Title	ABC-Type Periodic Terpolymer Synthesis by a One-Pot Approach Consisting of Oxirane- and Carbonyl-Derived Cyclic Acetal Generation and Subsequent Living Cationic Alternating Copolymerization with a Vinyl Monomer
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ABC-Type Periodic Terpolymer Synthesis by a One-Pot Approach Consisting of Oxirane- and Carbonyl-Derived Cyclic Acetal Generation and Subsequent Living Cationic Alternating Copolymerization with a Vinyl Monomer

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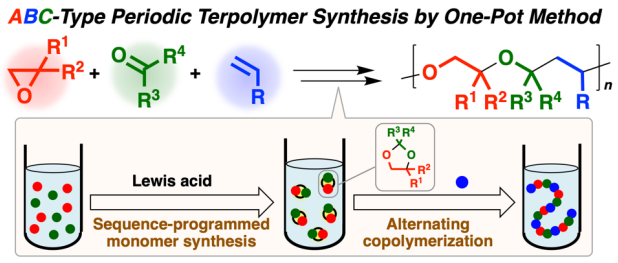


ABSTRACT. A one-pot synthesis of ABC-type periodic terpolymers with controllable molecular weights was achieved via an elaborately designed method consisting of sequence-programmed cyclic monomer synthesis and living cationic copolymerization of this cyclic monomer with a vinyl monomer. In this method, a cyclic acetal generated by a selective and quantitative Lewis acid-catalyzed cyclodimerization reaction of an oxirane and a carbonyl compound was subjected to subsequent copolymerization without any isolation or purification. Alternating copolymerization of the cyclic acetal and vinyl ether (VE) proceeded, yielding an ABC-type periodic terpolymer composed of oxirane, a carbonyl compound, and VE. Interestingly, the copolymerization proceeded in a living manner, which allowed simultaneous control of the molecular weight, molecular weight distribution, and chain ends in addition to the periodic sequence. Moreover, the terpolymers could be degraded by acid due to the periodically located acetal moieties. The use of various monomers also produced ABC-type sequence terpolymers. ABC-*b*-ABD-type periodic block quaterpolymers were synthesized by the sequential addition of vinyl monomers during the living copolymerization. These results surely provide a simple and efficient approach for the design of monomer sequences, polymer lengths, and chain ends in synthetic polymers.

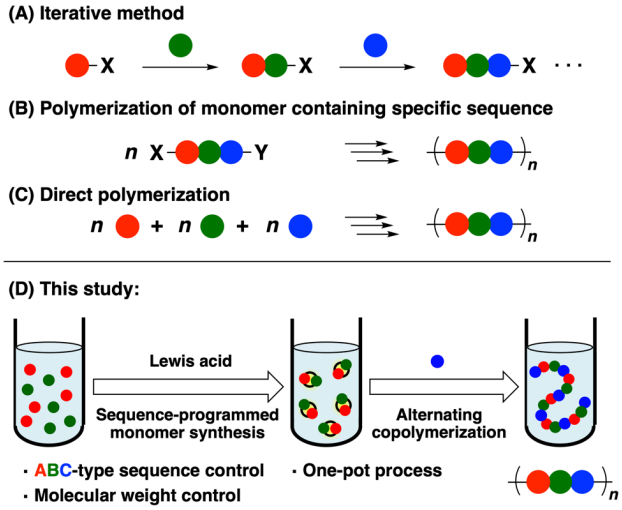
Introduction

Monomer sequences are important structural factors of polymers.[1–4] Natural macromolecules such as peptides and proteins exhibit sophisticated functions due to their perfectly regulated monomer sequences. In synthetic polymers, various methods have been developed to control the monomer sequences. One of the most reliable strategies is iterative single unit monomer addition

(Scheme 1A), such as polypeptide synthesis with the Merrifield resin, although considerable time and effort are required to prepare long polymers.[5–8] The polymerization of monomers containing a specific sequence (Scheme 1B) effectively produces sequence-regulated polymers;[9–19] however, the preparation of sequence-incorporated monomers generally requires a multistep reaction and challenging purification steps and/or results in low yield. The direct chain-growth polymerization of several monomers (Scheme 1C) is the simplest approach, although extremely high selectivity during the propagation reactions is indispensable for sequence regulation.[20–23] A simpler and more sophisticated method is desirable for facile access to sequence-controlled polymers.

A promising strategy for facile synthesis of sequence-controlled polymers is a successive one-pot process consisting of the synthesis of a sequence-incorporated monomer and subsequent polymerization with another monomer (Scheme 1D). A relevant and important study on the copolymerization of a sequence-incorporated monomer with another monomer describes the cycloaddition of an electron-deficient olefin and vinyl ether (VE) and the subsequent copolymerization of the cycloaddition product with oxirane,[24,25] although this example is not a one-pot process and requires purification and isolation of the cycloaddition product before polymerization with oxirane. To achieve a one-pot method, quantitative synthesis of a sequence-incorporated monomer without residual starting materials, the absence of byproducts, and the use of catalysts that do not disturb either the monomer synthesis or the polymerization are required.

Scheme 1. Schematic Illustration for (A), (B), (C) Synthesis of Sequence-Regulated Polymers and (D) the Method Designed in This Study: *In situ* Synthesis of a Sequence-Programmed Monomer and Subsequent Copolymerization with Another Monomer

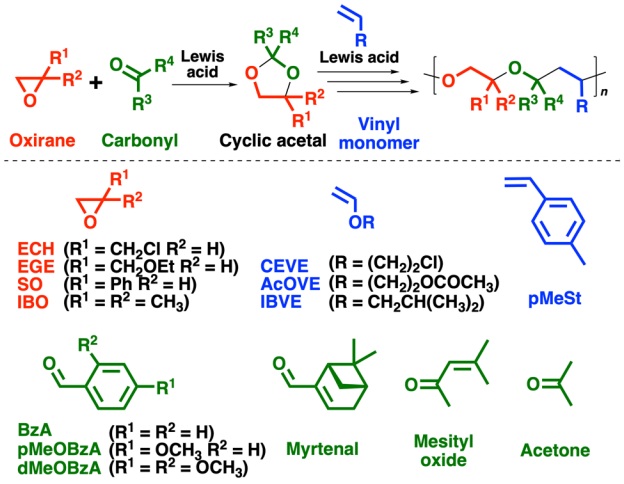


To satisfy these requirements, we devised a one-pot method that consists of the synthesis of a sequence-programmed cyclic acetal via selective cyclodimerization of oxirane and a carbonyl compound and the subsequent copolymerization of the cyclic acetal with a vinyl monomer. The cyclic acetal formation was reported to proceed from oxirane and acetone with the aid of a Lewis acid catalyst.[26–29] In addition, in our previous study, a cyclic acetal was generated as a byproduct in the cationic terpolymerization of oxirane, ketone, and VE,[23] which suggests that the cyclization reaction of oxirane and a carbonyl compound occurs even under the conditions required for cationic polymerization. The cationic copolymerization of cyclic acetals and vinyl monomers via the cationic mechanism was reported several decades ago.[30,31] Recently, we reported the controlled cationic copolymerization of VEs and cyclic acetals using a carefully designed initiating system based on the living cationic polymerization of vinyl monomers.[32] We also systematically

investigated the structural effects of cyclic acetals on copolymerization behavior.[33] The elaborate design of reaction conditions that enable both the quantitative synthesis of a sequence-programmed cyclic acetal and the subsequent alternating copolymerization of the cyclic acetal with a vinyl monomer can potentially afford ABC-type periodic terpolymers by a one-pot method.

In this study, we examined the one-pot synthesis of sequence-controlled terpolymers composed of oxiranes, carbonyl compounds, and vinyl monomers via the above-explained strategy (Scheme 2). Suitable combinations of aldehydes or ketones with oxiranes underwent selective and quantitative cyclodimerization reactions and yielded cyclic acetals without any byproducts under appropriately designed conditions. The generated cyclic acetals were successively copolymerized with VEs or styrene derivatives in a living manner, which afforded ABC-type periodic terpolymers with controlled molecular weights (MWs), molecular weight distributions (MWDs), and chain end structures. Furthermore, the sequential addition of VEs with different substituents, such as chloride or acetoxy moieties, produced unique block polymers consisting of blocks with different ABC-type periodic sequences.

