Sequence-Controlled Polymer Synthesis Derived from Alcohols, Cyclic Enol Ethers, and Vinyl Ethers: Selective Generation of 2-Alkoxy Cyclic Ethers Followed by Living Cationic Alternating Copolymerization by the One-Pot Process

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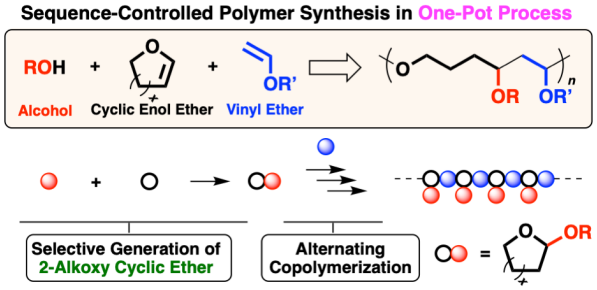


ABSTRACT: Syntheses of sequence-controlled copolymers with controllable molecular weights and chain ends composed of alcohols, cyclic enol ethers, and vinyl ethers were demonstrated using an approach consisting of selective monomer generation and subsequent alternating copolymerization. Acid-catalyzed additions of alcohols to 2,3-dihydrofuran or 3,4-dihydro-2*H*-pyran proceeded quantitatively to yield 2-alkoxy cyclic ethers (2-ACEs). Subsequent cationic alternating copolymerization of the 2-ACE and a vinyl ether proceeded successfully via concurrent ring-opening and vinyl-addition mechanisms, yielding copolymers with periodically arranged alcohol-derived side chain-containing cyclic enol ether and vinyl ether moieties in the repeating units. Complete degradation of the obtained copolymers into a single compound by alcoholysis confirmed the alternating sequences. The use of 2-propanol, (–)-menthol, and (1*R*)-*endo*-(+)-fenchyl alcohol was effective for syntheses of well-defined polymers, whereas the use of methanol resulted in oligomers. The bulkiness of the alkoxy groups of the 2-ACEs likely contributed to the preference for propagation rather than chain transfer.

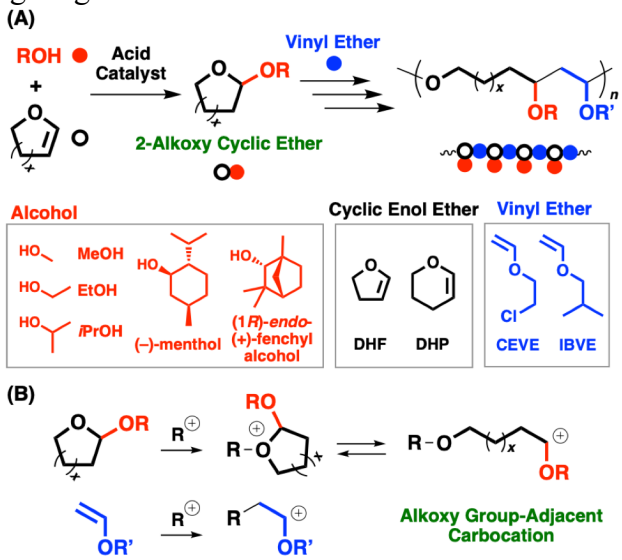
Introduction

Sequence control of synthetic polymers has attracted great interest and has been inspired by the possibility of sophisticated functions based on perfectly controlled structures of biopolymers.[1–4] For example, alternating sequences consisting of two types of monomers can uniformly introduce their functionalities throughout the polymer chains, which can lead to different properties compared to mixtures of homopolymers or block polymers. A well-known method for the synthesis of alternating sequences in chain-growth polymerization is radical copolymerization of monomers with large differences in electron densities, such as styrene and maleic anhydride.[5] Copolymerization of a bulky monomer with higher reactivity and a less reactive monomer is another route for inducing preferential crossover reactions over homopropagations due to steric repulsion.[6–11] Homopolymerization of elaborately designed monomers consisting of two or more monomer units also affords sequence-controlled polymers.[12–20] These methods produce specific sequences, although careful selection of monomers or multistep syntheses is needed for sequence-incorporated monomers. Developing a widely applicable approach from a simple compound will contribute substantially to the development of sequence-controlled polymer syntheses.

As a promising resource for polymer synthesis, we focused on alcohols, which are abundant in both nature and industrial fields. However, in cationic or anionic polymerization, the hydroxy groups of alcohols generally result in chain transfer reactions and/or irreversible termination via reaction with the propagating species. Therefore, transformation of hydroxyl groups into other structures is a practical approach for enabling participation of the alcohols in the polymerization reaction. In synthetic chemistry, acetals are widely used for protection of hydroxy groups. Among the synthetic approaches leading to acetals, the synthesis of 2-alkoxy cyclic ether (2-ACE) structures via acid-catalyzed addition of an alcohol to 2,3-dihydrofuran (DHF) or 3,4-dihydro-2*H*-pyran (DHP) [21–25] is a promising strategy for obtaining alcohol-derived comonomers that can be used in copolymerizations with vinyl monomers. In cationic polymerization, the resulting 2-ACE possibly generates a carbocation adjacent to an alkoxy group, which is structurally similar to the carbocation derived from a vinyl ether (VE), by ring-opening of the oxonium

