Electronic Supplementary Information for:

Spiroorthoesters as promising comonomers for degradable polymer synthesis by cationic copolymerization with vinyl ethers

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Contents:

Experimental Section

Materials. Isobutyl vinyl ether (IBVE; TCI, >99.0%) and isopropyl vinyl ether (IPVE; Wako, >97%) were washed with 10% aqueous sodium hydroxide solution and then with water, dried overnight over potassium hydroxide, and distilled twice over calcium hydride. 2-Methoxyethyl vinyl ether (MOVE; kindly supplied by Maruzen Petrochemical) was distilled over calcium hydride and then over metallic sodium. 2-Chloroethyl vinyl ether (CEVE; TCI; >97%) was washed with aqueous sodium hydroxide solution and then water, and distilled twice from calcium hydride under reduced pressure. Commercially available $B(C_6F_5)_3$ (TCI; >98%) was used without further purification after preparing a stock solution in dichloromethane. $GaCl_3$ (TCI; >98.0%), $SnCl_4$ (Sigma-Aldrich; 1.0 M solution in dichloromethane), triphenylmethylium tetrakis(pentafluorophenyl)borate ($Ph_3CB(C_6F_5)_4$; TCI, >98.0%), and triphenylmethylium hexafluorophosphate (Ph_3CPF_6; Sigma-Aldrich) were used without further purification.

Monomer synthesis. For the synthesis of SOE1 (2,2-dimethyl-1,4,6-trioxaspiro[4.6]undecane), 46 ml of ε-caprolactone (TCI; ≥99.0%), 184 ml of dichloromethane, 1.41 g of $GaCl_3$, and 30 ml of dichloromethane were added to a round-bottomed flask and the mixture was cool with ice bath. To the mixture, 43 ml of isobutylene oxide (TCI; ≥98.0%) and 61 ml of dichloromethane mixture were added dropwise. The reaction was occasionally monitored by ^1H NMR analysis and several milliliters of isobutylene oxide was added to promote the consumption of ε-caprolactone. After almost complete consumption of ε-caprolactone was confirmed, triethylamine was added to quench the reaction. The quenched mixture was washed with water and then saturated sodium chloride solution, and dried overnight over magnesium sulfate. Solvents were removed with a rotary evaporator and the crude product was purified by double distillation under reduced pressure from calcium hydride. SOE2 (2-ethyl-1,4,6-trioxaspiro[4.6]undecane) and SOE3 (2,2-dimethyl-1,4-dioxaspiro[4.5]decane) were synthesized according to similar procedures from the reaction of ε-caprolactone and 1,2-butylene oxide and the reaction of δ-valerolactone and isobutylene oxide, respectively.

SOE1 (2,2-dimethyl-1,4,6-trioxaspiro[4.6]undecane). ^1H NMR ($CDCl_3$; 500 MHz; Figure S1A): δ 3.84 (1H, d, 7.2–7.6 Hz), 3.70 (1H, d, 7.2–7.6 Hz), 3.71–3.62 (2H, m), 2.10 (2H, m), 1.80–1.50 (6H, m), 1.40 (3H, s), 1.26 (3H, s). ^{13}C NMR ($CDCl_3$; 125 MHz; Figure S2A): δ 124.1, 79.6, 74.7, 63.9, 38.5, 30.6, 29.3, 27.1, 26.7, 22.7. MS (ESI) [M + H^+], calcd: 187.1329, found: 187.1329.

SOE2 (2-ethyl-1,4,6-trioxaspiro[4.6]undecane). ^1H NMR ($CDCl_3$; 500 MHz; Figure S1B): major diastereomer, δ 4.25 (quin [dddd], 1H, 6.0–6.5 Hz), 4.12 (1H, dd, 7.0–7.5 Hz, 6.5–7.0 Hz), 3.75–3.63 (2H, m), 3.54 (1H, dd, 7.0–7.5 Hz, 6.0–6.5 Hz), 2.15–2.04 (2H, m), 1.84–1.48 (8H, m), 0.93 (3H, t, 7.5 Hz); minor diastereomer, 4.06 (1H, dd, 7.5 Hz, 6.5 Hz), 4.01 (1H, dq [dddd], 8.0 Hz, 6.5 Hz), 3.75–3.63 (3H, m), 2.15–2.04 (2H, m), 1.84–1.48 (8H, m), 0.95 ppm (3H, t, 7.5 Hz). ^{13}C NMR ($CDCl_3$; 125 MHz; Figure S2B): major diastereomer, δ 123.8, 76.6, 68.6, 64.1, 37.4, 30.8, 29.3, 26.5, 22.8, 9.5. minor diastereomer, δ 124.0, 78.5, 68.9, 64.1, 37.6, 30.6, 29.3, 27.3, 22.7, 10.2. MS (ESI) [M + H^+], calcd: 187.1329, found: 187.1326.

SOE3 (2,2-dimethyl-1,4-dioxaspiro[4.5]decane). ^1H NMR ($CDCl_3$; 500 MHz; Figure S1C): δ 3.87 (1H, d, 7.6 Hz), 3.85–3.76 (2H, m), 3.75 (1H, d, 7.6 Hz), 1.88–1.73 (4H, m), 1.53 (2H, m), 1.42 (3H, s), 1.28 (3H, s). ^{13}C NMR ($CDCl_3$; 125 MHz; Figure S2C): δ 119.3, 79.7, 74.7, 64.4, 33.3, 27.5, 26.9, 24.6, 21.6. MS (ESI) [M + H^+], calcd: 173.1172, found: 173.1170.

Polymerization procedures. The following is a typical polymerization procedure. A glass tube equipped with a three-way stopcock was dried using a heat gun (Ishizaki; PJ-206A; blow temperature: ~450 ºC) under dry nitrogen. Dichloromethane, hexane, VE, and SOE were added successively into the tube using dry syringes. The polymerization was started by the addition of a prechilled $Ph_3CB(C_6F_5)_4$ solution in dichloromethane at 0 ºC. After a predetermined period of time, the reaction was quenched with propanol containing a small amount of aqueous ammonia solution (2–3 vol%). The quenched mixture was diluted with dichloromethane and hexane and then washed with aqueous sodium hydroxide solution (approximately 0.6 M), followed by water. The volatiles were removed under reduced pressure at 40 ºC to yield a polymer. The monomer conversion was determined by gas chromatography (GC; column packing material: PEG-20M-Uniport HP or Gasukuropack; GL Sciences Inc.) using hexane as an internal standard.

Purification of polymers by reprecipitation. A typical procedure for reprecipitation in methanol is as follows: A polymer (0.2 g) dissolved in dichloromethane (0.8 mL) was poured into a large amount of methanol (20–40 mL) while stirring. After the mixture was stand for overnight in a freezer, an insoluble part was collected by filtration. The insoluble part left on filter paper was collected by dissolution in dichloromethane, removal of dichloromethane by an evaporator, and drying under reduced pressure.

Acid hydrolysis of polymers. Acid hydrolysis of the polymers was conducted with 0.5 M HCl (aq) in 1,2-dimethoxyethane and dichloromethane at room temperature for 3 h (polymer: approximately 0.5 wt%). The quenched mixture was diluted with dichloromethane and then washed with aqueous sodium hydroxide solution (approximately 0.6 M), followed by water. The volatiles were removed under atmospheric pressure at room temperature.

Characterization. The molecular weight distributions (MWDs) of the polymers were measured by gel permeation chromatography (GPC) in tetrahydrofuran at 30 ºC with two polystyrene gel columns [TSKgel GMH_{HR}-M × 2, flow rate = 0.7 mL/min] connected to a pump (Viscotek VE 1122) and a Viscotek TDA 305 detector. The number-average molecular weight (M_n) and the polydispersity ratio (weight-average molecular weight/number-average molecular weight [M_w/M_n]) were calculated from the refractive index chromatographs based on 16 polystyrene standards (Tosoh; $M_n = 5.0 \times 10^2$—1.09×10^6 , $M_w/M_n < 1.2$). Purification of polymers by preparative GPC was conducted in chloroform at room temperature with a polystyrene gel column [TSKgel $G3000H_{HR}$ (exclusion molecular weight = 6×10^4 ; bead size = 5 μm, column size = 21.5 mm i.d. × 300 mm); flow rate = 2.0 mL/min] connected to a JASCO PU2086 Plus pump, a JASCO UV-2075 ultraviolet detector, and a LAB-SYSTEM RI-2000AP refractive index detector. NMR spectra were recorded with JEOL JNM-ECA 500 spectrometer (500.16 MHz for ^1H), JEOL JNM-ECZN 500 spectrometer (500.16 MHz for ^1H and 125.77 MHz for ^{13}C), or JEOL JNM ECS400 spectrometer (395.88 MHz for ^1H) in chloroform-*d* or acetone-d_6 at 30 ºC. Electrospray ionization mass spectrometry (ESI-MS) was conducted with a Thermo Fisher Scientific Q-Exactive spectrometer. The transmittance of aqueous polymer solutions was measured with a JASCO V-500 UV-vis spectrometer equipped with a Peltier-type thermostatic cell holder (ETC-505). Dynamic light scattering (DLS) analysis was conducted with an Otsuka Electronics FPAR-1000HG analyzer (λ = 632.8 nm, scattering angle = 90 º). Differential scanning calorimetry (DSC) analysis was conducted with a Shimadzu DSC-60 Plus differential scanning calorimeter. Thermogravimetric analysis (TGA) was conducted with a Hitachi High Tech NEXTA STA under flowing nitrogen at a heating rate of 10 ºC min^{-1}.

