0$ = 2.5 mM, $[pMeSt]_{add}$ = 0.51 M, $[SnCl_4]_{add}$ = 10 mM, [ethyl acetate] = 1.0 M, in toluene at 0 ºC (b) $[IBVE]_0$ = 0.76 M, $[IBEA]_0$ = 4.0 mM, $[Et_{1.5}AlCl_{1.5}]_0$ = 5.0 mM, [ethyl acetate] = 50 mM, in CH_2Cl_2 at 0 ºC. *The subsequent addition of pMeSt was not conducted because the first segment was not synthesized precisely.

A considerable benefit of polymerization using acetal-containing macroinitiators is that both segments can be prepared under completely different reaction conditions. Although a past report[17] showed the successful sequential block copolymerization of methyl VE and styrene, i.e., monomers with a very large difference in reactivity, a drastic change of reaction conditions (the addition of a catalyst and the rise of temperature) after the addition of styrene was needed for the efficient synthesis of block copolymers. To confirm the superiority of the current method, sequential block copolymerizations of IBVE and pMeSt were examined under conditions suitable for the living polymerization of either of the two monomers. When the sequential block copolymerization was performed under the conditions optimized for IBVE, the polymerization of IBVE proceeded in a living manner, but the subsequent reaction of pMeSt did not occur [Figure 3 (B), (a)]. By contrast, the polymerization of IBVE was uncontrolled under the conditions suitable for the living cationic polymerization of pMeSt, yielding a polymer with a broad MWD [Figure 3 (B), (b)]. These results demonstrate that it is difficult to synthesize poly(IBVE)-*block*-poly(pMeSt) via sequential block copolymerization with the present system because of the significantly large differences in reactivity between IBVE and pMeSt.

Precision Synthesis of Graft Copolymer via the Polymerization of pMeSt Using a Macroinitiator Containing Acetal Moieties in Its Side Chains

The synthesis of graft copolymers was examined via the initiation of living cationic polymerization of pMeSt from the acetal moieties in the side chains of a poly(VE). Poly(IBVE-*co*-DMEVE)

(Scheme 2), a macroinitiator, was prepared via the living cationic copolymerization of IBVE with DMEVE, an acetal-containing monomer.[8] To synthesize the linear macroinitiator, the reactivity of acetal moiety of DMEVE was very important [the star-shaped copolymer was synthesized using high reactive acetal-containing VE (Supporting Information)]. The acetal moieties were intact during the copolymerization with $Et_{1.5}AlCl_{1.5}$ as a catalyst. Using this copolymer as a macroinitiator, the polymerization of pMeSt was conducted under similar conditions as those for the polymerization using TME as a cationogen and the synthesis of poly(IBVE)-*block*-poly(pMeSt). The polymerizations at the $[\text{acetal units}]_0/[TiCl_4]_0/[SnCl_4]_0$ ratio of 4.0 mM/5.0 mM/10 mM or 4.0 mM/10 mM/10 mM yielded the product with a narrow MWD, but the conversion of pMeSt plateaued (entry 1 in Table 2; circle symbols in Figure 4) or the product had a multimodal MWD (M_w/M_n = 2.10; entry 2 in Table 2; square symbols in Figure 4), respectively. The lower reactivity of the acetal moieties on the side chain than that at the chain end may be due to the electron-withdrawing inductive effect of the oxygen atom adjacent to the *β*-carbon. Quantitative consumption of pMeSt was achieved when the amount of $SnCl_4$ was increased ($[\text{acetal units}]_0/[TiCl_4]_0/[SnCl_4]_0$ = 4.0 mM/5.0 mM/20 mM). The monomer conversion neared 100% within 2 h, and a product with a unimodal MWD was obtained without the generation of any byproducts (entry 3 in Table 2; triangle symbols in Figure 4; Figure 5). ^{1}H NMR analysis revealed the disappearance of the acetal peak (peak *k*) and the appearance of the methine peak of the carbon–chlorine end at the poly(pMeSt) chain end (p-

Table 2. Synthesis of Graft Copolymer Containing Poly(pMeSt) by Macroinitiator-$TiCl_4/SnCl_4$ Initiating Systems[a]

entry	$[TiCl_4]_0$ (mM)	$[SnCl_4]_0$ (mM)	time	conv. (%)	$M_n \times 10^{-4}$ (GPC)[b]	M_w/M_n (GPC)[b]	NB[c]
1	5.0	10	20 h	40	2.85	1.20	4
2	10	10	24 h	100	2.44	2.10	–
3	5.0	20	2 h	94	5.69	1.22	4

[a] $[\text{pMeSt}]_0$ = 0.76 M, $[\text{acetal units}]_0$ = 4.0 mM, [DTBP] = 10 mM, [ethyl acetate] = 50 mM, in CH_2Cl_2 at 0 ºC. [b] Determined by GPC with polystyrene calibration. [c] The number of branches: calculated from ^{1}H NMR integral ratios.

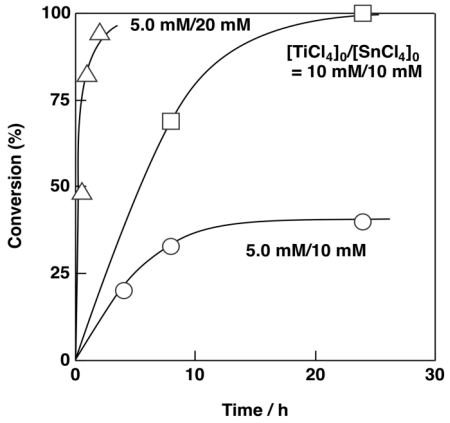


Figure 4. Time-conversion curves for the synthesis of poly(IBVE-*co*-DMEVE)-*graft*-poly(pMeSt) using poly(IBVE-*co*-DMEVE) as a macroinitiator: $[\text{pMeSt}]_0$ = 0.76 M, $[\text{acetal units}]_0$ = 4.0 mM, $[TiCl_4]_0$ = 5.0 or 10 mM, $[SnCl_4]_0$ = 10 or 20 mM, [DTBP] = 10 mM, [ethyl acetate] = 50 mM, in CH_2Cl_2 at 0 ºC; the data correspond to those listed in Table 2.

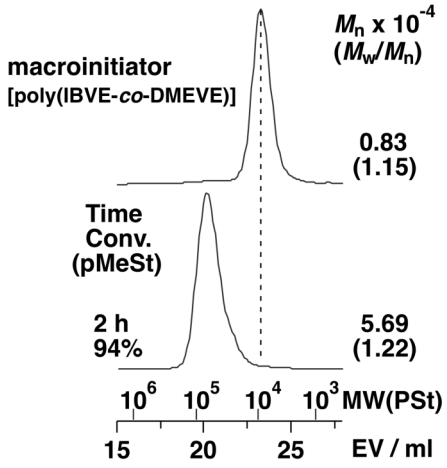


Figure 5. MWD curves for the synthesis of poly(IBVE-*co*-DMEVE)-*graft*-poly(pMeSt) using poly(IBVE-*co*-DMEVE) as a macroinitiator: $[pMeSt]_0$ = 0.76 M, $[acetal\ units]_0$ = 4.0 mM, $[TiCl_4]_0$ = 5.0 mM, $[SnCl_4]_0$ = 20 mM, [DTBP] = 10 mM, [ethyl acetate] = 50 mM, in CH_2Cl_2 at 0 ºC.

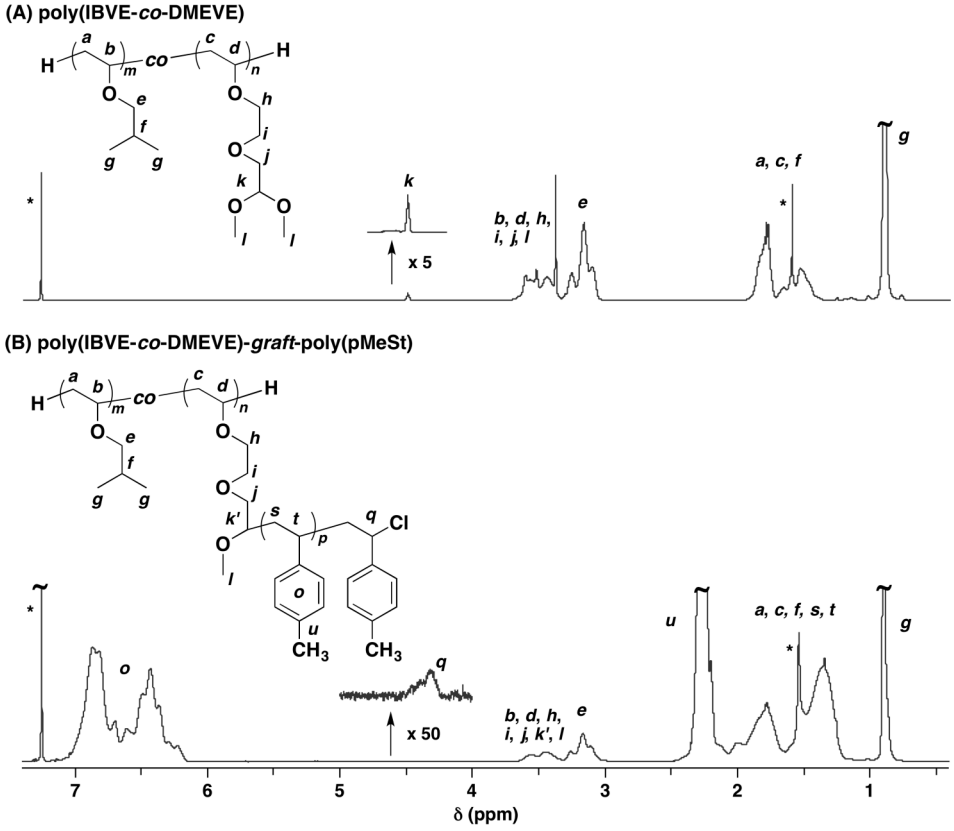


Figure 6. ^{1}H NMR spectra of the linear macroinitiator [M_n(GPC) = 0.83 × 10^4, M_w/M_n(GPC) = 1.15] (A) and poly(IBVE-*co*-DMEVE)-*graft*-poly(pMeSt) [M_n(GPC) = 5.02 × 10^4, M_w/M_n(GPC) = 1.24] (B) (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water).

eak *q*) after the polymerization (Figure 6). These results indicated that the pendant acetal moieties of the macroinitiator were activated quantitatively for the initiation reactions, and a graft copolymer of poly(pMeSt) graft chains was successfully synthesized with the use of the initiating system composed of appropriate concentrations of $TiCl_4$ and $SnCl_4$. The number of branch chains was estimated to be

approximately 4 by ^{1}H NMR, indicating quantitative initiation of the reaction by the copolymer macroinitiator.

The absolute molecular weight of the resulting poly(IBVE-*co*-DMEVE)-*graft*-poly(pMeSt) was determined by GPC analysis using RALS and LALS detectors. The resulting value (M_w = 11 × 10^4) was in good agreement with the calculated value (M_w = 9.8 × 10^4) and was larger than the relative M_w value obtained from the GPC analysis with polystyrene standards (M_w = 7.0 × 10^4), supporting the formation of a branched and compact structure. In addition, the exponent *a* of the Mark–Houwink–Sakurada equation was calculated to be 0.34 from the GPC data obtained with a viscosity detector. The *a* value of less than 0.5 also indicates the formation of a branched structure in the copolymer synthesized using the linear macroinitiator.

Solubility and Thermal Properties of the Resulting Copolymers

The solubilities of the resulting copolymers composed of poly(IBVE) and poly(pMeSt) segments were investigated. Although poly(IBVE) and poly(pMeSt) exhibit similar solubilities in various solvents, poly(IBVE) is soluble in acetone, whereas poly(pMeSt) exhibits upper critical solution temperature (UCST)-type phase separation. The resulting graft copolymer exhibited UCST-type phase separation in acetone, indicating that the solubilities of the resulting copolymers are likely governed largely by the poly(pMeSt) branches.

DSC analysis was also conducted to assess the thermal properties of the copolymers (Table 3, Figure 7). The resulting block copolymer had two glass transition temperatures (T_gs) of –19 °C and 110 °C. These values correspond to the T_gs of the poly(IBVE) and poly(pMeSt) segments, respectively. The T_g of the poly(pMeSt) segment was slightly higher than that of a pMeSt homopolymer because the former has a molecular weight larger than that of the analyzed homopolymer.[18] By contrast, the graft copolymer exhibited a single T_g of 85 °C, most likely because the thermal properties of the graft copolymer are governed mainly by the properties of the branch segments. The lower T_g of the graft copolymer is attributable to the larger amount of terminal end groups and larger free volume.[19]

Table 3. T_g Values of Polymers

polymer	T_g (ºC)[a]
poly(IBVE)	–19[b]
poly($IBVE_{110}$-*co*-$DMEVE_5$)[c]	–27
poly($pMeSt_{88}$)[d]	100
poly($IBVE_{138}$)-*block*-poly($pMeSt_{144}$)[e]	–19, 110
poly($IBVE_{78}$-*co*-$DMEVE_4$)-*graft*-poly($pMeSt_{179}$)[f]	85

[a] The heating and cooling rates were 10 ºC/min. [b] Reference 20. [c] M_n(GPC) = 1.19 × 10^4, M_w/M_n(GPC) = 1.13. [d] M_n(GPC) = 1.04 × 10^4, M_w/M_n(GPC) = 1.19. [e] M_n(GPC) = 3.81 × 10^4, M_w/M_n(GPC) = 1.12. [f] M_n(GPC) = 5.69 × 10^4, M_w/M_n(GPC) = 1.22.

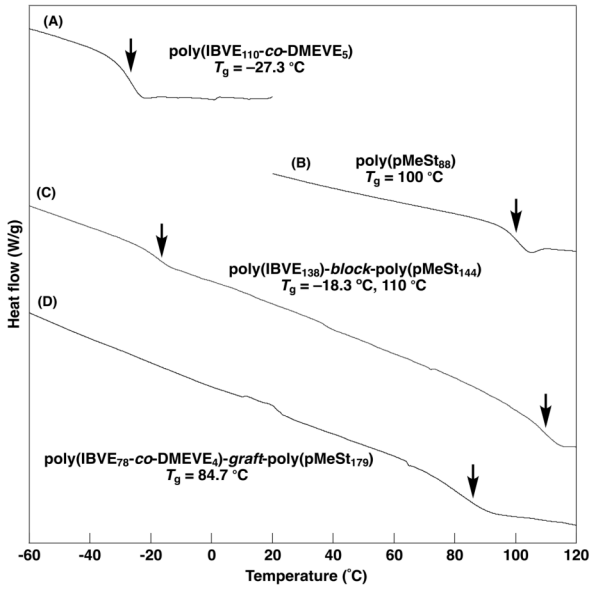
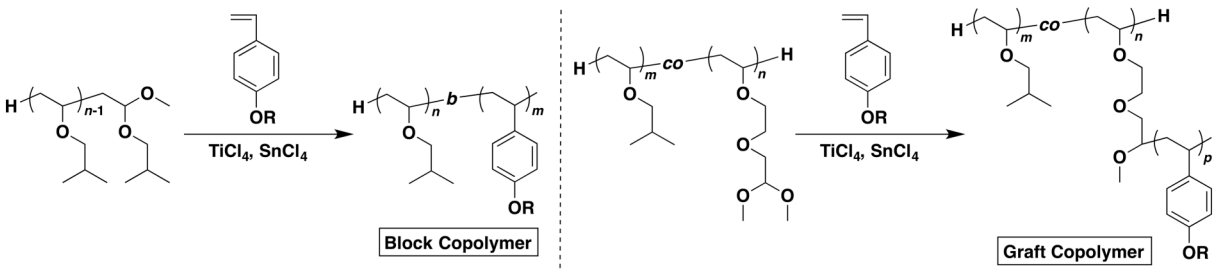


Figure 7. DSC thermograms for poly(IBVE$_{110}$-*co*-DMEVE$_5$) [M_n(GPC) = 1.19 × 10^4, M_w/M_n(GPC) = 1.13] (A), poly(pMeSt$_{88}$) [M_n(GPC) = 1.04 × 10^4, M_w/M_n(GPC) = 1.19] (B), poly(IBVE$_{138}$)-*block*-poly(pMeSt$_{144}$) [M_n(GPC) = 3.81 × 10^4, M_w/M_n(GPC) = 1.12] (C), and poly(IBVE$_{78}$-*co*-DMEVE$_4$)-*graft*-poly(pMeSt$_{179}$) [M_n(GPC) = 5.69 × 10^4, M_w/M_n(GPC) = 1.22] (D); the data correspond to those listed in Table 3.

Polymerizations of Alkoxystyrenes Using Macroinitiators

Copolymer syntheses using acetal-containing macroinitiators were also examined for the polymerization of alkoxystyrenes, which are styrene derivatives that are more reactive than pMeSt[21] (past studies showed that the sequential block copolymerization of IBVE and alkoxystyrenes proceed[22]) (Scheme 3). The cationic polymerizations of pMOS or tBOS were performed using an acetal end-containing poly(IBVE) as a macroinitiator under conditions similar to those for the polymerization of pMeSt, except that a larger amount of ethyl acetate was employed. The polymerizations proceeded smoothly, selectively producing block copolymers with narrow MWDs (M_w/M_n < 1.1) (Figure 8). These polymerizations were not accompanied by side reactions or unreacted macroinitiators.

Scheme 3. Synthesis of the Block and Graft Copolymers via Living Cationic Polymerization of Alkoxystyrens Using Macroinitiator.



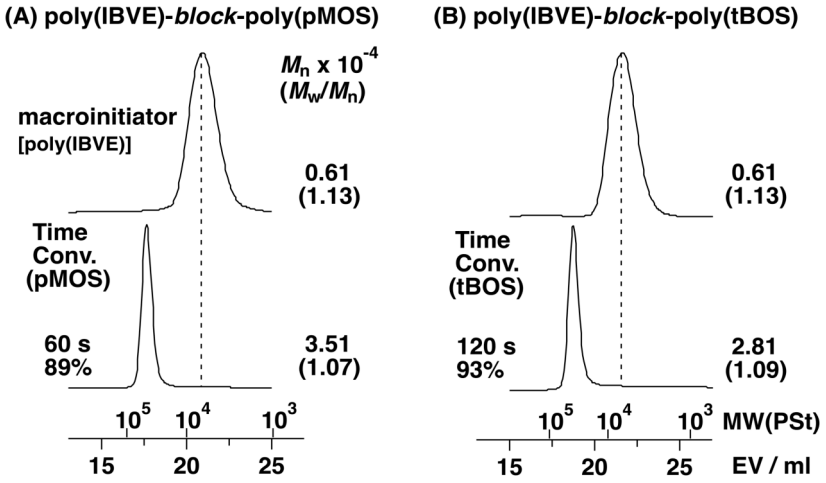


Figure 8. MWD curves for the synthesis of poly(IBVE)-*block*-poly(alkoxystyrene)s using poly(IBVE) as a macroinitiator: $[monomer]_0$ = 0.75 M (A) or 0.53 M (B), $[poly(IBVE)]_0$ = 4.0 mM, $[TiCl_4]_0$ = 5.0 mM, $[SnCl_4]_0$ = 10 mM, [DTBP] = 10 mM, [ethyl acetate] = 1.0 M (A) or 0.50 M (B), in CH_2Cl_2 at 0 ºC.

For the syntheses of graft copolymers containing poly(alkoxystyrene) segments the cationic polymerization of pMOS using poly(IBVE-*co*-DMEVE) as a macroinitiator was performed under similar conditions as for the synthesis of poly(IBVE)-*block*-poly(pMOS). The initiation efficiency of the synthesis of graft copolymers using pMOS was low when equimolar amounts of $TiCl_4$ and acetal units were employed (entry 1 in Table 4). In turn, the reaction using a higher concentration of $TiCl_4$ proceeded without the occurrence of any side reactions unlike the case of tBOS (vide infra). Very high initiation efficiencies were accomplished with the use of a five-fold molar excess of $TiCl_4$ to acetal units. The polymerization was complete in 3 min, yielding a product with a relatively narrow MWD (M_w/M_n = 1.30) [entry 2 in Table 4; Figure 9 (A)]. Approximately 90% of the acetal units on the side chains of the macroinitiator were activated during the polymerization, as confirmed by ^{1}H NMR spectroscopy [Figure 10 (A)]. The graft copolymerization using tBOS proceeded also smoothly, and a product with a unimodal MWD was obtained [entry 3 in Table 4; Figure 9 (B), (a)]. However, detailed ^{1}H NMR analysis revealed that half of the acetal moieties on the macroinitiator remained unactivated [Figure 10 (B)]. The polymerization was conducted with

Table 4. Synthesis of Graft Copolymer Containing Poly(alkoxystyrene) by Macroinitiator-$TiCl_4/SnCl_4$ Initiating Systems[a]

entry	monomer	$[TiCl_4]_0$ (mM)	time	conv. (%)	$M_n \times 10^{-4}$ (GPC)[b]	M_w/M_n (GPC)[b]	initiation efficiency (%)[c]	NB[d]
1	pMOS	10	3 min	59	2.86	1.34	~40	2
2		20	3 min	98	6.71	1.30	~90	4
3	tBOS	5.0	10 min	99	13.8	1.58	~50	4

[a] $[monomer]_0$ = 0.75 M (entries 1 and 2) or 0.53 M (entry 3), $[acetal\ units]_0$ = 4.0 mM (entries 1 and 2) or 4.8 mM (entry 3), $[SnCl_4]_0$ = 10 mM, [DTBP] = 10 mM (entries 1 and 3) or 20 mM (entry 2), [ethyl acetate] = 1.0 M (entries 1 and 2) or 0.50 M (entry 3), in CH_2Cl_2 at 0 ºC. [b] Determined by GPC with polystyrene calibration. [c] Determined by ^{1}H NMR analysis. [d] The number of branches: calculated from ^{1}H NMR integral ratios.

a larger concentration of $TiCl_4$ (10 mM) to improve the initiation efficiency. However, the polymerization was hampered by the side reaction between $TiCl_4$ and the *tert*-butoxy group[23] on tBOS [Figure 9 (B), (b)].

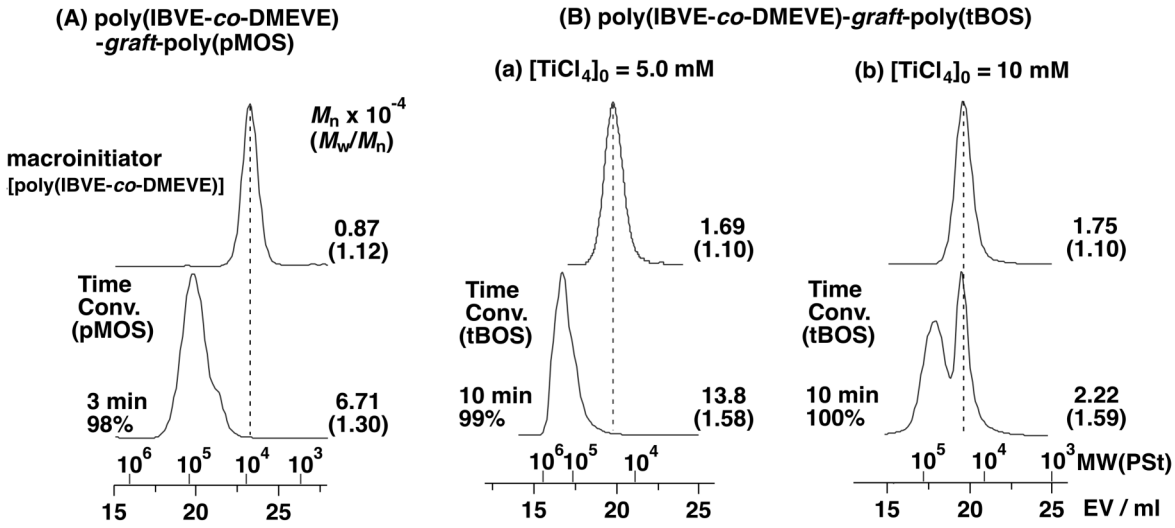


Figure 9. MWD curves for the synthesis of poly(IBVE-*co*-DMEVE)-*graft*-poly(alkoxystyrene)s using poly(IBVE-*co*-DMEVE) as a macroinitiator: $[monomer]_0$ = 0.75 M (A) or 0.53 M (B), $[acetal\ units]_0$ = 4.0 mM (A) or 4.8 mM (B), $[TiCl_4]_0$ = 20 mM (A) or 5.0 mM [(B), (a)] or 10 mM [(B), (b)], $[SnCl_4]_0$ = 10 mM, [DTBP] = 20 mM (A) or 10 mM (B), [ethyl acetate] = 1.0 M (A) or 0.50 M (B), in CH_2Cl_2 at 0 ºC.

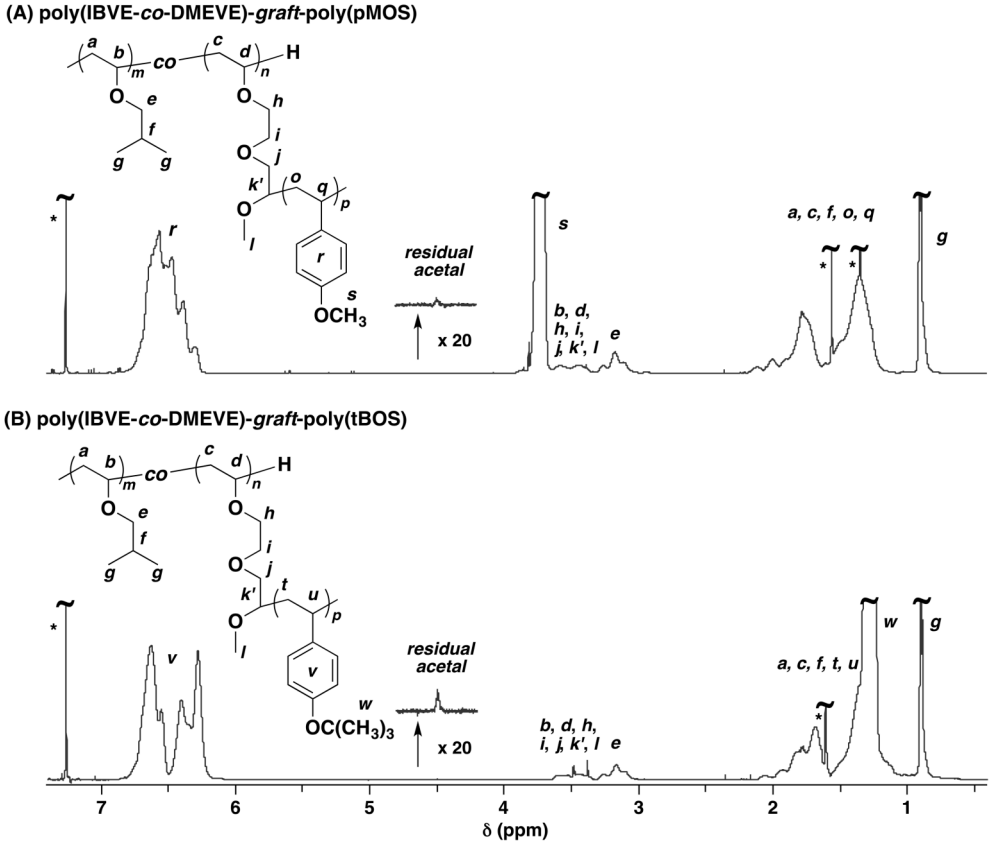


Figure 10. ^1H NMR spectra of poly(IBVE-*co*-DMEVE)-*graft*-poly(pMOS) [M_n(GPC) = 6.71 × 10^4, M_w/M_n(GPC) = 1.30] (A) and poly(IBVE-*co*-DMEVE)-*graft*-poly(tBOS) [M_n(GPC) = 13.8 × 10^4, M_w/M_n(GPC) = 1.58] (B) (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water, and vaseline).