Scheme 2. Synthesis of Sequence-Regulated Polymers via Selective Cyclodimerization of Oxiranes and Carbonyl Compounds and Subsequent Controlled Cationic Copolymerization with Vinyl Monomers (upper). Monomers Used in This Study (lower)



EXPERIMENTAL SECTION

Materials. Epichlorohydrin (ECH; TCI; >99.0%), ethyl glycidyl ether (EGE; TCI; >98.0%), styrene oxide (SO; Aldrich; 97.0%), *p*-methoxybenzaldehyde (pMeOBzA; Nacalai Tesque; ≥99.0%), benzaldehyde (BzA; Wako; >98.0%), and (1*R*)-(–)-myrtenal (myrtenal; Aldrich; ≥97.0%) were distilled twice over calcium hydride under reduced pressure. Mesityl oxide (Nacalai Tesque; ≥96.0%), isobutylene oxide (IBO; TCI; >97.0%), and ethyl acetate (Wako; >99.5%) were distilled twice over calcium hydride. 2-Chloroethyl VE (CEVE; TCI; >97.0%), *p*-methylstyrene (pMeSt; Aldrich; 96.0%), and isobutyl VE (IBVE; TCI; >99.0%) were washed with 10% sodium hydroxide solution and then water and distilled twice over calcium hydride under reduced (CEVE and pMeSt) or atmospheric (IBVE) pressure, respectively. 2-Acetoxyethyl VE (AcOVE) was synthesized by the substitution reaction of CEVE with sodium acetate and then distilled twice over

calcium hydride under reduced pressure.[34] 2,4-Dimethoxybenzaldehyde (dMeOBzA; TCI; >98.0%) was recrystallized from hexane and dried *in vacuo*. $SnCl_4$ (Sigma-Aldrich; 1.0 M solution in heptane), $TiCl_4$ (Sigma-Aldrich; 1.0 M solution in toluene), methanol (Nacalai Tesque; ≥99.8%), 3-buten-1-ol (TCI; >98.0%), ammonia water (Nacalai Tesque), triethylamine (Wako; >99.0%), 1,2-dimethoxyethane (Nacalai Tesque; ≥99.0%), hydrochloric acid (Nacalai Tesque; 35–37%), trifluoroacetic acid (Nacalai Tesque; ≥99.0%), sodium hydroxide (Nacalai Tesque; ≥97.0%), $In(OTf)_3$ (Sigma-Aldrich), potassium *tert*-butoxide (Wako; >85.0%), sodium iodide (Wako; >99.5%), *N*,*N*-dimethylformamide (Nacalai Tesque; >99.5%), and toluene (Nacalai Tesque; ≥99.5%) were used without further purification. Stock solutions of $FeCl_3$ in diethyl ether and $GaCl_3$ in hexane were prepared from $FeCl_3$ (Sigma-Aldrich; 99.99%) and $GaCl_3$ (Sigma-Aldrich; >99.999%), respectively. Dichloromethane (Wako; superdehydrated) was dried by passage through solvent purification columns (Glass Contour).

Synthesis of Cyclic Acetals via Selective Cyclodimerization. A typical reaction for the cyclodimerization of an oxirane and a carbonyl compound is as follows. A glass tube equipped with a three-way stopcock was dried using a heat gun (Ishizaki, PJ-206A; the air temperature was approximately 450 °C) under dry nitrogen. Dichloromethane and pMeOBzA were added into the tube using dry syringes. After cooling the solution to 0 °C, a solution of $SnCl_4$ (containing a small amount of heptane) in dichloromethane kept at 0 °C was added to the tube. The reaction was initiated by dropwise addition of a solution of ECH in dichloromethane (2 M). After 24 h, the reaction was terminated with methanol containing a small amount of an aqueous ammonia solution. Monomer conversion and the amount of cyclic acetal generated were determined by ^{1}H NMR spectroscopy of the quenched mixture. The quenched solution was diluted with dichloromethane and washed with water. The volatiles were then removed under reduced pressure to yield a

colorless cyclic acetal (see the Supporting Information for spectroscopic analysis of cyclic acetals). In the case of the one-pot process for the synthesis of a terpolymer, the reaction mixture was subjected to subsequent copolymerization with a vinyl monomer without quenching by methanol, as described below.

Polymerization Procedure. The following is a typical procedure for the copolymerization of a cyclic acetal and a vinyl monomer by a one-pot method. The glass tube containing the reaction mixture for cyclic acetal synthesis (explained above) was cooled at –96 °C. The polymerization was started by sequentially adding ethyl acetate, CEVE, and a solution of $SnCl_4$ in dichloromethane to the tube. 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. The residual cyclic acetal was removed by reprecipitation with methanol to yield a terpolymer. Monomer conversion was determined by ^{1}H NMR spectroscopy of the quenched reaction mixture using heptane as an internal standard.

Acid Hydrolysis. Acid hydrolysis of the obtained polymers was conducted with 0.50 M HCl (aq.) in 1,2-dimethoxyethane (sample: 0.5 wt%) at room temperature for 3 h. The quenched mixture was diluted with dichloromethane and washed with an aqueous sodium hydroxide solution and then water. The volatiles were removed at room temperature and atmospheric pressure.

Methanolysis. The polymer (30 mg) was dissolved in dichloromethane (3 mL), and then methanolysis was initiated by the addition of $In(OTf)_3$ (50 mg) in methanol (3 mL) at 50 °C. After

3 h, the reaction was quenched by aqueous sodium hydroxide solution, and the mixture was washed with water. The volatiles were removed under reduced pressure to yield a methanolysis product.

Formation of Vinyl Acetal Structure by Elimination of HCl. The polymer (15 mg) was dissolved in *N*,*N*-dimethylformamide (2 mL). Potassium *tert*-butoxide (50 mg) and sodium iodide (65 mg) were added to the reactor, and the reaction mixture was stirred for 16 h at room temperature. The reaction mixture was then diluted with toluene and washed with water. The volatiles were removed under reduced pressure.

Characterization. The MWD of the obtained polymer was measured by gel permeation chromatography (GPC) in chloroform at 40 °C with polystyrene gel columns [TSKgel GMH_{HR}-M × 2 (exclusion limit MW = 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 MW (M_n) and the polydispersity ratio (weight-average MW/number-average MW [M_w/M_n]) were calculated from the chromatographs based on 16 polystyrene standards (Tosoh; $M_n = 5.0 \times 10^2$–1.09×10^6, $M_w/M_n < 1.2$). The absolute M_n values were determined with a GPC system composed of a Viscotek VE 1122 pump, polystyrene gel columns (TSKgel GMH_{HR}-M × 2; flow rate = 0.7 mL/min), and a Viscotek TDA 305 triple detector [refractive index, laser light scattering (λ = 670 nm; 90° RALS and 7° LALS), and differential pressure viscometer] in tetrahydrofuran. NMR spectra were recorded by means of a JEOL JNM-ECA 500 spectrometer (500.16 MHz for ^1H and 125.77 MHz for ^{13}C) in chloroform-*d* at 30 °C. Electrospray ionization mass spectra (ESI-MS) were recorded using an LTQ Orbitrap XL (Thermo Scientific) spectrometer. The thermal properties of the polymers were examined with a Shimadzu DSC-60 Plus differential scanning

calorimeter for differential scanning calorimetry (DSC) analysis and PerkinElmer STA 6000 for thermal gravimetric analysis (TGA).

RESULTS AND DISCUSSION

Selective and Quantitative Synthesis of Sequence-Programmed Cyclic Acetal. To synthesize sequence-regulated monomers, the cyclodimerization reaction of various oxiranes and carbonyl compounds was examined using $SnCl_4$ as a Lewis acid in dichloromethane at 0 °C. $SnCl_4$ was used because this Lewis acid is highly effective for the living cationic polymerization of various VEs and styrene derivatives.[35] During the cyclodimerization reaction, complete consumption of both oxirane and carbonyl compounds is required because residual oxirane and carbonyl compounds would potentially react with VE during the subsequent cationic copolymerization.[36,37]

Very high selectivity was attained in the cyclodimerization of epichlorohydrin (ECH) with various aromatic aldehydes or conjugated ketones, among various combinations of monomers. The reactions effectively proceeded with almost complete consumption of both monomers, resulting in cyclic acetals consisting of ECH and a carbonyl compound (entries 1–5 in Table 1). In the case of *p*-methoxybenzaldehyde (pMeOBzA; entry 1 in Table 1), the ^{1}H NMR spectrum of the reaction mixture (Figure 1; see Figure S1 for ^{13}C NMR), which was recorded after quenching with an excess amount of methanol, exhibited peaks attributed to a cyclic acetal (98%) and a very small amount of residual pMeOBzA (2%; this resulted from the experimental error when using equimolar amounts of pMeOBzA and ECH), while no peaks attributed to residual ECH and undesired products, such as oxirane homopolymer, were observed. Similar results were obtained with 2,4-dimthoxybenzaldehyde (dMeOBzA; entry 2) and benzaldehyde (BzA; entry 3), which are more

and less reactive aromatic aldehydes than pMeOBzA, respectively. Moreover, the acyclic conjugated aldehyde (1*R*)-(–)-myrtenal (myrtenal; entry 4) and the conjugated ketone mesityl oxide (entry 5) also underwent an efficient cyclodimerization reaction with ECH.[38] However, the use of acetone resulted in the incomplete generation of a cyclic acetal and the partial formation of an ECH oligomer (entry 6), probably due to the smaller nucleophilicity of acetone than the conjugated aldehydes and ketones.