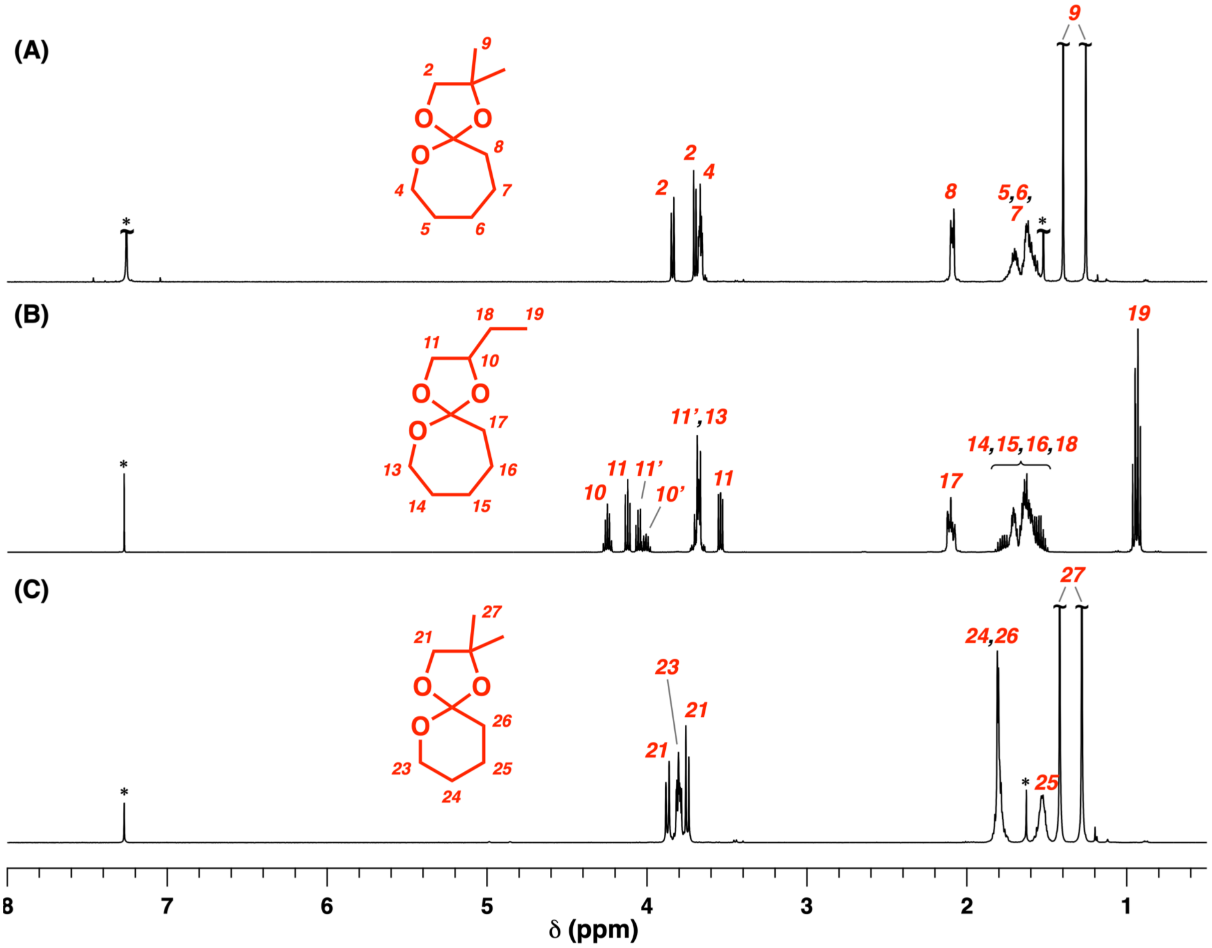


Figure S1. ^{1}H NMR spectra of (A) SOE1, (B) SOE2, and (C) SOE3. In $CDCl_3$ at 30 ºC. * Water or $CHCl_3$

Note for Figure S1: Very small amounts of ε-caprolactone or δ-valerolactone, which were not completely removed by the purification procedures (distillation), remained in the monomers as confirmed by peaks observed at 2.63 ppm (ε-caprolactone) or 2.57 ppm (δ-valerolactone). Amounts of the remained cyclic esters were 0.7% in SOE1 (Figure S1A), 0.9% in SOE2 (Figure S1B), and 0.1% in SOE3 (Figure S1C). These cyclic esters are considered to exhibit little effects on copolymerization because the remaining amounts were very small.

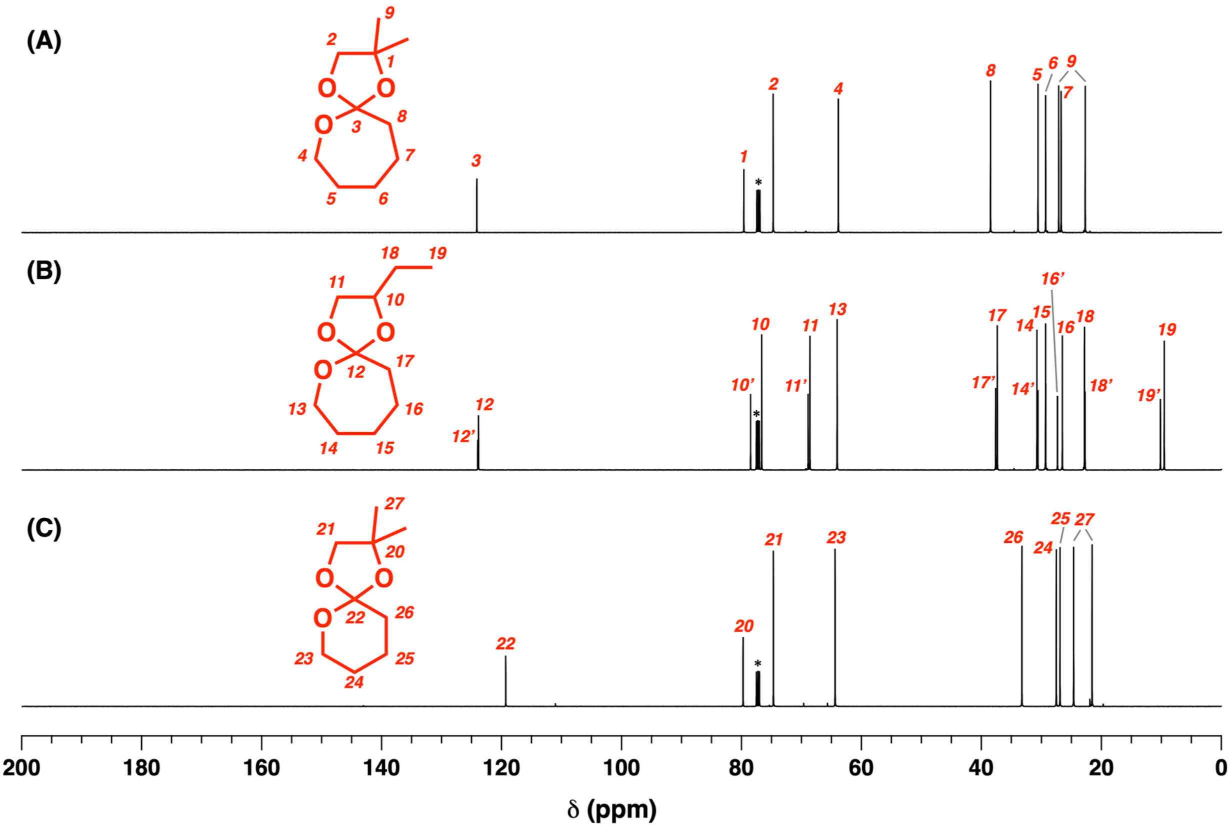


Figure S2. ^{13}C NMR spectra of (A) SOE1, (B) SOE2, and (C) SOE3. In $CDCl_3$ at 30 ºC. * $CDCl_3$.