The absolute molecular weight of the resulting poly(IBVE-*co*-DMEVE)-*graft*-poly(pMOS) (entry 2 in Table 4) was determined by GPC analysis using light scattering detectors. The resulting value (M_w = 15 × 10^4) was close to the calculated value (M_w = 11 × 10^4) and was larger than the relative M_w value obtained from the GPC analysis with polystyrene standards (M_w = 8.7 × 10^4). The exponent *a* of the Mark–Houwink–Sakurada equation was calculated to be 0.31. These results indicated the obtained copolymer having branched structure.

Conclusion

The precise synthesis of block and graft copolymers containing poly(alkyl VE) and poly(styrene derivatives) segments was successfully achieved using macroinitiators featuring acetal moieties at the chain ends or on the side chains. Living cationic polymerization of pMeSt, pMOS, or tBOS proceeded via initiation reactions from the acetal units with the use of the $TiCl_4$/$SnCl_4$ initiating system at appropriate concentration ratios. A notable benefit of the method used in this study is that each segment of the block or graft copolymers can be synthesized under completely different reaction conditions. In particular, a block copolymer was successfully obtained from IBVE and pMeSt, monomers that are incompatible under identical conditions and cannot be copolymerized via the sequential addition method. Thus, the synthetic method using macroinitiators with acetal units as latent initiating sites is expected to expand the strategies for the precise synthesis of copolymers with well-defined structures from monomers with very different reactivities.

References

1. (a) Allcock, H. R.; Powell, E. S.; Chang, Y.; Kim, C. *Macromolecules* **2004**, *37*, 7163–7167; (b) Olsen, B. D.; Segalman, R. A. *Macromolecules* **2005**, *38*, 10127–10137; (c) Schappacher, M.; Deffieux, A. *Macromol. Chem. Phys.* **1997**, *198*, 3953–3961; (d) Ryu, S. W.; Hirao, A. *Macromolecules* **2000**, *33*, 4765–4771.
2. (a) Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904–3920; (b) Notestein, J. M.; Lee, L.-B. W.; Regester, R. A. *Macromolecules* **2002**, *35*, 1985–1987.
3. (a) Grubbs, R. B.; Hawker, C. J.; Dao, J.; Fréchet, J. M. J. *Angew. Chem., Int. Ed.* **1997**, *36*, 270–272; (b) Liu, B.; Yuan, C. G.; Hu, C. P. *Macromol. Chem. Phys.* **2001**, *202*, 2504–2508; (c) Venkatesh, R.; Yajjou, L.; Koning, C. E.; Klumperman, B. *Macromol. Chem. Phys.* **2004**, *205*, 2161–2168; (d) Zhang, Y.; Shen, Z.; Yang, D.; Feng, C.; Hu, J.; Lu, G.; Huang, X. *Macromolecules* **2010**, *43*, 117–125; (e) Chung, T. C.; Lu, H. L.; Ding, R. D. *Macromolecules* **1997**, *30*, 1272–1278; (f) Villarroya, S.; Zhou, J.; Thurecht, K. J.; Howdle, S. M. *Macromolecules* **2006**, *39*, 9080–9086; (g) Beers, K. L.; Gaynor, S. G.; Matyjaszewski, K. *Macromolecules* **1998**, *31*, 9413–9415.
4. (a) Ross, S. G.; Müller, A. H. E.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 8331–8335; (b) Shinoda, H.; Matyjaszewski, K.; Okrasa, L.; Mierzwa, M.; Pakula, T. *Macromolecules* **2003**, *36*, 4772–

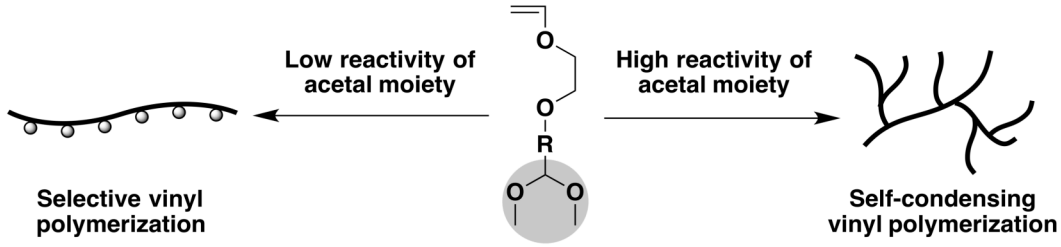
4778; (c) Muehlebach, A.; Rime, F. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3425–3439.

5. (a) Coca, S.; Matyjaszewski, K.; *Macromolecules* **1997**, *30*, 2808–2810; (b) Keszler, B.; Fenyvesi, Gy.; Kennedy, J. P. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 706–714; (c) Bernaerts, K. V.; Du Prez, F. E. *Polymer* **2005**, *46*, 8469–8482.
6. (a) Feldthusen, J.; Iván, B.; Müller, A. H. E. *Macromolecules* **1998**, *31*, 578–585; (b) Higashihara, T.; Feng, D.; Faust, R. *Macromolecules* **2006**, *39*, 5275–5279.
7. (a) Risse, W.; Grubbs, R. H.; *Macromolecules* **1989**, *22*, 1558–1562; (b) Kwon, Y.; Faust, R. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **2005**, *42*, 385–401.
8. Shimomoto, H.; Yoshida, H.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3703–3709.
9. Meirvenne, D. V.; Haucourt, N.; Goethals, E. J. *Polym. Bull.* **1990**, *23*, 185–190.
10. Haucourt, N.; Goethals, E. J.; Schappacher, M.; Deffieux, A. *Macromol. Chem., Rapid Commun.* **1992**, *13*, 329–336.
11. Satoh, K.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **2000**, *33*, 748–753.
12. (a) Higashimura, T.; Kamigaito, M.; Kato, M.; Hasebe, T.; Sawamoto, M. *Macromolecules* **1993**, *26*, 2670–2673; (b) Aoshima, S; Higashimura, T. *Macromolecules* **1989**, *22*, 1009–1013.
13. $LiBH_4$ was used to produce H-terminated polymers [Liu, Q.; Konas, M.; Davis, R. M.; Riffle, J. S. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1709–1717.].
14. Miyashita, K.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1994**, *27*, 1093–1098.
15. De, P.; Faust, R. *Macromolecules* **2005**, *38*, 5498–5505.
16. Sawamoto, M.; Higashimura, T. *Makromol. Chem., Macromol. Symp.* **1990**, *32*, 131–144.
17. Ohmura, T.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1994**, *27*, 3714–3720.
18. Fox, T. G.; Flory, P. J. *J. Appl. Phys.* **1950**, *21*, 581–591.
19. Roovers, J. E. L.; Toporowski, P. M. *J. Appl. Polym. Sci.* **1974**, *18*, 1685–1691.
20. Andrews, R. J.; Grulke, E. A. in *Polymer Handbook*, 4th ed.; Brandrup, J.; Immergut, E. H.; Grulke, E. A. Eds.; Wiley-Interscience: New York, 1999; Chapter VI, p 215.
21. Kolishetti, N.; Faust, R. *Macromolecules* **2008**, *41*, 3842−3851.
22. (a) Higashimura, T.; Mitsuhashi, M.; Sawamoto, M. *Macromolecules* **1979**, *12*, 178–182; (b) Kojima, K.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1991**, *24*, 2658–2662.
23. Flensberg, H.; Kops, J.; Iván, B. *Polym. Bull.* **1995**, *35*, 583–590.

Supporting Information

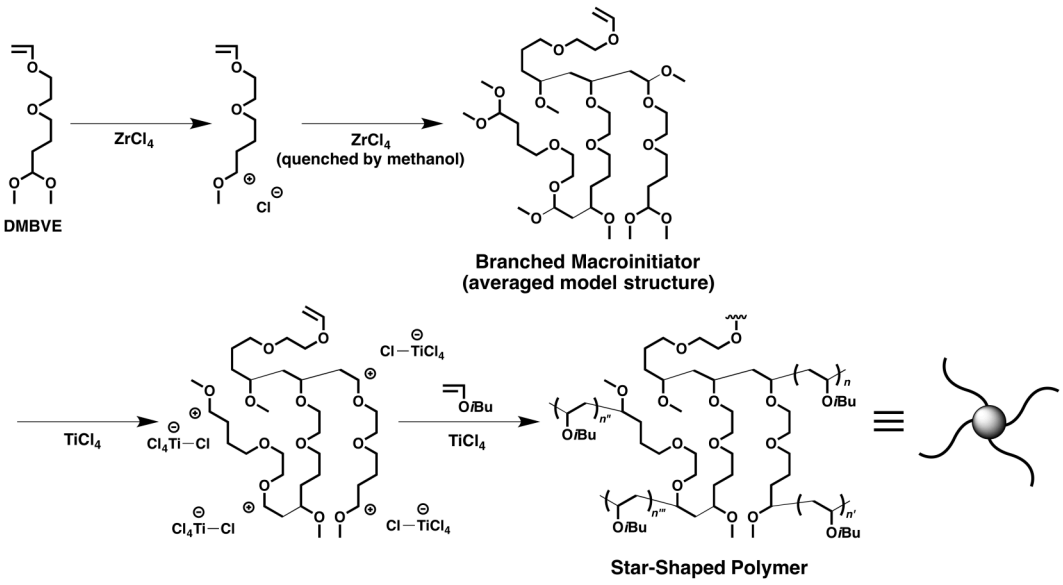
The reactivity of acetal can be adjusted by altering the electron density at the acetal carbon using electron-donating or electron-withdrawing substituents. Therefore, the reactivity of acetal moieties in cationic polymerization can also be adjusted through the design of acetal-containing monomers, which allows for the synthesis of polymers with various well-defined structures (Scheme S1).

Scheme S1. Control of Reactivity of Acetal Moiety of Acetal-Containing VE for Syntheses of Polymers with Various Structures.



The synthesis of star-shaped copolymers was examined using a branched oligomer, produced by the self-condensing vinyl polymerization of acetal-containing VE with butylene spacer (DMBVE), as a multifunctional macroinitiator (Scheme S2). First, the self-condensing vinyl polymerization of DMBVE was conducted with $ZrCl_4$ as a catalyst for the preparation of a hyperbranched macroinitiator. The reaction proceeded smoothly to reach quantitative conversion in 8 h (Figure S1, upper). The obtained DMBVE oligomer with an average of four acetal moieties in one molecule, derived from the quenching reaction using methanol, was used as a multifunctional macroinitiator to synthesize a star-shaped polymer via the "core-first" method. The cationic polymerization of IBVE using the macroinitiator was conducted with $TiCl_4$, a catalyst that is effective in the quantitative activation of acetal moieties. IBVE was steadily consumed to yield a polymer with a bimodal MWD (Figure S1, lower). The peak in the higher-MW region was assigned to a star-shaped polymer generated from the macroinitiator, whereas the peak in the lower-MW region was likely to be a linear poly(IBVE) derived from initiation by protic impurities, such as adventitious water. All of the acetal units of the macroinitiator were activated during the polymerization, resulting in the formation of a star-shaped polymer with an average of four polymer chain arms, as confirmed by ^{1}H NMR spectroscopy [Figure S2 (B)].

Scheme S2. Synthetic Route of the Star-Shaped Polymer via Living Cationic Polymerization Using Multi Functional Macroinitiator.



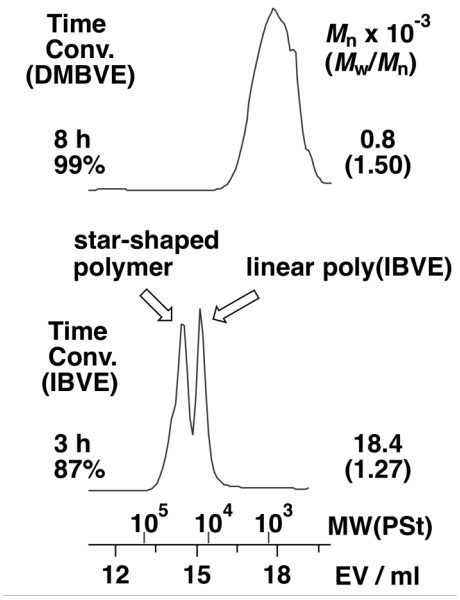


Figure S1. MWD curves for he polymerization of DMBVE and the synthesis of poly(IBVE)-*star* using poly(DMBVE) as a macroinitiator: $[DMBVE]_0$ = 0.24 M, $[ZrCl_4]_0$ = 10 mM, [DTBP] = 10 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC; $[IBVE]_0$ = 0.76 M, [acetal units]$_0$ = 4.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 20 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC.

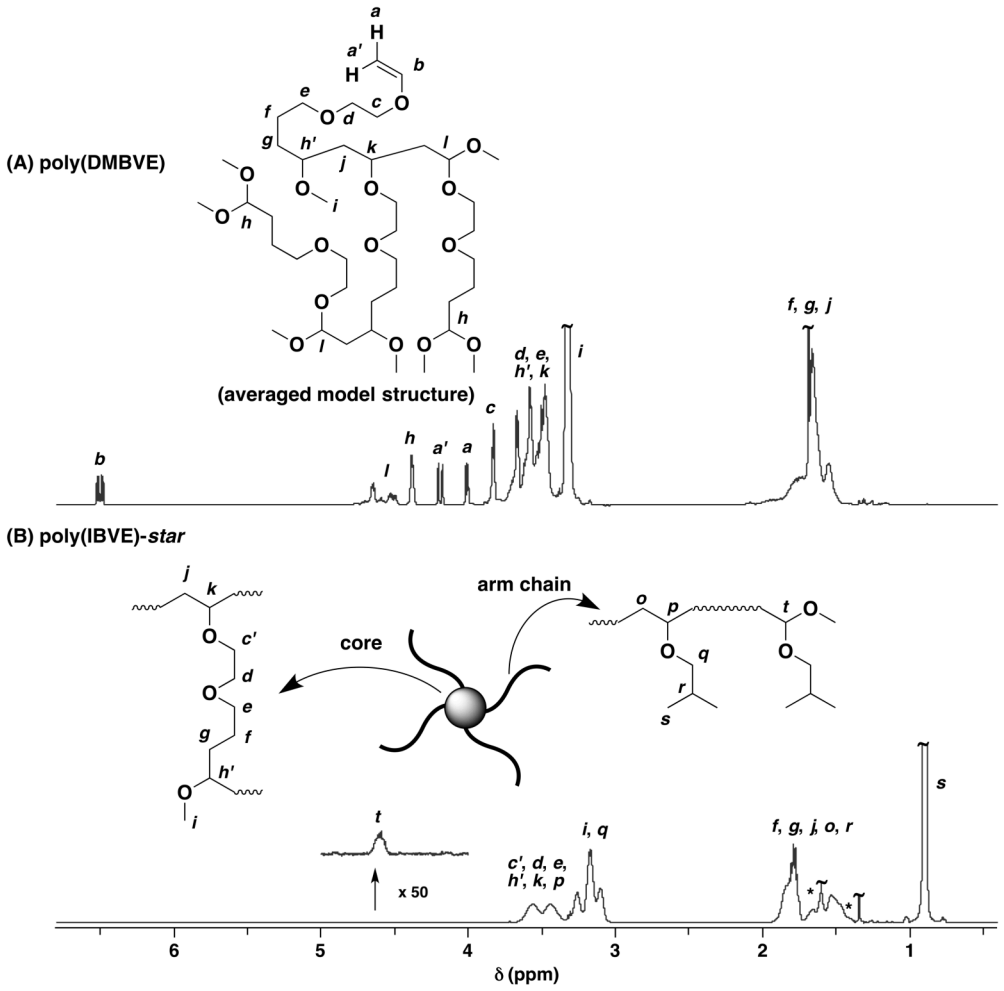


Figure S2. ^{1}H NMR spectra of the blanched macroinitiator [M_n(GPC) = 0.8 × 10^3, M_w/M_n(GPC) = 1.50] (A) and poly(IBVE)-*star* [M_n(GPC) = 18.4 × 10^3, M_w/M_n(GPC) = 1.27] (B) (500.16 MHz, in $CDCl_3$ at 30 ºC; *water, vaseline).

Chapter 3

End-Capping Reaction of Living Cationic Propagating Poly(Vinyl Ether)s Using Appropriate Alcohols: Precision Synthesis of Macromonomers for the Preparation of Graft Copolymers via a Grafting-Through Method

Introduction

Chain-end structures of polymers have appreciable effects on a variety of polymer properties such as stimuli responsivity, self-assembling behavior, and surface properties.[1,2] In addition, polymers containing a functional group at the chain end can be attached to functional molecules, such as drugs and biomolecules, to provide them with characteristic functions.[3–5] To effectively fulfill these functions, functional groups need to be incorporated quantitatively onto the chain ends of polymers. In this respect, living polymerization techniques are very useful for the precise synthesis of end-functionalized polymers containing definite terminal structures due to the absence of side reactions such as the chain-transfer reaction.[6–8] The following two methods are typically employed for the synthesis of end-functionalized polymers: (1) living polymerization via initiation with functional initiators and (2) end-capping reaction of living propagating chains by functional terminators. Moreover, telechelic polymers can be synthesized by combining these two methods.

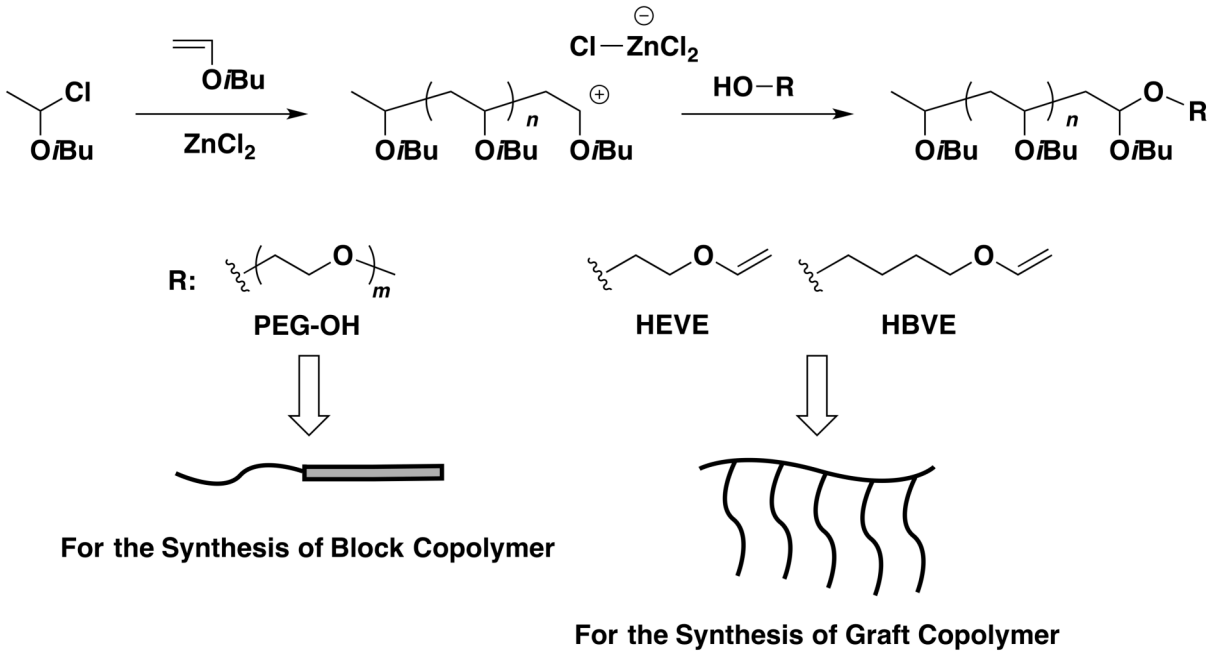
In the living cationic polymerization of vinyl ethers (VEs) or highly reactive styrene derivatives, end-functionalized polymers are easily prepared by quenching the polymerization reaction with nucleophilic compounds. When a nucleophilic compound is added to the reaction solution during living cationic polymerization, a substitution reaction occurs between the nucleophilic compound and the carbon–heteroatom bond, such as a carbon–halogen bond at the propagating chain end, resulting in the incorporation of the nucleophilic compound-derived moiety into the ω-end of the polymer chain. Various nucleophiles such as amines,[9] anilines,[10] malonate anions,[11] silyl ketene acetals,[12] silyl enol ethers,[13] and fullerene derivatives[14] have been used as quenchers for the living cationic polymerization of VEs, which successfully yielded ω-end functionalized poly(VE)s. Alcohols have also been employed as nucleophilic compounds for the synthesis of end-functionalized poly(VE)s.[15,16] The acetal moiety generated at the ω-end by the reaction with an alcohol[17] can be used as the initiating site for the subsequent living cationic polymerization of VEs or styrene derivatives through activation with appropriate catalysts.[18]

Macromonomers can also be synthesized by end-capping reactions using a quencher that has a vinyl group. In fact, macromonomers containing a poly(VE) segment have been prepared by quenching the living cationic polymerization of VEs with alcohols having a vinyl group.[19,20] The acryloyl in methacryloyl group-containing macromonomers obtained via such methods can be polymerized via a radical mechanism

to yield graft polymers. In contrast, cationic polymerizations of macromonomers bearing a vinyloxy group were difficult because the acetal moiety of the macromonomers, which was generated via the reaction between the VE-derived carbocation and the hydroxy group of the alcohol quencher, was degraded by Lewis acid catalysts. Therefore, Lewis acid catalysts that catalyze the propagating reaction but are inert toward acetal moieties are needed for the cationic polymerization of these macromonomers.

The present chapter focuses on the synthesis of end-functionalized poly(VE)s using various alcohols as quenchers for living cationic polymerization (Scheme 1). In particular, macromonomers are prepared using alcohol quenchers and subsequently (co)polymerized using highly selective Lewis acid catalysts.[18,21] To elucidate the effect of alcohol quenchers on the stabilities of the resulting acetal end structures, quenching reactions are first examined using primary, secondary, and tertiary alcohols. Based on the obtained results, macromonomers containing a vinyloxy group are synthesized using appropriate alcohols. Subsequently, graft copolymers are synthesized via cationic copolymerization of these macromonomers.

Scheme 1. Quenching Reactions of Living Cationic Polymerization of IBVE with Various Alcohols.



Experimental

Materials

Ethylene glycol monovinyl ether (HEVE; TCI; >98.0%) and tetramethylene glycol monovinyl ether (HBVE; TCI; >97.0%) were distilled over calcium hydride under reduced pressure. Ethanol (Nacalai Tesque; ≥99.5%), 2-propanol (Nacalai Tesque; 99%), *tert*-butyl alcohol (Aldrich; >99.5%), and triethylamine (TEA; Wako; >99.0%) were used as received. α-Hydroxy-ω-methoxy polyethylene glycol (PEG-OH; NOF Corporation; SUNBRIGHT® MEH-50H; $M_n = 5.1 \times 10^3$, $M_w/M_n = 1.02$) was dried by the azeotropic method using toluene before use. Other materials were prepared and used as described in Chapter 2.

Polymerization Procedure

Synthesis of the Macromonomer

The polymerization was performed under a dry nitrogen atmosphere in a glass tube with a three-way stopcock. The glass tube was baked using a heat gun (Ishizaki; PJ-206A; blow temperature ~450 °C) under dry nitrogen for 10 min before use. The polymerization of isobutyl VE (IBVE) in toluene at –30 °C and the subsequent quenching reaction using HEVE as the quencher are described as a representative example. The polymerization of IBVE was initiated by the addition of a prechilled $ZnCl_2$ solution in toluene (0.40 mL; 50 mM) to a mixture (3.6 mL) of toluene, ethyl acetate, IBVE, and IBVE–HCl at 0 °C using a dry syringe. After a predetermined period, the polymerization was terminated using chilled HEVE containing a small amount (1 wt%) of TEA (2.0 mL). The quenched reaction mixture was diluted with hexane and then washed with water to remove the initiator residues. The volatiles were then removed under reduced pressure. The monomer conversion was determined by a gravimetric method.

Synthesis of the Graft Copolymer by Copolymerization of a Macromonomer

For the copolymerization of a macromonomer and IBVE, a solution in toluene (0.80 mL) of a predried macromonomer, ethyl acetate, IBVE, and a solution of cationogen (IBVE–HCl) in toluene (0.10 mL; 20 mM) were successively added to the tube using dry syringes. To this solution, $ZnCl_2$ in toluene (0.10 mL; 25 mM) was added to start the copolymerization. After a predetermined period, the polymerization was terminated using chilled methanol containing a small amount (0.1%) of aqueous ammonia solution (1.0 mL). The quenched reaction mixture was diluted with CH_2Cl_2 and then washed with water to remove the initiator residues. The volatiles were then removed under reduced pressure. The conversion of macromonomer and IBVE were determined by a gravimetric method and ^{1}H NMR analysis.

Characterization

The MWD of the polymers and NMR spectra were measured as described in Chapter 2. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI–TOF–MS) was conducted on a Shimadzu/Kratos AXIMA-CFR spectrometer (linear mode; voltage, 20 kV; pressure, $<1.9 \times 10^{-3}$ Pa) using dithranol and sodium trifluoroacetate as matrix and ion source, respectively. A solution (2−3 μL) containing the polymer, matrix, and ion source (polymer/matrix/ion source = 2 mg/7 mg/1 mg in 1 mL of THF) was cast onto a stainless steel sample plate (Shimadzu Biotech, DE1580TA) and loaded into the spectrometer.

Results and Discussion

Effects of the Structure of Alcohol on the Stability of the Acetal End

To determine the appropriate structure of alcohol for the synthesis of end-functionalized poly(VE)s by the end-capping technique, quenching reactions using ethanol, 2-propanol, and *tert*-butyl

alcohol were examined in the living cationic polymerization of IBVE. The living cationic polymerization was conducted using the IBVE–HCl/$ZnCl_2$ initiating system in the presence of ethyl acetate in toluene at 0 °C. In the living cationic polymerization, when methanol was used as a quencher, the obtained poly(IBVE) had an acetal moiety at the *ω*-end quantitatively. Then, the other employed alcohols successfully quenched the polymerization reaction, resulting in the cessation of monomer consumption. ^{1}H NMR analysis of the product polymers, however, revealed that the efficiency of the chain-end functionalization obviously became low due to the bulkiness of the quencher. The quenching reaction using ethanol quantitatively yielded poly(IBVE) with an acetal moiety at the chain end in near quantitative yield (95%) in similar to that using methanol. In contrast, the acetal functionality of the polymer obtained using 2-propanol as the quencher was 88%. Moreover, the functionality was 43% when *tert*-butyl alcohol was used as the quencher.