Table 1. Selective Cyclodimerization of Various Oxiranes and Carbonyl Compounds[a]

			conv (%)[b]		
entry	oxirane	carbonyl	oxirane	carbonyl	CE(%)[c]
1	ECH	pMeOBzA	100	98	>99
2		dMeOBzA	100	99	>99
3		BzA	100	99	>99
4		myrtenal	100	97	>99
5		mesityl	100	98	>99
6		acetone	90	97	72
7	EGE	pMeOBzA	100	68	64
8		dMeOBzA	100	94	98
9	SO	pMeOBzA	100	82	83
10		dMeOBzA	87	70	71
11	IBO	pMeOBzA	100	75	78
12		dMeOBzA	100	83	88

[a] $[\text{oxirane}]_0 = 0.50$ (except for entry 8) or 1.0 (entry 8) M, $[\text{carbonyl compound}]_0 = 0.50$ (except for entry 8) or 1.0 (entry 8) M, $[SnCl_4]_0 = 20$ (entries 1, 2, 7, and 9–12) or 5.0 (entries 3–6, and 8) mM in dichloromethane at 0 ºC (except for entries 9 and 10) or –78 ºC (entries 9 and 10) for 24 h. [b] Determined by ^{1}H NMR analysis. [c] Cyclization efficiency: the ratio of the generated cyclic acetal to the feeds of oxiranes ($[\text{cyclic}]/[\text{oxirane}]_0$) determined by ^{1}H NMR analysis.

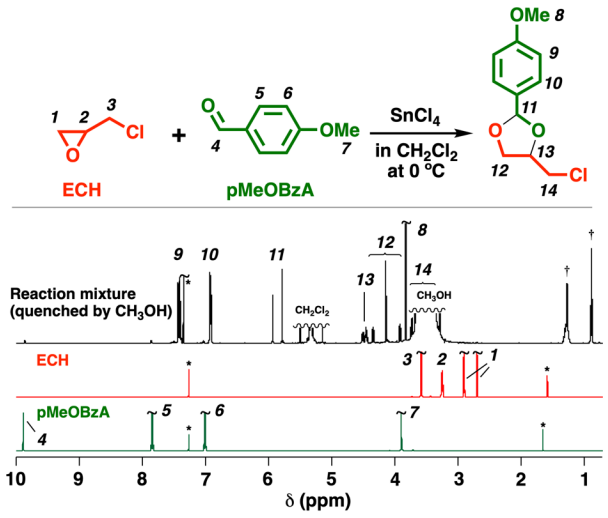


Figure 1. ^{1}H NMR spectra of the reaction mixture quenched by methanol (upper; entry 1 in Table 1), ECH monomer (middle), and pMeOBzA monomer (lower). In $CDCl_3$ at 30 ºC. * $CHCl_3$ and water. † heptane.

Oxiranes other than ECH also generated cyclic acetals when combined with appropriate carbonyl compounds, although the selectivity was inferior to that of ECH. The reaction of ethyl glycidyl ether (EGE) and dMeOBzA produced a cyclic acetal without any byproducts (entry 8 in Table 1). However, when pMeOBzA was used, the selectivity of the cyclodimerization reaction was relatively low because the oligomerization of EGE also occurred (entry 7). The selective cyclodimerization of EGE and pMeOBzA proceeded when the amount of pMeOBzA was twice that of EGE (entry 1 in Table S1). The cyclodimerization of pMeOBzA with styrene oxide (SO), which generates a benzyl-type carbocation by a ring-opening reaction, effectively proceeded at a lower temperature (–78 °C), although a slight amount of SO oligomer was also produced (entry 9 in Table 1, entry 3 in Table S1). In the case of isobutylene oxide (IBO), which generates a tertiary carbocation by the ring-opening reaction, IBO oligomers containing a homodimer were partly

generated at an equimolar feed of both monomers (entries 11 and 12 in Table 1). When an excess of pMeOBzA (2 equiv. with respect to SO or 4 equiv. with respect to IBO) was charged, selective cyclodimerization proceeded successfully (entries 2 and 4 in Table S1). The ESI-MS spectra of the obtained products also corroborated the generation of the corresponding cyclic acetals ("Characterization of Cyclic Acetals" in the Supporting Information). As demonstrated here, various oxiranes were used for cyclodimerization; however, equimolar amounts of both oxirane and carbonyl compounds need to be used because residual monomers disturb the sequence control of the subsequent copolymerization.

An appropriate choice of a Lewis acid catalyst is important for the efficient cyclodimerization reaction (Table S2). Among the various Lewis acids examined, $SnCl_4$ was superior in terms of activity and selectivity in the cyclodimerization reaction of SO and BzA. Lewis acids such as $FeCl_3$, $TiCl_4$, and $GaCl_3$ did not result in complete consumption of SO (Table S2). These differences probably stemmed from the difference in the interaction between the Lewis acids and BzA, partly arising from the difference in oxophilicity of the Lewis acids.[36,39]

Synthesis of an ABC-Type Periodic Terpolymer: Controlled Cationic Copolymerization of a Sequence-Programmed Cyclic Acetal and a Vinyl Monomer. Cationic copolymerization of the above-obtained cyclic acetal and CEVE was subsequently conducted to synthesize an ABC-type sequence-regulated terpolymer with an initiating system that is effective for the controlled cationic copolymerization of CEVE and cyclic acetals (entries 1 and 2 in Table 2; Figure 2).[32,40] First, the selective cyclodimerization of ECH and pMeOBzA was performed as explained above (at higher concentrations of monomers than those in Table 1; Table S3). After cooling the reaction solution to –96 °C, without any purification processes, ethyl acetate, CEVE, and $SnCl_4$ were added to the solution. Ethyl acetate was used as a Lewis basic additive to suppress side reactions such as

chain transfer reactions during cationic polymerization.[35] The additional $SnCl_4$ was used to compensate for the deficiency of the catalytic activity at lower temperatures. Milder reaction conditions, such as higher temperatures and lower catalyst loading, would be feasible by tuning reaction conditions, such as the amount of ethyl acetate. The copolymerization proceeded with the consumption of both monomers, yielding a polymer with a unimodal MWD (Figure 2A and 2C).[41] Interestingly, the MWD curves of the terpolymers shifted to the high-MW region as copolymerization proceeded, indicating the generation of long-lived species (Figure 2C). The M_n values measured by GPC with polystyrene standards (circle symbols in Figure 2B) or light-scattering detectors (square symbols) were consistent with the values calculated from the conversion of both monomers and the amounts of the first portion of $SnCl_4$ (5.0 mM), which also suggests propagation in a living manner. Livingness of the copolymerization is slightly inferior to that of the homopolymerization of CEVE under similar conditions, as indicated by the slight broadening of MWDs of the high MW terpolymers. The broadening probably resulted from the additional initiation from the cyclic acetal via the interaction with $SnCl_4$. Polymers with higher MWs are potentially obtained by the increase in the feed of oxiranes, carbonyl compounds, and vinyl monomers.

Table 2. Controlled Cationic Copolymerization of Sequence-Programmed Cyclic Acetals and Vinyl Monomers[a]

					conv (%)[b]				units per block[d]		
entry	oxirane	carbonyl	vinyl	time	cyclic	vinyl	$M_n \times 10^{-3}$[c]	M_w/M_n[c]	oxirane	carbony	vinyl
1	ECH	pMeOBzA	CEVE	15 min	8	32	5.4	1.26	1.0	1.0_5	1.0_5
2				50 min	25	95	12.4	1.51	1.0	1.0_0	1.0_5
3		dMeOBzA		50 min	13	49	4.3	1.19	1.0	1.0_1	1.0_9
4		BzA		24 h	12	42	5.3	1.69	1.0	1.0_7	1.2_0
5		myrtenal		40 min	24	99	9.5	1.54	1.0	1.0_0	1.2_4
6		mesityl oxide		24 h	1	68	2.1	1.21	1.0	1.0	4.1
7	ECH	pMeOBzA	AcOVE	30 min	24	81	12.8	1.43	1.0	1.0_0	1.0_3
8			IBVE	46 h	9	73	15.7	1.71	1.0	0.9_9	2.1
9			pMeSt	93 h	6	68	3.0	1.18	1.0	1.0	3.4
10	EGE	pMeOBzA	pMeSt	96 h	30	76	2.4	1.19	1.0	1.0	4.8
11	IBO	pMeOBzA	pMeSt	96 h	36	38	2.3	1.15	1.0	1.0	13

[a] Reaction conditions for the synthesis of cyclic acetals: $[\text{oxirane}]_0 = 1.0$ (entries 1–9), 0.50 (entry 10), or 0.25 (entry 11) M; $[\text{carbonyl compound}]_0 = 1.0$ M; $[SnCl_4]_0 = 5.0$ (entries 1–8) or 20 (entries 9–11) mM; in dichloromethane at 0 °C for 24 h. Polymerization conditions: $[\text{cyclic acetal}]_0 = 1.0$ (entries 1–9), 0.50 (entry 10), or 0.25 (entry 11) M; $[\text{vinyl monomer}]_{add} = 0.25$ (entries 1–9) or 0.50 (entries 10 and 11) M; $[\text{ethyl acetate}]_{add} = 0.25$ (entries 1, 2, 5, and 7) or 1.0 (entry 8) M; $[SnCl_4]_{add} = 10$ (entries 1–5 and 7), 20 (entry 6), or 5.0 (entry 8) mM; $[EtSO_3H]_{add} = 10$ mM (entries 10 and 11); in dichloromethane at –96 (entries 1, 2, 5, 7, and 8), –78 (entries 3, 4, and 6), or 0 (entries 9–11) ºC. [b] Determined by ^{1}H NMR analysis. [c] Determined by GPC (polystyrene standards). [d] Evaluated by ^{1}H NMR analysis.