ion (Scheme 1B). Indeed, our group reported controlled cationic copolymerizations of various cyclic acetals and vinyl monomers.[26] Moreover, we devised a one-pot synthesis of ABC-type sequence-regulated terpolymers based on a successive process comprising selective generation of sequence-incorporated cyclic acetals and subsequent alternating copolymerization.[27] Cationic ring-opening copolymerization of substituted tetrahydrofurans (THFs), such as 2-methyltetrahydrofuran or 3-methyltetrahydrofuran, with 1,3-dioxolane was reported several decades ago, whereas homopolymerization of substituted THFs is rare because the conformations of substituted THFs thermodynamically disfavor the polymerization reaction.[28–30] Therefore, an elaborate design of reaction conditions affording both selective synthesis of 2-ACEs and subsequent alternating copolymerization with a vinyl monomer would potentially enable one-pot syntheses of sequence-controlled polymers using alcohol as a starting material.

Scheme 1. (A) The Synthesis of Alcohol, Cyclic Enol Ether, and VE-Derived Sequence-Controlled Copolymers in One-Pot Approach and (B) Propagating Species Generated at 2-Alkoxy Cyclic Ethers (2-ACEs) or VE-Derived Propagating Ends.



In this study, we aimed to develop one-pot syntheses of sequence-controlled copolymers using various alcohols as monomeric precursors (Scheme 1A). The addition reactions of various alcohols, such as primary and secondary alcohols, including naturally occurring alcohols, to DHF or DHP, which are inexpensive and commercially available cyclic enol ethers, are used to selectively generate the corresponding 2-ACEs under suitable reaction conditions. These 2-ACEs were subsequently copolymerized

with 2-chloroethyl VE (CEVE) without purification, yielding alternating copolymers with well-defined molecular weights (MWs), molecular weight distributions (MWDs), and chain end fidelity.

Experimental

See the Supporting Information for the Materials and Characterization Subsections and NMR and ESI-MS characterization data of 2-alkoxy cyclic ethers.

Synthesis of 2-Alkoxy Cyclic Ethers via Addition of Alcohols to Cyclic Enol Ethers

Procedure A: A typical reaction for addition of an alcohol to a cyclic enol ether proceeds as follows. A glass tube equipped with a three-way stopcock was dried using a heat gun (Ishizaki, PJ-206A; air temperature of approximately 450 °C) under a N_2 atmosphere. Then, dichloromethane, hexane (as an internal standard for calculation of monomer conversion), alcohol, and cyclic enol ether were added into the tube using dry syringes. After cooling the solution at 0 °C for 10 min, a solution of $ZrCl_4$ (containing a small amount of ethyl acetate) in dichloromethane kept at 0 °C was added to the tube to initiate the reaction. After 1 h, an excess amount of methanol containing a small amount of an aqueous ammonia solution was added to the solution to terminate the reaction. Monomer conversion and the amount of 2-alkoxy cyclic ether (2-ACE) generated were determined by ^{1}H NMR analysis of the quenched mixture. The quenched mixture was diluted with dichloromethane and washed with water. The volatiles were then removed under reduced pressure to yield the 2-ACE. For the case of a one-pot process, the reaction mixture was directly subjected to subsequent copolymerization with a VE without quenching by methanol, as described below.

Procedure B: In the cases of 2-methoxytetrahydrofuran, 2-ethoxytetrahydrofuran, and 2-isopropoxytetrahydrofuran, 2-ACEs were synthesized under bulk conditions and without solvent for NMR and mass spectrometry analyses of the obtained products. In contrast, syntheses of copolymers were conducted with procedure A, and the reaction mixture was directly subjected to subsequent copolymerization with a VE. The following is a typical procedure for procedure B: alcohol and *p*-toluenesulfonic anhydride were added to a dried glass tube, and the mixture was cooled at 0 °C. After 10 min, DHF was added to the tube to

start the reaction. After 1 h, a few drops of the reaction mixture were extracted for NMR and mass spectrometric analyses.

Polymerization Procedure. The following is a typical procedure used for copolymerization of 2-ACE and VE in a one-pot process. A glass tube containing the reaction mixture of 2-ACE, which was obtained as described above, was cooled to –78 °C. The copolymerization was started by sequential addition of CEVE and a solution of $SnCl_4$ in dichloromethane kept at 0 °C. After a predetermined interval, the polymerization was terminated with methanol or 3-buten-1-ol containing a small amount of aqueous ammonia or triethylamine, respectively. The quenched reaction mixture was diluted with dichloromethane and then washed with water. The volatiles were evaporated under reduced pressure at 50 °C. When the monomers were insoluble in water, the residual cyclic monomer was removed by reprecipitation with methanol. Monomer conversion was determined from the ^{1}H NMR spectrum of the quenched reaction mixture with hexane or ethyl acetate used as an internal standard.

Alcoholysis. Alcoholysis of the obtained polymers was conducted with 0.50 M HCl (aq.) (Nacalai Tesque; 35−37%) in dichloromethane/*n*-butanol (Nacalai Tesque; >99.0%) or methanol (1/1 v/v) (sample: 0.5 wt%) at 50 °C for 3 h. The reaction mixture was diluted with dichloromethane and washed with an aqueous sodium hydroxide solution and then water. The volatiles were removed under reduced pressure to obtain the products.