The low efficiency of chain-end functionalization using secondary and tertiary alcohols as quenchers was most likely due to the low stability of acetal moieties consisting of secondary or tertiary alkoxy groups. It was reported that the hydrolysis reaction of diisopropyl acetal proceeded under milder conditions than those for the reaction of dimethyl acetal.[22] In the present study, some of the acetal moieties generated from the isopropoxy or *tert*-butoxy groups via the quenching reaction appeared to decompose during the purification steps. Indeed, peaks for the aldehyde moieties that were most likely derived from the hydrolysis of acetal moieties were observed in the ^{1}H NMR spectrum of the poly(IBVE) obtained by quenching with *tert*-butyl alcohol. Therefore, primary alcohols should be used as quenchers for the synthesis of end-functionalized polymers by living cationic polymerization.

A polymer containing a primary alcohol structure at the chain end was also useful as a macroterminator for an efficient quenching reaction. When the monomer conversion reached approximately 90% in the living cationic polymerization of IBVE, PEG-OH (M_n = 5.1 × 10^3), which has a primary hydroxy group at the chain end, was added as the quencher (Figure 1). The molar ratio of the quencher to the living

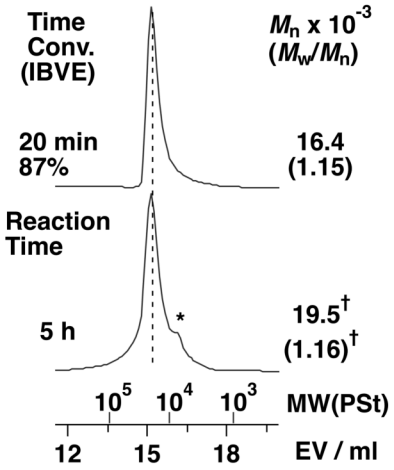


Figure 1. MWD curves for the synthesis of poly(IBVE)-*block*-PEG using PEG-OH as a macroterminator. IBVE polymerization: $[IBVE]_0$ = 0.76 M, $[IBVE–HCl]_0$ = 4.0 mM, $[ZnCl_2]_0$ = 5.0 mM, [ethyl acetate] = 1.0 M, in toluene at 0 ºC. Coupling reaction: $[PEG\text{-}OH]_{add}/[IBVE–HCl]_0$ = 10. †For a main peak. *Residual macroterminator.

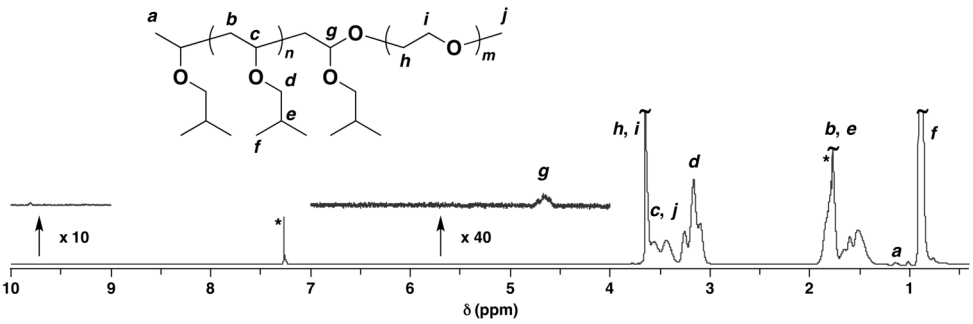


Figure 2. ^{1}H NMR spectrum of poly(IBVE)-*block*-PEG [M_n(GPC) = 19.5 × 10^3, M_w/M_n(GPC) = 1.16] (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water).

propagating chains was set to 10. The reaction between the living propagating end and the hydroxy group successfully proceeded to result in the efficient incorporation of the PEG moiety into the ω-end of the poly(IBVE) chain. The efficiency of the end functionalization was determined to be approximately 93% by ^{1}H NMR spectroscopy (Figure 2).

Synthesis of Macromonomer Using VEs Containing a Hydroxy Group as Quenchers

For the synthesis of macromonomers bearing a VE moiety, primary hydroxy group-containing VEs were employed as quenchers for living cationic polymerization. When HEVE was added into a reaction solution of the living polymerization of IBVE, the polymerization reaction stopped immediately. The ratio of the acetal moiety generated at the ω-end (4.7 ppm) to the α-end moiety (1.1 ppm) was found to be almost quantitative by ^{1}H NMR analysis. However, the MALDI–TOF–MS spectrum of the obtained polymer had two series of peaks [Figure 3 (A), (a)]. The *m*/*z* values of the main peaks agreed with the mass values of the ideal polymer structures with the ω-end derived from HEVE. In contrast, the *m*/*z* values of the other series of peaks (+88 from the main peaks) were in good agreement with the mass values of the polymer chains with two HEVE units. This result suggests that a cationic vinyl addition reaction of the vinyl ether moiety of HEVE with the propagating chain occurred before the quenching reaction by the hydroxyl moiety of HEVE. After the polymerization reactions were examined under various conditions, such side reactions were found to be suppressed by quenching the polymerization reaction at lower temperature, –30 °C, resulting in one series of peaks in the MALDI spectrum of the product polymer [Figure 3 (A), (b)]. The propagation rate was slow at a lower temperature, resulting in suppression of extra addition of HEVE. Under the same conditions, HBVE, a hydroxy group-containing VE with a longer alkylene chain than HEVE, also functioned as a quencher to yield a polymer with a vinyloxy group at the ω-end without any side reactions [Figure 3 (B)]. Thus, two types of macromonomers were synthesized quantitatively using primary hydroxy group-containing VEs as quenchers at low temperature.

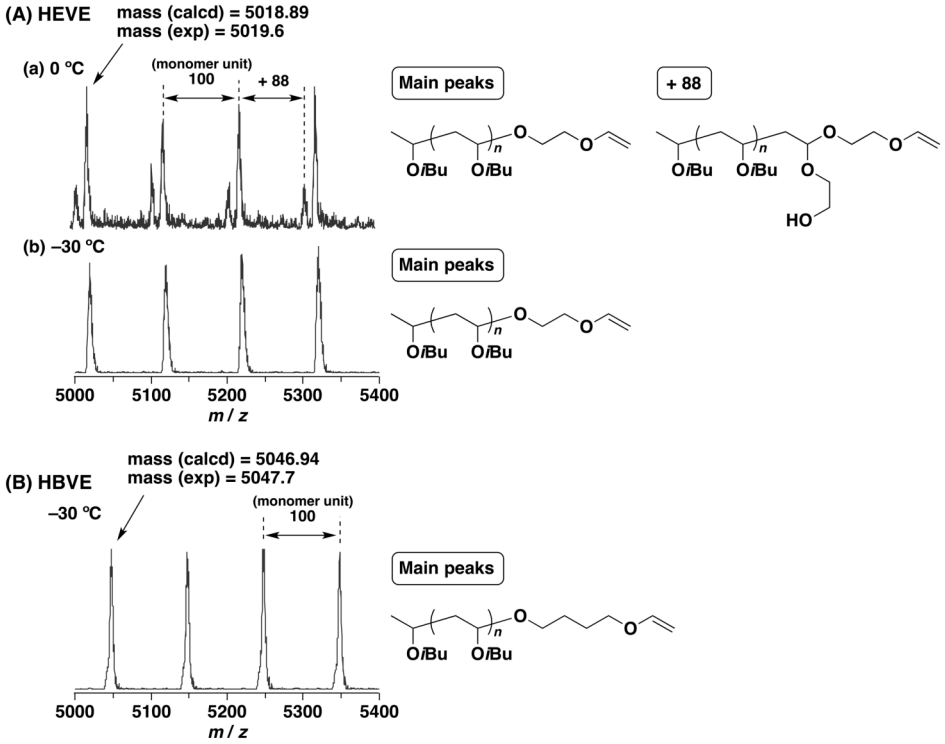


Figure 3. MALDI–TOF–MS spectra of end-functionalized poly(IBVE)s obtained using HEVE (A) and HBVE as a quencher (B) {(A) (a): M_n(GPC) = 7.4 × 10^3, M_w/M_n(GPC) = 1.07; (b) M_n(GPC) = 6.3 × 10^3, M_w/M_n(GPC) = 1.04; (B) M_n(GPC) = 5.7 × 10^3, M_w/M_n(GPC) = 1.03 (polymerization conditions: $[IBVE]_0$ = 0.76 M, $[IBVE–HCl]_0$ = 10 mM, $[ZnCl_2]_0$ = 5.0 mM, [ethyl acetate] = 1.0 M, in toluene at 0 or –30 ºC)}.

Synthesis of Graft Copolymers Using Macromonomers Having a VE Structure

The macromonomers obtained from the quenching reaction using HEVE [poly(IBVE)-EVE] and HBVE [poly(IBVE)-BVE] were cationically polymerized for the synthesis of graft copolymers via the grafting-through method. $ZnCl_2$ was used as a catalyst to avoid the degradation of the acetal moiety[18,21] of the macromonomers. The reactions of both macromonomers proceeded smoothly to result in the quantitative consumption of vinyl groups, as confirmed by the ^{1}H NMR spectra. However, the peak of the product obtained from poly(IBVE)-EVE in GPC analysis was very similar to that of the original macromonomer [Figure 4 (A)]. ^{1}H NMR analysis revealed that a five-membered cyclic acetal moiety was generated after the reaction [Figure 5 (B)]. A possible mechanism for the generation of the cyclic acetal structure is shown in Scheme 2. After the reaction of the initiating or propagating carbocation with the vinyl group of the macromonomer, the generated carbocation abstracted the alkoxy group of the acetal moiety of the macromonomer to form the cyclic acetal structure.[23] This reaction generated a new propagating chain derived from the poly(IBVE) moiety of the macromonomer, which triggered the subsequent similar reactions. In the case of poly(IBVE)-BVE, the seven-membered cyclic acetal was generated in a similar manner [Figure 5 (D)], but oligomers were partly produced through the vinyl-addition reactions [Figure 4 (B)]. The difference between poly(IBVE)-EVE and poly(IBVE)-BVE most likely stemmed from the efficiency of the formation of five- and seven-membered cyclic acetal structures.[24]

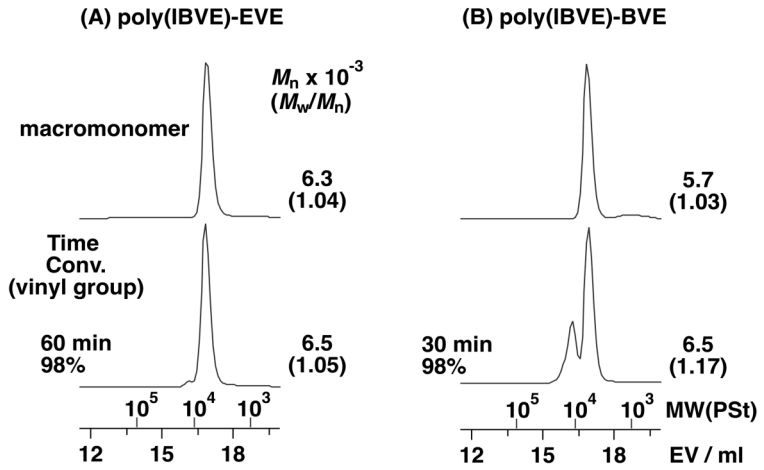


Figure 4. MWD curves for the polymerization of poly(IBVE)-EVE (A) or poly(IBVE)-BVE (B): $[\text{macromonomer}]_0$ = 20 mM, $[\text{IBVE–HCl}]_0$ = 2.0 mM, $[ZnCl_2]_0$ = 2.5 mM, [ethyl acetate] = 1.0 M, in toluene at 0 ºC.

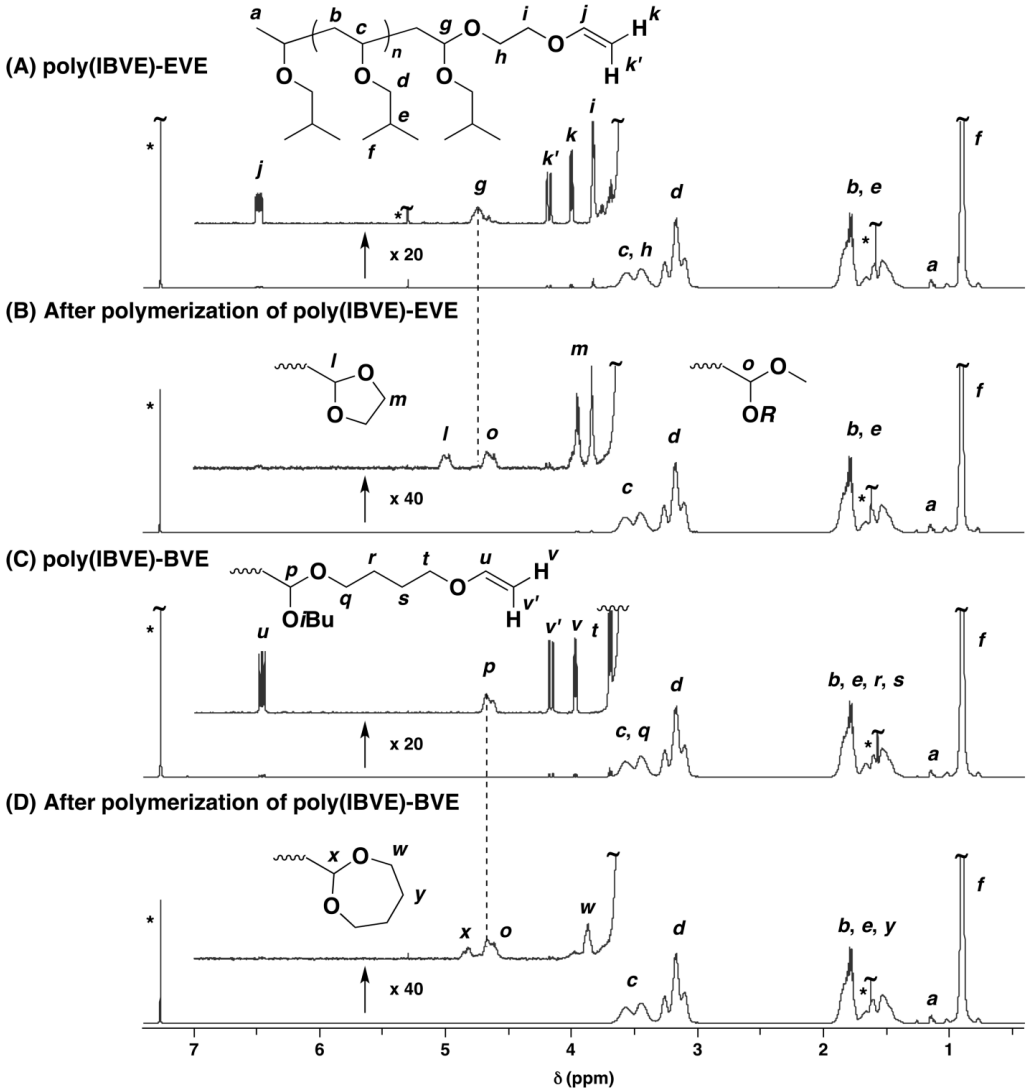
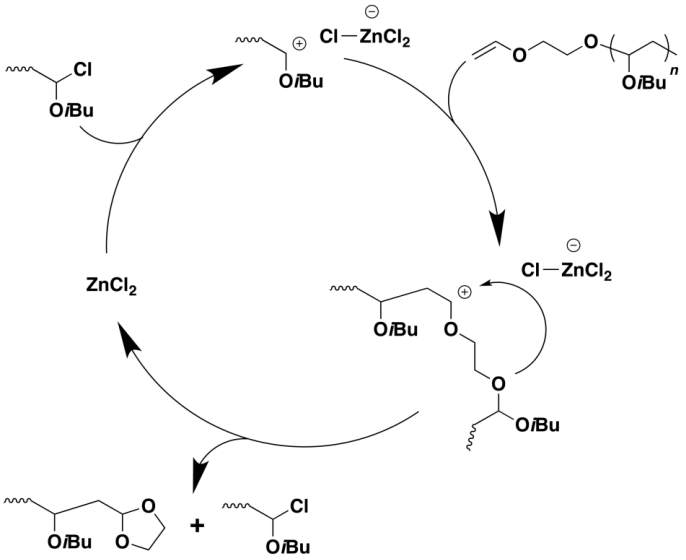


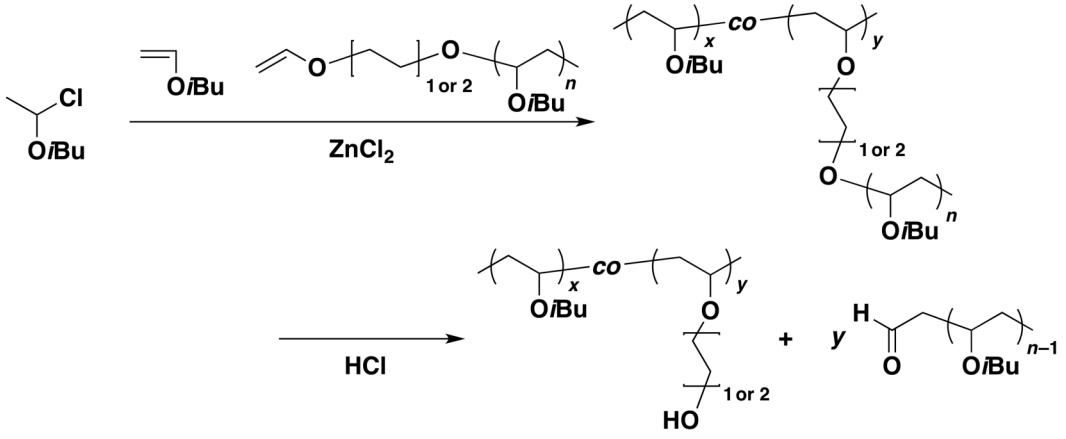
Figure 5. ^{1}H NMR spectra of poly(IBVE)-EVE (A) [M_n(CPC) = 6.3 × 10^3, M_w/M_n(GPC) = 1.04], the product of the polymerization of poly(IBVE)-EVE (B) [M_n(GPC) = 6.5 × 10^3, M_w/M_n(GPC) = 1.05], poly(IBVE)-BVE (C) [M_n(GPC) = 5.7 × 10^3, M_w/M_n(GPC) = 1.03], and the product of the polymerization of poly(IBVE)-BVE (D) [M_n(GPC) = 6.5 × 10^3, M_w/M_n(GPC) = 1.17] (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, CH_2Cl_2, and water).

Scheme 2. Postulated Mechanism for the Cyclization Reaction of Poly(IBVE)-EVE.



Steric hindrance of the macromonomers was considered to be responsible for the decrease in the rate of the propagation reactions and the preferential cyclization reactions forming cyclic acetal structures. Copolymerizations of macromonomers with IBVE were examined under similar conditions to those of the homopolymerization reactions (Scheme 3, upper). The copolymerization of poly(IBVE)-EVE and IBVE proceeded smoothly via the consumption of both monomers to yield high MW products. The MW of the products, however, did not increase with the increase in monomer conversion values [Figure 6 (A)]. The uncontrolled copolymerization was attributed to the side reaction that formed the five-membered cyclic acetal structure in a manner similar to the homopolymerization of poly(IBVE)-EVE, as confirmed by the ^{1}H NMR spectrum [Figure 7 (A)]. In contrast, the peak of the MWD curves of the products obtained in the copolymerization of poly(IBVE)-BVE and IBVE shifted to the higher MW region [Figure 6 (B)]. In addition, the ^{1}H NMR spectrum reveals that the copolymerization proceeded without the generation of cyclic acetal

Scheme 3. Synthesis of Graft Copolymers Using Grafting-Through Method via Cationic Polymerization and Acid Hydrolysis of Acetal Moieties at Connecting Points of Branch Segments.



structures [Figure 7 (B)]. Thus, the synthesis of graft copolymers via the cationic copolymerization of an acetal-containing macromonomer was accomplished by using a macromonomer with an appropriate structure. The absolute MW of the obtained polymer (M_w = 75 × 10^3), determined by GPC analysis using light scattering detectors, was obviously larger than the relative MW (M_w = 37 × 10^3) calculated based on

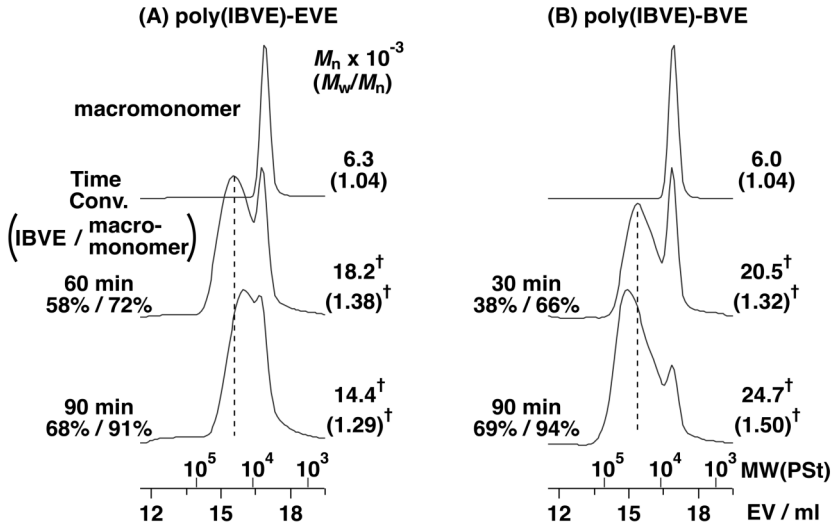


Figure 6. MWD curves for the copolymerization of IBVE with poly(IBVE)-EVE (A) or poly(IBVE)-BVE (B): $[IBVE]_0$ = 1.5 M, $[macromonomer]_0$ = 20 mM, $[IBVE–HCl]_0$ = 2.0 mM, $[ZnCl_2]_0$ = 2.5 mM, [ethyl acetate] = 1.0 M, in toluene at 0 ºC. †For main peaks.

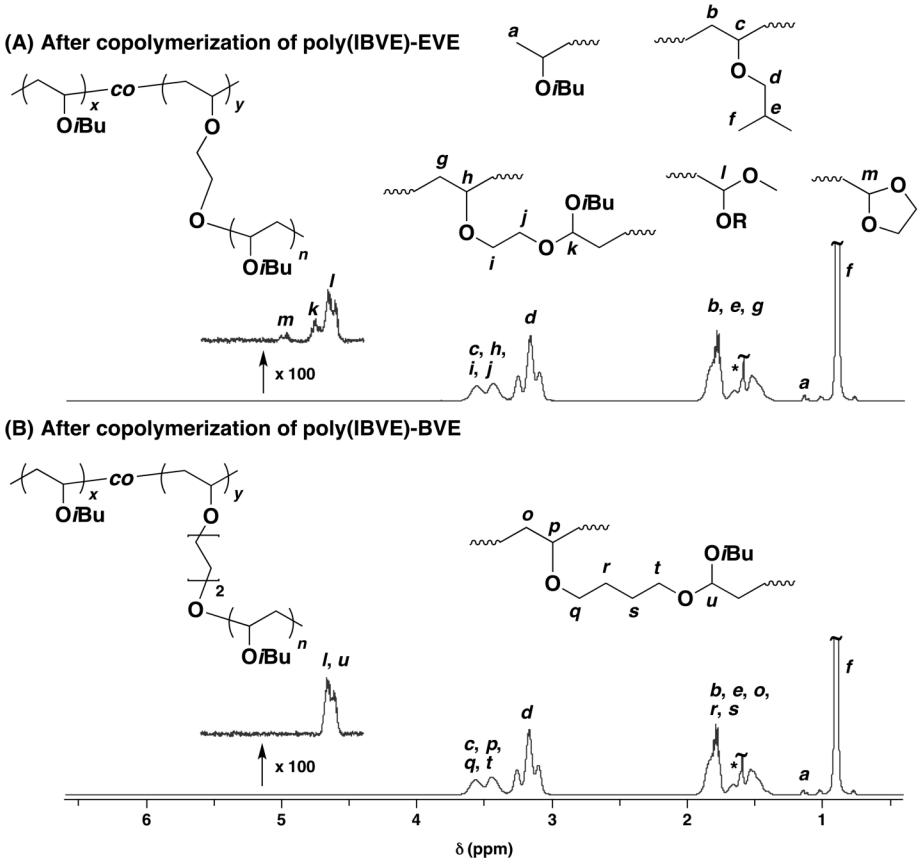


Figure 7. ^{1}H NMR spectra of the products of the copolymerizations of IBVE with poly(IBVE)-EVE (A) [M_n(GPC) = 14.4 × 10^3, M_w/M_n(GPC) = 1.29], and poly(IBVE)-BVE (B) [M_n(GPC) = 24.7 × 10^3, M_w/M_n(GPC) = 1.50] (500.16 MHz, in $CDCl_3$ at 30 ºC; *water).

polystyrene calibration. In addition, the value of the exponent *a* of the Mark–Houwink–Sakurada equation was smaller (a = 0.57) than the values of linear poly(IBVE) ($a \sim 0.7$). These results also support the generation of a polymer containing a branched structure.

Because the graft copolymer obtained by the copolymerization of poly(IBVE)-BVE and IBVE contained acetal structures on the side chains derived from the macromonomer, the branch segments were completely cleaved from the backbone under acidic conditions (Scheme 3, lower). The decomposition reaction was conducted using 0.5 M HCl(aq) in 1,2-dimethoxyethane at room temperature for 3 h (Figure 8).[25] After the acid hydrolysis reaction, the MWD curve in the GPC analysis shifted to the lower MW region, and a new peak appeared instead in a similar region to the peak of the original macromonomer. This result indicates that the backbone and the poly(IBVE) segments derived from the macromonomer were separated through the degradation of the acetal moieties by acid hydrolysis.

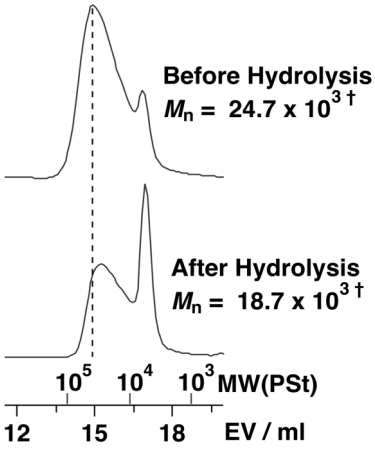


Figure 8. MWD curves for the copolymer (upper) and its hydrolysis product (lower). Hydrolysis conditions: 0.5 M HCl(aq) in 1,2-dimethoxyethane (3 mg/mL polymer) at room temperature for 3 h. †For main peaks.