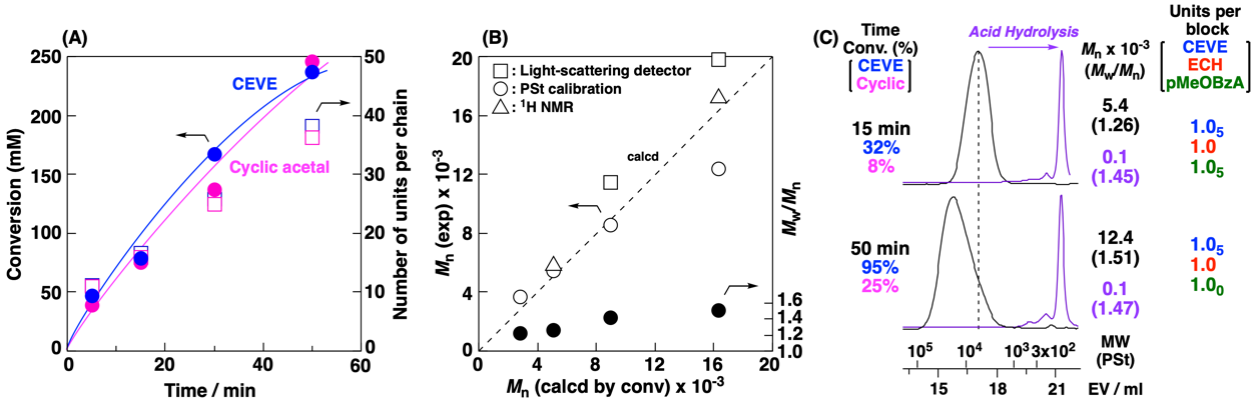


Figure 2. (A) Time–conversion curves for the copolymerization of CEVE and the cyclic acetal synthesized by the selective cyclodimerization of ECH and pMeOBzA (circle) and the average number of monomer units per chain (square; calculated from ^{1}H NMR analysis and MW values measured by GPC analysis), (B) the M_n (open) determined by GPC (circle; polystyrene standards, square; light-scattering detector) or NMR (triangle; from the main chain and the ω-ends) and M_w/M_n (filled) values of the polymers, and (C) MWD curves of poly(CEVE-*co*-cyclic acetal)s (black) and acid hydrolysis products (purple). Hydrolysis conditions: 0.50 M HCl in 1,2-dimethoxyethane (0.5 wt% polymer) at room temperature for 3 h. The data correspond to entries 1 and 2 in Table 2.

The ^{1}H NMR analysis of the obtained terpolymers indicated the occurrence of extremely frequent crossover reactions between CEVE and the cyclic acetal (Figure 3A; Figures S2–S5 for ^{13}C and 2D NMR spectra). Peaks assigned to acetal and *sec*-benzyl ether structures, which were generated by the crossover reaction from CEVE to the cyclic acetal and from the cyclic acetal to CEVE, respectively, were detected (peaks 9 and 4). Moreover, a peak attributed to an aromatic acetal was not observed at 5–6 ppm, indicating that homopropagation of the cyclic acetal did not occur. The absence of homopropagation is consistent with the result that the homopolymerization of the cyclic acetal did not proceed under the same conditions (Table S4, $[\text{cyclic acetal}]_0 = 1.0$ M). From the integral ratios of the aromatic peaks (peaks 5 and 6), the peaks of acetal and *sec*-benzyl ether (peaks 9 and 4), and the peaks of the CEVE-derived methylene group in the main chain (peak 8), the average number of ECH, pMeOBzA, and CEVE units per block was estimated to be 1.0, 1.0_5, 1.0_5, respectively (entry 1 in Table 2), suggesting that the copolymerization of CEVE and the cyclic acetal occurred in an alternating manner; thus, the terpolymer has ABC-type periodic

sequences. The terpolymers obtained at different degrees of monomer conversion also had similar ABC-type periodic sequences (entries 1 and 2 in Table 2; Figure 2).

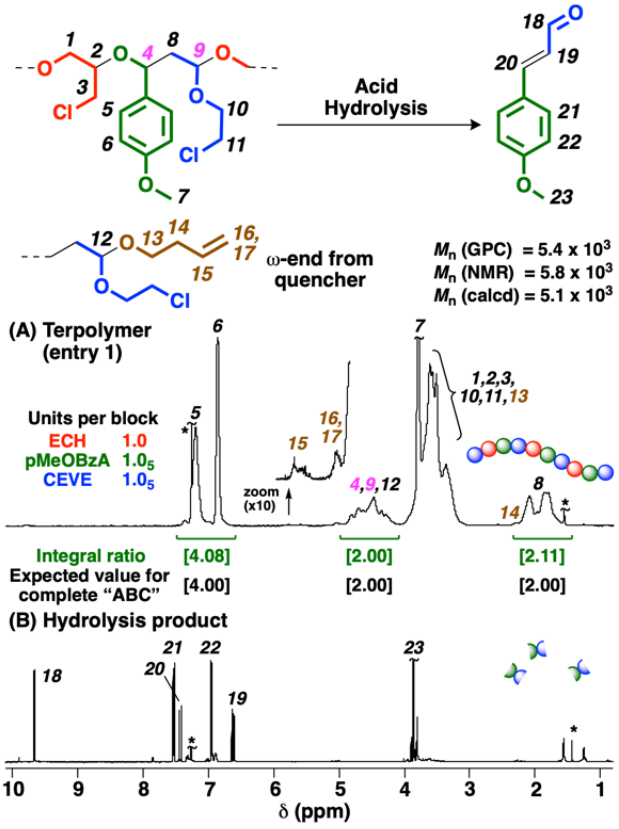
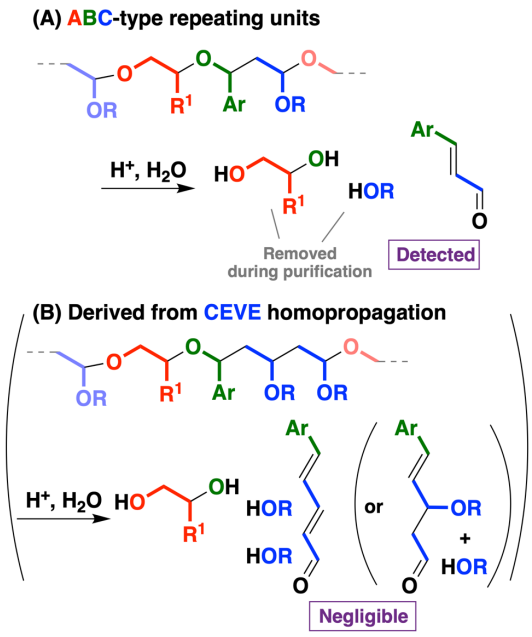


Figure 3. ^{1}H NMR spectra of (A) ECH–pMeOBzA–CEVE terpolymer (entry 1 in Table 2) and (B) its hydrolysis product. In $CDCl_3$ at 30 ºC. * $CHCl_3$ and water.

The ABC-type periodic sequences derived from alternating copolymerization were also corroborated by acid hydrolysis of the obtained terpolymers. In the ^{1}H NMR spectrum of the hydrolysis product, peaks assigned to *p*-methoxycinnamaldehyde, which was derived from one CEVE unit and one pMeOBzA unit, were exclusively observed (Figure 3B). This compound was generated via acid hydrolysis of the acid-labile acetal and *sec*-benzyl ether structures of the ECH–

pMeOBzA–CEVE–ECH sequence and the subsequent dehydration reaction (Scheme 3A). 3-Chloro-1,2-propanediol and 2-chloroethanol, which are derived from the ECH and CEVE units, respectively, were most likely removed during purification. Importantly, other possible hydrolysis products, such as compounds derived from two or more CEVE units, were not observed in the ^{1}H NMR spectrum (Scheme 3B; see Figure S23 in the case of compounds derived from VE units observed after hydrolysis), which indicates the negligible occurrence of CEVE homopropagation during alternating copolymerization. The very sharp peaks in the low-MW region of the MWD curves of the hydrolysis products also suggest the ABC-type periodic sequences of the original terpolymer (Figure 2C, purple). In addition, the methanolysis result of the terpolymer was consistent with the periodic sequences consisting of ECH, pMeOBzA, and CEVE (Figures S6–S8).