Results and Discussion

For selective generation of 2-ACEs from alcohols and cyclic enol ethers, we examined the effects of various reaction conditions, such as catalysts, alcohols, cyclic enol ethers, and solvents, on reaction selectivity (Table 1). In the subsequent copolymerization with VE, residual alcohols result in chain transfer reactions and/or irreversible termination. In addition, residual cyclic enol ethers potentially react as monomers with the propagating species and are incorporated into the main chain. Therefore, complete

consumption of both alcohol and cyclic enol ether is strongly required for successive 2-ACE generation and subsequent copolymerization.

Table 1. Synthesis of 2-ACEs via Addition of Alcohol to Cyclic Enol Ethers[a]

entry	alcohol	enol ether	solvent	time	conv. (%)[b]		RE[c]
					alcohol	enol ether	
1	*i*PrOH	DHF	tol	1 h	100	100	>99
2			DCM	1 h	100	100	>99
3		DHP	tol	1 h	38	37	–
				24 h	100	100	>99
4			DCM	1 h	100	100	>99
5	MeOH	DHF	tol	1 h	100	100	>99
6	EtOH		tol	1 h	100	100	>99
7	(–)-menthol		tol	1 h	100	100	>99
8	(1*R*)-endo-(+)-fenchyl alcohol		DCM	1 h	100	100	>99

[a] $[alcohol]_0$ = 0.50 M, $[cyclic\ enol\ ether]_0$ = 0.50 M, $[ZrCl_4]_0$ = 5.0 mM, [ethyl acetate] = 0.10 M at 0 ºC. [b] Determined by ^{1}H NMR analysis. [c] Reaction efficiency: the ratio of the generated 2-ACE to the feeds of cyclic enol ether ($[2\text{-ACE}]/[cyclic\ enol\ ether]_0$) determined by ^{1}H NMR analysis. tol: toluene. DCM: dichloromethane.

Among the various Brønsted and Lewis acids examined, $ZrCl_4$, one of the efficient catalysts for synthesis of tetrahydropyranyl ether by addition of alcohol to DHP,[24] provided the best performance in terms of reaction rate and selectivity (entry 1 in Table 1; Table S1). Other catalysts, such as *p*-toluenesulfonic anhydride, a conventional Brønsted acid, and $SnCl_4$, which is a Lewis acid used for living cationic polymerizations of various vinyl monomers,[31] also induced selective addition reactions, but these acids required longer reaction times (entries 1 and 2 in Table S1). The ^{1}H NMR spectrum of the reaction mixture recorded after quenching with methanol (Figures S1 and S2) exhibited peaks attributed to 2-isopropoxytetrahydrofuran (2-*i*PrO-THF), while peaks attributed to 2-propanol (*i*PrOH), DHF, and other undesired products were not observed. Moreover, the amount of 2-*i*PrO-THF, which was calculated from the integrated peaks of 2-*i*PrO-THF and hexane used as an internal standard, corresponded to the original feeds of DHF and 2-propanol (~0.50 M), indicating quantitative generation of the cyclic monomer.

Addition of alcohols to DHP instead of DHF quantitatively generated the corresponding 2-ACEs (entries 3 and 4 in Table 1). For the case of DHP, the reaction in toluene was slower than the case of DHF

(entry 3). The use of dichloromethane as a solvent was effective for the faster reaction (entry 4) as in the case of cationic polymerization of vinyl monomers. This difference most likely arose because the reactivity of DHP is lower than that of DHF.

A series of alcohols was also used to generate the corresponding 2-ACEs (entries 5–8 in Table 1). Methyl (MeOH), primary (EtOH), secondary (*i*PrOH), and naturally occurring alcohols with bulky substituents, such as (–)-menthol and (1*R*)-endo-(+)-fenchyl alcohol, were selectively transformed into 2-ACEs by reaction with DHF, which indicated that the structural differences of alcohols affected the selectivity of the addition reactions negligibly.

Controlled cationic copolymerization of the resulting 2-ACEs and CEVE proceeded successfully without isolation or purification of the 2-ACEs when using an initiating system that is effective for living cationic polymerizations of VEs (Table 2 and Figure 1). The reaction solution containing the obtained 2-*i*PrO-THF was cooled to –78 °C, and CEVE and $SnCl_4$ solutions were added to start the copolymerization (entry 1 in Table 2; Figure 1). The $SnCl_4$ catalyst was employed to enable complete propagation at low temperature.[31] The copolymerization resulted in copolymers with very narrow MWDs (Figures 1A and 1C). The MWD curves for the copolymers shifted to higher MWs as the reaction progressed, indicating generation of long-lived species. Moreover, the M_n values measured by GPC analysis were consistent with the theoretical values calculated from the formula based on the amounts of monomers and $ZrCl_4$ (M_n(calcd) = [(formula weight of 2-*i*PrO-THF; 130) × [2-*i*PrO-THF]$_0$ × (conversion of 2-*i*PrO-THF) + (formula weight of CEVE; 106.5) × [CEVE]$_0$ × (conversion of CEVE)] / [$ZrCl_4$]$_0$), suggesting the living nature of the copolymerization (Figure 1B). The dependence of M_n values on [$ZrCl_4$]$_0$ was supported by the copolymerization results with 10 mM of $ZrCl_4$ (Figure S3). The role of $ZrCl_4$ in the generation of propagating chains is discussed below.