Conclusion

In conclusion, end-functionalized polymers were synthesized using primary alcohols as quenchers for the living cationic polymerization of IBVE. The quenching reactions using ethanol, 2-propanol, and *tert*-butyl alcohol indicated that primary alcohols were suitable for end functionalization due to the stability of the acetal ω-ends. A block copolymer was also synthesized in high yield by the quenching reaction using a polymer containing a primary hydroxy group at the chain end as a macroterminator. In addition, macromonomers were prepared by the end-capping method using primary alcohols containing a vinyloxy group as quenchers for the living cationic polymerization of IBVE under appropriate conditions. The structure adjacent to the vinyloxy group of the macromonomer was very important to obtain efficient cationic copolymerization reactions that proceeded without cyclization reactions. A macromonomer prepared from HBVE was successfully copolymerized with IBVE using an appropriate catalyst, yielding graft copolymers in high yield. The end-capping method demonstrated in this study will contribute to the precise synthesis of end-functionalized poly(VE)s with a variety of functional groups at the ω-end.

References

1. Tasdelen, M. A.; Kahveci, M. U.; Yagci, Y. *Prog. Polym. Sci.* **2011**, *36*, 455–567.
2. Verso, F. L.; Likos, C. N. *Polymer* **2008**, *49*, 1425–1434.
3. Roberts, M. J.; Bentley, M. D.; Harris, J. M. *Adv. Drug Deliv. Rev.* **2002**, *54*, 459–476.
4. Klok, H.-A. *Macromolecules* **2009**, *42*, 7990–8000.
5. Velonia, K. *Polym. Chem.* **2010**, *1*, 944–952.
6. Jagura-Grodzinski, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2116–2133.
7. Ouchi, M.; Terashima, T.; Sawamoto, M. *Chem. Rev.* **2009**, *109*, 4963–5050.
8. Aoshima, S; Kanaoka, S. *Chem. Rev.* **2009**, *109*, 5245–5287.
9. Miyamoto, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1985**, *18*, 123–127.
10. Sawamoto, M.; Enoki, T.; Higashimura, T. *Polym. Bull.* **1987**, *18*, 117–122.
11. Sawamoto, M.; Enoki, T.; Higashimura, T. *Macromolecules* **1987**, *20*, 1–6.
12. Verma, A.; Nielsen, A.; McGrath J. E.; Riffle, J. S. *Polym. Bull.* **1990**, *23*, 563–570.
13. Fukui, H.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1993**, *26*, 7315–7321.
14. Okamura, H.; Minoda, M.; Komatsu, K.; Miyamoto, T. *Macromol. Chem. Phys.* **1997**, *198*, 777–786.
15. Goethals, E. J.; Haucourt, N. H.; Verheyen, A. M.; Habimana, J. *Makromol. Chem., Rapid Commun.* **1990**, *11*, 623–627.
16. Percec, V.; Lee, M.; Tomazos, D. *Polym. Bull.* **1992**, *28*, 9–15.
17. Sawamoto, M.; Higashimura, T. *Makromol. Chem., Macromol. Symp.* **1990**, *32*, 131–144.
18. Chapter 2 in this thesis: Yokoyama, N.; Yoshida, H.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Polym. Chem.* **2015**, *6*, 6316–6324.
19. Goethals, E. J.; Reyntjens, W.; Lievens, S. *Macromol. Symp.* **1998**, *132*, 57–64.
20. Reyntjens, W.; Jonckhere, L.; Goethals, E. J.; Du Prez, F. E. *Macromol. Symp.* **2001**, *164*, 293–300.
21. Shimomoto, H.; Yoshida, H.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3703–3709.
22. Sandri, J.; Viala, J. *Synthesis* **1995**, 271–274.
23. Kanazawa, A.; Kanda, S.; Kanaoka, S.; Aoshima, S. *Macromolecules* **2014**, *47*, 8531–8540.
24. Hill, H. S.; Hibbert, H. *J. Am. Chem. Soc.* **1923**, *45*, 3124–3132.
25. The acid hydrolysis of the graft copolymer was conducted with 0.5 M HCl(aq) in 1,2-dimethoxyethane at room temperature for 3 h (sample: approximately 3 mg/mL). The quenched mixtures were diluted with CH_2Cl_2 and then successively washed with an aqueous sodium hydroxide solution and water. The volatiles were removed under reduced pressure.

Part II

Development of Two-Staged Latent Initiator for Synthesis of Branched Copolymers Having Well-Defined Structure

Chapter 4

Synthesis of Block Copolymers by a Combination of Living Cationic Polymerization and Ring-Opening Anionic Polymerization Using Cyclic Acetal as a "Two-Staged Latent Initiator"

Introduction

Numerous methods for the synthesis of block copolymers have been developed to produce polymeric materials that exhibit suitable properties, such as microphase separation or formation of micelles, for emerging technologies (e.g., microelectronics and biomedicine). In particular, the syntheses of block copolymers from monomers that polymerize via different mechanisms have been attracting much interest because a variety of segments can be incorporated into block copolymers.[1,2] For example, the synthesis of block copolymers by the direct transformation of an active species into another type of active species[3–6] or by coupling reactions of two types of living propagating chains[7–9] were developed with the use of living polymerization techniques. Moreover, methods using macroinitiators are highly efficient for the synthesis of block copolymers with highly controlled structures since each segment can be prepared under conditions that are most favorable for each monomer.[10–12]

In most cases, using macroinitiators that are prepared by cationic polymerization, post polymerization modification is required to introduce initiating sites before the second polymerization reaction due to the limitation of functional groups that are tolerant to conditions used in cationic polymerization.[13–15] Since a carbocation is easily deactivated by anionic species or by polar functional groups such as amino and hydroxy groups, it is difficult to directly synthesize macroinitiators by cationic polymerization using initiators or terminators containing these functional groups. For instance, in the combination of cationic polymerization and subsequent ring-opening anionic polymerization, a hydroxy group, as an initiating site for ring-opening polymerization, must be protected using protective groups that are inert to Lewis acids and carbocationic species, such as acetyl and *tert*-butyldimethylsilyl groups, before conducting cationic polymerization.[16,17]

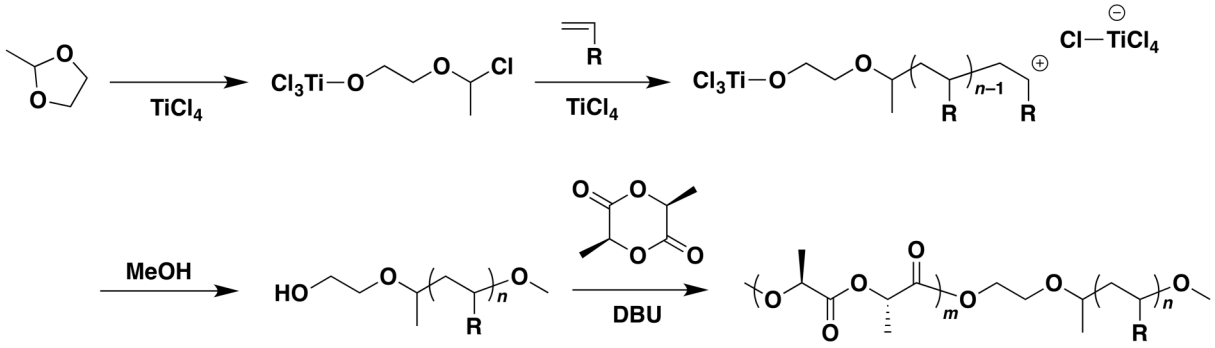
Macroinitiator synthesis that is free from protection and deprotection procedures is highly attractive as an efficient and reasonable method. In cationic polymerization, the introduction of a hydroxy group at the α-end without a post polymerization reaction was achieved using a cyclic acetal with trimethylsilyl iodide (TMSI) for the polymerization of vinyl ether (VE)[18] or using an epoxy compound with $TiCl_4$ for the polymerization of isobutene.[19] In these cases, alkoxy–TMS or alkoxy–titanium bonds were formed through the generation of cationic species via the ring-opening reaction of cyclic acetal or epoxy moieties. After efficient propagation reactions via carbocationic species without deactivation by alkoxide groups, polymers containing a hydroxy group at the α-end were obtained by the transformation of

alkoxy–TMS or alkoxy–titanium bonds to hydroxy groups by a reaction with alcohol quenchers.

In chapter 2, the author demonstrated that quantitative initiation reactions from an acyclic acetal occurred in the living cationic polymerization of styrene derivatives with the use of oxophilic metal chlorides such as $TiCl_4$. This method was applicable for the synthesis of block or graft copolymers that are derived from monomers with completely different reactivities using a macroinitiator containing acetal moieties. Thus, cyclic acetals may also function as an efficient initiator when combined with oxophilic Lewis acids, which will allow for the quantitative introduction of a hydroxy group at the α-end of poly(VE)s and poly(styrene derivative)s, in a manner similar to the examples discussed above.[18,19]

In this chapter, block copolymers are synthesized by living cationic polymerization and subsequent ring-opening anionic polymerization using a cyclic acetal as a "two-staged latent initiator" that generates a new initiating site after the first polymerization reaction (Scheme 1). First, the cationic polymerization of isobutyl VE (IBVE) is examined using several cyclic acetals as initiators. Subsequently, the synthesis of block copolymers by the anionic ring-opening polymerization of lactide is examined using poly(IBVE) containing a hydroxy group at the α-end, which is obtained by polymerization with a suitable cyclic acetal as a macroinitiator. In addition, a block copolymer containing a poly(alkoxystyrene) segment is synthesized in a similar manner.

Scheme 1. Synthesis of Block Copolymers Using Cyclic Acetal as a Two-Staged Latent Initiator.



Experimental

Materials

2-Methyl-1,3-dioxolane (MDOL; TCI; >98.0%), 1,3-dioxolane (DOL; Wako; >99.0%), and 2,2-dimethyl-1,3-dioxolane (DMDOL; TCI; >98.0%) were distilled twice over calcium hydride. 2-Benzyl-1,3-dioxolane (BnDOL; TCI; >98.0%) and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU; TCI; >98.0%) were distilled twice over calcium hydride under reduced pressure. 2-Methyl-1,3-dioxane (MDOX) was prepared by reacting paraldehyde (TCI; >98.0%) with 1,3-propandiol (TCI; >98.0%) according to a literature method[20] and was then distilled twice over calcium hydride. L-(–)-Dilactide (LLA; TCI; >98.0%) was recrystallized twice from ethyl acetate and toluene and vacuum dried for more than 3 h prior to use. Imidazole (Nacalai Tesque; 99%) and *tert*-butyldimethylchlorosilane ($tBuMe_2SiCl$; Nacalai Tesque; ≥98%)

were used as received. Other materials were prepared and used as described in Chapter 2.

Polymerization Procedure

Cationic polymerizations were conducted in a similar manner to that described in Chapter 2.

Silylating Reaction Procedure

The silyl ether moiety was introduced by the reaction of a hydroxy group and a silylating agent as described below.[21] A solution of $tBuMe_2SiCl$ (0.28 mmol) in CH_2Cl_2 (3.0 mL) was added dropwise to a mixture of poly(IBVE) containing a hydroxy group at α-end (8.0×10^{-3} mmol) and imidazole (0.56 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C under a nitrogen atmosphere. The mixture was stirred for 6 h at 0 °C and then washed with water. After the organic solvents were removed by evaporation, the product was purified by reprecipitation into a large excess of methanol. The product was recovered after evaporation of the methanol under reduced pressure and then vacuum-dried overnight.

Synthesis of the Block Copolymer Using a Macroinitiator

The polymerization was performed under a dry nitrogen atmosphere in a glass tube with a three-way stopcock. The glass tube was baked using a heat gun (Ishizaki; PJ-206A; blow temperature ~450 °C) under dry nitrogen for 10 min before use. A typical example for the synthesis of poly(IBVE)-*block*-poly(LLA) in CH_2Cl_2 at 25 °C is as follows: For the block copolymerization of LLA, a DBU solution (0.30 mL in CH_2Cl_2; 50 mM) was added to a solution (2.70 mL) containing CH_2Cl_2, LLA, and poly(IBVE) with a hydroxy group at the α-end at 25 °C. After a predetermined period, the polymerization was terminated with acetic acid (0.1 mL). The quenched reaction mixture was diluted with CH_2Cl_2 and then washed with water to remove the initiator residues. The volatile materials were then removed under reduced pressure. The monomer conversion was determined by a gravimetric method and ^1H NMR analysis.

Characterization

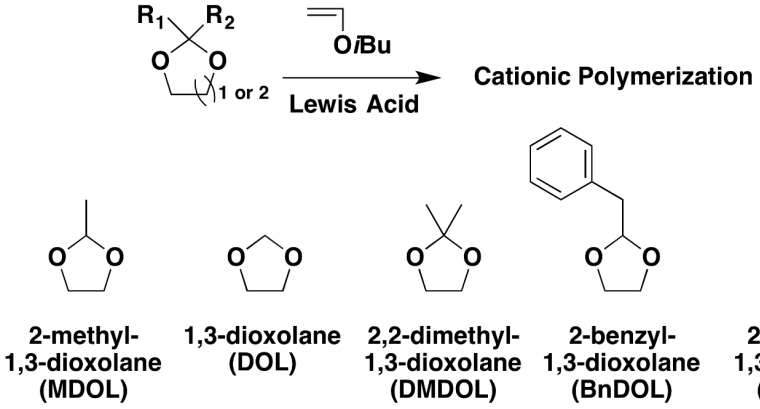
The MWD of the polymers and their NMR spectra were determined as described in Chapter 2.

Results and Discussion

Cationic Polymerizations Using Cyclic Acetals as Initiators: Effect of the Structure on Initiator Efficiency

The cationic polymerizations of IBVE using cyclic acetal/Lewis acid initiating systems were examined to optimize the reaction conditions for polymerization with quantitative initiator efficiency (Scheme 2). The reactions were conducted at 0 °C in the presence of ethyl acetate as an added base and 2,6-di-*tert*-butylpyridine (DTBP) as a proton trap reagent (Table 1). The polymerizations using MDOL as an initiator produced polymers with molecular weights (MW) much higher than the theoretical values when

Scheme 2. Cationic Polymerization of IBVE Using a Cyclic Acetal as an Initiator.



$EtAlCl_2$ and $ZrCl_4$ were used as catalysts (entries 1 and 2 in Table 1), indicating that these catalysts were not suited for quantitative activation of the initiator. In contrast, the M_n values of the polymers obtained using $TiCl_4$ as a catalyst were smaller than the calculated values. ^{1}H NMR analysis of the product suggests that the polymer chains were generated from both the cyclic acetal and protic impurities such as adventitious water (entry 3 in Table 1). Then, the polymerization was conducted using a higher concentration of DTBP in CH_2Cl_2. As a result, the polymerization proceeded smoothly to yield a polymer with a very narrow MWD (M_w/M_n = 1.04) (entry 4 in Table 1). The M_n value of the obtained polymer was consistent with that calculated from the monomer-to-initiator ratio [Figure 1 (B)]. ^{1}H NMR analysis of the product indicates a quantitative initiation reaction from MDOL. Moreover, the M_n values increased linearly in proportion to the amount of monomer that was converted, indicating that the polymerization proceeded in a living manner.

Table 1. Cationic Polymerization of IBVE by Cyclic Acetal/Lewis Acid Initiating Systems[a]

entry	initiator	Lewis acid	DTBP (mM)	solvent	time	conv. (%)	$M_n \times 10^{-3}$ (GPC)[b]	$M_n \times 10^{-3}$ (calcd)	M_w/M_n (GPC)[b]	IE[c]	M_n(NMR)/ M_n(calcd)[d]
1	MDOL	$EtAlCl_2$	5.0	toluene	8 h	27	37.9	4.1	1.14	0.20	5.1
2		$ZrCl_4$	5.0	toluene	8 h	26	9.9	4.0	1.24	0.47	2.1
3		$TiCl_4$	5.0	toluene	48 h	92	10.8	14.0	1.05	~1.0	0.76
4		$TiCl_4$	10	CH_2Cl_2	90 min	84	12.5	12.8	1.04	~1.0	0.95
5	DOL	$TiCl_4$	10	CH_2Cl_2	90 min	47	14.6	7.2	1.13	~0	1.8
6	DMDOL	$TiCl_4$	10	CH_2Cl_2	90 min	52	6.6	7.9	1.05	0.63	0.79
7	BnDOL	$TiCl_4$	10	CH_2Cl_2	90 min	72	9.4	11.0	1.05	~1.0	0.93
8	MDOX	$TiCl_4$	10	CH_2Cl_2	90 min	40	4.5	6.1	1.19	~1.0	0.79

[a] $[IBVE]_0$ = 0.76 M, $[initiator]_0$ = 5.0 mM, $[Lewis\ acid]_0$ = 20 mM (except for entry 2) or 10 mM (entry 2), [DTBP] = 5.0 mM (entries 1–3) or 10 mM (entries 4–8), [ethyl acetate] = 1.0 M, at 0 ºC. [b] Determined by GPC with polystyrene calibration. [c] Initiator efficiency determined by the M_n(calcd) value calculated from the $[monomer]_0/[initiator]_0$ ratio and the monomer conversion value, the M_n(NMR) value determined from the integral ratio between the peaks of the side chains and the peak of the ω-end, and comparison of the integral ratio between the peaks of the α-end and the ω-end in the ^{1}H NMR spectra. [d] The value of M_n(NMR) determined from ^{1}H NMR/M_n(calcd) calculated from the monomer conversion value. A small value is obtained when many chains are generated via initiation reactions from protic impurities.

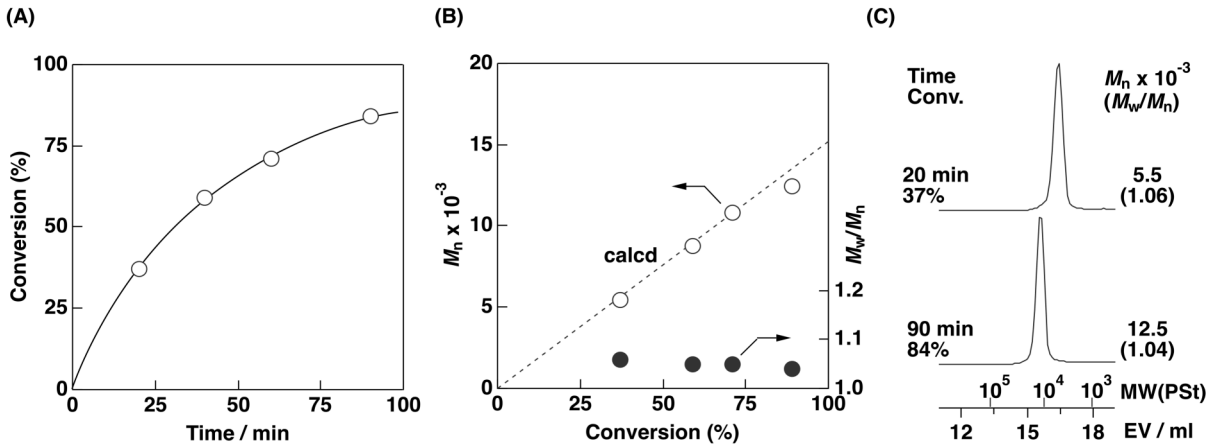
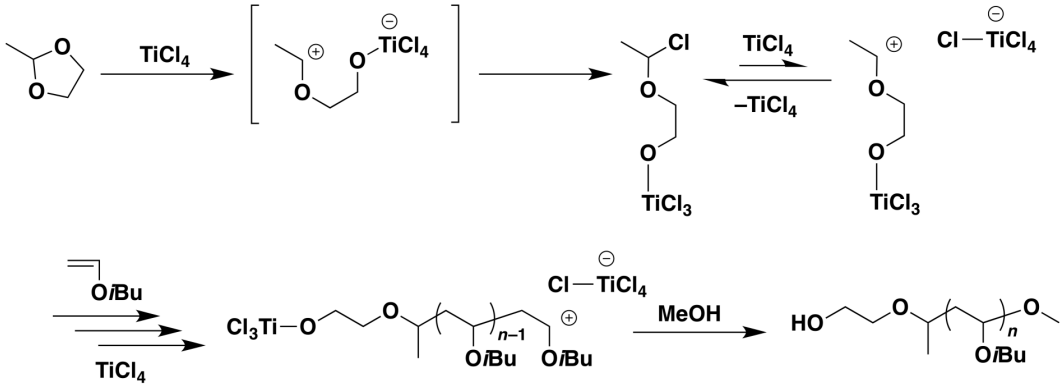


Figure 1. (A) Time–conversion curve, (B) M_n and M_w/M_n–conversion plots, and (C) MWD curves of the poly(IBVE)s obtained using the MDOL/$TiCl_4$ system: $[IBVE]_0$ = 0.76 M, $[MDOL]_0$ = 5.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 10 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC.

The postulated mechanism for the polymerization with the MDOL/$TiCl_4$ initiating system is shown in Scheme 3. The reaction between the oxygen atom of the cyclic acetal and $TiCl_4$ formed a Ti–O bond and subsequently produced a species having a structure similar to a VE–HCl adduct through the transfer of a chloride anion from the Ti species to the acetal carbon. The ring-opening reaction via such mechanisms may involve the transient formation of a zwitterionic species that consists of a carbocationic center and a negatively charged Ti atom.[19] The generation of the VE–HCl adduct and the formation of the Ti–oxygen bond were demonstrated by ^{1}H NMR analysis of an equimolar mixture of MDOL and $TiCl_4$ (Figure 2). The spectrum, however, indicated that a part of the cyclic acetal remained intact, unlike the quantitative reactions using acyclic acetals under the same conditions.[22] The lower reactivity of cyclic acetals compared with acyclic acetals is likely responsible for the difference in the reaction efficiency.[23–25] In the polymerization reaction, the use of excess $TiCl_4$ appeared to contribute to the quantitative generation of the VE–HCl adduct and the quantitative initiator efficiency. The propagation reactions were catalyzed by the presence of extra $TiCl_4$ species that were not consumed in the initiation reaction. Moreover, the Ti–O bond was decomposed in the quenching reaction with methanol, which led to the generation of a hydroxy group at the α-end.

Scheme 3. Postulated Reaction Mechanism for Cationic Polymerization of IBVE Using MDOL/$TiCl_4$ Initiating System.



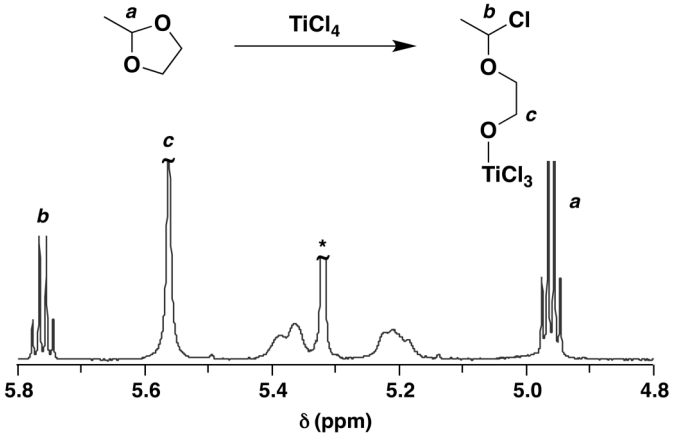


Figure 2. ^{1}H NMR spectrum of the mixture of MDOL, ethyl acetate, and $TiCl_4$ in CD_2Cl_2 at 0 ºC: $[MDOL]_0$ = 40 mM, [ethyl acetate] = 1.0 M, $[TiCl_4]_0$ = 40 mM. *CH_2Cl_2 and $CDHCl_2$.

To confirm the quantitative introduction of a hydroxy group at the α-end, the silylation reaction of the hydroxy group was examined. The reaction was conducted using $tBuMe_2SiCl$ with imidazole in CH_2Cl_2 at 0 °C for 6 h. ^{1}H NMR analysis of the product that was obtained revealed the incorporation of a *tert*-butyldimethylsilyl group. The ratio of the initiator fragment (peak *d*), the acetal moiety at the ω-end (peak *j*), and the silyl group (peak *p*) was in good agreement with the theoretical value [*d*:*j*:*p* = 1.0:3.2:5.9 (the calculated ratio is 1.0:3.0:6.0)] (Figure 3). This result indicated that poly(IBVE) with a hydroxy group at the α-end was successfully produced without post polymerization modification reactions.

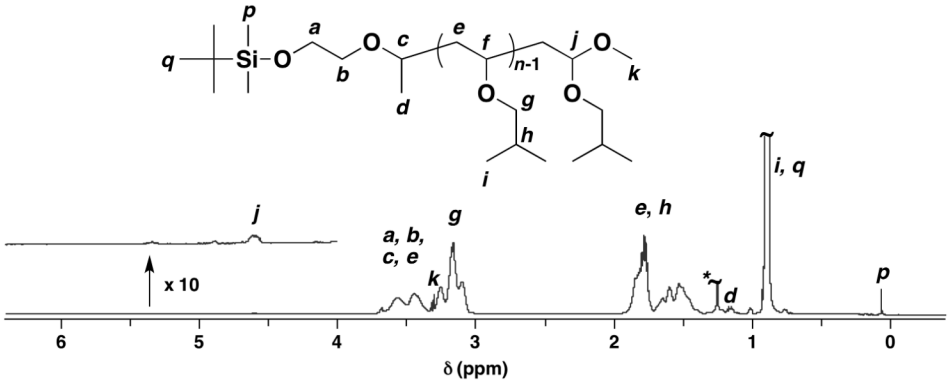


Figure 3. ^{1}H NMR spectrum of poly(IBVE) obtained after silylation reaction {silylation conditions: $[poly(IBVE)]_0$ = 1.0 mM, $[imidazole]_0$ = 70 mM, $[tBuMe_2SiCl]_0$ = 35 mM, in CH_2Cl_2 at 0 ºC for 6 h; 500.16 MHz, in $CDCl_3$ at 30 ºC; *vaseline}.

The number of substituents on the acetal carbon of cyclic acetals was very important for the quantitative initiating reaction with $TiCl_4$. The polymerization using DOL, a non-substituted five-membered cyclic acetal as a cationogen, produced a poly(IBVE) with a high MW (entry 5 in Table 1). The ^{1}H NMR spectrum of the polymer did not contain a peak that could be assigned to a DOL moiety, which suggests that the polymer chains were generated only from protic impurities [Figure 4 (A)]. The initiating reaction from DOL by $TiCl_4$ was not induced due to the low reactivity of the cyclic acetal.[26] In contrast, the polymerization using DMDOL, a five-membered cyclic acetal with two methyl groups on the acetal carbon, yielded a

polymer with a MW similar to the calculated value (entry 6 in Table 1). The analysis of the product by ^{1}H NMR, however, revealed that approximately 40% of the polymer chains had α-ends that were derived from protons [Figure 4 (B)]. The high reactivity of the ketal moiety of DMDOL to acid[26] is likely responsible for the low initiator efficiency. A carbocation generated from DMDOL may be decomposed at 0 ºC through processes such as a β-proton elimination reaction,[27] although the details are not clear at the present time. Thus, non- or di-substituted five-membered cyclic acetals were unsuitable for the quantitative introduction of hydroxy groups at the α-end, unlike a monosubstituted cyclic acetal. Indeed, BnDOL, a monosubstituted cyclic acetal with a benzyl group on the acetal carbon, was also efficient as a cationogen for the polymerization with quantitative initiator efficiency, in a manner similar to MDOL. The obtained polymer had an α-end that was derived from the initiating reaction with BnDOL [entry 7 in Table 1, Figure 4 (C)].