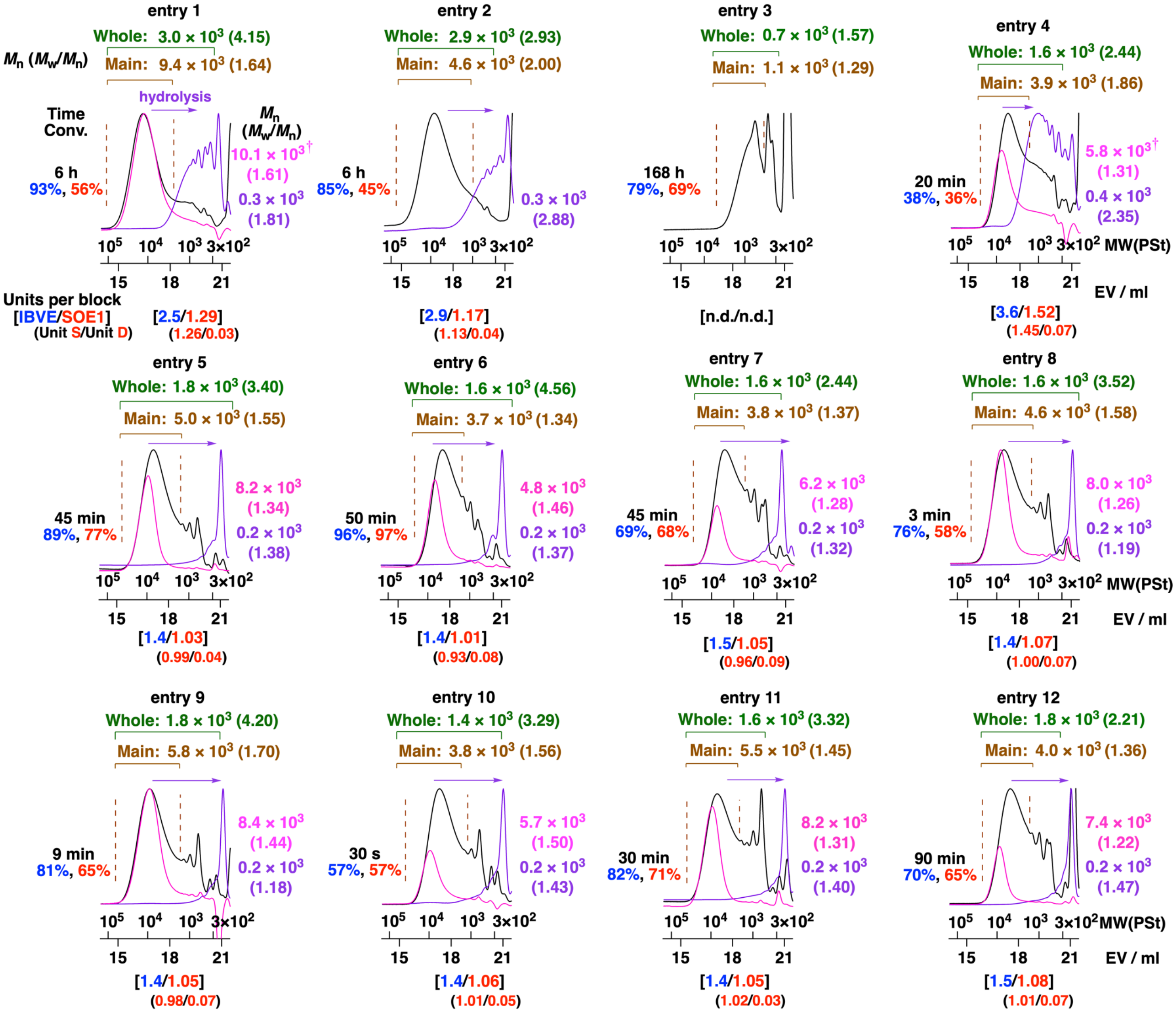


Figure S3. MWD curves of the poly(IBVE-*co*-SOE1)s listed in Table 1 (black: the original product, pink: after purification by reprecipitation in methanol, purple: acid hydrolysis products). See the footnote of Table 1 for the polymerization conditions. The M_n values of whole part (green), main portion (brown; the MW region over approximately 10^3), polymer after purification by reprecipitation in methanol (pink), and product of acid hydrolysis (purple) are listed. The M_n values of the "main" portions were calculated by arbitrarily determining the calculated areas. This is because it is difficult to precisely differentiate "polymer" and "oligomer" portions from the shapes of the MWD curves. The regions used for the M_n calculation were shown with brown broken lines. † Values for a main peak (entries 1 and 4, pink curves).

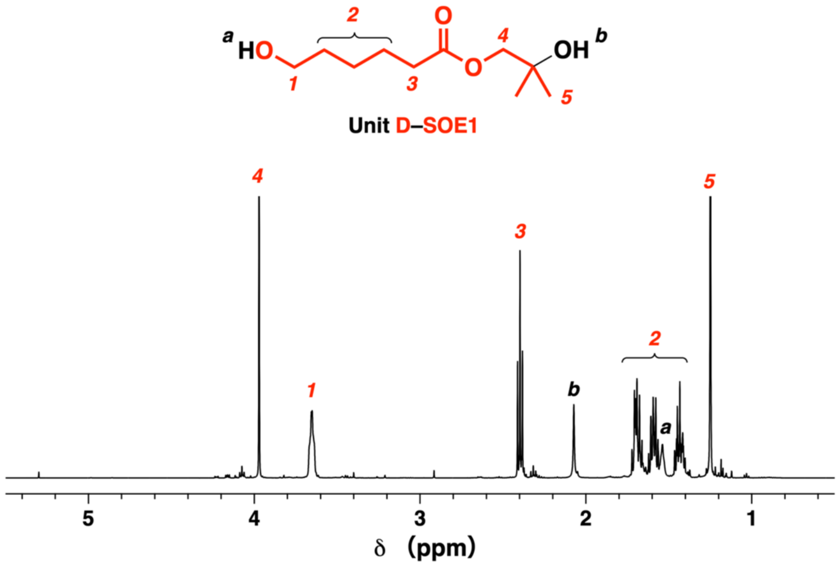


Figure S4. ^{1}H NMR spectrum of the SOE1 homopolymerization product (entry 13 in Table 1; in $CDCl_3$ at 30 ºC).

Note for homopolymerization (entry 13 in Table 1, Figure S4):

A polymer was not obtained in the reaction at an initial SOE1 concentration of 0.80 M. Instead, a ester moiety-containing product was obtained as suggested by the ^{1}H NMR spectrum (Figure S4). A possible formation mechanism is hydrolysis of SOE1 oligomers, such as a cyclic SOE1 dimer, during the workup process consisting of quenching by methanol, washing with water, evaporation, and drying. The orthoester moieties in SOE1 homosequences are easily hydrolyzed.

When polymerization was conducted at an initial monomer concentration of 4.80 M, the reaction solution became viscous. A polymer was likely generated; however, a polymer was not isolated after purification procedure consisting of dilution, washing, and evaporation. The unstable orthoester moieties in a main chain were likely decomposed during the purification procedure by some species such as initiator residues.

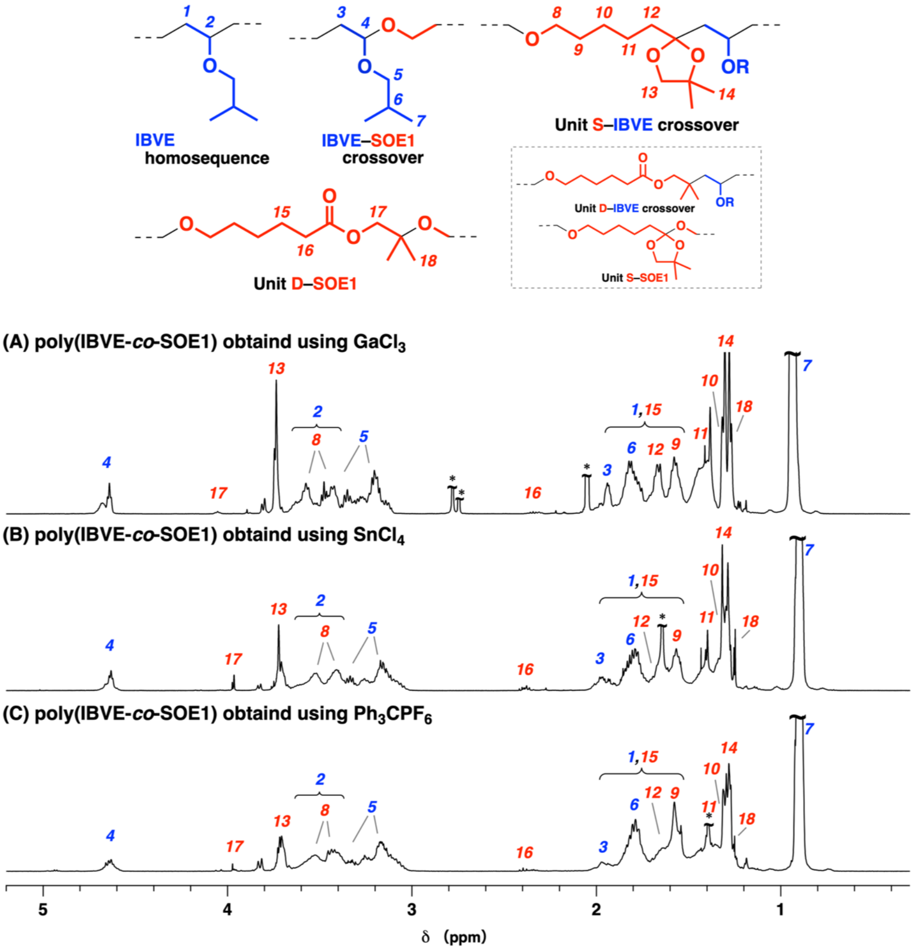


Figure S5. ^{1}H NMR spectra of poly(IBVE-*co*-SOE1)s obtained with (A) $GaCl_3$ (entry 1 in Table 1; recorded in acetone-d_6), (B) $SnCl_4$ (entry 2 in Table 1; recorded in $CDCl_3$), or (C) Ph_3CPF_6 (entry 4 in Table 1) (in $CDCl_3$ at 30 ºC). See the footnote of Table 1 for the polymerization conditions. * Acetone or water.