Table 2. Synthesis of 2-ACEs and Subsequent Cationic Copolymerization of the 2-ACEs and CEVE[a]

entry	alcohol	enol ether	time	conv. (%)[b]		$M_n \times 10^{-3}$ [c]	M_w/M_n [c]	units per block[d]	
				cyclic	CEVE			cyclic	CEVE
1	*i*PrOH	DHF	16 h	54	99	11.8	1.10	0.98	1.01
2	EtOH	DHF	8 h	49	88	6.2	1.26	0.99	1.09
3	(–)-menthol	DHF	2 h	50	99	15.0	1.10	1.00	1.11
4	(1*R*)-endo-(+)-fenchyl alcohol	DHF	2 h	50	99	4.3	1.30	1.00	1.06
5	*i*PrOH	DHP	2 h	44	99	9.0	1.18	0.99	1.11
6	*i*PrOH	DHF	16 h	59	76	15.8	1.11	0.99	1.17
7	MeOH	DHF	16 h	51	99	0.2	1.42	–	–

[a] Reaction conditions for the synthesis of 2-ACEs: $[alcohol]_0$ = 0.50 M, $[cyclic\ enol\ ether]_0$ = 0.50 M, $[ZrCl_4]_0$ = 5.0 mM, [ethyl acetate] = 0.10 M (derived from the stock solution of $ZrCl_4$), in toluene (entries 1, 2, 6, and 7) or dichloromethane (entries 3–5) at 0 °C for 1 h. Polymerization conditions: $[2\text{-ACE}]_0$ = 0.50 M, $[CEVE]_{add}$ = 0.25 (entries 1–5 and 7) or 0.50 (entry 6) M, $[SnCl_4]_{add}$ = 20 mM, in toluene (entries 1, 2, 6, and 7) or dichloromethane (entries 3–5) at –78 °C. [b] Determined by ^{1}H NMR analysis. [c] Determined by GPC (polystyrene standards). [d] Estimated by ^{1}H NMR.