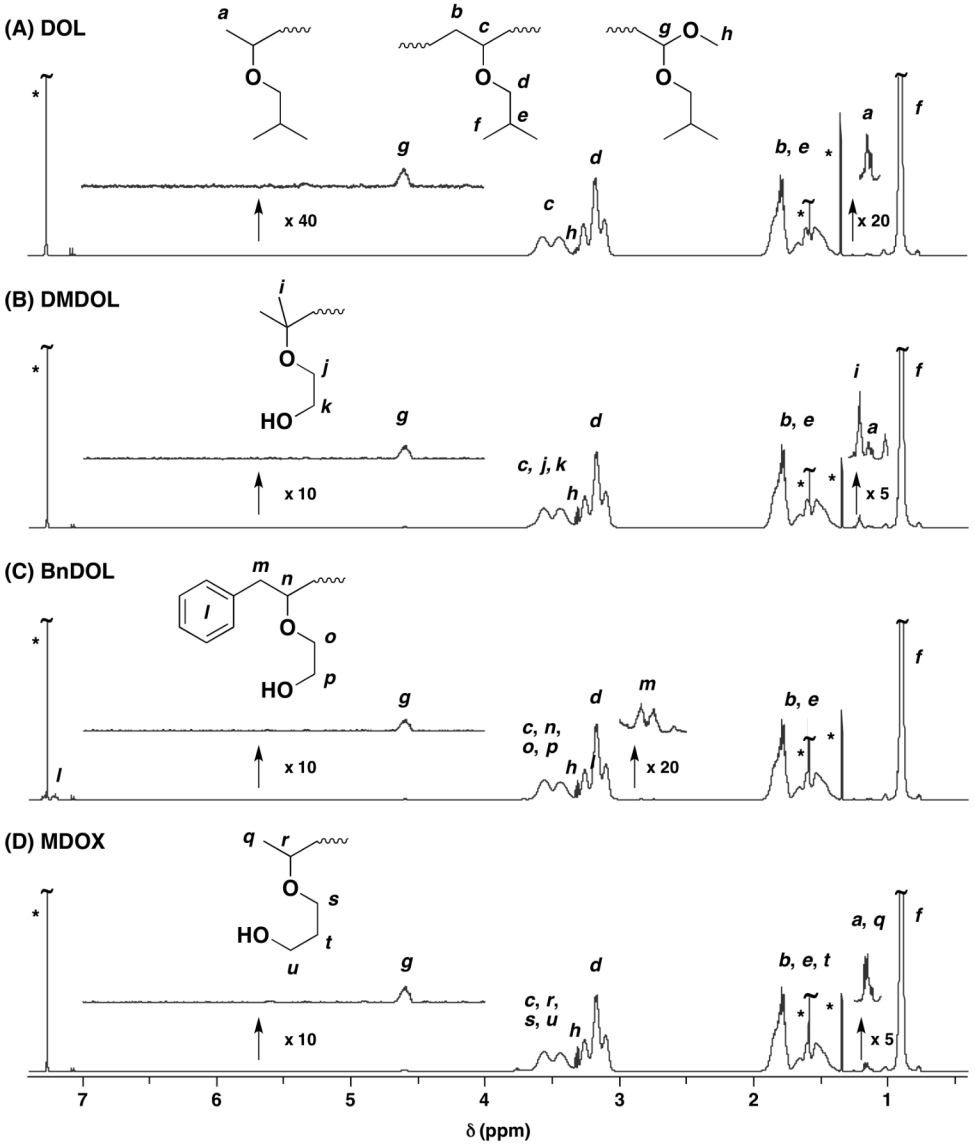


Figure 4. ^{1}H NMR spectra of the products obtained in the polymerization using DOL (A) [M_n(GPC) = 14.6 × 10^3, M_w/M_n(GPC) = 1.13], DMDOL (B) [M_n(GPC) = 6.6 × 10^3, M_w/M_n(GPC) = 1.05], BnDOL (C) [M_n(GPC) = 6.0 × 10^3, M_w/M_n(GPC) = 1.07] and MDOX as initiators (D) [M_n(GPC) = 4.4 × 10^3, M_w/M_n(GPC) = 1.16] (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water, and vaseline).

The number of ring members of cyclic acetals also influenced the ability to control the polymerization. The polymerization using MDOX, a six-membered cyclic acetal containing a methyl group at the acetal carbon, as an initiator proceeded smoothly with quantitative initiator efficiency [entry 8 in Table 1, Figure 4 (D)]. However, the MWD of the polymer obtained was broader (M_w/M_n = 1.19) compared to the polymer produced by the initiation reaction using the monosubstituted five-membered cyclic acetals. In addition, an undesired initiating reaction appeared to have occurred, as deduced from the M_n value smaller than the calculated value, and from the ^{1}H NMR analysis (1.1 ppm). The less-controlled polymerization using MDOX, compared to the case using MDOL, most likely stemmed from the low reactivity of the six-membered cyclic acetal. In fact, the reactivity of monosubstituted 1,3-dioxanes in hydrolysis reactions was reported to be lower than that of monosubstituted 1,3-dioxolanes.[28,29]

An end-functionalized poly(styrene derivative) with a hydroxy group at the α-end was also synthesized by the cationic polymerization of *p*-methoxystyrene (pMOS), which is a styrene derivative less reactive than IBVE,[30] using DMOL as an initiator. A quantitative initiating reaction was achieved when the polymerization was conducted under the same conditions as those for the living cationic polymerization of IBVE (Figure 5). Although the rate of polymerization was low, due to the low reactivity of pMOS, the polymerization was highly controlled and yielded poly(pMOS) with a very narrow MWD (M_w/M_n = 1.05). In addition, the integral ratio of the α-end (peaks *a*–*d*) and the ω-end (peaks *i* and *j*) in the ^{1}H NMR spectrum accorded with the calculated value [a:(b + c + d + i):j = 1.0:1.9:0.97 (the calculated ratio is 1.0:2.0:1.0)], indicating that almost all of the α-ends of the poly(pMOS) chains were derived from the cyclic acetal (Figure 6).

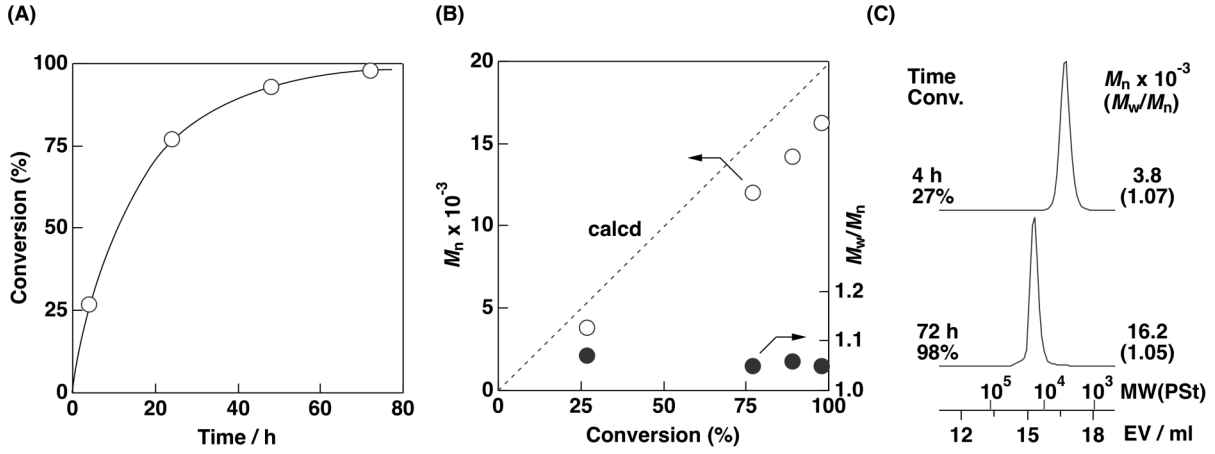


Figure 5. (A) Time–conversion curve, (B) M_n and M_w/M_n–conversion plots, and (C) MWD curves of the obtained poly(pMOS)s using the MDOL/$TiCl_4$ system: $[pMOS]_0$ = 0.74 M, $[MDOL]_0$ = 5.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 10 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC.

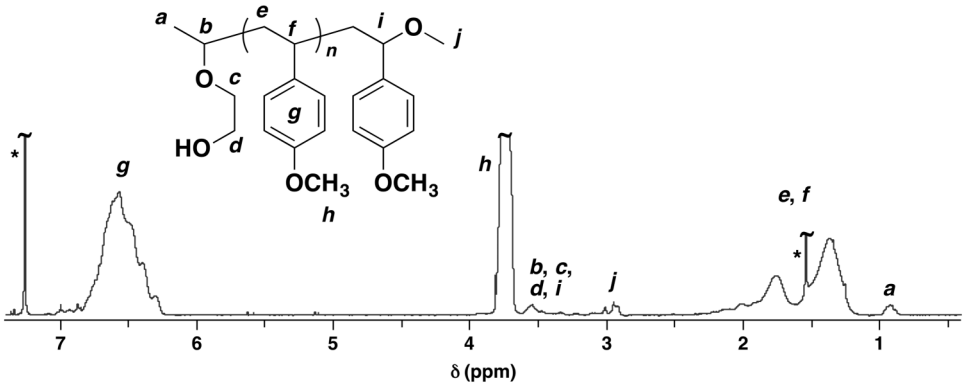


Figure 6. ^{1}H NMR spectrum of poly(pMOS) obtained using MDOL/$TiCl_4$ initiating system [M_n(GPC) = 3.8 × 10^3, M_w/M_n(GPC) = 1.07] (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water).

Syntheses of Block Copolymers via Polymerization of Lactide Using Macroinitiators Containing Hydroxy Groups at the α-End

The syntheses of block copolymers bearing a polylactide segment were examined using polymers that contained a hydroxy group at the α-end which was obtained by polymerization using MDOL, as macroinitiators for ring-opening polymerization of L-lactide (Scheme 1). The reaction was conducted in CH_2Cl_2 with DBU as a catalyst.[31] The polymerization using poly(IBVE) that contained a hydroxy group at the α-end as a macroinitiator, proceeded smoothly without unreacted macroinitiators to yield a block copolymer with a very narrow MWD (M_w/M_n = 1.06) [Figure 7 (A)]. Although a small amount of homopoly(LLA) was generated from protic impurities, the polymerization proceeded in a highly controlled manner as confirmed by ^{1}H NMR analysis (Figure 8). In particular, the quantitative synthesis of a block copolymer was verified by the integral ratio of the peaks of both chain ends (peaks *a* and *p*) and the

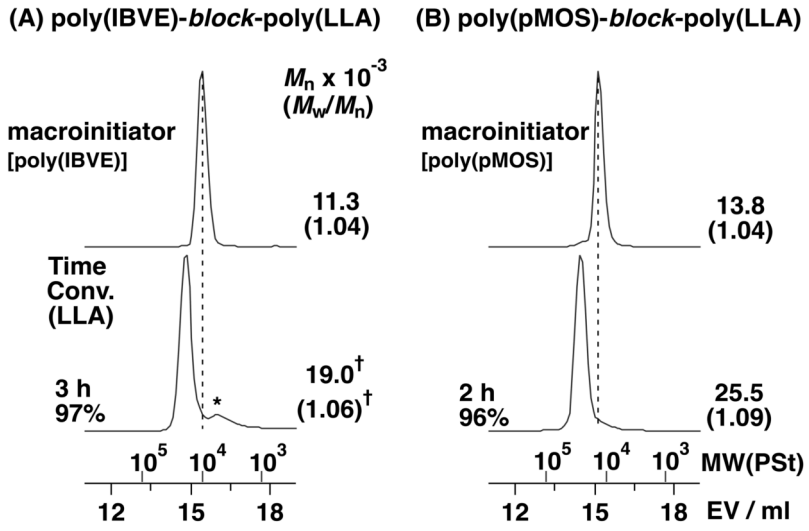


Figure 7. MWD curves for the synthesis of poly(IBVE)-*block*-poly(LLA) (A) and poly(pMOS)-*block*-poly(LLA) (B) using poly(IBVE) or poly(pMOS) as macroinitiators: $[LLA]_0$ = 0.20 M, $[macroinitiator]_0$ = 4.0 mM, $[DBU]_0$ = 5.0 mM, in CH_2Cl_2 at 25 ºC. †For a main peak. *Homopoly(LLA) derived from protic impurities.

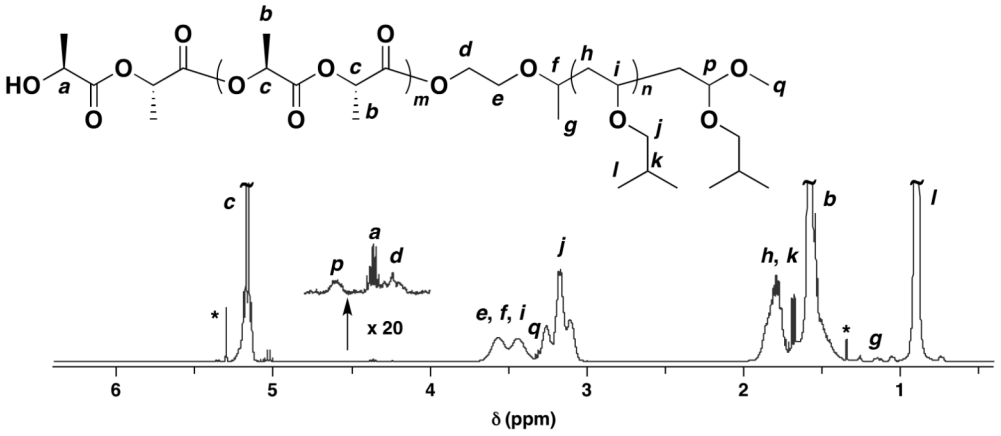


Figure 8. ^{1}H NMR spectrum of the poly(IBVE)-*block*-poly(LLA) [M_n(GPC) = 19.0 × 10^3, M_w/M_n(GPC) = 1.06] (500.16 MHz, in $CDCl_3$ at 30 ºC; *CH_2Cl_2, vaseline).

MDOL-derived moiety (peaks *d* and *g*) [(*a* + *d)*:*g*:*p* = 3.1:3.2:1.0 (the calculated ratio is 3.0:3.0:1.0)]. In addition, the polymerization of lactide using the hydroxy group-functionalized poly(pMOS) as a macroinitiator proceeded as it did with poly(IBVE), yielding a block copolymer with a well-defined structure [Figure 7 (B)]. These results demonstrated that block copolymers were synthesized using MDOL as a two-staged latent initiator for living cationic polymerization and subsequent ring-opening anionic polymerization without post-polymerization modification.

Conclusion

This chapter presented the syntheses of block copolymers using a cyclic acetal as a two-staged latent initiator for living cationic polymerization of VE or pMOS and the subsequent ring-opening anionic polymerization of lactide. Living cationic polymerization of IBVE using the MDOL/$TiCl_4$ initiating system in CH_2Cl_2 with a high concentration of a proton trap reagent quantitatively produced polymers containing a hydroxy group at the α-end. The numbers of both substituents and ring members of cyclic acetals were very important for conducting living cationic polymerization with quantitative initiator efficiency. MDOL was also useful as a cationogen for the living cationic polymerization of pMOS. The reaction yielded poly(pMOS) with a hydroxy group at the initiating end. A notable benefit of the method that is demonstrated in this chapter is that hydroxy groups can be incorporated into chain ends without post-polymerization modification. The end-functionalized polymers were employed as macroinitiators for the syntheses of block copolymers via ring-opening anionic polymerization of LLA. The polymerizations proceeded in a controlled manner to yield block copolymers containing a poly(LLA) segment. It is expected that the syntheses of polymeric compounds with more complicated structures than block copolymers will be possible using appropriate cyclic acetal moieties as two-staged initiating sites.

References

1. Bernaerts, K. V.; Prez, F. E. D. *Prog. Polym. Sci.* **2006**, *31*, 671–722.

2. Yagci, Y.; Tasdelen, M. A. *Prog. Polym. Sci.* **2006**, *31*, 1133–1170.
3. Nomura, R.; Endo, T. *Macromolecules* **1995**, *28*, 1754–1757.
4. Nomura, R.; Shibasaki, Y.; Endo, T. *Polym. Bull.* **1996**, *37*, 597–601.
5. Aoshima, H.; Satoh, K.; Kamigaito, M. *Macromol. Symp.* **2013**, *323*, 64–74.
6. Sugihara, S.; Konegawa, N.; Maeda, Y. *Macromolecules* **2015**, *48*, 5120–5131.
7. Richards, D. H.; Kingston, S. B.; Souel, T. *Polymer* **1978**, *19*, 68–72.
8. Creutz, S.; Vandooren, C.; Jérôme, R.; Teyssié, P. *Polym. Bull.* **1994**, *33*, 21–28.
9. Tsutsumiuchi, K.; Aoi, K.; Okada, M. *Macromol. Rapid Commun.* **1995**, *16*, 749–755.
10. Jakubowski, W.; Matyjaszeski, K. *Macromol. Symp.* **2006**, *240*, 213–223.
11. Ouchi, M.; Terashima, T.; Sawamoto, M. *Chem. Rev.* **2009**, *109*, 4963–5050.
12. Jagur-Grodzinski, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2116–2133.
13. Feldthusen, J.; Iván, B.; Müller, A. H. E. *Macromolecules* **1997**, *30*, 6989–6993.
14. Keszler, B.; Fenyvesi, Gy.; Kennedy, J. P. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 706–714.
15. Martinez-Castro, N.; Lanzendörfer, M. G.; Müller, A. H. E.; Cho, J. C.; Acar, M. H.; Faust, R. *Macromolecules* **2003**, *36*, 6985–6994.
16. Kwon, Y.; Faust, R.; Chen, C. X.; Thomas, E. L. *Macromolecules* **2002**, *35*, 3348–3357.
17. Kim, M. S.; Faust, R. *Polym. Bull.* **2002**, *48*, 127–134.
18. Meirvenne, D. V.; Haucourt, N.; Goethals, E. J. *Polym. Bull.* **1990**, *23*, 185–190.
19. Puskas, J. E.; Brister, L. B.; Michel, A. J.; Lanzendörfer, M. G.; Jamieson, D.; Pattern, W. G. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 444–452.
20. Hibbert, H.; Timm, J. A. *J. Am. Chem. Soc.* **1924**, *46*, 1283–1290.
21. Sugihara, S.; Hashimoto, K.; Matsumoto, Y.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3300–3312.
22. Chapter 2 in this thesis: Yokoyama, N.; Yoshida, H.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Polym. Chem.* **2015**, *6*, 6316–6324.
23. Vollhardt, K. P. C.; Schore, N. E. in *Organic Chemistry: Structure and Function*, 6th ed.; Freeman: New York, 2010; Chapter 17.
24. Satchell, D. P. N.; Satchell, R. S. *Chem. Soc. Rev.* **1990**, *19*, 55–81.
25. Namikoshi, T.; Hashimoto, T.; Urushisaki, M. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 4855–4866.
26. Salomaa, P.; Kankaanperä, A. *Acta Chem. Scand.* **1961**, *15*, 871–878.
27. Yonezumi, M.; Takaku, R.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 2202–2211.
28. Leutner, R. *Monatsh. Chem.* **1932**, *60*, 317–352.
29. Jacques, S. A.; Leriche, G.; Mosser, M.; Nothisen, M.; Muller, C. D.; Remy, J.-S.; Wagner, A. *Org. Biomol. Chem.* **2016**, *14*, 4794–4803.

30. Sawamoto, M.; Ohtoyo, T.; Higashimura, T.; Gührs, K.-H.; Heublein, G. *Polym. J.* **1985**, *17*, 929–933.
31. Lohmeijer, B. G. G.; Pratt, R. C.; Leibfarth, F.; Logan, J. W.; Long, D. A.; Dove, A. P.; Nederberg, F.; Choi, J.; Wade, C.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 8574–8583.

Chapter 5

A Novel Strategy to Synthesize a Highly Defined Graft Copolymer via a Repetitive Reaction Using a Cyclic Acetal Moiety

Introduction

Graft copolymers have been studied as model branched polymers in terms of their properties in solution, such as critical micelle concentration or viscosity, and in the bulk state including their morphology.[1] Recently, graft copolymers have attracted much attention in commercial applications for use as adhesives and compatibilizing agents due to characteristics derived from their branched compact structure and many terminal functional groups.[2] For the syntheses of graft copolymers, a variety of precise synthetic methods using prepolymers have been developed in recent years utilizing living/controlled polymerization techniques,[3,4] while conventional studies mainly employed transfer reactions of propagating species for branch formation.[5] The methods are classified into three main strategies: "grafting-from", "granting-onto", and "grafting-through" methods. In the "grafting-from" method, a polymer with initiating sites on the side chains is used as a macroinitiator for the generation of graft chains. Graft copolymers are obtained in high yield without residual unreacted prepolymer due to the minimal steric hindrance of other graft chains.[6,7] Graft copolymers consisting of a backbone and branch chains with well controlled molecular weights (MW) are synthesized by the "grafting-onto" method because graft copolymers are prepared by the direct reaction between living polymers and a backbone polymer.[8,9] In the "grafting-through" method, a polymer with a pendant polymerizable unit, or a macromonomer, is polymerized to prepare graft copolymers having graft chains in high density. Bottlebrush polymers can also be synthesized using this method.[10–12]

Recently, the synthesis of graft copolymers with highly defined structures was achieved through both the elaborate design of synthetic strategies and the development of living polymerization reactions. The structure of a graft copolymer is defined by the following three parameters: (i) MW of the backbone chain, (ii) MW of the branched chains, and (iii) the number of and the distance between branched chains (Figure 1). To obtain the desired functions, these three parameters need to be controlled very precisely because minute differences of grafting positions have been reported to influence the morphology of graft copolymers in the bulk state.[13] Motivated by these results, Paraskeva and Hadjichristidis[14] achieved the synthesis of the "exact graft copolymer", a graft copolymer consisting of a precisely defined backbone and branch structures, by combining living anionic polymerization and repetitive polymer coupling reactions. In addition, Hirao and co-workers[15–21] have developed synthetic methods for graft and star-shaped copolymers with precisely defined structures using repetitive cycles of living anionic polymerization and post-polymerization reactions.

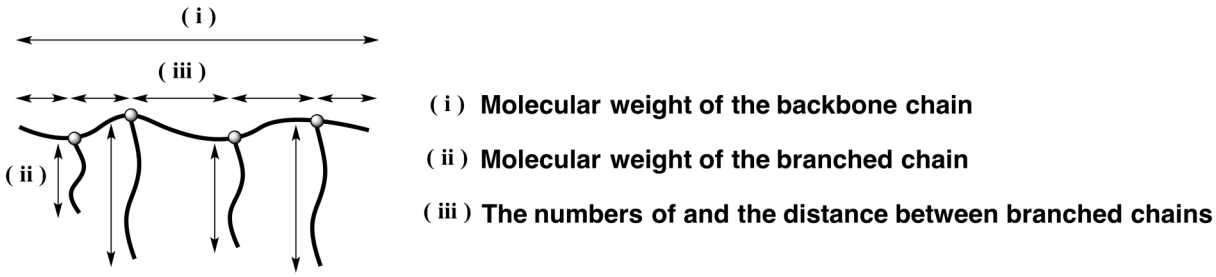
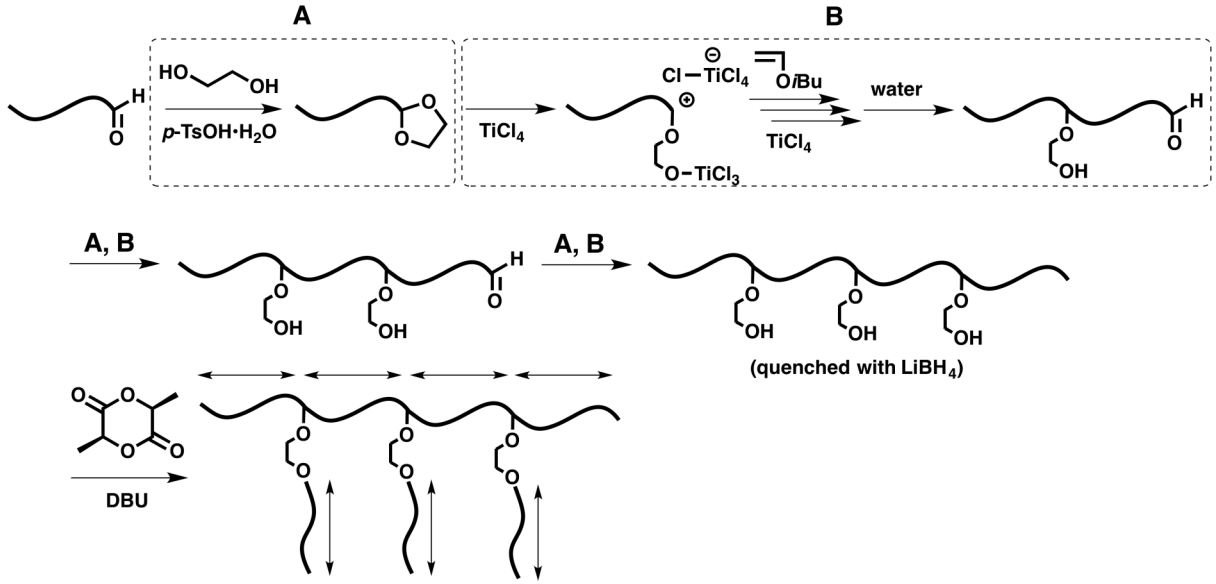


Figure 1. Three parameters defining the structure of a graft polymer.

In this chapter, graft copolymers with precisely defined structures are synthesized using a combination of living cationic polymerization of vinyl ethers (VEs) and ring-opening anionic polymerization of lactide using cyclic acetal moieties as two-staged latent initiating sites. A cyclic acetal moiety is quantitatively introduced into the *ω*-end of a poly(VE) chain by a post-polymerization modification reaction. A three-arm star-shaped polymer is then prepared using the cyclic acetal moiety at the *ω*-end as a two-staged latent initiating site for the living cationic polymerization of VE and subsequent anionic ring-opening polymerization of lactide. A polymer containing two or three hydroxy groups on the side chains, which is achieved by repeatedly introducing a cyclic acetal moiety and living cationic polymerization, is used as a macroinitiator for the syntheses of graft copolymers with an exact number of branch chains and controlled chain length (Scheme 1).