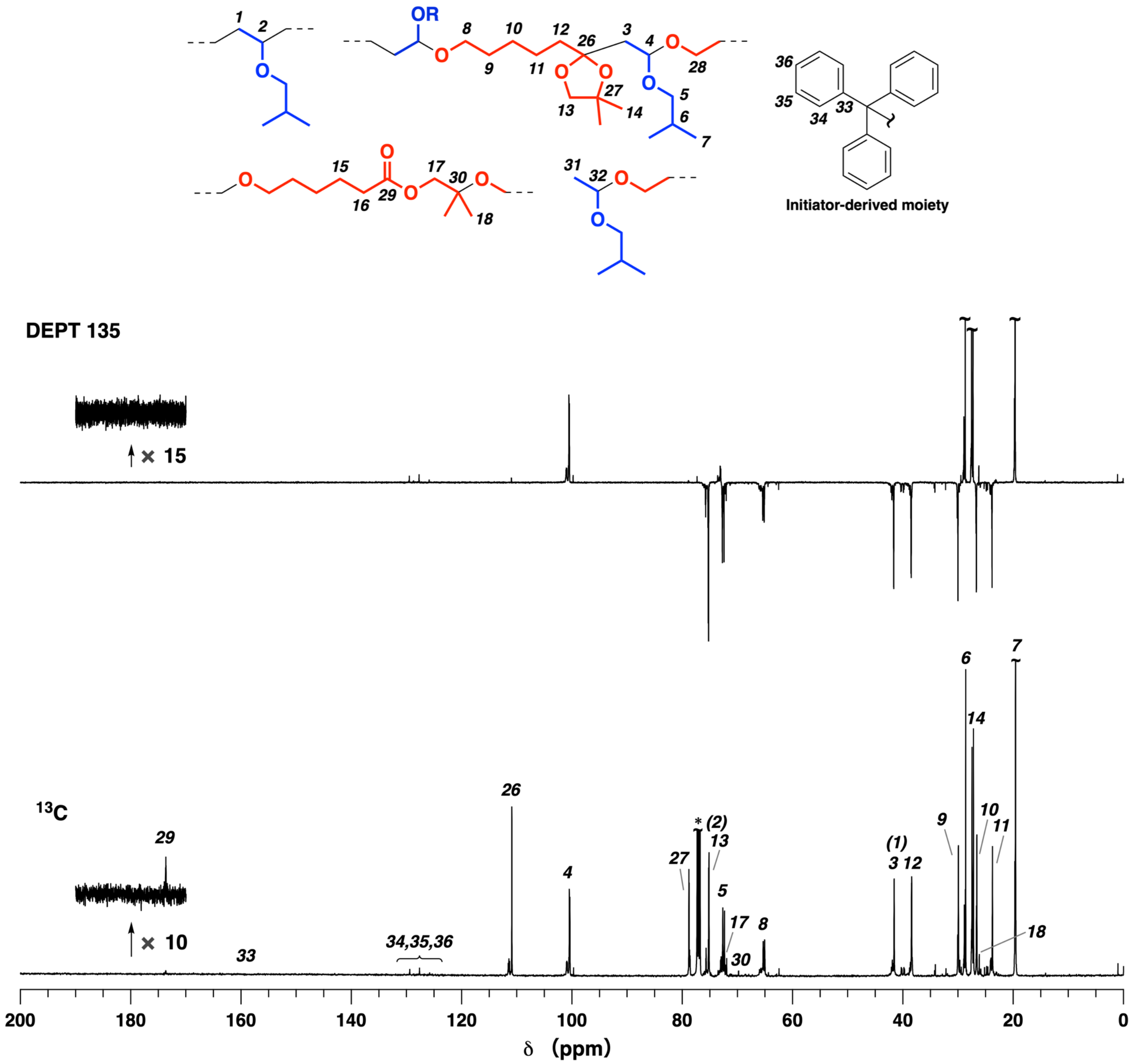


Figure S6. ^{13}C and DEPT 135 NMR spectra of the IBVE–SOE1 copolymer (entry 9 in Table 1; $[IBVE]_0 = 0.80$ M, $[SOE1]_0 = 0.80$ M, $[Ph_3CB(C_6F_5)_4]_0 = 3.0$ mM in toluene/CH_2Cl_2 (9/1 v/v) at 30 ºC; after purification by reprecipitation in methanol [M_n(GPC) = 8.4×10^3, M_w/M_n(GPC) = 1.44]) (in $CDCl_3$ at 30 ºC). * $CDCl_3$.

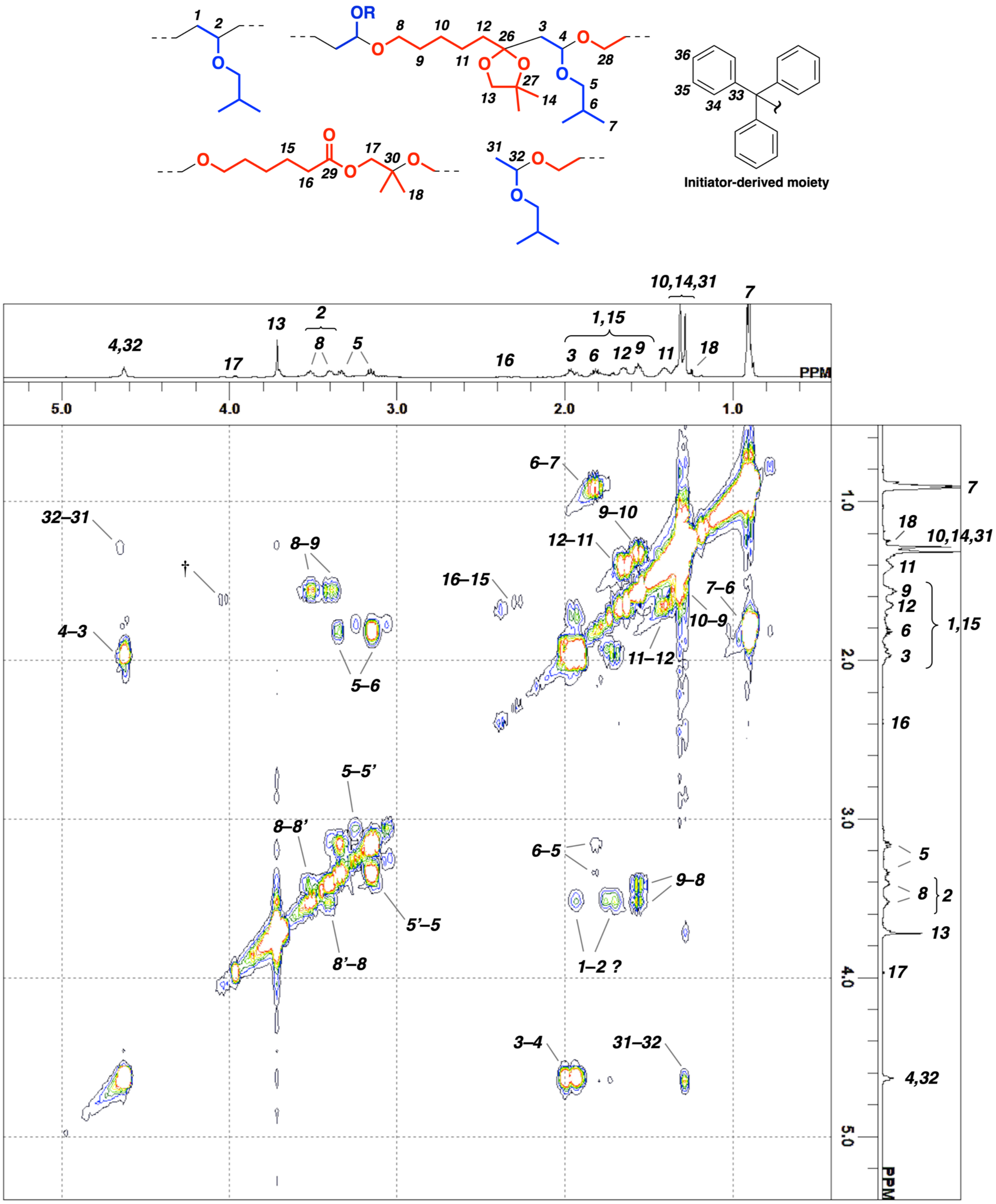


Figure S7. ^{1}H–^{1}H COSY NMR spectrum of the IBVE–SOE1 copolymer (entry 9 in Table 1; after purification by reprecipitation in methanol) (in $CDCl_3$ at 30 ºC). † This correlation is likely assigned to a hydrolysis product of an ester structure resulting from SOE1 homopropagation by the single ring-opening reaction (cf. c-(1,2) [elim] and c-(2,2) [elim] in Figure S12).