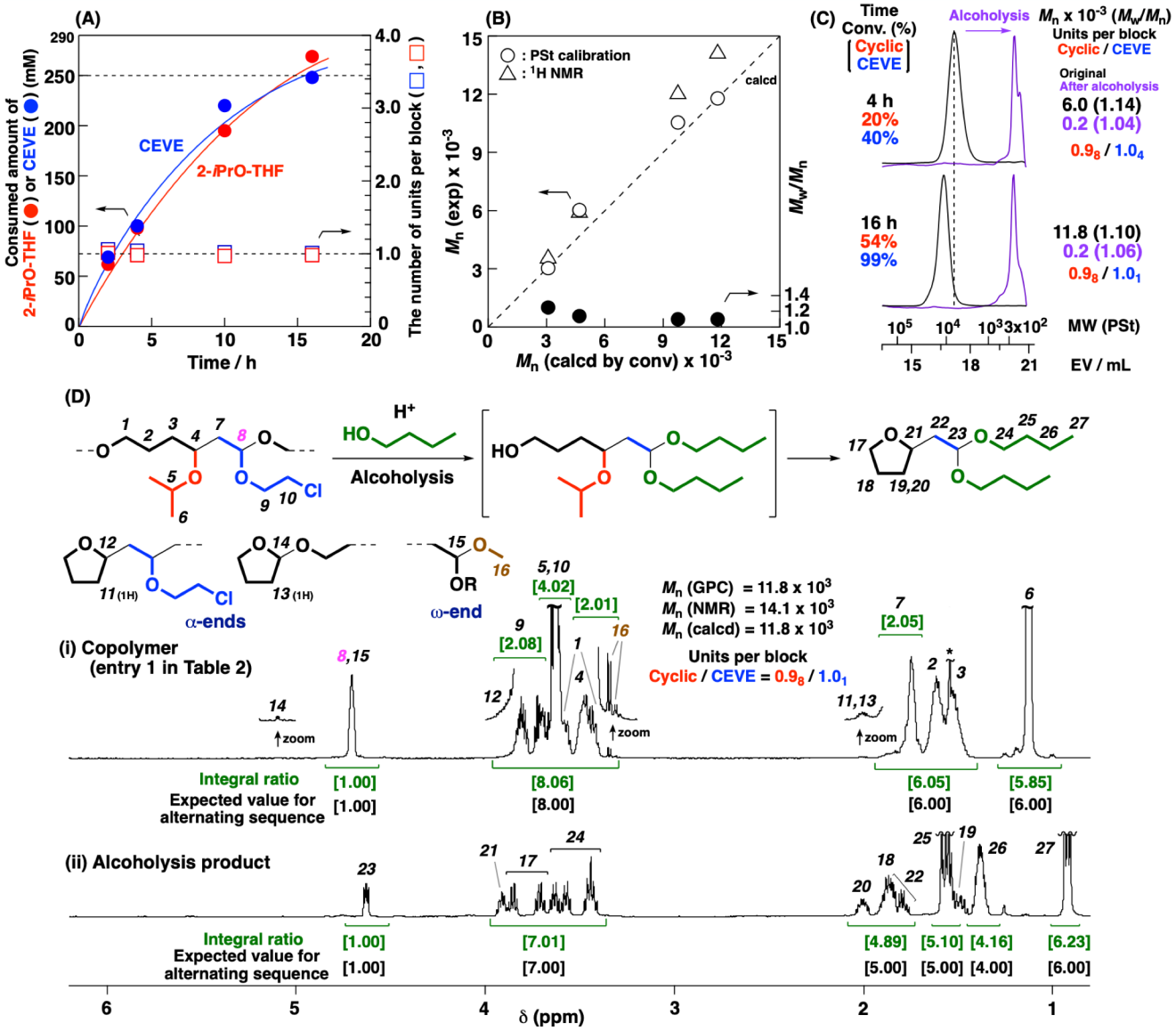


Figure 1. (A) Consumed amounts of CEVE (blue) and 2-*i*PrO-THF (red) in the copolymerization (circle) and the average number of monomer units per block (square: calculated from ^{1}H NMR analysis); (B) the

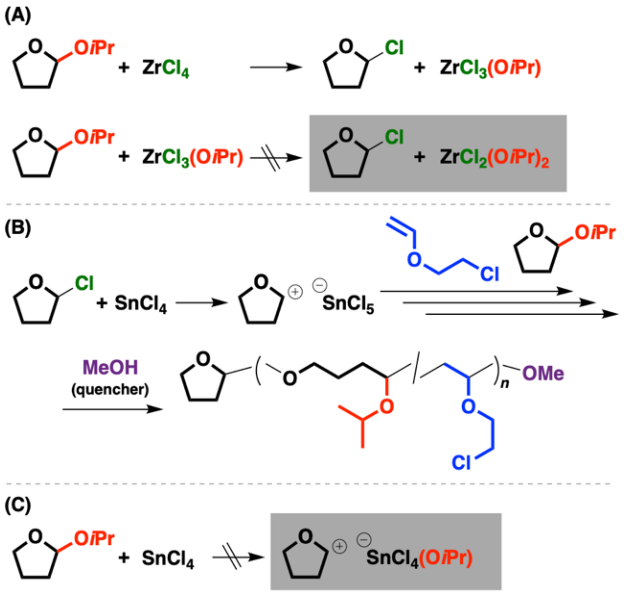
M_n determined by GPC (open circle) or ^{1}H NMR analysis (triangle) and M_w/M_n (filled circle) values of the polymers; (C) MWD curves of poly(CEVE-*co*-2-*i*PrO-THF)s (black) and alcoholysis products (purple); and (D) ^{1}H NMR spectra of *i*PrOH–DHF–CEVE copolymer and its alcoholysis product (in $CDCl_3$ at 30 ºC; * water). The data correspond to entry 1 in Table 2.

^{1}H NMR analysis revealed that the copolymers showed alternating sequences of 2-ACE and CEVE (Figure 1D(i); see Figures S5–S8 for ^{13}C and 2D NMR spectra). The peak at 4.7 ppm was assigned to the acetal structures derived from the crossover reaction from CEVE to the 2-*i*PrO-THF (peak 8), while the peaks at 3.5 ppm were assigned to the structure derived from the crossover reaction from the cyclic ether to CEVE (peak 4). The integral ratio for the methyl protons (peak 6) of the isopropyl group was almost six times that of the acetal proton derived from the crossover reaction (peak 8) and three times that of the methylene proton of the CEVE units in the main chain (peak 7), indicating negligible homopropagation of the cyclic ether. Indeed, homopolymerization of 2-*i*PrO-THF did not occur under the same conditions as those used for copolymerization (Table S2). Moreover, from the integral ratios of the acetal peak (peak 8), the methylene peaks of the CEVE units (peak 7), and the peaks for the isopropyl group (peak 6), the average numbers of 2-*i*PrO-THF and CEVE units per block were calculated to be 0.98 and 1.01, respectively, indicating the occurrence of alternating copolymerization.

The alcoholysis products obtained from the copolymers also supported the presence of alternating sequences in the copolymers. To examine the structures of the repeating units of the copolymers, a transacetalization reaction was conducted with hydrochloric acid and 1-butanol as an acid catalyst and an alcohol, respectively. In the ^{1}H NMR spectrum of the alcoholysis products (Figure 1D(ii)), peaks assigned to the acetal compound derived from one 2-*i*PrO-THF unit and one CEVE unit were selectively observed. This compound was likely generated via transacetalization of the acetal structures derived from crossover from CEVE to the cyclic ether and the intramolecular cyclization reaction accompanied by elimination of *i*PrOH (Figure 1D; see Figures S9–S11 for ^{13}C and 2D NMR spectra). The MWD curves for the alcoholysis products showed a very sharp peak in the low-MW region, suggesting the occurrence of alternating propagation (Figure 1C purple).

Chain-end analyses of the copolymers indicated the livingness of the copolymerization. In the ^{1}H NMR spectrum of the obtained copolymer (Figure 1D(i)), the peaks at 3.3–3.4 ppm (peak 16) were assigned to the ω-end structure derived from methanol, which was used as a quencher. The M_n value calculated from the integral ratio of the ω-end structure (14.1×10^3; calculated from the integral ratios of the acetal peaks (peaks 8 and 15) and the methoxy peak (peak 16), M_n(NMR) = (sum of the formula weights of 2-ACE(*i*PrOH-DHF) and CEVE; 237) × (integral ratio of peaks 8 and 15) / [(integral ratio of peak 16) / 3]; Figure 1B triangle) was comparable to both the value measured by GPC analysis (11.8×10^3; Figure 1B circle) and the theoretical value (11.8×10^3; Figure 1B). The incorporation of an alcohol quencher into the ω-ends was also confirmed by the use of 3-buten-1-ol instead of methanol (Figure S12). These results suggested negligible occurrence of side reactions such as chain transfer reactions.