Scheme 3. Possible Mechanism of Acid Hydrolysis of the Terpolymers with ABC-Type Periodic Sequences



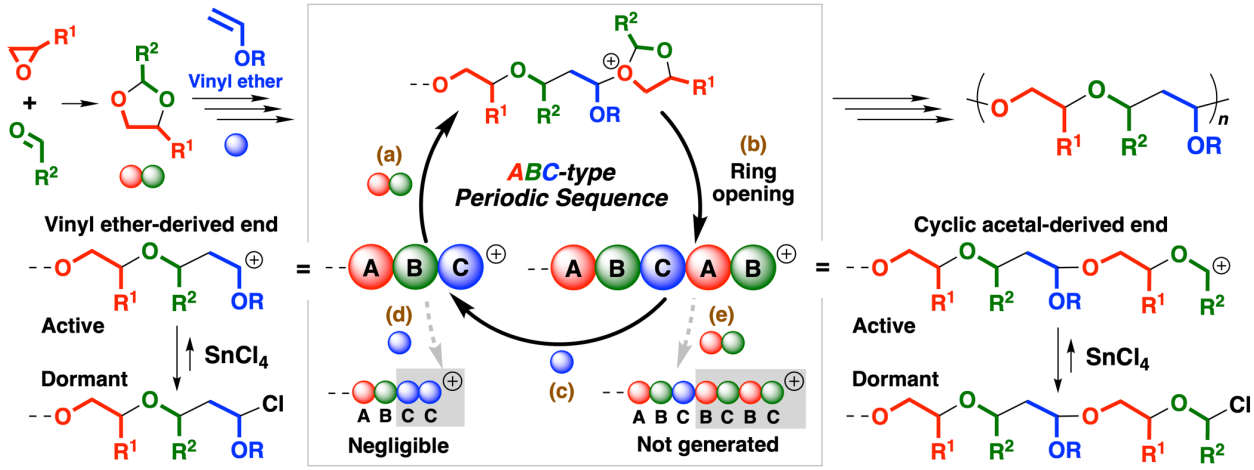
The livingness of the copolymerization was confirmed by the incorporation of a quencher into the chain ends and the monomer-addition experiment. In the ^{1}H NMR spectrum (Figure 3A), the peaks at 2.3, 5.1, and 5.8 ppm (peaks 14–17) were assigned to the ω-end structure derived from 3-buten-1-ol, which was used as a quencher.[42] The M_n value calculated from the integral ratio of the peaks of the main chain to those of the ω-end (5.8×10^3; Figure 2B triangle) was comparable to both the theoretical value based on the conversion of both monomers (5.1×10^3) and the value measured by GPC analysis (5.4×10^3; Figure 2B open circle, Figure 2C upper). This result suggests that copolymerization proceeded in a highly controlled manner via an appropriate dormant-active equilibrium at the propagating chain ends. Moreover, when the second portion of CEVE was added to the reaction mixture after almost complete consumption of the first portion of CEVE (conversion = 95%), the unimodal MWD curve shifted smoothly to the high-MW region without any tailings (Figure S9), indicating the occurrence of living polymerization.

The copolymerization mechanism is summarized in Scheme 4. Successful regulation of the ABC-type periodic sequence was achieved as a result of the nonhomopolymerizability of the cyclic acetal and the frequent crossover reactions from VE to cyclic acetal. A cyclic acetal adds to the VE-derived propagating carbocation to form an oxonium ion (Scheme 4a), which is subsequently converted to a carbocation via a ring-opening reaction (Scheme 4b). The selective scission of an acetal moiety rather than an ether moiety during the ring-opening reaction occurs because an alkoxy-adjacent carbocation is more stable than an alkyl-adjacent carbocation.[43,44] At the cyclic acetal-derived propagating end, the homopropagation of cyclic acetals did not proceed (Scheme

4e), which is consistent with the nonhomopolymerizability of 2-aryl-1,3-dioxolanes under the adopted conditions (Table S4).[45] The instability of an aromatic acetal structure in the main chain, which results from the homopropagation of the cyclic acetal, may be responsible for the nonhomopolymerizability. Therefore, the selective addition of VE to the cyclic acetal-derived propagating end proceeds (Scheme 4c), exclusively generating an oxirane–carbonyl–VE sequence. The acid hydrolysis of the obtained terpolymer (Figure 3B) also suggested an ABC-type periodic sequence, as explained above. The frequent crossover reactions from VE to cyclic acetal (Scheme 4a), which is also consistent with the copolymerization of VEs and 2-aryl-1,3-dioxolanes,[46] most likely stem from the higher reactivity of the cyclic acetal than of CEVE and the efficient occurrence of the ring-opening reaction. The monomer reactivity ratios determined by the Kelen–Tüdõs method also supported the frequent occurrence of crossover reactions (Figure S10 and Table S5; M_1 = CEVE, M_2 = cyclic acetal consisting of ECH and pMeOBzA).[47,48] An r_1 value of less than 1 ($r_1 = 0.41$) and an r_2 value of approximately zero ($r_2 = 0.03$) indicate the favorable crossover from VE to cyclic acetal (Scheme 4a) over the homopropagation (Scheme 4d) and the nonhomopolymerizability of the cyclic acetal (Scheme 4e), respectively. To completely suppress the homopropagation of CEVE (Scheme 4d), the charged amount of CEVE was one-fourth the amount of cyclic acetal (Figure 2), resulting in alternating copolymerization. The initiation reaction most likely occurs via ring opening of the cyclic acetal with the first portion of $SnCl_4$ in a manner similar to the acetal-initiated living cationic polymerization of VEs or styrene derivatives.[49–53] The reaction of CEVE with the cyclic acetal-derived carbocation generates the CEVE-derived propagating end, which is followed by smooth propagation reactions as explained above (Scheme S1). The living copolymerization most likely proceeded via a dormant-active

equilibrium consisting of the reversible activation of carbon–chlorine bonds at the propagating ends in a similar manner to the living cationic polymerization of vinyl monomers.[32,40]

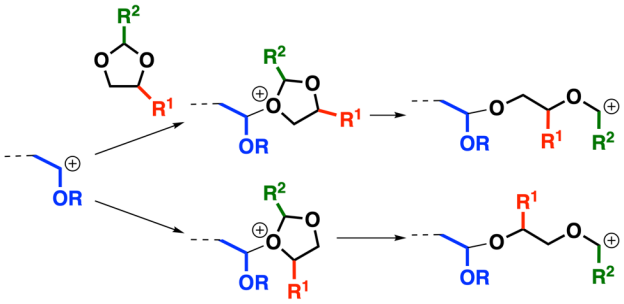
Scheme 4. Copolymerization Mechanisms (Counteranions are omitted; R^1 = CH_2Cl, R^2 = $C_6H_4OCH_3$, R = CH_2CH_2Cl)



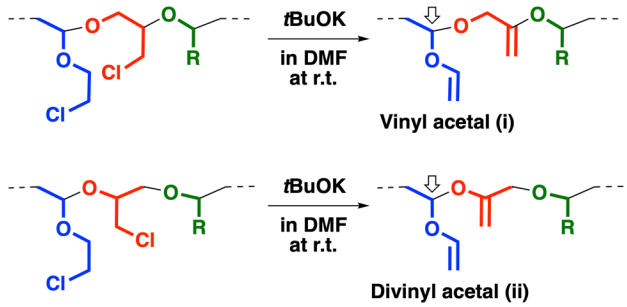
The microstructures of the ABC-type periodic terpolymer were investigated with a focus on the ring-opening mode of the cyclic acetal. The cyclodimerization reaction of an oxirane and a carbonyl compound generates a 2,4-disubstituted asymmetric cyclic acetal via the α-scission or β-scission of an oxirane (Scheme S2). During copolymerization, the asymmetric cyclic acetal reacts with a VE-derived propagating species via the reaction of the oxygen atom at the 1-position or that at the 3-position, resulting in different microstructures (Scheme 5). The ratio of the two microstructures in the main chain was determined by the transformation of the VE–ECH sequence into vinyl acetal (i) and divinyl acetal (ii) structures with tBuOK (Scheme 6). The (i)/(ii) ratio was

calculated to be 64/36 by 13C NMR (Figure S12) and 63/37 by 1H NMR (Figure S11; see Figures S13–15 for the 2D NMR spectra), which indicates that the reaction of the cyclic acetal at the 1-position was preferential over that at the 3-position probably due to the less steric hindrance around the 1-position (Scheme 5). The main chains of the obtained terpolymers were not cleaved by the transformation under the basic conditions.