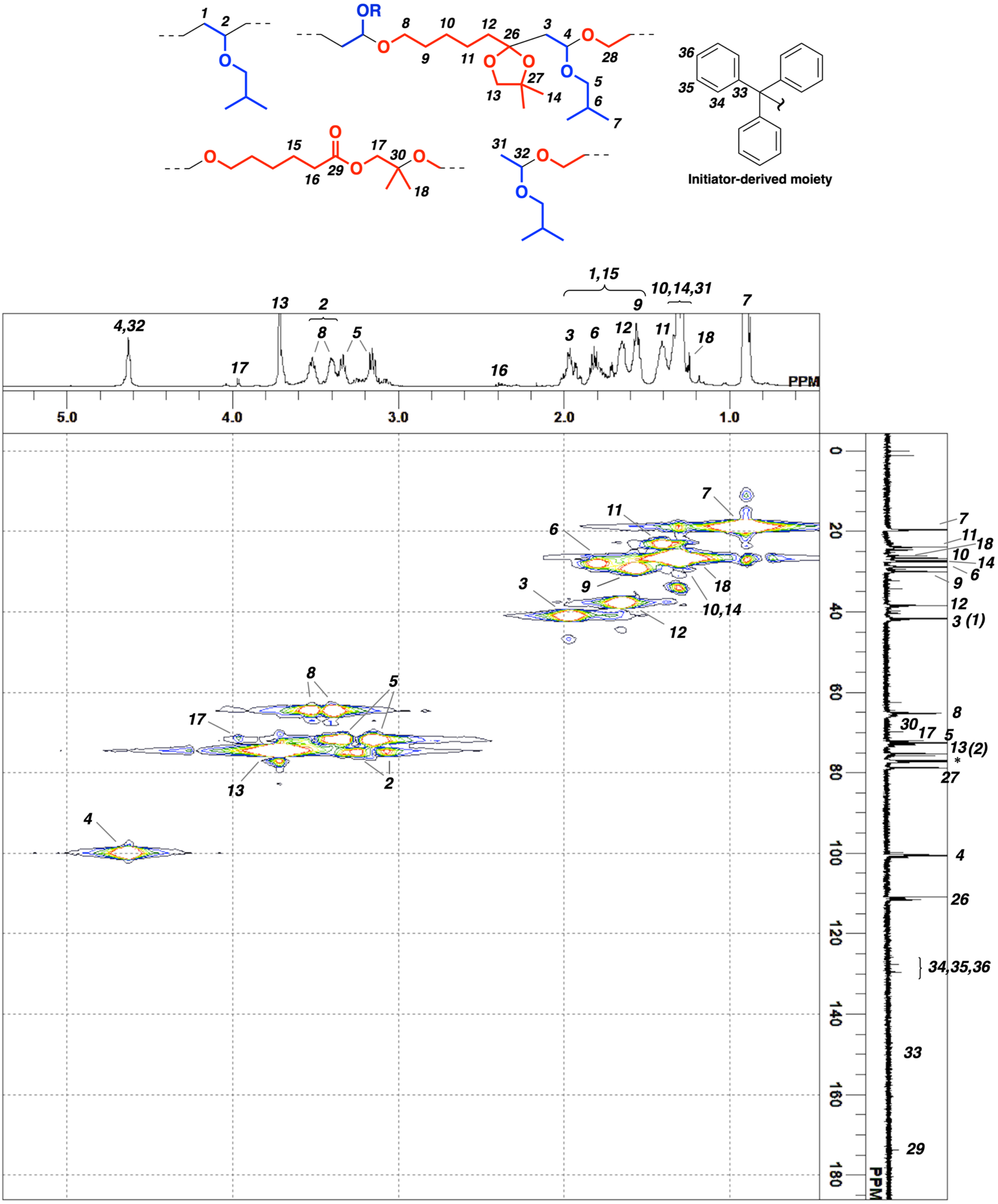


Figure S8. ^{1}H–^{13}C HSQC NMR spectrum of the IBVE–SOE1 copolymer (entry 9 in Table 1; after purification by reprecipitation in methanol) (in CDCl$_3$ at 30 ºC).

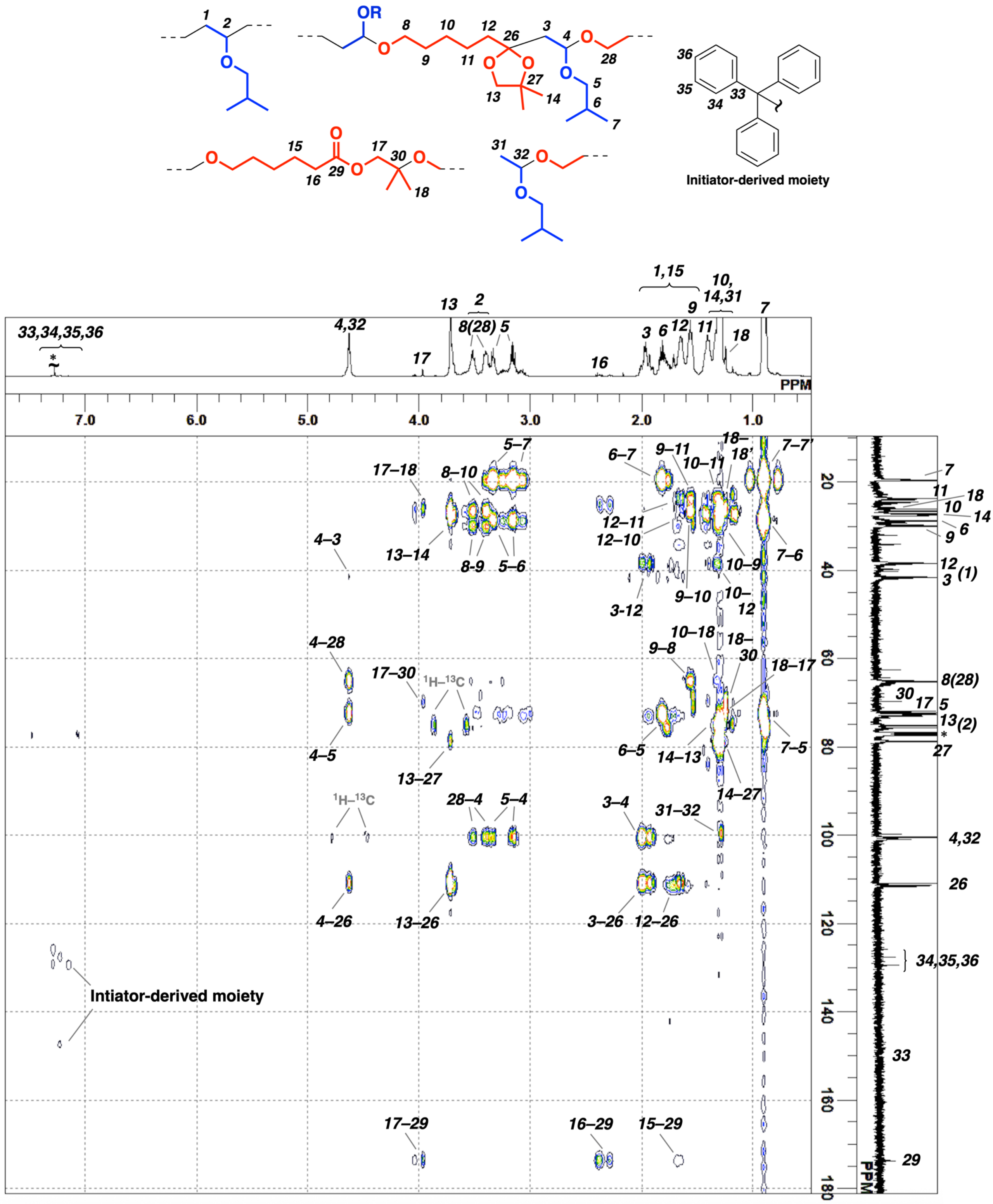
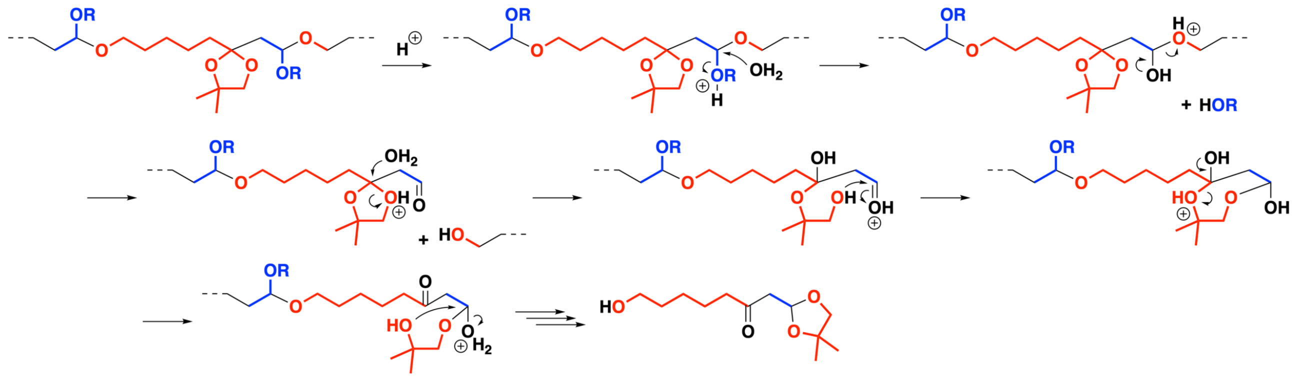