Scheme 1. Synthetic Route of Highly Defined Graft Copolymers.



Experimental

Materials

Ethylene glycol (Nacalai Tesque; ≥99.0%) and *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O; TCI; >98.0%) were used without further purification. Tetrahydrofuran (THF; Wako; >99.9%, stabilizer free) was used as received. Other materials were prepared and used as described in Chapters 2 and 4.

Polymerization Procedure

Cationic polymerization, ring-opening anionic polymerization, and silylating reactions were performed in a manner similar to those described in Chapters 2 and 4.

Cyclic Acetalization Procedure

The aldehyde group in a poly(VE) chain was converted into a cyclic acetal moiety as described below.[22] Poly(isobutyl VE) [poly(IBVE)] containing an aldehyde group at the *ω*-end was dissolved in toluene to prepare a 2.0 mM solution. Ethylene glycol (two equivalents relative to the aldehyde group) and *p*-TsOH·H_2O (one-fifth equivalents relative to the aldehyde group) were then added into the solution. The mixture was magnetically stirred with a stir bar at 80 °C for 8 h. The reaction was quenched by the addition of ice-cold saturated aqueous $NaHCO_3$. The organic layer was washed with saturated aqueous $NaHCO_3$ and water. The volatile substances were then removed under reduced pressure.

Acid Hydrolysis of the Silyl Protecting Group

The silyl ether pendant was converted into a hydroxy group as described below.[23] Poly(IBVE) containing silyl ether pendants was dissolved in THF to prepare a 2 wt% solution. Aqueous (3.0 M) hydrogen chloride-ethanol [aqueous HCl:ethanol = 1:3 (v/v)] (100 equivalents relative to the silyl group) was then added into the solution. The mixture was magnetically stirred with a stir bar at 0 °C for 6 h. The mixture was neutralized with $NaHCO_3$, and then insoluble residues were filtered off. After the organic solvents were removed by evaporation, the product was purified by reprecipitation from CH_2Cl_2 into a large excess of methanol. The product was recovered by the evaporation of methanol under reduced pressure and then vacuum-dried overnight.

Characterization

The MWD of the polymers and NMR spectra were measured as described in Chapter 2.

Results and Discussion

Introduction of a Cyclic Acetal Moiety into the Polymer ω-End and Synthesis of a Three-Arm Star-Shaped Polymer Using the Cyclic Acetal Moiety

A five-membered cyclic acetal moiety was introduced into the chain end of a VE polymer by the reaction between ethylene glycol and an aldehyde group at the ω-end under acidic conditions. Poly(IBVE) with an aldehyde group at the ω-end was prepared by quenching the living cationic polymerization of IBVE with water (M_n = 14.0 × 10^3, M_w/M_n = 1.07).[24] Subsequently, the acetalization reaction using ethylene glycol was conducted at 80 °C in toluene with *p*-TsOH·H_2O as a catalyst for 8 h. The progress of the reaction without any side reactions and the quantitative conversion of the aldehyde group (peak *h*) into a cyclic acetal moiety (peaks *j* and *k*) were confirmed by ^{1}H NMR analysis (Figure 2). Thus, an end-functionalized polymer containing a cyclic acetal moiety at the ω-end was quantitatively obtained by the living cationic polymerization and the subsequent post-polymerization reaction.

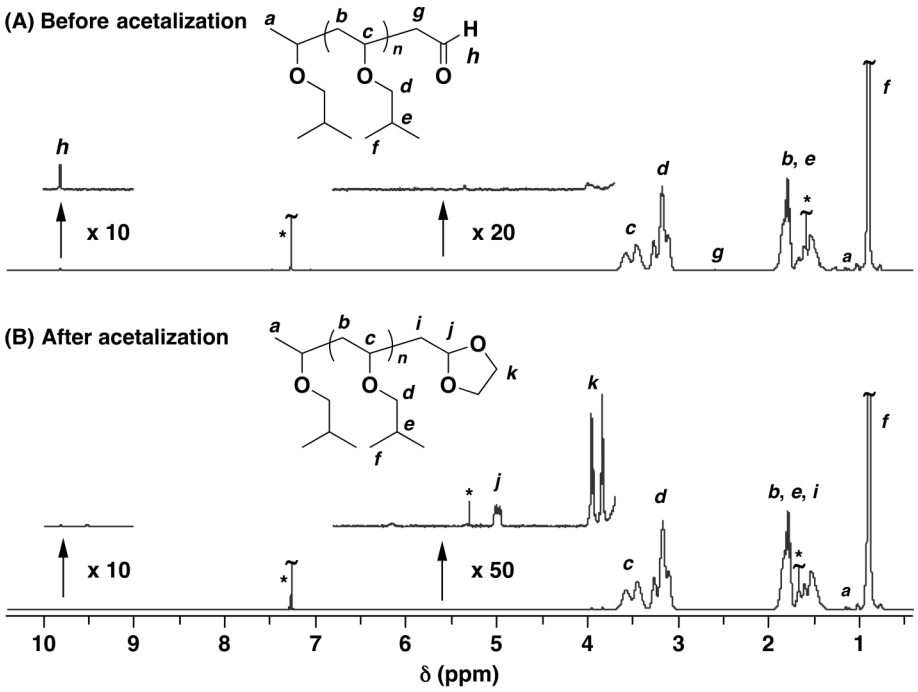
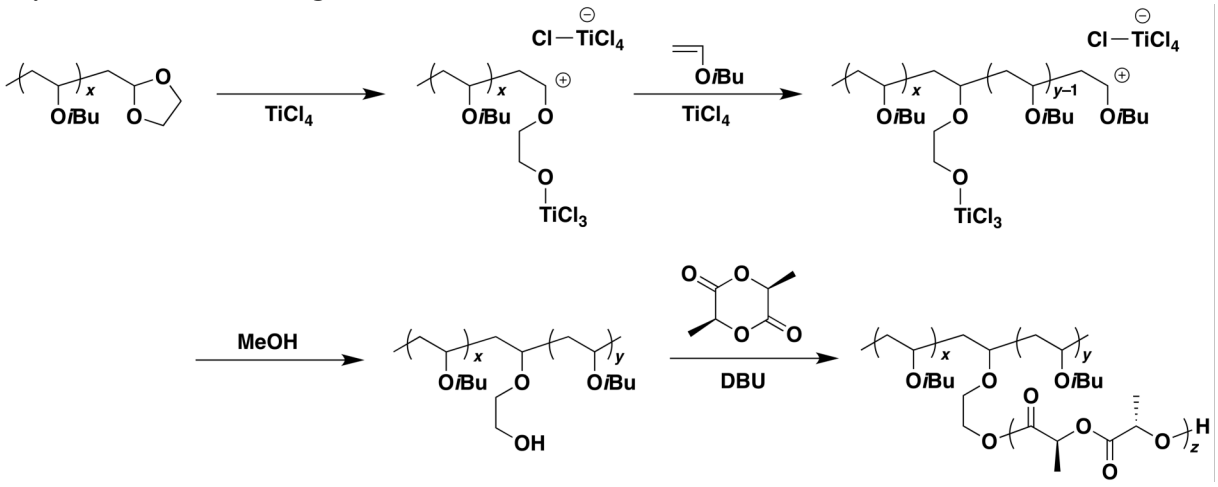


Figure 2. ^{1}H NMR spectra of (A) poly(IBVE) with an aldehyde group at the ω-end and (B) poly(IBVE) obtained after cyclic acetalization reaction {polymerization conditions: $[IBVE]_0$ = 0.76 M, $[IBEA]_0$ = 4.0 mM, $[EtAlCl_2]_0$ = 20 mM, [ethyl acetate] = 1.0 M, in hexane at 0 ºC for 4 h; acetalization conditions: $[poly(IBVE)]_0$ = 2.0 mM, $[ethylene\ glycol]_0$ = 4.0 mM, $[p\text{-}TsOH\cdot H_2O]_0$ = 0.42 mM, in toluene at 80 ºC for 8 h; 500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, CH_2Cl_2, and water}.

The synthesis of a three-arm star-shaped polymer was studied using the poly(IBVE) with a cyclic acetal moiety at the ω-end as a two-staged latent macroinitiator (Scheme 2). First, the living cationic polymerization of IBVE from the cyclic acetal moiety at the chain end was performed in CH_2Cl_2 at 0 °C using $TiCl_4$ as a catalyst in the presence of ethyl acetate as an added base and 2,6-di-*tert*-butylpyridine

Scheme 2. Synthesis of a Three-Arm Star-Shaped Copolymer Using Poly(IBVE) Containing a Cyclic Acetal Moiety at *ω*-End as a Two-Staged Latent Macroinitiator.



(DTBP) as a proton trap reagent. The polymerization proceeded smoothly from the macroinitiator to yield a polymer with a very narrow MWD (M_w/M_n = 1.07) (Figure 3, middle portion). Because the polymerization was initiated from the cationic species derived from the ring-opening reaction of the cyclic acetal moiety by $TiCl_4$ in a manner similar to the reaction demonstrated in Chapter 4, a hydroxy group was introduced into a mid-chain position through the reaction between an alcohol quencher and the Ti-alkoxide bond generated along with the cationic species. Subsequently, the polymerization of L-lactide (LLA) using the hydroxy group as an initiating site was conducted with 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) as a catalyst in CH_2Cl_2 at 25 °C. The polymerization proceeded smoothly with high conversion of LLA. In addition, the MWD curves of the obtained polymers shifted toward the higher MW region than that of the macroinitiator

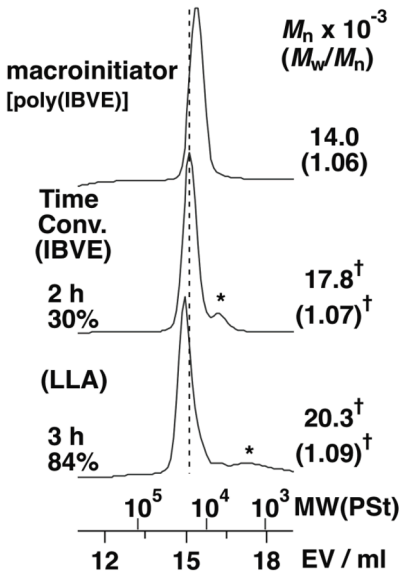


Figure 3. MWD curves for the synthesis of three-arm star-shaped polymer: $[IBVE]_0$ = 0.76 M, $[macroinitiator]_0$ = 5.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 20 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC; $[LLA]_0$ = 0.20 M, $[macroinitiator]_0$ = 4.0 mM, $[DBU]_0$ = 5.0 mM, in CH_2Cl_2 at 25 ºC. †For main peaks. *Homopolymers derived from protic impurities.

(Figure 3, bottom portion). This indicates that the polymerization proceeded in a highly controlled manner, although a small amount of an LLA homopolymer, which was easily removed by reprecipitation, was also produced through the initiation reaction from protic impurities. In the ^{1}H NMR spectrum of the product (Figure 4), the integral ratio of the peaks of both chain ends of the poly(IBVE) segment (peaks *a* and *n*), the chain end of the poly(LLA) segment (peak *m*), and the junction point (peak *j*) were in good agreement with the calculated value [*a*:(*j* + *m*):*n* = 3.3:3.0:1.0 (the calculated ratio is 3.0:3.0:1.0)], indicating that the quantitative initiation reaction of the LLA polymerization occurred from the macroinitiator. Thus, a three-arm star-shaped polymer consisting of two poly(IBVE) chains and one polylactide chain was successfully synthesized by the living cationic polymerization of IBVE and subsequent ring-opening anionic polymerization of LLA using poly(IBVE) with a cyclic acetal moiety at the *ω*-end as a two-staged latent macroinitiator.

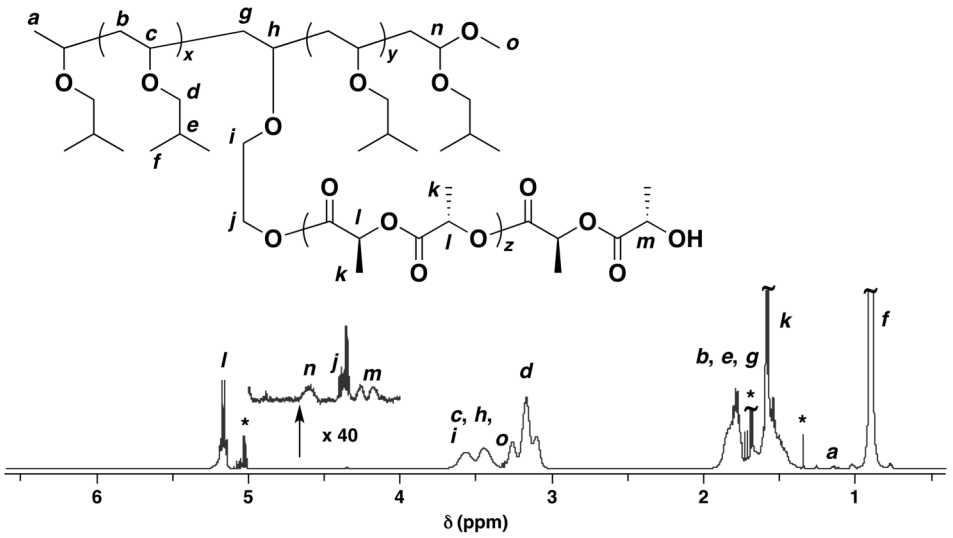


Figure 4. ^{1}H NMR spectrum of three-arm star-shaped polymer [M_n(GPC) = 20.3 × 10^3, M_w/M_n(GPC) = 1.09] (500.16 MHz, in $CDCl_3$ at 30 ºC; *LLA, water, and vaseline).

Synthesis of Highly Defined Graft Copolymers by Repetitive Cycles of Cyclic Acetalization Reaction and Living Cationic Polymerization

To synthesize graft copolymers with highly controlled structures, the synthesis of a macroinitiator containing several hydroxy groups on the side chains was studied through repetitive cyclic-acetalization reaction and living cationic polymerization (Scheme 1). First, the living cationic polymerization of IBVE using a cyclic acetal-containing poly(IBVE) as a macroinitiator was quenched with water to introduce an aldehyde group at the *ω*-end (Figure 5, upper portion). The aldehyde group was then transformed to a cyclic acetal structure using ethylene glycol in a similar manner to the first step. The cyclic acetal moiety was further used as an initiating site for the living cationic polymerization of IBVE. However, a relatively large amount of homopolymer was produced as a side product in the polymerization (the bottom curve in Figure 5). The hydroxy group at the mid-chain position was most likely responsible for the uncontrolled polymeriz-

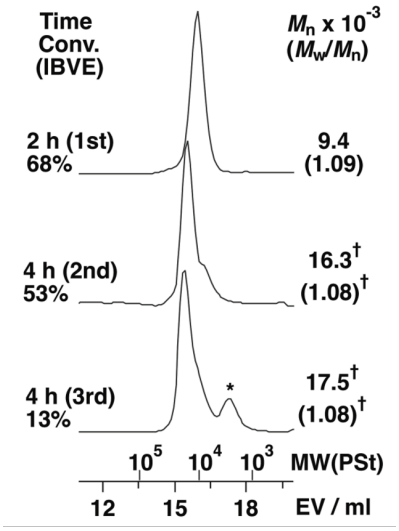


Figure 5. MWD curves for the products obtained in the repetitive polymerization of IBVE using macroinitiators: (1st) $[IBVE]_0$ = 0.76 M, $[IBEA]_0$ = 4.0 mM, $[EtAlCl_2]_0$ = 20 mM, [ethyl acetate] = 1.0 M, in hexane at 0 ºC; (2nd, 3rd) $[IBVE]_0$ = 0.76 M, $[macroinitiator]_0$ = 5.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 20 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC. †For main peaks. *Homopolymer derived from protic impurities.

ation. Specifically, the initiation reaction from a proton generated through the reaction of the hydroxy group with $TiCl_4$ resulted in the homopolymer generation. Therefore, the hydroxy group must be protected to inhibit the reaction with $TiCl_4$.

The hydroxy group at the mid-chain position of the poly(IBVE) chain was protected by a silylation reaction using $tBuMe_2SiCl$. The integral ratio of the α-end (peak *a*), the cyclic acetal moiety at the ω-end (peak *p*), and the silyl group (peak *k*) in the ^{1}H NMR spectrum of the silylated product was in good agreement with the theoretical value [*a*:*k*:*p* = 3.3:5.9:1.0 (the calculated ratio is 3.0:6.0:1.0)] (Figure 6), indicating the quantitative protection of the hydroxy group. The cationic polymerization of IBVE using the obtained polymer as a macroinitiator proceeded in a highly controlled manner without the generation of homopolymers, yielding a poly(IBVE) with a silyloxy group and a hydroxy group in the side chains [the upper curve in Figure 7 (A)].

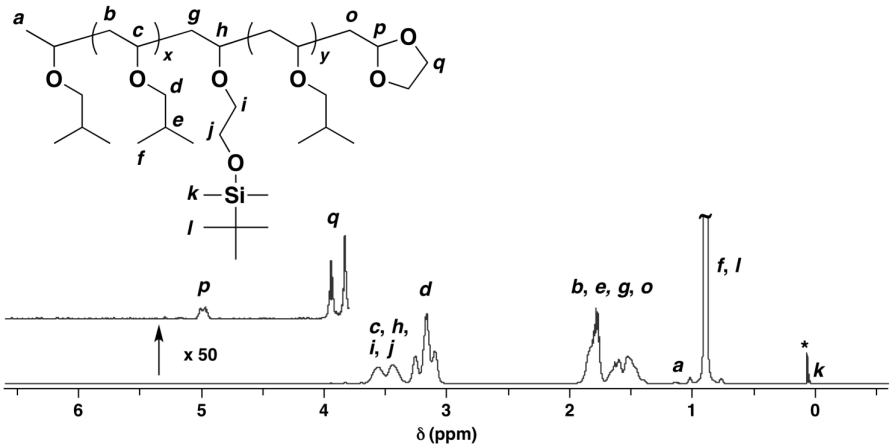


Figure 6. ^{1}H NMR spectrum of poly(IBVE) after silylation reaction {silylation conditions: $[poly(IBVE)]_0$ = 1.0 mM, $[imidazole]_0$ = 70 mM, $[tBuMe_2SiCl]_0$ = 35 mM, in CH_2Cl_2 at 0 ºC for 6 h; 500.16 MHz, in $CDCl_3$ at 30 ºC; *grease}.

Graft copolymers with well-defined structures were synthesized by the ring-opening polymerization of LLA using macroinitiators containing two or three hydroxy groups on the side chains. The silyloxy group of the poly(IBVE) obtained above was deprotected under acidic conditions to yield poly(IBVE) containing two hydroxy groups on the side chains. This polymer was used as a macroinitiator for the polymerization of LLA. The controlled polymerization proceeded smoothly to yield a graft copolymer containing two poly(LLA) segments as branched chains [the bottom curve in Figure 7 (A); Figure 8]. Additionally, a poly(IBVE) with three hydroxy groups on the side chains at intervals of approximately 100 IBVE units [poly(IBVE)$_{96}$-OH-poly(IBVE)$_{113}$-OH-poly(IBVE)$_{118}$-OH-poly(IBVE)$_{94}$] (M_n = 42.2 × 10^3) was synthesized through a repetitive cycle consisting of the introduction of a cyclic acetal moiety, the protection of the hydroxy group, the living cationic polymerization of IBVE, and the deprotection reaction [Figure 7 (B)]. A graft copolymer with three branch chains containing approximately 14 LLA units in each branch was prepared by the polymerization of LLA using the poly(IBVE) containing three hydroxy groups as a macroinitiator [Figure 7 (B), bottom portion]. The MW, the number of and the distances between branch chains can be adjusted using this methodology.

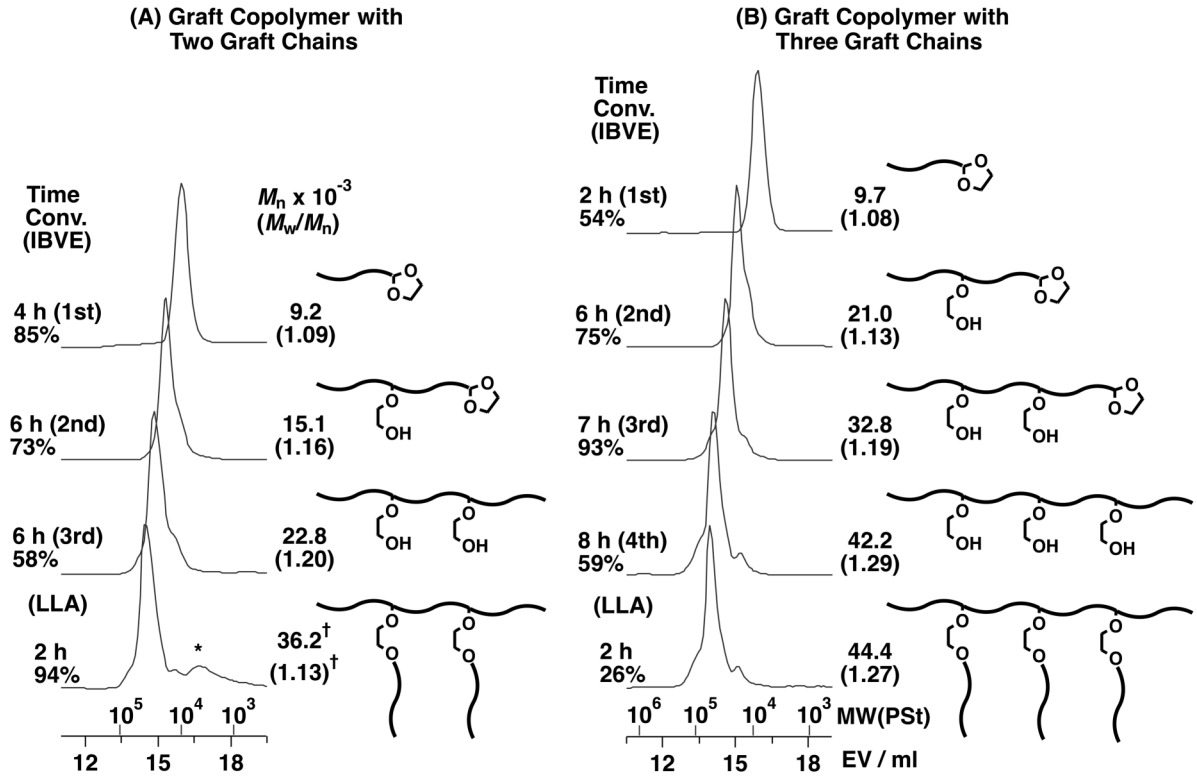


Figure 7. MWD curves for the synthesis of graft copolymers: (1st) $[IBVE]_0$ = 0.76 M, $[IBEA]_0$ = 4.0 mM, $[EtAlCl_2]_0$ = 20 mM, [ethyl acetate] = 1.0 M, in hexane at 0 ºC; (2nd–4th) $[IBVE]_0$ = 0.76 M, [macroinitiator]$_0$ = 5.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 20 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at 0 ºC; $[LLA]_0$ = 0.20 M, [hydroxy group]$_0$ = 4.0 mM, $[DBU]_0$ = 5.0 mM, in CH_2Cl_2 at 25 ºC. †For a main peak. *Homopolymer derived from protic impurities.

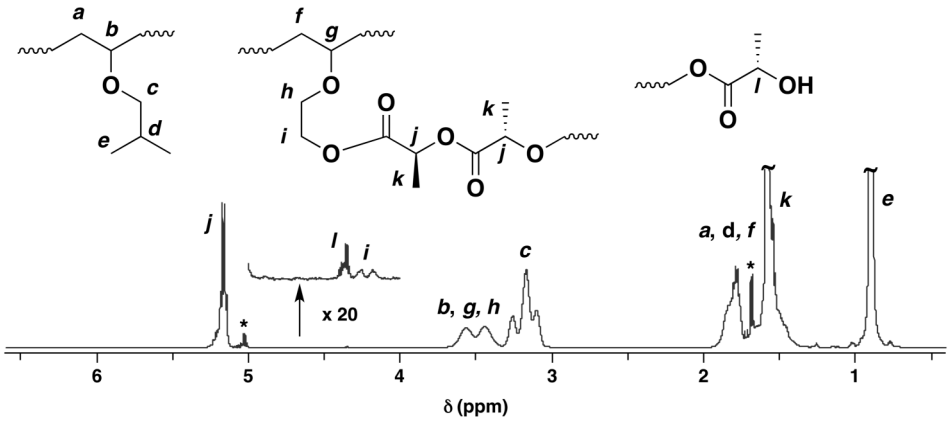


Figure 8. ^{1}H NMR spectrum of poly(IBVE)-*graft*-poly(LLA) [M_n(GPC) = 36.2 × 10^3, M_w/M_n(GPC) = 1.13] (500.16 MHz, in $CDCl_3$ at 30 ºC; *LLA, water).

The comparison of the absolute MWs determined by GPC with RALS and LALS detectors and the relative MWs determined by GPC using a polystyrene calibration indicated that the obtained polymers had branched structures. The absolute MW (M_w = 53 × 10^3) of the graft copolymer containing two branch chains was larger than the relative MW value obtained from the GPC analysis with polystyrene standards (M_w = 41 × 10^3). Additionally, the absolute MW was in relatively good agreement with the value calculated from the MW of the macroinitiator and the conversion of LLA (M_w = 48 × 10^3). In addition, the value of the exponent a of the Mark–Houwink–Sakurada equation was smaller (a = 0.55) than the values of linear poly(IBVE) and poly(LLA) (a ~ 0.7).[25] Similar results were obtained for the graft copolymer with three branch chains [M_w(absolute) = 63 × 10^3, M_w(relative) = 55 × 10^3, M_w(calcd) = 61 × 10^3, a = 0.50].

Conclusion

The synthesis of graft copolymers with highly defined structures was achieved by repetitive cycles of the introduction of cyclic acetal moieties and living polymerization. A VE polymer containing a cyclic acetal moiety at the ω-end was prepared by the post-polymerization modification of an aldehyde group using ethylene glycol. A three-arm star-shaped polymer was synthesized using the cyclic acetal moiety as a two-staged latent initiating site for the living cationic polymerization of IBVE and subsequent ring-opening anionic polymerization of LLA. The protection of the hydroxy groups with a silylating agent was necessary to allow for iterative reactions consisting of cyclic acetalization reaction and living cationic polymerization to yield macroinitiators containing several hydroxy groups on the side chains. These macroinitiators were employed for the synthesis of graft copolymers by ring-opening anionic polymerizations of LLA. The control of the number of branches, the MW of both backbone and branch chains, and the distances between the branch chains of the graft copolymers was feasible using this method because each segment was precisely synthesized via living polymerization. The branch chains of the graft copolymers synthesized in this chapter had uniform lengths and compositions as a result of the simultaneous synthesis of all branch segments; however, graft copolymers having diverse types of backbone and branch

segments may be obtained through step-by-step living polymerization using different types of monomers.