Copolymer chains were demonstrated to have α-ends derived from the initiation reaction from the carbocations generated by the abstraction of the *i*PrO group of 2-ACE(*i*PrOH-DHF) (Scheme 2) from matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) and electrospray ionization mass spectrometry (ESI-MS) analyses of the copolymers (Figure S13). The amount of the carbocations generated from 2-ACE(*i*PrOH-DHF) corresponds to the amount of $ZrCl_4$, which was supported by the copolymerization result that the M_n values of the products corresponded to the values calculated based on the amounts of $ZrCl_4$ (vide supra; 5.0 mM for Figure 1 and 10 mM for Figure S3). Specifically, an HCl adduct of DHF was likely generated through the reaction of 2-ACE and $ZrCl_4$ (Scheme 2A) as in our previous studies on the cationic polymerization using acetals or alcohols as cationogens.[32–34] A carbocation was generated from the HCl adduct by $SnCl_4$ to trigger polymerization (Scheme 2B), while a carbocation was not efficiently generated from 2-ACE and $SnCl_4$ (Scheme 2C). Oxophilicity and chlorophilicity of metal halides are responsible for the difference in the activity.[33] Peaks assignable to the α-ends were also detected in the ^{1}H NMR spectrum (peaks 11–14 in Figure 1D). In addition, $ZrCl_3$(O*i*Pr), which was likely generated from $ZrCl_4$ and 2-ACE, did not abstract an *i*PrO group from ACE (Scheme 2A).

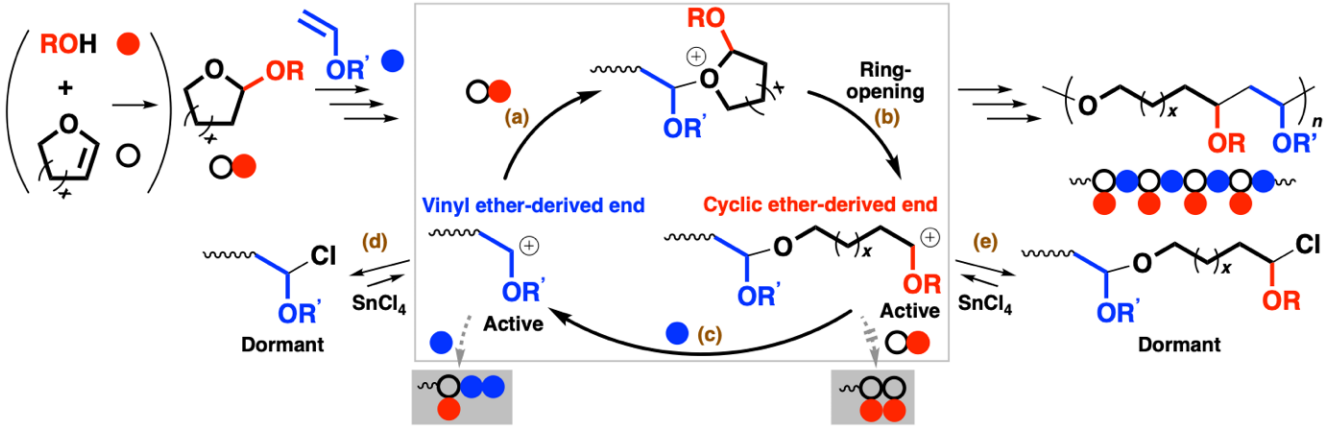


Scheme 2. Postulated mechanisms of (A) the cationogen generation from 2-ACE and $ZrCl_4$, (B) the initiation reaction and polymerization with $SnCl_4$, and (C) inertness of $SnCl_4$ for 2-ACE activation.

The exceptional copolymerizability of 2-ACEs in copolymerizations with CEVE was most likely attributable to the stabilities of carbocations derived from the 2-ACEs and the negligible homopolymerizability of 2-ACEs (Scheme 3). In the propagating reaction, the oxygen at the 1-position of a 2-ACE reacts with the CEVE-derived propagating species (Scheme 3a) to form an oxonium ion species, which is subsequently transformed into a carbocation via a ring-opening reaction (Scheme 3b). The stable carbocation adjacent to the alkoxy group is structurally identical to the carbocation derived from a VE, which is responsible for smooth crossover from the cyclic monomer-derived carbocation to CEVE (Scheme 3c). The negligible homopolymerizability of 2-ACE under the conditions used, which probably stems from a small change in the Gibbs free energy for the homopropagation reaction (Table S2), also contributes to the exclusive crossover to CEVE. In general, polymerization of a THF derivative with a substituent at the 2-position proceeds negligibly because of steric repulsion.[28–30] Similar effects were possibly responsible for the inertness of 2-ACEs to homopropagation. Preferential occurrence of the crossover reaction from CEVE to the cyclic ethers (Scheme 3a) instead of CEVE homopropagation likely stems from the higher reactivities of cyclic ethers toward the propagating carbocations in comparison with that of CEVE. The