Scheme 5. The Addition Mode of the Cyclic Acetal in the Copolymerization with a VE (Counteranions are omitted)



Scheme 6. Determination of Microstructure Distribution by Elimination Reaction (R = $C_6H_4OCH_3$)



The one-pot synthesis of the ABC-type terpolymer demonstrated above exhibited adequate controllability in terms of sequences and MWs, even when compared with the polymerization of an isolated cyclic acetal and CEVE, whereas this method was obviously superior to the direct

terpolymerization of ECH, pMeOBzA, and CEVE. The cationic copolymerization of CEVE and the cyclic acetal that was isolated and purified after the cyclodimerization reaction of ECH and pMeOBzA resulted in an ABC-type periodic terpolymer with similar degrees of sequence and MW control (Figure S16). In contrast, the direct cationic terpolymerization of ECH, pMeOBzA, and CEVE did not proceed under the same conditions as those used for the copolymerization of the cyclic acetal and CEVE (entries 2 and 3 in Table S6), likely because the Lewis basicities of the ECH and pMeOBzA monomers suppressed the catalytic activity of $SnCl_4$ at –96 °C. At a higher temperature (0 °C), terpolymerization proceeded; however, both ECH and pMeOBzA reacted with the CEVE-derived propagating species, resulting in a statistical sequence rather than an ABC-type periodic sequence (entry 1 in Table S6, Figure S17). These results indicate that the selective synthesis of the sequence-incorporated monomer is significantly important for the sequence regulation of the terpolymer.

The use of other monomers was also effective for the synthesis of ABC-type periodic terpolymers. When dMeOBzA was used instead of pMeOBzA, frequent crossover reactions between CEVE and the cyclic acetals generated quantitatively from ECH and dMeOBzA occurred, yielding ABC-type periodic terpolymers (entry 3 in Table 2; Figure S18; ECH/dMeOBzA/CEVE = $1.0/1.0_1/1.0_9$ units per block). The use of BzA or myrtenal-derived cyclic acetal also generated ABC-type sequence-controlled terpolymers, although CEVE homosequences were partly generated (entries 4 and 5 in Table 2; Figures S19 and S20; ECH/BzA/CEVE = $1.0/1.0_7/1.2_0$ units per block, ECH/myrtenal/CEVE = $1.0/1.0_0/1.2_4$ units per block). In the case of mesityl oxide, however, the number of CEVE units per block was obviously large (entry 6 in Table 2; Figure S21; ECH/mesityl oxide/CEVE = 1.0/1.0/4.1 units per block). The difference in the substituents

at the 2-position of cyclic acetals most likely affected the efficiency of the crossover reaction from VEs to cyclic acetals.

The difference in vinyl monomers mainly affected the length of vinyl monomer units. The use of 2-acetoxyethyl VE (AcOVE), which has an electron-withdrawing ester group and exhibits reactivity comparable to that of CEVE, also generated an ABC-type periodic terpolymer by copolymerization with ECH- and pMeOBzA-derived cyclic acetals (entry 7 in Table 2; Figure S22; ECH/pMeOBzA/AcOVE = $1.0/1.0_0/1.0_3$ units per block). In addition, the M_n values corresponded to the calculated values, indicating the livingness of the copolymerization (Figure 4). Copolymerization with isobutyl VE (IBVE), which is a more reactive VE than CEVE, resulted in a terpolymer containing a larger number of IBVE units per block (entry 8 in Table 2; Figure S23; ECH/pMeOBzA/IBVE = $1.0/0.9_9/2.1$ units per block). These results indicate that the use of VEs with low reactivity is important for the construction of ABC-type periodic sequences. The copolymerization of *p*-methylstyrene (pMeSt), which exhibits a smaller reactivity than CEVE,[54] and the cyclic acetal resulted in a terpolymer with several pMeSt units per block (entry 9 in Table 2; Figure S24; ECH/pMeOBzA/pMeSt = 1.0/1.0/3.4 units per block), which probably stemmed from the difference in the reactivity of the carbocations derived from pMeSt and VEs. The longer reaction time was required for the copolymerization with less reactive pMeSt. Faster polymerization is possibly achieved by tuning reaction conditions (e.g., higher reaction temperatures, larger amounts of the catalyst, etc.) without losing controllability. Interestingly, in the case of pMeSt, terpolymers with ABC-type sequences were successfully generated even when an excess amount of pMeOBzA was charged for the selective cyclodimerization with EGE or IBO. Unreacted pMeOBzA did not disturb the subsequent copolymerization (entries 10 and 11 in Table 2; Figures S25 and S26; EGE/pMeOBzA/pMeSt = 1.0/1.0/4.8 units per block,

IBO/pMeOBzA/pMeSt = 1.0/1.0/13 units per block. See the caption of Table 2 or entries 1 and 4 in Table S1 for the reaction conditions for the synthesis of cyclic acetals). Indeed, during the copolymerization of pMeSt and pMeOBzA under similar conditions, negligible crossover reactions occurred between pMeSt and pMeOBzA (Figure S27).

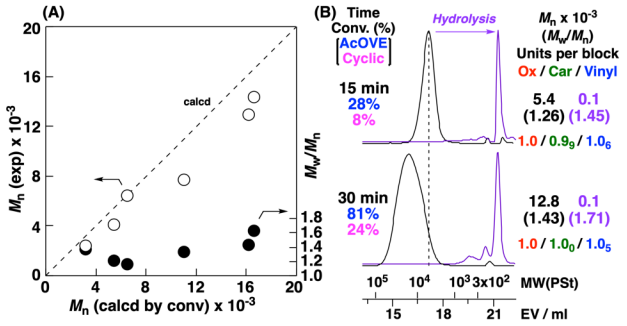


Figure 4. (A) M_n (open) and M_w/M_n (filled) values (by GPC) of the copolymers obtained and (B) MWD curves of poly(AcOVE-*co*-cyclic acetal)s (black) and acid hydrolysis products (purple). The data correspond to entry 7 in Table 2.

Synthesis of a Block Quaterpolymer with Periodic Sequences. The livingness of the copolymerization was effective for the synthesis of block polymers consisting of blocks with different ABC-type periodic sequences, such as an ABC-*b*-ABD quaterpolymer, by a one-pot process (Figure S28). The alternating cationic copolymerization of the ECH- and pMeOBzA-derived cyclic acetal with CEVE was conducted using four equivalents of the cyclic acetal with respect to CEVE (Figure S28 upper; CEVE/ECH/pMeOBzA = 1.0_3/1.0/1.0_1 units per block). At the late stage of copolymerization, a fresh portion of AcOVE was added to the reaction mixture, which triggered the subsequent copolymerization of AcOVE and the residual cyclic acetal. The sequential monomer addition afforded a high-MW polymer via frequent crossover reactions between AcOVE and the cyclic acetal (Figure S28 lower; CEVE/ECH/pMeOBzA/AcOVE =

$1.0_3/1.0/1.0_0/1.3_3$ units per block), resulting in a block polymer consisting of blocks with ECH–pMeOBzA–CEVE and ECH–pMeOBzA–AcOVE periodic sequences.

Thermal Properties of an ABC-Type Periodic Terpolymer. The thermal properties of the ECH–pMeOBzA–CEVE terpolymers with different sequences were examined by DSC analysis (Figure 5). The glass transition temperature (T_g) of the ABC-type periodic terpolymer (T_g = –3 °C; Figure 5A; see Figure S29 for TGA) was lower than that of the statistical terpolymer (T_g = 9 °C; Figure 5C). The ABC-type periodic monomer sequences probably affected the lower T_g value than that of the statistical sequences. In copolymerization of two kinds of monomers, the differences of T_g between alternating and statistical sequences were reported in several past studies.[55–58] However, whether alternating copolymers exhibit higher or lower T_g than statistical copolymers depends on the combinations of monomers. Further investigation is needed to clarify the T_g difference in the present study. Interestingly, the T_g of the ABC$_n$-type sequence-controlled terpolymer containing CEVE homosequences (T_g = –2 °C; Figure 5B) was comparable to that of the ABC-type periodic-sequence terpolymer, which suggests that regular incorporation rather than statistical incorporation of the three monomers in the order of ECH, pMeOBzA, and CEVE into polymer chains also affected the thermal properties.