References

1. Lutz, P. J.; Peruch, F. in *Polymer Science: A Comprehensive Reference*, 1st ed.; Matyjaszewski, K.; Möller, M. Eds.; Elsevier Science: Amsterdam, 2012; Chapter 6.14, 511–542.
2. Uhrig, D.; Mays, J. *Polym. Chem.* **2011**, *2*, 69–76.
3. Börner, H. G.; Matyjaszewski, K. *Macromol. Symp.* **2002**, *177*, 1–15.
4. Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Mays, J. *Prog. Polym. Sci.* **2006**, *31*, 1068–1132.
5. Haas, H. C.; Kamath, P. M.; Schuler, N. W. *J. Polym. Sci.* **1957**, *24*, 85–92.
6. Beers, K. L.; Gaynor, S. G.; Matyjaszewski, K. *Macromolecules* **1998**, *31*, 9413–9415.
7. Chung, T. C.; Lu, H. L.; Ding, R. D. *Macromolecules* **1997**, *30*, 1272–1278.
8. Schappacher, M.; Deffieux, A. *Macromol. Chem. Phys.* **1997**, *198*, 3953–3961.
9. Ryu, S. W.; Hirao, A. *Macromolecules* **2000**, *33*, 4765–4771.
10. Ross, S. G.; Müller, A. H. E.; Matyjaszewski, K. *Macromolecules* **1999**, *32,* 8331–8335.
11. Shinoda, H.; Matyjaszewski, K.; Okrasa, L.; Mierzwa, M.; Pakula, T. *Macromolecules* **2003**, *36*, 4772–4778.
12. Muehlebach, A.; Rime, F. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3425–3439.
13. Takano, A.; Kondo, K.; Ueno, M.; Ito, K.; Kawahara, S.; Isono, Y.; Suzuki, J.; Matsushita, Y. *Polym. J.* **2001**, *33*, 732–740.
14. Paraskeva, S.; Hadjichristidis, N. *J. Polym. Sci. Part A: Polym. Chem.* **2000**, *38*, 931–935.
15. Hirao, A.; Hayashi, M.; Haraguchi, N. *Macromol. Rapid. Commun.* **2000**, *21*, 1171–1184.
16. Zhao, Y.; Higashihara, T.; Sugiyama, K.; Hirao, A. *J. Am. Chem. Soc.* **2005**, *127*, 14158–14159.
17. Hirao, A.; Watanabe, T.; Kurokawa, R. *Macromolecules* **2009**, *42*, 3973–3981.
18. Hirao, A.; Murano, K.; Kurokawa, R.; Watanabe, T.; Sugiyama. K. *Macromolecules* **2009**, *42*, 7820–7827.
19. Hirao, A.; Murano, K.; Abouelmagd A.; Uematsu, M.; Ito, S.; Goseki, R.; Ishizone, T. *Macromolecules* **2011**, *44*, 3302–3311.
20. Hirao, A.; Uematsu, M.; Kurokawa, R.; Ishizone, T.; Sugiyama, K. *Macromolecules* **2011**, *44*, 5638–5649.
21. Ito, S.; Ishizone, T.; Hirao, A. *Macromolecules* **2015**, *48*, 8307–8314.
22. Kuramochi, Y.; Sandanayaka, A. S. D.; Satake, A.; Araki, Y.; Ogawa, K.; Ito, O.; Kobuke, Y. *Chem. Eur. J.* **2009**, *15*, 2317–2327.
23. Sugihara, S.; Hashimoto, K.; Matsumono, Y.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci. Part A: Polym. Chem.* **2003**, *41*, 3300–3312.
24. Verma, A.; Nielsen, A.; Bronk, J. M.; McGrath, J. E.; Riffle, J. S. *Makromol, Chem., Macromol, Symp.* **1991**, *47*, 239–251.

25. Dorgan, J. R.; Janzen, J.; Knauss, D. M.; Hait, S. B.; Limoges, B. R.; Hutchinson, M. H. *J. Polym. Sci. Part B: Polym. Chem.* **2005**, *43*, 3100–3111.

Chapter 6

Synthesis of Block Copolymers Using Aromatic Acetal as a "Two-Staged Latent Initiator" for Iterative Living Cationic Polymerizations

Introduction

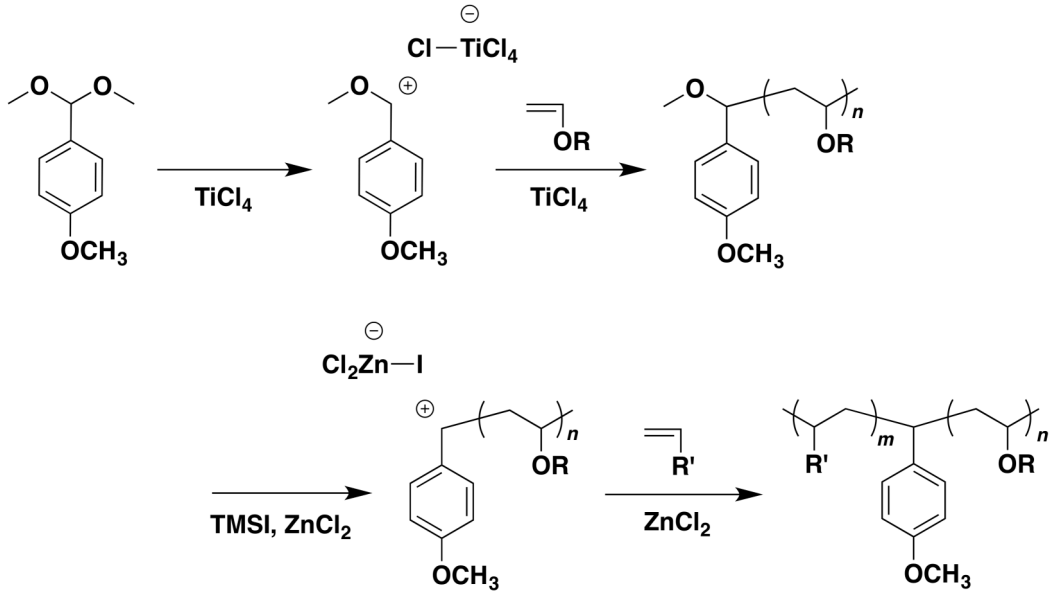
Precision syntheses of polymers having predetermined numbers of functional groups at predetermined positions have recently been attracting much attention in the field of synthetic polymers.[1,2] Methods for the introduction of a functional group into a pinpoint position of a polymer chain via chain polymerization reactions have been devised via the development of living polymerization techniques. For instance, functionalization of polymer chain ends has been demonstrated using reagents with functional groups, such as non-homopolymerizable monomers, terminators, and initiators, in living polymerization.[3–6] Polymers having functional groups at a mid-chain position were successfully obtained using macroinitiators with a functional group.[3,7] Feeding a small amount of highly reactive comonomers, such as maleimides or conjugated aldehydes, at a predetermined time during the living polymerization of monomers such as styrene or vinyl ethers (VEs), respectively, was also highly efficient for the synthesis of polymers with functional groups at predetermined positions along their main chain.[8–10] In addition, polymerization of oligomers having a specific sequence[11–14] and polymerization via iterative single-monomer addition reactions[15–18] can generate polymers with functional groups at precisely defined positions.

In Chapter 4, block copolymers were synthesized by the combination of living cationic polymerization and subsequent ring-opening anionic polymerization using a cyclic acetal as a two-staged latent initiator. Since the moiety derived from the two-staged latent initiator remains between the poly(VE) and poly(lactide) segments of the block copolymer, this method is applicable for the introduction of a functional group into a specific position in a main chain. Therefore, the author focused on aromatic acetals as a two-staged latent initiator for living cationic polymerization. A benzyl ether moiety, a possible initiating site for the second polymerization, is generated at the α-end of the resulting polymer chain through the selective initiation reaction from an aromatic acetal. Because a benzyl ether moiety is relatively stable, as expected from its use for protection of hydroxy groups,[19,20] a macroinitiator with a benzyl ether moiety will be obtained via simple isolation and purification steps. Indeed, Aoshima and co-workers[21] achieved controlled cationic polymerization of VEs through a highly efficient initiation reaction from the benzyl ether moiety at the ω-end of poly(*p*-methoxystyrene) [poly(pMOS)].

This chapter describes the syntheses of block copolymers by controlled cationic polymerization reactions using an aromatic acetal as a two-staged latent initiator. First, polymerization of VEs is examined using *p*-anisaldehyde dimethyl acetal as a cationogen with Lewis acids as catalysts. The quantitative

introduction of a benzyl ether moiety into the α-end of the obtained polymer is achieved using an appropriate Lewis acid at low temperature. Subsequently, the obtained poly(VE) containing a benzyl ether moiety at the α-end is used as a macroinitiator for the syntheses of block copolymers by the second cationic polymerization from the α-end (Scheme 1).

Scheme 1. Synthesis of Block Copolymers Using an Aromatic Acetal as a Two-Staged Latent Initiator.



Experimental

Materials

Isopropyl VE (IPVE; Wako; >97.0%) was distilled twice over calcium hydride. *p*-Anisaldehyde dimethyl acetal (TCI; >97.0%) was distilled twice over calcium hydride under reduced pressure. 1,4-Dioxane (Wako; >99.5%) was dried overnight over molecular sieves 3A and 4A and distilled over calcium hydride and then lithium aluminum hydride. Trimethylsilyl iodide (TMSI; TCI; >95.0%) was used without further purification. Other materials were prepared and used as described in Chapters 2 and 3.

Polymerization Procedure

Polymerizations were carried out in a similar manner to that described in Chapter 2.

Characterization

The MWD of the polymers and NMR spectra were measured as described in Chapter 2.

Results and Discussion

Cationic Polymerizations Using an Aromatic Acetal as an Initiator for Synthesis of a Polymer Containing a Benzyl Ether End

Cationic polymerizations of IPVE using *p*-anisaldehyde dimethyl acetal as a cationogen were investigated with several metal chlorides as catalysts to determine suitable conditions for the synthesis of a polymer having a benzyl ether moiety at the α-end [Scheme 1 (upper)]. The reactions were conducted in CH_2Cl_2 at 0 °C in the presence of ethyl acetate as an added base and 2,6-di-*tert*-butylpyridine (DTBP) as a proton trap reagent (Table 1). The polymerizations proceeded smoothly with any of the catalysts to yield polymers with molecular weights (MWs) relatively similar to their calculated values (entries 1–3 in Table 1). In particular, the polymer synthesized with $TiCl_4$, an effective Lewis acid for the activation of acetal moieties,[22] had a very narrow MWD (M_w/M_n = 1.07) (entry 3 in Table 1). ^{1}H NMR analysis of the products indicated that the polymer chains were generated via the initiation reaction from *p*-anisaldehyde dimethyl acetal. However, the benzyl ether moiety, which resulted from the carbocation generation from the acetal moiety and the subsequent addition reaction of a VE monomer, was not quantitatively retained at the α-end in any polymerization, regardless of catalyst, at 0 °C. A fraction of the benzyl ether head groups were most likely activated during the polymerization reaction through the abstraction of the methoxy group, which triggered the generation of an extra propagating species from the initiator fragment [peaks *c'* and *d'* in Figure 1 (A)–(C)].

The selective initiation reaction from *p*-anisaldehyde dimethyl acetal was achieved by conducting the polymerization at low temperature. The polymerization of IPVE using $TiCl_4$ at −78 °C proceeded at a slower rate than that at 0 °C, yielding a polymer with a narrow MWD and an MW similar to the theoretical value (entry 4 in Table 1, Figure 2). In the ^{1}H NMR of the product, no peak of the structure resulting from the activation of the benzyl ether group was detected [Figure 1 (D)], indicating that the undesired initiation

Table 1. Cationic Polymerization of VEs by *p*-Anisaldehyde Dimethyl Acetal/Lewis Acid Initiating Systems[a]

entry	monomer	Lewis acid	temp. (ºC)	time	conv. (%)	$M_n \times 10^{-3}$ (GPC)[b]	$M_n \times 10^{-3}$ (calcd)	M_w/M_n (GPC)[b]	$f_{\alpha\text{-end}}$[c]
1	IPVE	$EtAlCl_2$	0	2 min	92	16.0	13.8	1.50	0.95
2		$ZrCl_4$	0	4 min	71	11.1	10.6	1.77	0.90
3		$TiCl_4$	0	8 min	96	12.1	14.4	1.07	0.93
4		$TiCl_4$	–78	30 h	94	12.4	14.1	1.07	>0.99
5	IBVE	$TiCl_4$	0	4 h	90	12.1	13.7	1.12	0.74
6		$TiCl_4$	–78	960 h	32	3.7	4.9	1.14	0.84

[a] $[monomer]_0$ = 0.85 M (entries 1–4) or 0.76 M (entries 5, 6), [*p*-anisaldehyde dimethyl acetal]$_0$ = 5.0 mM, [Lewis acid]$_0$ = 20 mM (except for entry 2) or 10 mM (entry 2), [DTBP] = 10 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2. [b] Determined by GPC with polystyrene calibration. [c] The number of benzyl ether head group/the number of ω-ends determined by ^{1}H NMR.

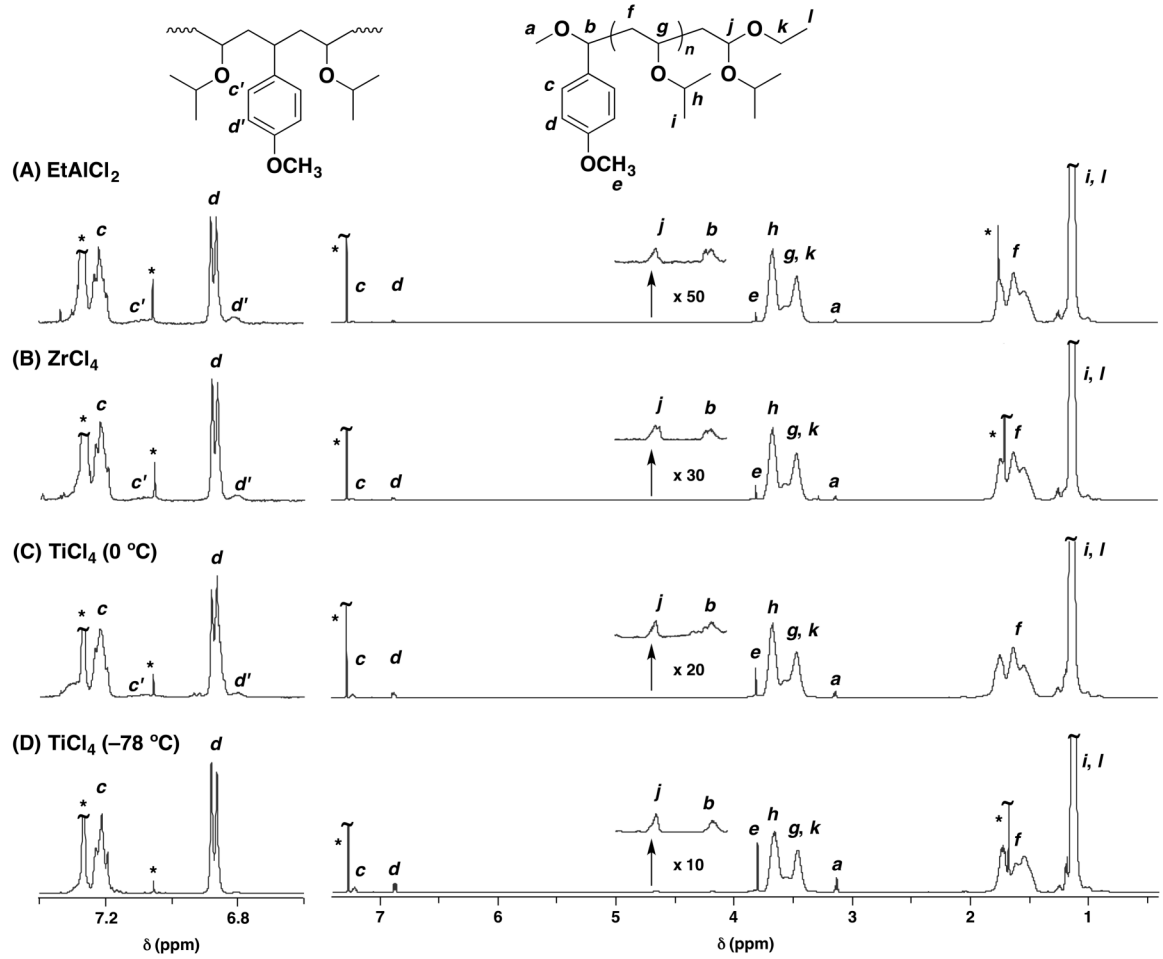


Figure 1. ^{1}H NMR spectra of poly(IPVE)s obtained using the *p*-anisaldehyde dimethyl acetal/Lewis acid initiating systems (A): M_n(GPC) = 16.0 × 10^3, M_w/M_n(GPC) = 1.50, (B): M_n(GPC) = 3.0 × 10^3, M_w/M_n(GPC) = 4.47, (C): M_n(GPC) = 5.2 × 10^3, M_w/M_n(GPC) = 1.13, (D): M_n(GPC) = 4.6 × 10^3, M_w/M_n(GPC) = 1.24 (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water).

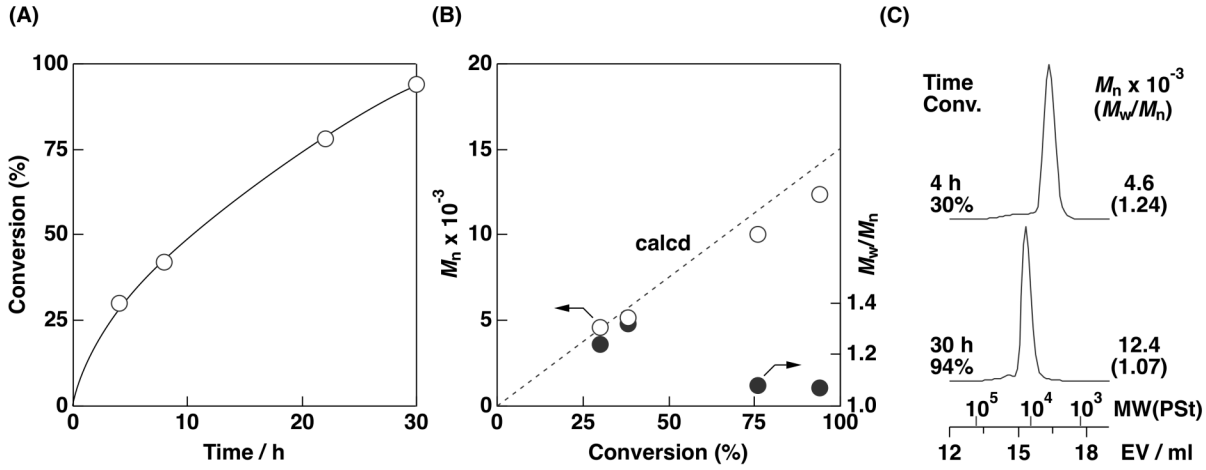


Figure 2. (A) Time–conversion curve, (B) M_n and M_w/M_n–conversion plots, and (C) MWD curves of the poly(IPVE)s obtained using the *p*-anisaldehyde dimethyl acetal/$TiCl_4$ system: $[IBVE]_0$ = 0.76 M, [*p*-anisaldehyde dimethyl acetal]$_0$ = 5.0 mM, $[TiCl_4]_0$ = 20 mM, [DTBP] = 10 mM, [ethyl acetate] = 1.0 M, in CH_2Cl_2 at –78 ºC.

reaction from the initiator fragment was completely suppressed at −78 °C. It should also be noted that the quantitative initiation efficiency from *p*-anisaldehyde dimethyl acetal was retained at this temperature, as confirmed by the GPC and ^{1}H NMR analyses of the products. Thus, the cationic polymerization of IPVE using *p*-anisaldehyde dimethyl acetal as an initiator proceeded in a controlled manner at low temperature using a suitable catalyst, yielding a polymer having a benzyl ether moiety at the α-end with quantitative functionality.

The use of a highly reactive monomer, IPVE, was also essential for the selective initiation reaction without the activation of the benzyl ether end. When isobutyl VE (IBVE), a VE less reactive than IPVE,[23] was polymerized using the *p*-anisaldehyde dimethyl acetal/$TiCl_4$ initiating system at 0 °C, the undesired initiation reaction occurred from approximately a quarter of the benzyl ether ends, as confirmed by ^{1}H NMR analysis (entry 5 in Table 1, Figure 3). This ratio was much higher than with IPVE (approximately 7%) at 0 °C. The longer reaction time for the polymerization due to the smaller reactivity of IBVE is most likely responsible for the more frequent side reactions compared to IPVE. The selectivity in the initiation reaction was improved at −78 °C, although the polymerization proceeded at a very slow rate, and a fraction of the benzyl ether ends were still activated (entry 6 in Table 1).

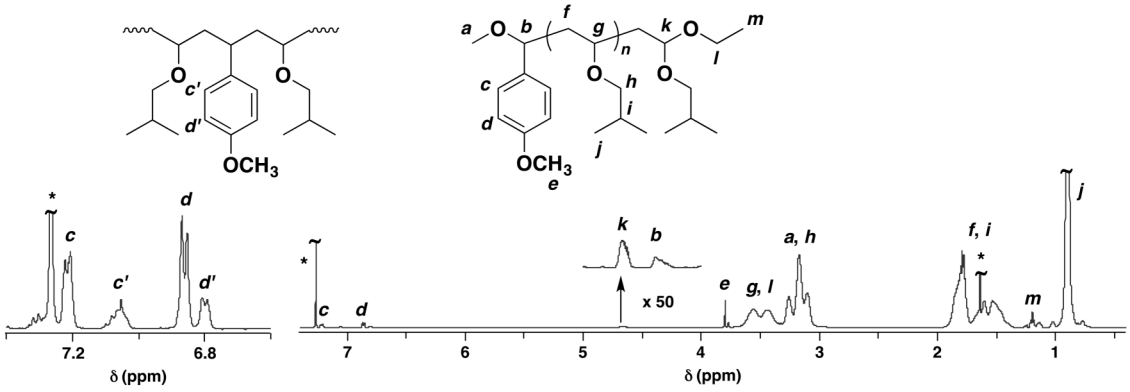


Figure 3. ^{1}H NMR spectrum of poly(IBVE) obtained using the *p*-anisaldehyde dimethyl acetal/$TiCl_4$ initiating system [M_n(GPC) = 4.6 × 10^3, M_w/M_n(GPC) = 1.11] (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water).

Syntheses of Block Copolymers by Cationic Polymerizations Using Poly(IPVE) Having a Benzyl Ether Moiety as a Macroinitiator

The syntheses of block copolymers were examined using poly(IPVE) containing a benzyl ether moiety at the α-end as a macroinitiator [Scheme 1 (lower)]. The macroinitiator was prepared by quenching the living cationic polymerization of IPVE using $LiBH_4$ as a quencher to avoid the formation of an acetal moiety at the ω-end.[24] Cationic polymerization of IBVE using metal chlorides as Lewis acid catalysts proceeded from the macroinitiator in toluene at 0 °C (entries 1–3 in Table 2). However, a part of the macroinitiator remained unreacted after polymerization with all catalysts employed, as confirmed from the MWD curves (Figure 4). This is in sharp contrast to the almost quantitative initiation efficiency in the polymerization using the benzyl ether moiety-containing poly(pMOS) as a macroinitiator in conjunction with

Table 2. Synthesis of Block Copolymers by Polymerization of IBVE Using the Poly(IPVE)/Lewis Acid Systems[a]

entry	Lewis acid	$M_n \times 10^{-3}$ (macroinitiator)	time	conv. (%)	$M_n \times 10^{-3}$ (GPC)[b]	M_w/M_n (GPC)[b]	initiation efficiency[c]
1	$EtAlCl_2/SnCl_4$	11.1	20 min	45	28.8	1.15	0.68
2	$TiCl_4$	12.4	24 h	31	22.6	1.13	0.46
3	$TiCl_4/SnCl_4$	11.7	15 min	71	32.9	1.19	0.76
4	$TMSI/ZnCl_2$	2.8	80 min	86	10.7	1.12	0.36

[a] $[IBVE]_0$ = 0.76 M, $[poly(IPVE)]_0$ = 4.0 mM, $[Lewis\ acid]_0$ = 10 mM/5.0 mM (entries 1 and 3), 20 mM (entry 2) or 6.0 mM/5.0 mM (entry 4), [DTBP] = 5.0 mM, [added base] = 1.0 M (ethyl acetate for entries 1–3) or 1.2 M (1,4-dioxane for entry 4), in toluene at 0 ºC. [b] Determined by GPC with polystyrene calibration (for main peaks). [c] Calculated from the area ratio of block copolymers and residual macroinitiators in GPC curves detected by UV absorption (254 nm).

$EtAlCl_2$ and $SnCl_4$ as catalysts.[21] The same catalysts were not effective for the activation of the benzyl ether end of poly(IPVE) [entry 1 in Table 2, Figure 4 (A)]. Additionally, the initiating systems using $TiCl_4$ or $TiCl_4/SnCl_4$, which were effective for the activation of an acetal moiety,[22,25] resulted in inefficient initiation reactions from the macroinitiator [entries 2 and 3 in Table 2, Figure 4 (B) and (C)]. The initiation efficiencies of these polymerization reactions, calculated from the area ratio of the UV-detected curves (254 nm; Figure 4 broken line) derived from the absorption of the aromatic ring, were 46–76%.[26]

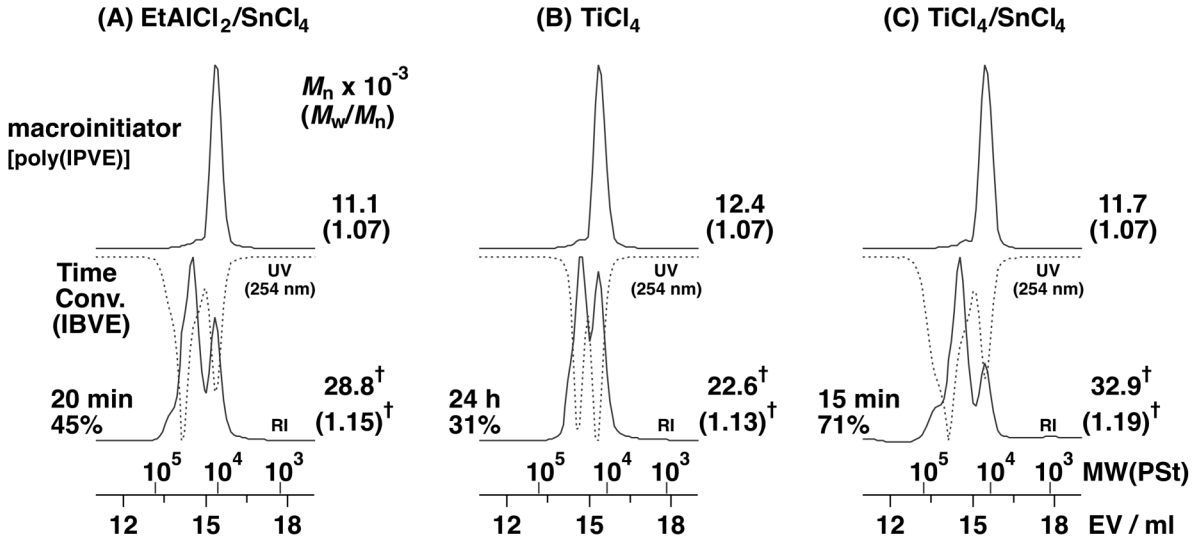


Figure 4. MWD curves for the synthesis of poly(IPVE)-*block*-poly(IBVE) using poly(IPVE) as a macroinitiator: $[IBVE]_0$ = 0.76 M, $[poly(IPVE)]_0$ = 4.0 mM, $[Lewis\ acid]_0$ = 10 mM/5.0 mM [(A), (C)] or 20 mM (B), [DTBP] = 5.0 mM, [ethyl acetate] = 1.0 M, in toluene at 0 ºC. †For main peaks.