Figure S9. ^{1}H–^{13}C HMBC NMR spectrum of the IBVE–SOE1 copolymer (entry 9 in Table 1; after purification by reprecipitation in methanol) (in $CDCl_3$ at 30 ºC).



Scheme S1. A plausible acid hydrolysis mechanism of poly(IBVE-co-SOE1).

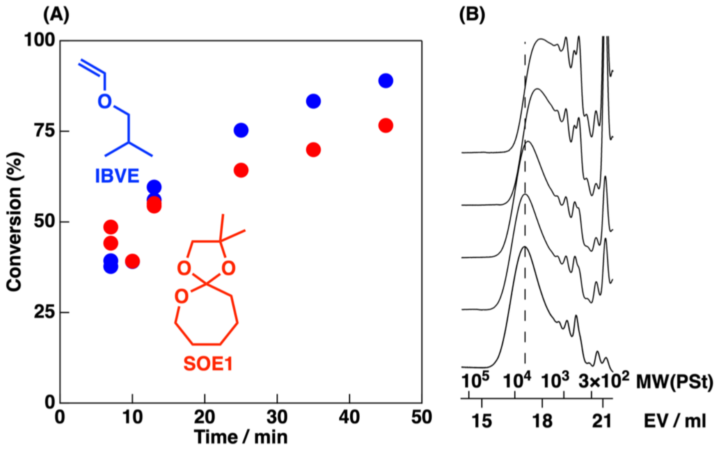


Figure S10. (A) Time–conversion curves for the copolymerization of IBVE and SOE1, and (B) MWD curves of poly(IBVE-co-SOE1)s. Polymerization conditions: $[\mathrm{IBVE}]_0$ = 0.80 M, $[\mathrm{SOE1}]_0$ = 0.80 M, $[\mathrm{Ph_3CB(C_6F_5)_4}]_0$ = 3.0 mM, in dichloromethane at 0 °C. Conversion was determined by GC. The data correspond to those listed in Table S1.

Table S1. Copolymerization of IBVE and SOE1[a]

entry	time	conv (%)		$M_n \times 10^{-3}$ [b] (main)	M_w/M_n [b] (main)
		IBVE	SOE1		
1	7 min	38	44	3.1	1.25
2	7 min	39	49	2.3	1.28
3	10 min	39	39	2.4	1.28
4	13 min	56	54	3.1	1.30
5	13 min	60	55	3.3	1.28
6	25 min	75	64	3.9	1.45
7	35 min	83	70	4.2	1.53
8	45 min	89	77	5.0	1.55

[a] $[\mathrm{IBVE}]_0$ = 0.80 M, $[\mathrm{SOE1}]_0$ = 0.80 M, $[\mathrm{Ph_3CB(C_6F_5)_4}]_0$ = 3.0 mM, in dichloromethane at 0 °C. [b] Determined by GPC (polystyrene calibration). The values of the main portions (the MW region over approximately 10^3). The data correspond to those shown in Figure S10.

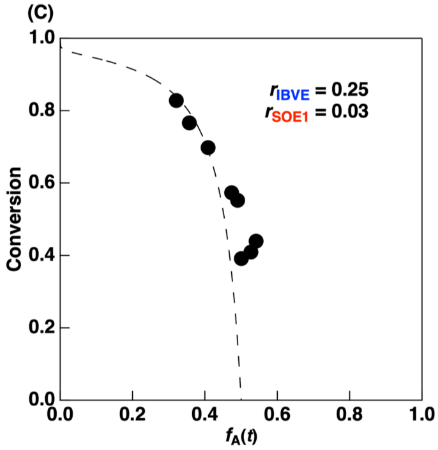


Figure S11. A graph for the determination of the monomer reactivity ratios by the Meyer–Lowry method (IBVE]$_0$ = 0.80 M, [SOE1]$_0$ = 0.80 M, [$Ph_3CB(C_6F_5)_4$]$_0$ = 3.0 mM, in dichloromethane at 0 °C). The polymerization data shown in Figure S10 and Table S1 were used.

Note for Figure S11 (the determination of the monomer reactivity ratios): The broken line in Figure S11 was drawn with r_{IBVE} and r_{SOE1} values of 0.25 and 0.03 by the Meyer–Lowry method. The data obtained at low monomer conversion (entries 1–5 in Table S1) did not fit a curve well. A possible reason is inaccurate SOE1 conversion due to several reasons such as oligomer formation, decomposition of residual SOE1 monomers after quenching, and experimental error associated with GC analysis of residual SOE1 monomers.