higher basicities of 2-ACEs compared to cyclic acetals, which undergo frequent crossover reactions with VEs,[26,27] are also likely responsible for the frequent crossover reactions.[29] The initiation reaction most likely occurs via the abstraction of the *i*PrO group of 2-ACE(*i*PrOH-DHF) with $ZrCl_4$ as mentioned above (Scheme 2).[32,35–37] The living cationic copolymerization proceeded via a dormant-active equilibrium involving reversible activation of carbon-chlorine bonds at the VE-type propagating ends derived from both monomers in a manner similar to those of living cationic polymerizations of VEs (Scheme 3d and 3e; using $SnCl_4$ as a Lewis acid catalyst).[31]

Scheme 3. Copolymerization Mechanisms (Counteranions Are Omitted.).



The one-pot syntheses of copolymers demonstrated above indicated adequate controllability compared with conventional syntheses using isolated monomers (Figure S14). Copolymers obtained by cationic copolymerization of CEVE and 2-*i*PrO-THF, which was obtained via acid-catalyzed addition of iPrOH to DHF and subsequent threefold distillation over calcium hydride, had values comparable (2-*i*PrO-THF/CEVE = 0.98/1.01 units per block, $M_n = 13.4 \times 10^3$; Figure S14) to those obtained by the one-pot method in terms of monomer sequences and MWs (2-ACE(*i*PrOH-DHF)/CEVE = 0.98/1.01 units per block, $M_n = 11.8 \times 10^3$; entry 1 in Table 2). In contrast, the one-pot method was superior to direct polymerization of *i*PrOH, DHF, and CEVE, which did not proceed (Table S3) because *i*PrOH acted as a terminator and/or a chain transfer agent. These results showed that selective generation of the alcohol-derived cyclic monomer is highly important for one-pot syntheses of copolymers with well-defined structures.

The use of other alcohols or cyclic enol ethers also resulted in highly controlled copolymerizations (entries 2–5 in Table 2; Figure 2). A cyclic ether derived from EtOH, (–)-menthol or (1*R*)-*endo*-(+)-fenchyl alcohol, which has simple or bulky substituents, and DHF underwent efficient copolymerization with CEVE (Figure S15–S17; 2-ACE(EtOH-DHF)/CEVE = $0.9_9/1.0_9$ units per block, 2-ACE((–)-menthol-DHF)/CEVE = $1.0_0/1.1_1$ units per block, 2-ACE((1*R*)-*endo*-(+)-fenchyl alcohol-DHF)/CEVE = $1.0_0/1.0_6$ units per block). A six-membered 2-ACE obtained from DHP instead of DHF also produced alternating copolymers with narrow MWDs (Figure S18; 2-ACE(*i*PrOH-DHP)/CEVE = $0.9_9/1.1_1$ units per block). The alcoholysis products of the obtained copolymers exhibited sharp MWDs in the low-MW region, supporting the occurrence of efficient crossover reactions (Figure 2). In addition, an increased proportion of the CEVE monomer led to an increase in the M_n value of the well-defined copolymer (entry 6 in Table 2; Figure S19). The M_n value obtained from GPC analysis (15.8×10^3) was highly consistent with the theoretical values calculated for conversion of both monomers (15.8×10^3), suggesting that high-MW copolymers were generated by polymerizations that occurred in a living manner. However, the higher conversion of CEVE than that of 2-ACE was attained in this case, which suggests that CEVE homosequences were partly generated in the main chain. To suppress the CEVE homosequences and obtain alternating copolymers, the CEVE concentration was set to the half of the 2-ACE concentrations in most cases. In addition, the use of isobutyl VE (IBVE), which is a more reactive VE than CEVE, resulted in the increase in VE homosequences. Copolymers with 2-ACE(*i*PrOH)/IBVE units per block of 1.0/2.5 were obtained at equal concentrations of 2-ACE(*i*PrOH) and IBVE (Figure S20). The use of dichloromethane instead of toluene enabled faster copolymerization (Figure S4).