Trimethylsilyl iodide (TMSI) was examined as an activator for the benzyl ether moiety of the macroinitiator instead of metal chlorides. TMSI has been used for activation of benzyl ethers in organic chemistry[27,28] and for initiation reactions from cyclic acetals in living cationic polymerization.[29,30] Prior to the use of TMSI for the initiation reaction, a model reaction was carried out under similar conditions to those for the polymerization. The reaction was composed of the activation of the benzyl ether moiety of the

macroinitiator and the subsequent addition of ethanol. If a carbon–iodine bond is formed via the activation of the benzyl ether end by TMSI, a substitution reaction will occur between ethanol and the carbon–iodine bond by the addition of ethanol to generate an ethoxy group at the α-end. The conversion from the methoxy group to an ethoxy group was monitored by ^{1}H NMR spectroscopy. As shown in Figure 5, the peak of the methine group adjacent to the methoxy group completely disappeared after the reaction, and a new peak appeared downfield instead. The peak was assigned to the methine proton adjacent to the ethoxy group, which indicates that TMSI successfully activated the benzyl ether moiety with high efficiency [Figure 5 (B)].

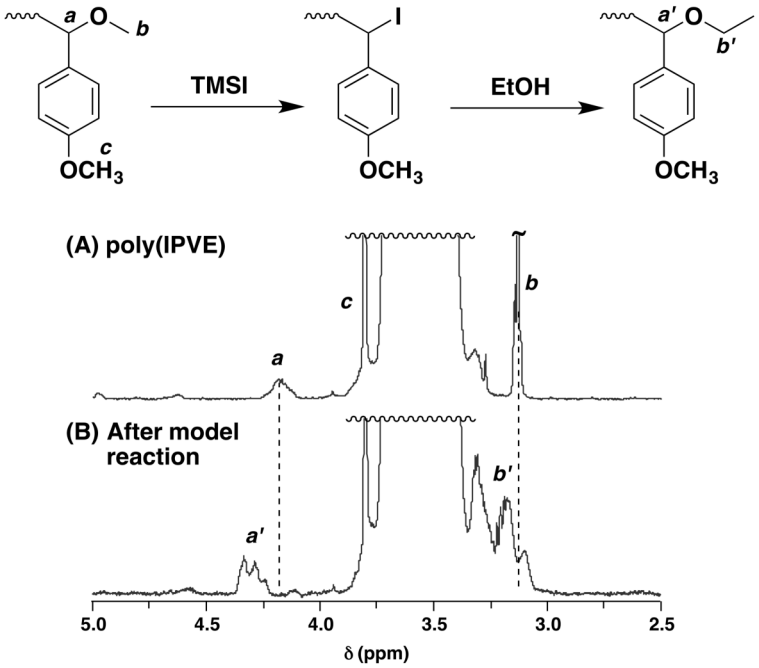


Figure 5. ^{1}H NMR spectra of (A) poly(IPVE) and (B) the product of a model reaction using TMSI as an activator and ethanol as a quencher {reaction conditions: $[poly(IPVE)]_0$ = 4.0 mM, $[TMSI]_0$ = 6.0 mM, [DTBP] = 5.0 mM, [1,4-dioxane] = 1.2 M, in toluene at 0 ºC for 20 min; 500.16 MHz, in $CDCl_3$ at 30 ºC}.

Based on the result of the model reaction, the cationic polymerization of IBVE from the macroinitiator was examined using TMSI as an activator. $ZnCl_2$ was used as a catalyst for the propagation reaction because TMSI has been reported to be ineffective for the propagation reaction of cationic polymerization.[29–32] The polymerization of IBVE proceeded smoothly; however, a large amount of the macroinitiator remained unreacted as confirmed by the UV-detected MWD curve of the product (entry 4 in Table 2, Figure 6).[33]

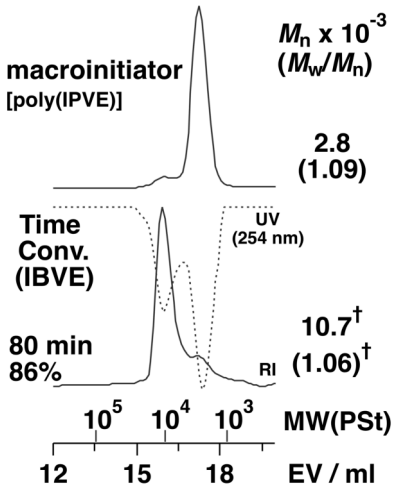


Figure 6. MWD curves for the synthesis of poly(IPVE)-*block*-poly(IBVE) using poly(IPVE) as a macroinitiator: $[IBVE]_0$ = 0.76 M, $[poly(IPVE)]_0$ = 4.0 mM, $[TMSI]_0$ = 6.0 mM, $[ZnCl_2]_0$ = 5.0 mM, [DTBP] = 5.0 mM, [1,4-dioxane] = 1.2 M, in toluene at 0 ºC. †For a main peak.

Alkoxystyrenes were then employed as monomers for polymerization using the macroinitiator because fewer active carbon–halogen ends will be generated from the monomers with lower reactivity than was the case using IBVE.[34,35] First, the cationic polymerization of pMOS was performed under similar conditions to those for the polymerization of IBVE. The polymerization proceeded smoothly with the generation of long-lived species [Figure 7 (A)]. The MWD curves of the products had a very sharp and unimodal peak in the high MW region, which suggests that the desired block copolymer was successfully obtained through the initiation reaction from the macroinitiator. A small amount of a peak in the low MW region was most likely generated via the initiation reaction from protic impurities. The quantitative initiation reaction from the macroinitiator was also confirmed by ^{1}H NMR spectroscopy. No peak assignable to the residue of the unreacted benzyl ether moiety was detected in the spectrum of the obtained polymer (Figure 8). In addition, the MW value of the block copolymer (M_n = 14.8 × 10^3), obtained by GPC analysis, was in relatively good agreement with the value calculated from the MW of the macroinitiator and the conversion of pMOS (M_n = 16.3 × 10^3), which also indicated that the cationic polymerization proceeded with high initiation efficiency.

The cationic polymerization of *p*-*tert*-butoxystyrene (tBOS), an alkoxystyrene less reactive than pMOS,[35] was also efficient for the block copolymerization using the macroinitiator, although the rate of polymerization was very low. The product obtained under similar conditions to those for the pMOS polymerization had a unimodal MWD. Moreover, the peak shifted toward the higher MW region with the consumption of monomers [Figure 7 (B)]. The MW value obtained by GPC (M_n = 3.7 × 10^3) was similar to the calculated MW value (M_n = 5.0 × 10^3), indicating the polymerization proceeded from the macroinitiator with high initiation efficiency.

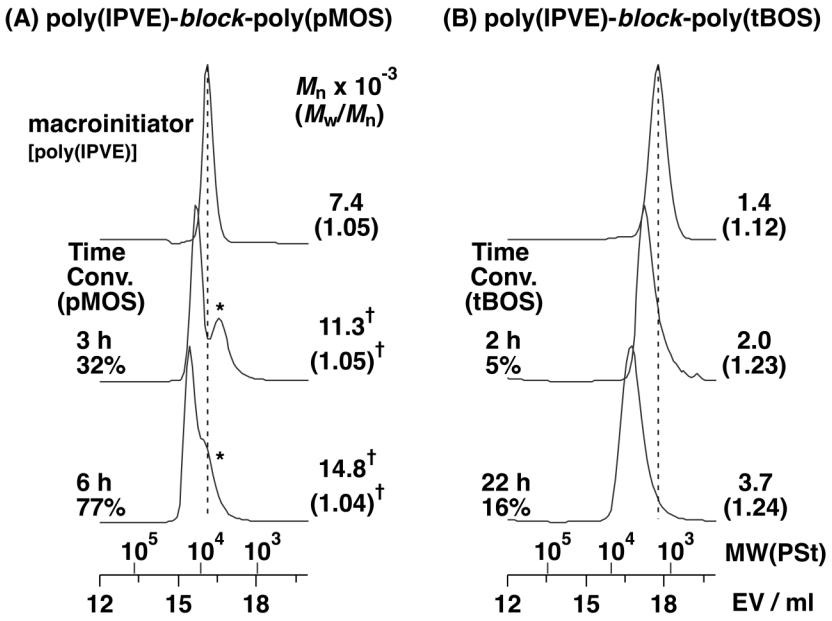


Figure 7. MWD curves for the synthesis of poly(IPVE)-*block*-poly(alkoxystyrenes) using poly(IPVE) as a macroinitiator: $[monomer]_0$ = 0.37 M (A) or 0.53 M (B), $[poly(IPVE)]_0$ = 4.0 mM, $[TMSI]_0$ = 4.0 mM, $[ZnCl_2]_0$ = 10 mM, [DTBP] = 5.0 mM, [1,4-dioxane] = 1.2 M, in toluene at 0 ºC. †For main peaks. *Homopolymers derived from protic impurities.

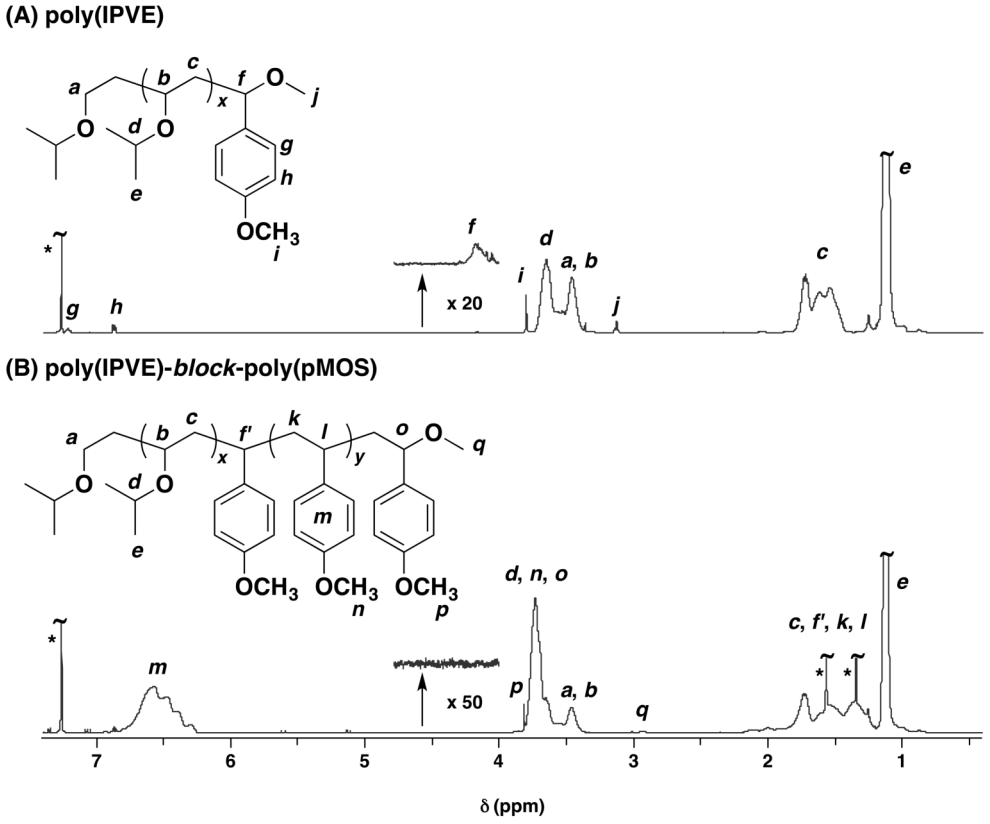


Figure 8. ^{1}H NMR spectra of poly(IPVE) [M_n(GPC) = 7.4 × 10^4, M_w/M_n(GPC) = 1.05] (A) and poly(IPVE)-*block*-poly(pMOS) [M_n(GPC) = 14.8 × 10^3, M_w/M_n(GPC) = 1.04] (B) (500.16 MHz, in $CDCl_3$ at 30 ºC; *$CHCl_3$, water, and vaseline).

Conclusion

In this chapter, the synthesis of block copolymers was investigated using an aromatic acetal as a two-staged latent initiator. Living cationic polymerization of IPVE was achieved using the *p*-anisaldehyde dimethyl acetal/$TiCl_4$ initiating system in CH_2Cl_2 at low temperature. The quantitative introduction of a benzyl ether moiety into the α-end of poly(IPVE) without side reactions was confirmed by ^{1}H NMR spectroscopy. Both the use of IPVE, a highly reactive monomer, and low polymerization temperature were essential for the selective initiation reaction. The benzyl ether end of the poly(IPVE) macroinitiator was quantitatively activated using TMSI, which was confirmed by the model reaction. Based on the result of the model reaction, cationic polymerizations of alkoxystyrenes from the benzyl ether moiety was conducted using the TMSI/$ZnCl_2$ initiating system, resulting in the synthesis of block copolymers, without remaining unreacted macroinitiators. Thus, the syntheses of block copolymers in high initiation efficiency were achieved by repetitive cationic polymerization of monomers with different reactivities using *p*-anisaldehyde dimethyl acetal as a two-staged latent initiator. The introduction of a variety of functional groups between two block segments will be feasible using aromatic acetals having various functional groups.

References

1. Lutz, J.-F. *Acc. Chem. Res.* **2013**, *46*, 2696–2705.
2. Ouchi, M.; Badi, N.; Lutz, J.-F.; Sawamoto, M. *Nat. Chem.* **2011**, *3*, 917–924.
3. Hirao, A.; Hayashi, M.; Loykulnant, S.; Sugiyama, K.; Ryu, S. W.; Haraguchi, N.; Matsuo, A.; Higashihara, T. *Prog. Polym. Sci.* **2005**, *30*, 111–182.
4. Jagura-Grodzinski, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2116–2133.
5. Ouchi, M.; Terashima, T.; Sawamoto, M. *Chem. Rev.* **2009**, *109*, 4963–5050.
6. Aoshima, S; Kanaoka, S. *Chem. Rev.* **2009**, *109*, 5245–5287.
7. Ogura, Y.; Terashima, T.; Sawamoto, M. *J. Am. Chem. Soc.* **2016**, *138*, 5012–5015.
8. Pfeifer, S.; Lutz, J.-F. *J. Am. Chem. Soc.* **2007**, *129*, 9542–9543.
9. Chan-Seng, D.; Zamfir, M.; Lutz, J.-F. *Angew. Chem., Int. Ed.* **2012**, *51*, 12254–12257.
10. Kawamura, M.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Polym. Chem.* **2015**, *6*, 4102–4108.
11. Cho, I.; Hwang, K. M. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1079–1081.
12. Zhang, J.; Matta, M. E.; Hillmyer, M. A. *ACS Macro Lett.* **2012**, *1*, 1383–1387.
13. Satoh, K.; Ozawa, S.; Mizutani, M.; Nagai, K.; Kamigaito, M. *Nat. Commun.* **2010**, *1*, 6.
14. Hibi, Y.; Ouchi, M.; Sawamoto, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 7434–7437.
15. Minoda, M.; Sawamoto, M.; Higashimura, T. *Polym. Bull.* **1990**, *23*, 133–139.
16. Houshyar, S.; Keddie, D. J.; Moad, G.; Mulder, R. J.; Saubern, S.; Tsanaktsidis, J. *Polym. Chem.* **2012**, *3*, 1879–1889.
17. Vandenbergh, J.; Reekmans, G.; Adriaensens, P.; Junkers, T. *Chem. Commun.* **2013**, *49*, 10358–10360.
18. Oh, D.; Ouchi, M.; Nakanishi, T.; Ono, H.; Sawamoto, M. *ACS Macro Lett.* **2016**, *5*, 745–749.

19. Czernecki, S.; Georgoulis, C.; Provelenghiou, C. *Tetrahedron Lett.* **1976**, *17*, 3535–3536.
20. White, J. D.; Reddy, G. N.; Spessard, G. O. *J. Am. Chem. Soc.* **1988**, *110*, 1624–1626.
21. Okada, N.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Polym. Prepr. Jpn.* **2014**, *63(2)*, 4094–4095.
22. Shimomoto, H.; Yoshida, H.; Kanaoka, S.; Aoshima, S. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3703–3709.
23. Hatada, K.; Nagata, K.; Yuki, H.; *Bull. Chem. Soc. Jpn.* **1970**, *43*, 3195–3198.
24. Liu, Q.; Konas, M.; Davis, R. M.; Riffle, J. S. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1709–1717.
25. Chapter 2 in this thesis: Yokoyama, N.; Yoshida, H.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. *Polym. Chem.* **2015**, *6*, 6316–6324.
26. Such low initiation efficiencies of the polymerization using metal chlorides appeared to stem from that the catalyst became less reactive due to the interaction with the isopropoxy side chains and/or the benzyl ether moiety became less reactive due to the electron-withdrawing inductive effect of the isopropoxy group at the penultimate unit.
27. Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761–3764.
28. Onishi, Y.; Nishimoto, Y.; Yasuda, M.; Baba, A. *Chem. Lett.* **2011**, *40*, 1223–1225.
29. Meirvenne, D. V.; Haucourt, N.; Goethals, E. J. *Polym. Bull.* **1990**, *23*, 185–190.
30. Haucourt, N.; Goethals, E. J.; Schappacher, M.; Deffieux, A. *Macromol. Chem., Rapid Commun.* **1992**, *13*, 329–336.
31. Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1990**, *23*, 4896–4901.
32. Kamigaito, M.; Sawamoto, M.; Higashimura, T. *J. Polym. Sci., Part A: Polym. Chem.* **1991**, *29*, 1909–1915.
33. The result was likely due to more efficient activation of the carbon–iodine or carbon–chloride bonds at the propagating ends derived from IBVE compared to the activation of the benzyl ether moiety-derived carbon–iodine bond via the $ZnCl_2$ catalysis [Kojima, K.; Sawamoto, M.; Higashimura, T. *Polym. Bull.* **1990**, *23*, 149–156.].
34. Sawamoto, M.; Ohtoyo, T.; Higashimura, T.; Gührs, K.-H.; Heublein, G. *Polym. J.* **1985**, *17*, 929–933.
35. Kojima, K.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1991**, *24*, 2658–2662.

Chapter 7

Summary

Copolymers having specially designed architectures, such as graft copolymers, have attracted much attention in various fields from basic research to medical and industrial fields because their properties in solution and in the bulk state are completely different from those of linear polymers. In particular, the highly defined structures of these copolymers are very responsible for the sufficient functions as high-performance materials. In this regard, the stepwise synthesis using prepolymers is a highly effective strategy for the precise synthesis of polymers with complicated structures since each segment can be prepared under the best conditions for each monomer. However, prepolymers need to satisfy several prerequisites, such as quantitatively incorporated reactive sites and sufficient stability of reactive sites under ambient conditions, to achieve the precise synthesis. Thus, the author focused on acetal structures, which are stable under neutral and basic conditions but efficiently activated by an acid catalyst, as reactive sites that satisfy the prerequisites. The purpose of this thesis was to develop the method of the precise synthesis of block, graft, and star-shaped copolymers with precisely designed structures using prepolymers via living cationic polymerization with the use of acetal moieties.

Part I described the precise syntheses of copolymers containing branched structures by step-by-step or one-step controlled cationic polymerization reactions based on the catalyst-selectivity of acetal moieties. Block copolymers, graft copolymers, and star-shaped polymers were synthesized via the selective activation of acetal moieties incorporated into monomers and side chains or a chain end of polymers.

Chapter 2 presented the syntheses of block and graft copolymers containing segments derived from monomers with very different reactivities using macroinitiators that have acetal moieties as initiating sites. First, the $TiCl_4/SnCl_4$ initiating system was designed for the living cationic polymerization of pMeSt using TME as an acetal cationogen. The initiating system allowed for living cationic polymerizations of pMeSt using the poly(IBVE) having an acetal end, prepared by living cationic polymerization, as a macroinitiator, which yielded a block copolymer. Moreover, acetal moieties in the side chains of poly(IBVE-*co*-DMEVE), a polymer synthesized by selective vinyl copolymerization of DMEVE and IBVE, were employed as initiating sites for cationic polymerization of pMeSt to yield well-controlled graft copolymers in quantitative yield. In addition, the precision synthesis of block and graft copolymers was also feasible using alkoxystyrenes, styrene derivatives that are more reactive than pMeSt, in a similar manner.

Chapter 3 focused on the quantitative syntheses of end-functionalized polymers using alcohols as quenchers for living cationic polymerization. The results of the quenching reactions using ethanol,

2-propanol, and *tert*-butyl alcohol showed that primary alcohols were suitable for the end-functionalization from the viewpoint of the stability of acetal ω-ends. A block copolymer was also synthesized in high yield by the quenching reaction using a PEG containing a primary hydroxy group at the chain end as a macroterminator. In addition, macromonomers were prepared using primary alcohols containing a vinyloxy group as quenchers for living cationic polymerization. A macromonomer that has a butylene spacer between the vinyloxy group and the acetal moiety derived from the quenching reaction was successfully copolymerized with IBVE using $ZnCl_2$, a low reactive catalyst for acetals, yielding graft copolymers in high yield. The long alkylene spacer of the macromonomer was highly important for the selective copolymerization without side reactions of acetal moieties.

Part II demonstrated the syntheses of block copolymers using cyclic or aromatic acetals as two-staged latent initiators. Additionally, graft copolymers with highly defined structures were prepared by introducing these acetal moieties into the chain ends and using them as initiating sites.

Chapter 4 dealt with the syntheses of block copolymers using a cyclic acetal as a two-staged latent initiator for living cationic polymerization and subsequent ring-opening anionic polymerization. Living cationic polymerization of IBVE using MDOL, a five-membered cyclic acetal, as an initiator in conjunction with $TiCl_4$ as a catalyst proceeded through the generation of carbocation derived from the ring-opening reaction to yield polymers containing a hydroxy group at the α-end. The numbers of both substituents and ring members of cyclic acetals were essential for living cationic polymerization with quantitative initiator efficiency. The MDOL/$TiCl_4$ initiating system was also useful for living cationic polymerization of pMOS. In addition, block copolymers were synthesized by ring-opening polymerization of LLA from the hydroxy groups of the polymers obtained by the living cationic polymerizations using MDOL, demonstrating that the cyclic acetal was usable as a two-staged latent initiator.

Based on the function of cyclic acetals as a two-staged latent initiator as demonstrated in Chapter 4, the synthesis of graft copolymers with highly defined structures was performed by repetitive cycles consisting of the introduction of cyclic acetal moieties into the chain end of poly(VE) and living cationic polymerization reactions (Chapter 5). A polymer containing a five-membered cyclic acetal moiety at the ω-end was prepared by the post-polymerization modification of an aldehyde group at the chain end of poly(IBVE) using ethylene glycol. Then, a three-arm star-shaped polymer was prepared using the cyclic acetal moiety as a two-staged latent initiating site for living cationic polymerization of IBVE and subsequent ring-opening anionic polymerization of LLA. Moreover, the polymers containing several hydroxy groups at the side chains were prepared by the repetitive cycle consisting of the introduction of a cyclic acetal moiety into the chain end, living cationic polymerization, and the protection of the hydroxy group. These polymers were used as macroinitiators for the synthesis of graft copolymers by ring-opening anionic polymerizations of LLA. The control of the number of branches, the MW of both backbone and branch chains, and the distances between the branch chains of the graft copolymers was feasible using this method since each

segment was precisely synthesized via living polymerization reactions respectively.

In Chapter 6, the syntheses of block copolymers via cationic polymerization were investigated using an aromatic acetal as a two-staged latent initiator. First, living cationic polymerization of IPVE proceeded using the *p*-anisaldehyde dimethyl acetal/$TiCl_4$ initiating system at low temperature to yield a polymer containing a benzyl ether moiety at the α-end quantitatively. Both the use of IPVE, a highly reactive monomer, and low polymerization temperature were highly important for the selective initiation reaction. The benzyl ether α-end of the poly(IPVE) macroinitiator was quantitatively activated using TMSI, which was confirmed by the model reaction. Additionally, cationic polymerizations of alkoxystyrenes from the benzyl ether moiety was conducted using the TMSI/$ZnCl_2$ initiating system, resulting in the synthesis of block copolymers with a high initiation efficiency of the macroinitiator.

In conclusion, this thesis described the precise syntheses of copolymers having specially designed architectures by step-by-step living polymerization reactions using prepolymers with acetal moieties as reactive sites. The control of the reactivity of acetal moieties through the structural design and the use of appropriate Lewis acid catalysts depending on the purpose were highly important to achieve the precise synthesis of polymers via selective polymerization reactions. The author hopes that the research conducted in this thesis will be a threshold for the precise synthesis of polymer materials having more complex structures.

List of Publications

1. Norifumi Yokoyama, Hirotoshi Yoshida, Arihiro Kanazawa, Shokyoku Kanaoka, and Sadahito Aoshima
   "Synthesis of Block or Graft Copolymers Containing Poly(Styrene Derivative) Segments by Living Cationic Polymerization Using Acetal Moieties as Latent Initiating Sites"
   Polym. Chem. **2015**, *6*, 6316–6324.
   (Corresponding to Chapter 2)

2. Norifumi Yokoyama, Arihiro Kanazawa, Shokyoku Kanaoka, and Sadahito Aoshima
   "End-Capping Reaction of Living Cationic Propagating Poly(Vinyl Ether)s Using Appropriate Alcohols: Precision Synthesis of Macromonomers for the Preparation of Graft Copolymers via a Grafting-Through Method"
   to be submitted.
   (Corresponding to Chapter 3)

3. Norifumi Yokoyama, Arihiro Kanazawa, Shokyoku Kanaoka, and Sadahito Aoshima
   "Synthesis of Highly Defined Graft Copolymers Using a Cyclic Acetal Moiety for a Combination of Living Cationic Polymerization and Ring-Opening Anionic Polymerization"
   to be submitted.
   (Corresponding to Chapters 4 and 5)