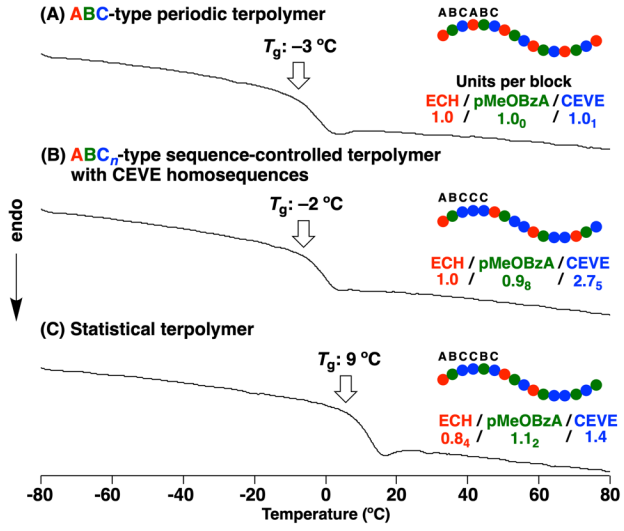


Figure 5. DSC thermogram of the ECH–pMeOBzA–CEVE terpolymers with (A) ABC-type periodic sequences (entry 1 in Table S5), (B) ABC$_n$-type sequences with CEVE homosequences (entry 4 in Table S5), and (C) statistical sequences (Figure S17) (the second heating scan; heating rate: 10 ºC/min).

CONCLUSION

A one-pot strategy consisting of the quantitative synthesis of a sequence-programmed monomer and the subsequent copolymerization reaction was developed using oxiranes, carbonyl compounds, and vinyl monomers as monomers. The selective cyclodimerization reaction of oxiranes and carbonyl compounds quantitatively produced sequence-programmed cyclic acetals, even when both monomers were charged in equimolar amounts. The subsequent cationic copolymerization with vinyl monomers proceeded in an alternating manner to give terpolymers with an ABC-type periodic monomer sequence. Moreover, the livingness of the copolymerization enabled the simultaneous control of the MW, MWD, and chain end structures. The sequential addition of vinyl monomers yielded unique ABC-*b*-ABD-type quaterpolymers. The use of oxiranes with sufficient reactivity and low tendency to homocyclization, aldehydes with an electron-donating group, and VEs with low reactivity is of great importance for the selective cyclodimerization and alternating polymerization reactions. This strategy is expected to provide a concept for the simple conversion of various types of commercially available monomers, such as vinyl, cyclic, and carbonyl monomers, into ter- or quaterpolymers with a high degree of sequence and MW control. Further progress in both the efficient synthesis of sequence-programmed monomers and the occurrence of exclusive crossover reactions between different types of monomers will contribute to the

construction of polymers with unique properties from various types of monomers and to the development of novel technologies with sequence-controlled polymers.

ASSOCIATED CONTENT

Supporting Information.

The Supporting Information is available free of charge on the ACS Publications website. Characterization of cyclic acetals; NMR spectra of cyclic acetals, polymerization products, and methanolysis product; polymerization data; ESI-MS spectrum of the methanolysis product; and the mechanisms of the initiation reaction and the selective cyclodimerization.

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Notes

The authors declare no competing financial interest.

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REFERENCES

1. Lutz, J.-F.; Ouchi, M.; Liu, D. R.; Sawamoto, M. Sequence-Controlled Polymers. *Science* **2013**, *341*, No. 1238149.
2. Lutz, J.-F. Defining the Field of Sequence-Controlled Polymers. *Macromol. Rapid Commun.* **2017**, *38*, No. 1700582.
3. Szymański, J. K.; Abul-Haija, Y. M.; Cronin, L. Exploring Strategies To Bias Sequence in Natural and Synthetic Oligomers and Polymers. *Acc. Chem. Res.* **2018**, *51*, 649–658.
4. Meier, M. A. R.; Barner-Kowollik, C. A New Class of Materials: Sequence-Defined Macromolecules and Their Emerging Applications. *Adv. Mater.* **2019**, *31*, No. 1806027.
5. Merrifield, R. B. Solid Phase Peptide Synthesis. I. The Synthesis of a Tetrapeptide. *J. Am. Chem. Soc.* **1963**, *85*, 2149–2154.
6. Trinh, T. T.; Laure, C.; Lutz, J.-F. Synthesis of Monodisperse Sequence-Defined Polymers Using Protecting-Group-Free Iterative Strategies. *Macromol. Chem. Phys.* **2015**, *216*, 1498–1506.
7. Solleder, S. C.; Schneider, R. V.; Wetzel, K. S.; Boukis, A. C.; Meier, M. A. R. Recent Progress in the Design of Monodisperse, Sequence-Defined Macromolecules. *Macromol. Rapid Commun.* **2017**, *38*, No. 1600711.

8. Hill, S. A.; Gerke, C.; Hartmann, L. Recent Developments in Solid-Phase Strategies towards Synthetic, Sequence-Defined Macromolecules. *Chem.—Asian J.* **2018**, *13*, 3611–3622.
9. Cho, I.; Hwang, K. M. Ring-Opening Metathesis Polymerization of 4-Methyl-6-Phenylcyclooctene. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1079–1081.
10. Cho, I. New Ring-Opening Polymerizations for Copolymers Having Controlled Microstructures. *Prog. Polym. Sci.* **2000**, *25*, 1043−1087.
11. Zhang, J.; Matta, M. E.; Hillmyer, M. A. Synthesis of Sequence-Specific Vinyl Copolymers by Regioselective ROMP of Multiply Substituted Cyclooctenes. *ACS Macro Lett.* **2012**, *1*, 1383–1387.
12. Yokota, K. Periodic Copolymers. *Prog. Polym. Sci.* **1999**, *24*, 517−563.
13. Satoh, K.; Ozawa, S.; Mizutani, M.; Nagai, K.; Kamigaito, M. Sequence-Regulated Vinyl Copolymers by Metal-Catalysed Step-Growth Radical Polymerization. *Nat. Commun.* **2010**, *1*, 6.
14. Miyajima, M.; Satoh, K.; Horibe, T.; Ishihara, K.; Kamigaito, M. Multifactor Control of Vinyl Monomer Sequence, Molecular Weight, and Tacticity via Iterative Radical Additions and Olefin Metathesis Reactions. *J. Am. Chem. Soc.* **2020**, *142*, 18955–18962.
15. Zhang, C.; Ling, J.; Wang, Q. Radical Addition-Coupling Polymerization (RACP) toward Periodic Copolymers. *Macromolecules* **2011**, *44*, 8739–8743.
16. Schulz, M. D.; Wagener, K. B. Precision Polymers through ADMET Polymerization. *Macromol. Chem. Phys.* **2014**, *215*, 1936–1945.
17. Gutekunst, W. R.; Hawker, C. J. A General Approach to Sequence-Controlled Polymers Using Macrocyclic Ring Opening Metathesis Polymerization. *J. Am. Chem. Soc.* **2015**, *137*, 8038–8041.

18. Yang, C.; Flynn, J. P.; Niu, J. Facile Synthesis of Sequence-Regulated Synthetic Polymers Using Orthogonal SuFEx and CuAAC Click Reactions. *Angew. Chem. Int. Ed.* **2018**, *57*, 16194–16199.
19. Kreye, O.; Tóth, T.; Meier, M. A. R. Introducing Multicomponent Reactions to Polymer Science: Passerini Reactions of Renewable Monomers. *J. Am. Chem. Soc.* **2011**, *133*, 1790–1792.
20. Saegusa, T.; Kobayashi, S.; Kimura, Y. Polymerization via Zwitterion. 12. Novel 1:1:1 Alternating Terpolymerizations of 2-Phenyl-1,3,2-Dioxaphospholane, Electron Deficient Vinyl Monomers of Acrylonitrile and Acrylate, and Carbon Dioxide. *Macromolecules* **1977**, *10*, 68–72.
21. Hsieh, H. L. Terpolymerization of Cyclic Ethers with Cyclic Anhydride. *J. Macromol. Sci., Part A: Chem.* **1973**, *7*, 1525−1535.
22. Kanazawa, A.; Aoshima, S. Exclusive One-Way Cycle Sequence Control in Cationic Terpolymerization of General-Purpose Monomers via Concurrent Vinyl-Addition, Ring-Opening, and Carbonyl-Addition Mechanisms. *ACS Macro Lett.* **2015**, *4*, 783–787.
23. Mimura, M.; Kanazawa, A.; Aoshima, S. ABC Pseudo-Periodic Sequence Control by Cationic Orthogonal Terpolymerization of Vinyl Ether, Oxirane, and Ketone. *Macromolecules* **2019**, *52*, 7572–7583.
24. Yokozawa, T.; Suzuki, T. Spontaneous Copolymerization of the Cyclobutane Adduct of Tetracyanoethylene and Vinyl Ether with Oxiranes. *Macromolecules* **1996**, *29*, 22–25.
25. Yokozawa, T.; Tagami, M.; Takehana, T.; Suzuki, T. Synthesis of Terpolymers by Spontaneous Copolymerization of the Cyclobutane Adducts of Electron-Acceptor Olefins and Vinyl Ether with 2-Oxazolines. *Tetrahedron* **1997**, *53*, 15603–15616.