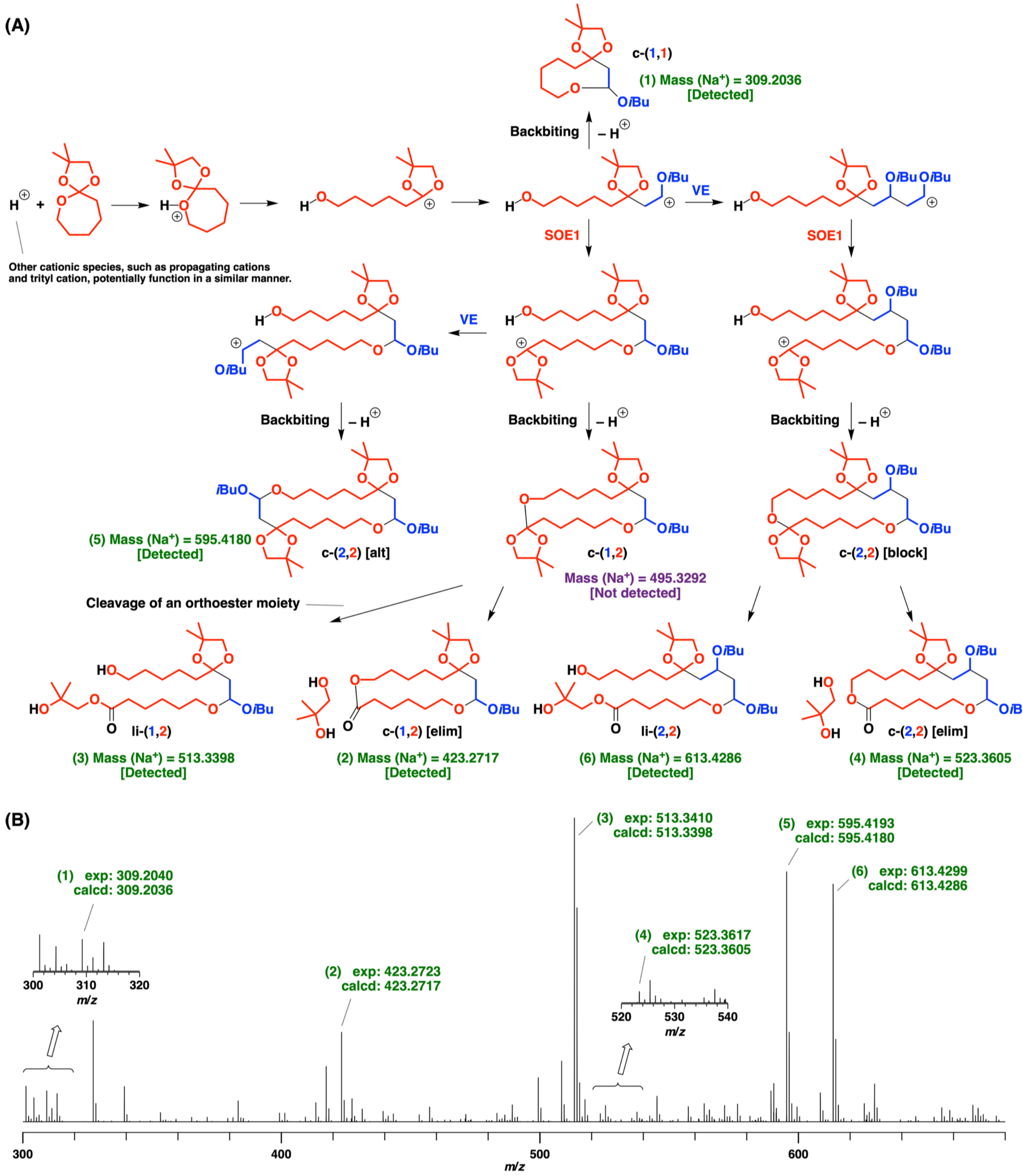


Figure S12. (A) Plausible mechanisms of backbiting reactions and hydrolysis products of the cyclic oligomers. (B) ESI-MS analysis of poly(IBVE-*co*-SOE1) (entry 5 in Table 1) .

Note for Figure S12: In the ESI-MS spectrum of the copolymerization product, several large peaks were detected in the oligomer region. The *m*/*z* values of peaks (1) and (5) corresponded to the sum of the masses of one IBVE and one SOE1 units and that of two IBVE and two SOE1 units, respectively. Plausible structures assigned to these peaks are cyclic oligomers [c-(1,1) and c-(2,2) in Figure S12A], which were most likely generated from initiation reaction from a proton or other cationic species, addition reactions of monomers, and backbiting reaction. The *m*/*z* values of peaks (2) and (4) agreed with the masses of IBVE and SOE1 unit-derived structures from which a –$OCH_2C(CH_3)O$– moiety was eliminated. The *m*/*z* values of peaks (3) and (6) agreed with the masses of IBVE and SOE1 unit-derived structures with an additional H_2O moiety. These peaks were most likely assigned to structures generated by hydrolysis of an orthoester moiety resulting from homopropagation reactions of SOE1 [c-(1,2) [elim], c-(2,2) [elim], li-(1,2), and li-(2,2) in Figure S12A].

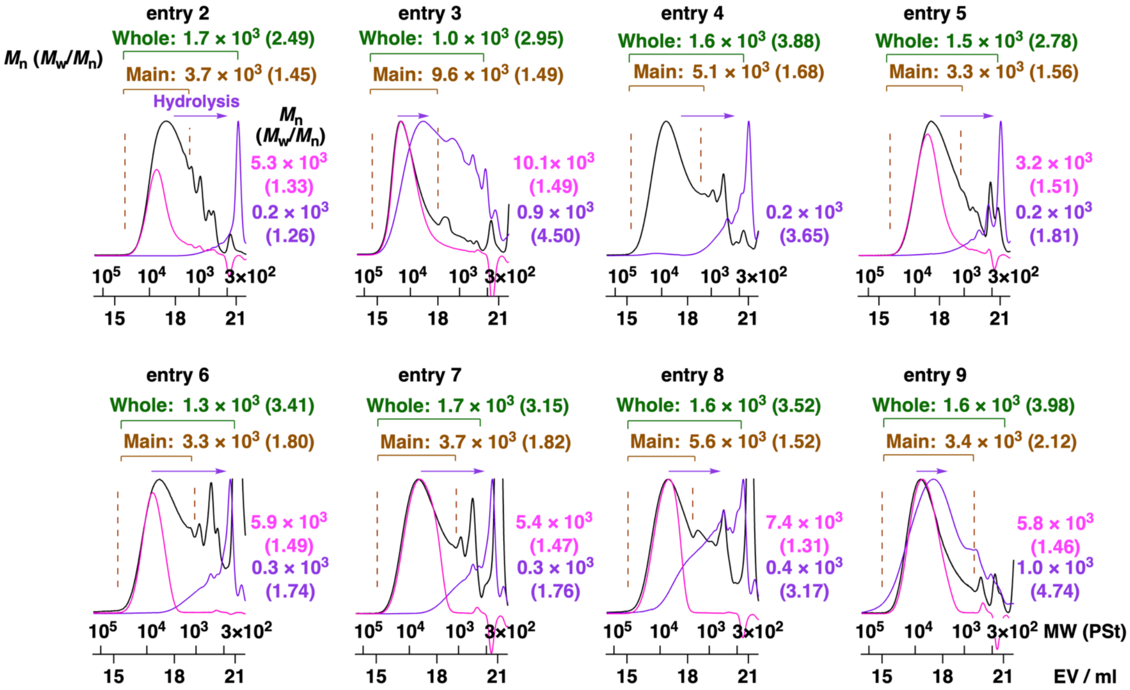


Figure S13. MWD curves of the copolymers listed in Table 2 (black: the original product, pink: after purification by reprecipitation in methanol [entries 2, 3, and 5] or preparative GPC (entries 6–9), purple: acid hydrolysis products. See the footnote of Table 2 for the polymerization conditions. The M_n values of whole part (green), main portion (brown; the MW region over approximately 10^3), polymer after purification by reprecipitation in methanol (pink), and product of acid hydrolysis (purple) are listed. The M_n values of the "main" portions were calculated by arbitrarily determining the calculated areas. This is because it is difficult to precisely differentiate "polymer" and "oligomer" portions from the shapes of the MWD curves. The regions used for the M_n calculation were shown with brown broken lines.

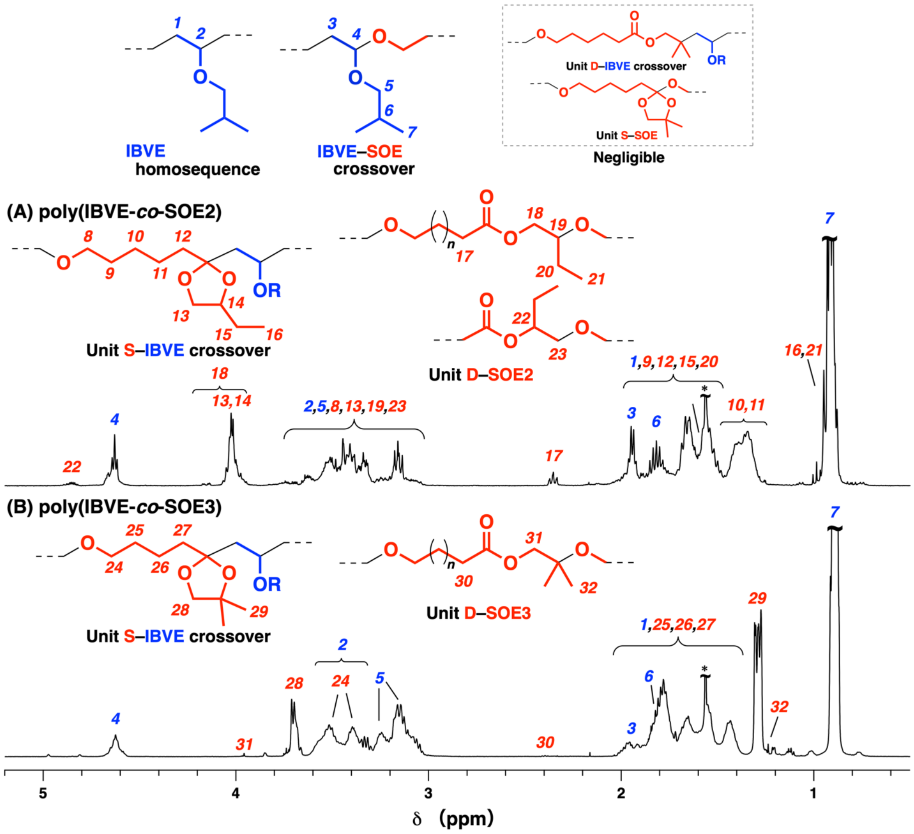


Figure S14. ^{1}H NMR spectra of (A) poly(IBVE-*co*-SOE2) (entry 2 in Table 2) and (B) poly(IBVE-*co*-SOE3) (entry 3) (in $CDCl_3$ at 30 ºC). See the footnote of Table 2 for the polymerization conditions. * Water.