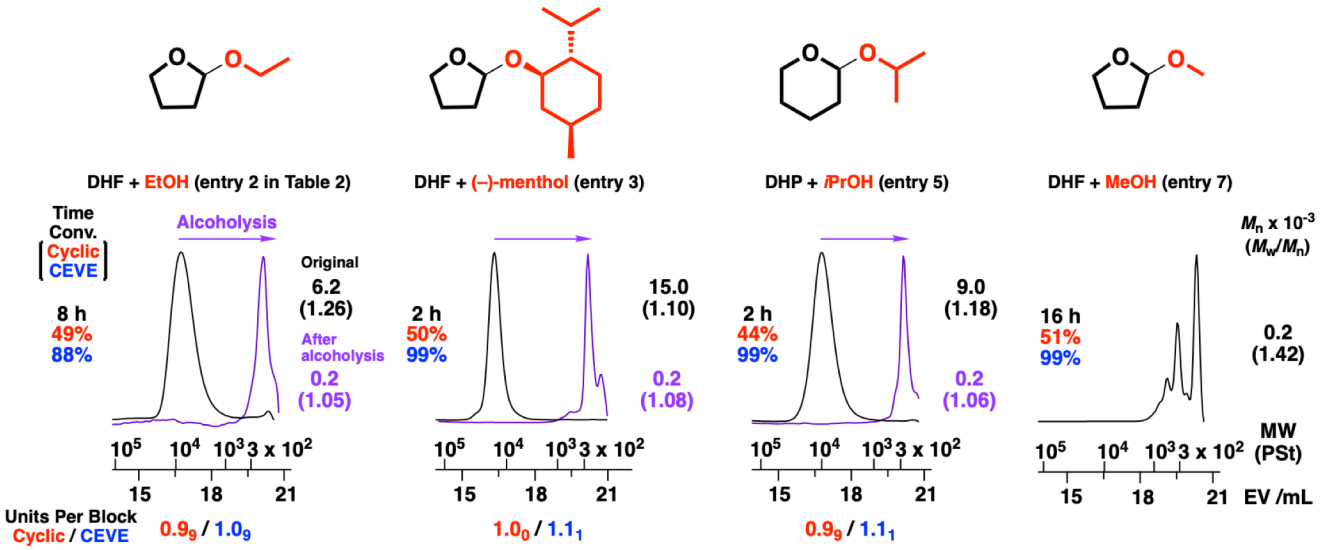
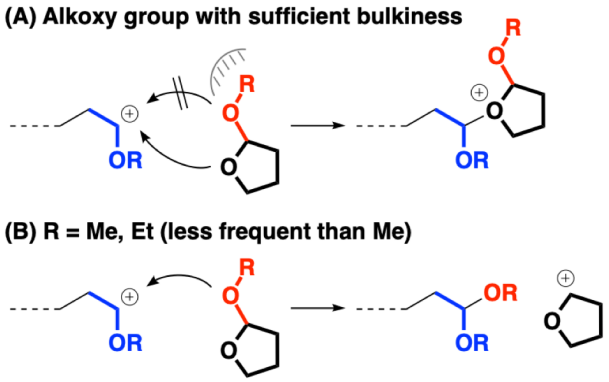


Figure 2. MWD curves of poly(CEVE-*co*-2-ACE)s (black) and alcoholysis products (purple). The data correspond to entries 2, 3, 5, and 7 in Table 2.

Interestingly, cationic copolymerizations of methanol-derived 2-ACE and CEVE produced low-MW compounds (entry 7 in Table 2; Figures 2 and S21). ^{1}H and ^{1}H–^{1}H COSY NMR analyses of the products showed that the major products were oligomers consisting of one or a few CEVE units with a THF structure at the α-end and a methoxy group at the ω-end, suggesting that the methanol-derived 2-ACE acted as a chain transfer agent rather than a monomer (Figures S21 and S22). The reaction of the alkoxy group at the 2-position of 2-ACE results in an acetal chain end and an oxygen atom-adjacent cyclic carbocation (Schemes 4B and S1). Subsequent addition of CEVE to the cyclic carbocation generates another chain with a THF structure at the α-end. Such chain transfer reactions also occurred in the copolymerization of 2-ACE(EtOH-DHF) and CEVE (vide infra) as suggested by the relatively low M_n value (entry 2 in Table 2) and MALDI-TOF-MS and ESI-MS analyses of the copolymer (Figure S23) although the frequency of the chain transfer reactions was lower than the case with the methanol-derived 2-ACE. Therefore, the bulkiness of the alkoxy groups in the 2-ACE most likely contributed to the selectivity for crossover reactions (Scheme 4A).



Scheme 4. The reaction of a propagating carbocation and 2-ACE.

The thermal properties of the obtained polymers were examined with differential scanning calorimetry (DSC) measurements (Figure S24). The glass transition temperatures (T_g) of the obtained polymers were tunable depending on their alkoxy substituents derived from 2-ACEs. Bulkier alkoxy substituents resulted in a higher T_g (*i*PrOH–DHF–CEVE copolymer: T_g = –24 °C, entry 1 in Table 2; (–)-menthol–DHF–CEVE copolymer: T_g = 6 °C, entry 3 in Table 2). The use of VEs with a bulkier alkoxy group, such as cyclohexyl VE, will also lead to further increase in T_g. In addition, the number of carbons in the repeating unit in the main chain, which is tunable by using 5- or 6- membered cyclic enol ethers, slightly affected the T_g values (*i*PrOH–DHP–CEVE copolymer: T_g = –28 °C, entry 5 in Table 2).

Conclusion

In conclusion, a sequential process consisting of selective monomer generation and subsequent alternating copolymerization was demonstrated to generate well-defined copolymers from simple compounds such as alcohols, cyclic enol ethers, and a VE. The use of a series of alcohols, cyclic enol ethers, and acid catalysts provided effective and selective syntheses of 2-ACEs with corresponding structures. Subsequent copolymerizations of the 2-ACEs with CEVE produced alternating copolymers with well-defined structures. The results obtained in this study provide a facile strategy for producing sequence-controlled copolymers with various types of monomers obtained from diverse sources. Other vinyl

monomers possessing appropriate reactivities, such as styrene derivatives, can also be potentially useful for the copolymerization with 2-ACEs, which will be demonstrated in our future study.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website.
Experimental sections; NMR spectra of 2-ACEs and polymerization products; and polymerization data.

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Notes

The authors declare no competing financial interest.

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