26. Krompiec, S.; Penkala, M.; Szczubiałka, K.; Kowalska, E. Transition Metal Compounds and Complexes as Catalysts in Synthesis of Acetals and Orthoesters: Theoretical, Mechanistic and Practical Aspects. *Coord. Chem. Rev.* **2012**, *256*, 2057–2095.
27. Bogert, M. T.; Roblin, R. O. The Formation of Cyclic Acetals from Aldehydes or Ketones and Alkylene Oxides. *J. Am. Chem. Soc.* **1933**, *55*, 3741–3745.
28. Saha, S.; Mandal, S. K.; Roy, S. C. Fe(III) Chloride Catalyzed Conversion of Epoxides to Acetonides. *Tetrahedron Lett.* **2008**, *49*, 5928–5930.
29. Nagata, T.; Takai, T.; Yamada, T.; Imagawa, K.; Mukaiyama, T. Direct and Stereoselective Preparation of Optically Active 1,3-Dioxolanes from the Corresponding Chiral Styrene Oxides. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2614–2616.
30. Okada, M.; Yamashita, Y.; Ishii, Y. Cationic Copolymerization of 1,3-Dioxolane with Styrene. *Makromol. Chem.* **1966**, *94*, 181–193.
31. Okada, M.; Yamashita, Y. Cationic Copolymerization of Cyclic Formals and Vinyl Ethers. *Makromol. Chem.* **1969**, *126*, 266−275.
32. Shirouchi, T.; Kanazawa, A.; Aoshima, S. Controlled Cationic Copolymerization of Vinyl Monomers and Cyclic Acetals via Concurrent Vinyl-Addition and Ring-Opening Mechanisms. *Macromolecules* **2016**, *49*, 7184–7195.
33. Maruyama, K.; Kanazawa, A.; Aoshima, S. Controlled Cationic Copolymerization of Vinyl Monomers and Cyclic Acetals *via* Concurrent Vinyl-Addition and Ring-Opening Mechanisms: The Systematic Study of Structural Effects on the Copolymerization Behavior. *Polym. Chem.* **2019**, *10*, 5304–5314.
34. Aoshima, S.; Nakamura, T.; Uesugi, N.; Sawamoto, M.; Higashimura, T. Living Cationic Polymerization of Vinyl Ethers with a Functional Group. 1. Polymerization of 2-

Acetoxyethyl Vinyl Ether and Synthesis of Polyalcohols with a Narrow Molecular Weight Distribution. *Macromolecules* **1985**, *18*, 2097–2101.

35. Aoshima, S.; Kanaoka, S. A Renaissance in Living Cationic Polymerization. *Chem. Rev.* **2009**, *109*, 5245–5287.
36. Ishido, Y.; Aburaki, R.; Kanaoka, S.; Aoshima, S. Controlled Cationic Copolymerization of Benzaldehyde with Isobutyl Vinyl Ether Using Base-assisting System. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 1838–1843.
37. Ishido, Y.; Aburaki, R.; Kanaoka, S.; Aoshima, S. Well-Defined Alternating Copolymers of Benzaldehydes with Vinyl Ethers: Precision Synthesis by Cationic Copolymerization and Quantitative Degradation to Cinnamaldehydes. *Macromolecules* **2010**, *43*, 3141–3144.
38. The slightly different values between the conversion of carbonyl compounds and cyclization efficiency were due to the experimental errors in using equimolar amounts of carbonyl compounds and oxiranes.
39. Kanazawa, A.; Kanaoka, S.; Aoshima, S. Major Progress in Catalysts for Living Cationic Polymerization of Isobutyl Vinyl Ether: Effectiveness of a Variety of Conventional Metal Halides. *Macromolecules* **2009** *42*, 3965–3972.
40. Kimura, R.; Yamada, M.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. Monomer-Selective Domino Living Cationic Copolymerization of a Variety of Vinyl Ethers and Styrene Derivatives. *Polym. Prepr., Jpn.* **2013**, *62*, 2412.
41. Each diastereomer of the cyclic acetal was equally consumed as indicated by ^{1}H NMR analysis of the quenched reaction mixtures.

42. To characterize the end groups of the obtained terpolymers, ESI-MS and MALDI-TOF-MS analysis were conducted under various conditions. However, the analysis of the samples was difficult because the signal intensity was very small.
43. Goethals, E.; Duprez, F. Carbocationic Polymerizations. *Prog. Polym. Sci.* **2007**, *32*, 220–246.
44. Deslongchamps, P.; Dory, Y. L.; Li, S. The Relative Rate of Hydrolysis of a Series of Acyclic and Six-Membered Cyclic Acetals, Ketals, Orthoesters, and Orthocarbonates. *Tetrahedron* **2000**, *56*, 3533–3537.
45. Okada, M. Polymerization of 1,3-Dioxolane. *Makromol. Chem.* **1964**, *80*, 196–207.
46. The cationic copolymerization of CEVE and 2-phenyl-1,3-dioxolane using $SnCl_4$ proceeded via extremely frequent crossover reactions even at equimolar concentrations of both monomers (unpublished data). The carbocation generated via ring-opening reaction of the oxonium ion derived from 2-phenyl-1,3-dioxolane received the resonance stabilization from the adjacent aromatic ring, which probably contributes to the high copolymerizability.
47. Kelen, T.; Tüdõs, F. A New Improved Linear Graphical Method for Determining Copolymerization Reactivity Ratios. *Kinet. Catal. Lett.* **1974**, *1*, 487−492.
48. Kennedy, J. P.; Kelen, T.; Tüdõs, F. Analysis of the Linear Methods for Determining Copolymerization Reactivity Ratios. II. A Critical Reexamination of Cationic Monomer Reactivity Ratios. *J. Polym. Sci., Polym. Chem. Ed.* **1975**, *13*, 2277−2289.
49. Van Meirvenne, D.; Haucourt, N.; Goethals, E. J. A New Initiating System for the "Living" Polymerization of Vinyl Ethers Leading to Hydroxy-Terminated Polymers. *Polym. Bull.* **1990**, *23*, 185–190.

50. Haucourt, N. H.; Goethals, E. J.; Schappacher, M.; Deffieux, A. Re-activation of Acetal-Terminated Poly(vinyl ether)s. *Makromol. Chem. Rapid Commun.* **1992**, *13*, 329–336.
51. Satoh, K.; Kamigaito, M.; Sawamoto, M. Aromatic Acetals as New Initiators for Cationic Polymerization of Isobutyl Vinyl Ether. *Macromolecules* **2000**, *33*, 748–753.
52. Shimomoto, H.; Yoshida, H.; Kanaoka, S.; Aoshima, S. Synthesis of Graft Copolymers Based on Selective Living Cationic Polymerization Using an Acetal Group with a Combination of Lewis Acids. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3703–3709.
53. Yokoyama, N.; Kanazawa, A.; Kanaoka, S.; Aoshima, S. Synthesis of Highly Defined Graft Copolymers Using a Cyclic Acetal Moiety as a Two-Stage Latent Initiating Site for Successive Living Cationic Polymerization and Ring-Opening Anionic Polymerization. *Macromolecules* **2018**, *51*, 884–894.
54. Masuda, T.; Higashimura, T.; Okamura, S. Cationic Copolymerization of 2-Chloroethyl Vinyl Ether with Styrene Derivatives. *Polym. J.* **1970**, *1*, 19–26.
55. Hirooka, M.; Kato, T. Glass Transition Temperature and Sequential Structure of Equimolar Copolymers. *J. Polym. Sci. Polym. Lett. Ed.* **1974**, *12*, 31–37.
56. Mori, Y.; Sumi, H.; Hirabayashi, T.; Inai, Y.; Yokota, K. Synthesis of Sequence-Ordered Copolymers. 4. Glass Transition and Melting Temperatures of Sequence-Ordered and Unordered Ethylene-Vinyl Alcohol and Ethylene-Vinyl Acetate Copolymers. *Macromolecules* **1994**, *27*, 1051–1056.
57. Denizli, B. K.; Lutz, J.-F.; Okrasa, L.; Pakula, T.; Guner, A.; Matyjaszewski, K. Properties of Well-Defined Alternating and Random Copolymers of Methacrylates and Styrene Prepared by Controlled/Living Radical Polymerization. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 3440–3446.

58. Liu, G.; Meng, Z.; Wang, W.; Zhou, Y.; Zhang, L. Sequence Distribution Effects on Glass Transition Temperatures of Copolymers: An Extended Gibbs−DiMarzio Equation in View of Bond Rotation Flexibility. *J. Phys. Chem. B* **2008**, *112*, 93–99.