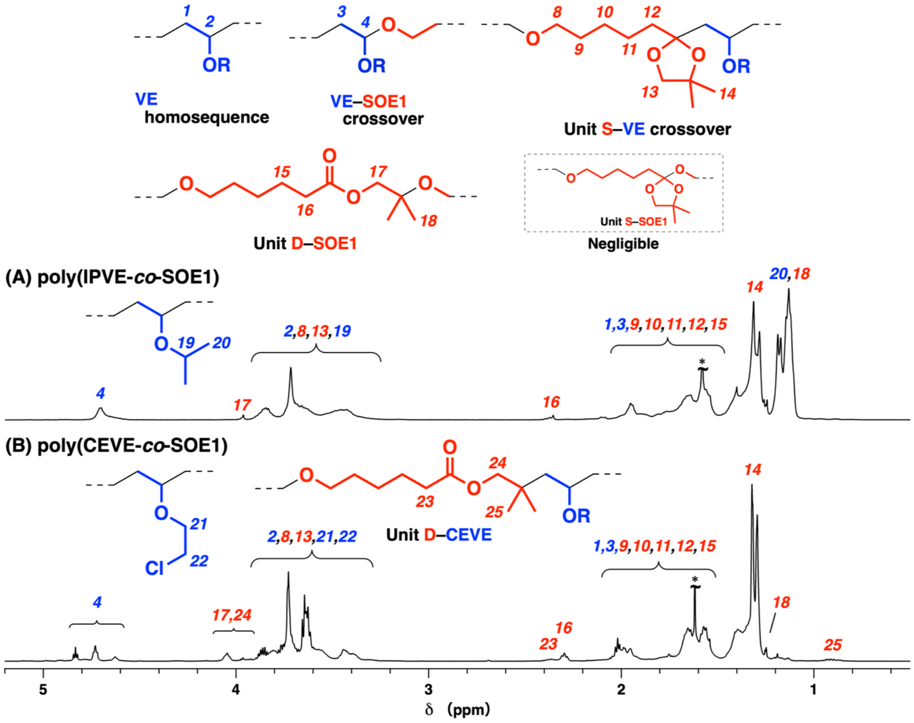


Figure S15. ^{1}H NMR spectra of (A) poly(IPVE-*co*-SOE1) (entry 4 in Table 2) and (B) poly(CEVE-*co*-SOE1) (entry 5) (in $CDCl_3$ at 30 ºC). See the footnote of Table 2 for the polymerization conditions. * Water.

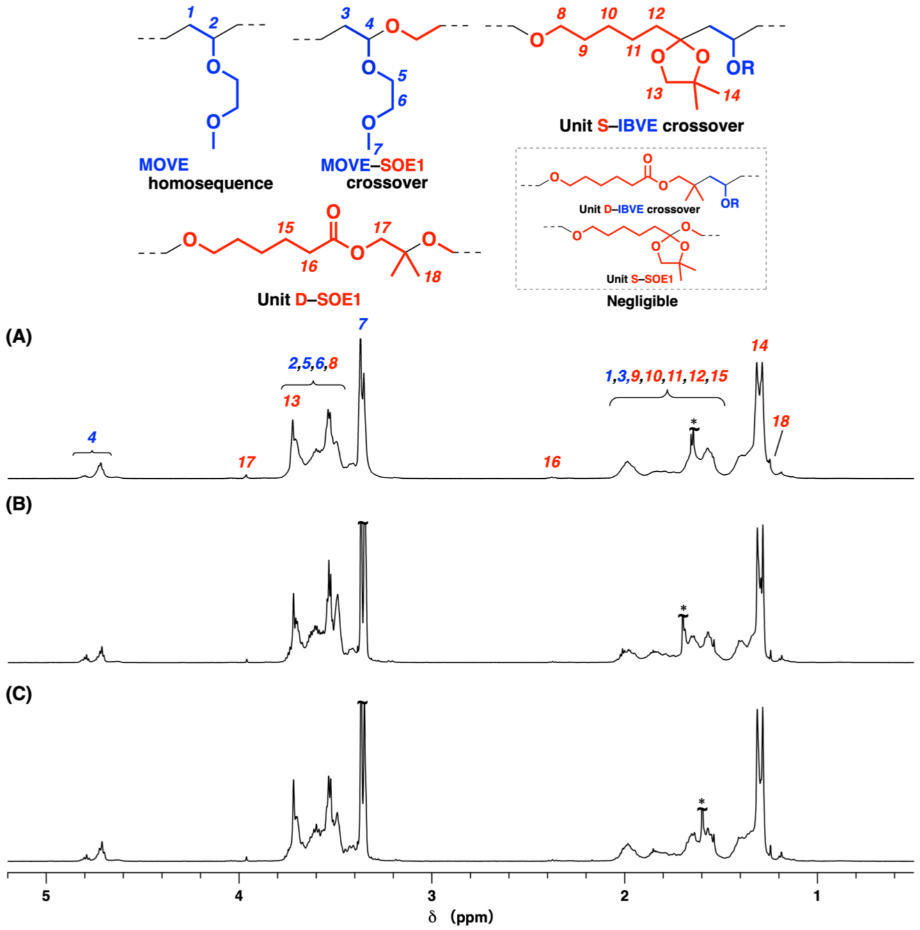


Figure S16. ^{1}H NMR spectra of poly(MOVE-*co*-SOE1)s [entries (A) 6, (B) 7, and (C) 8 in Table 2] (in $CDCl_3$ at 30 ºC). See the footnote of Table 2 for the polymerization conditions. * Water.

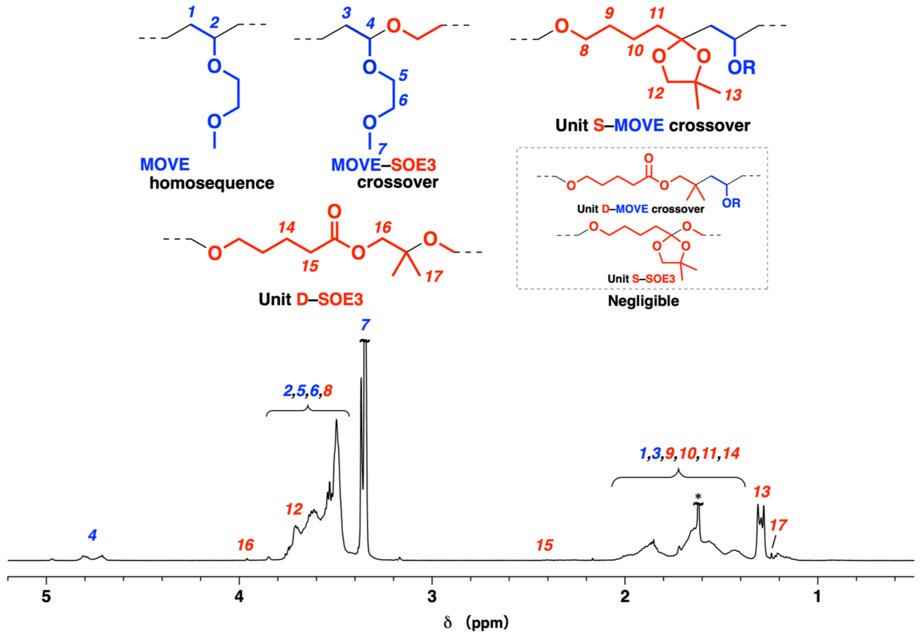


Figure S17. ^{1}H NMR spectrum of poly(MOVE-*co*-SOE3) (entry 9 in Table 2) (in $CDCl_3$ at 30 ºC). See the footnote of Table 2 for the polymerization conditions. * Water.

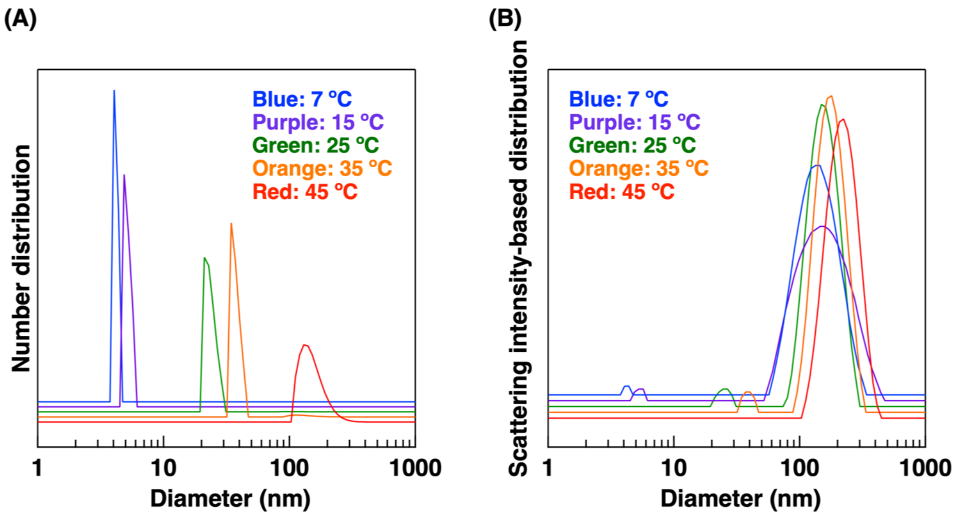


Figure S18. DLS analysis of poly(MOVE-*co*-SOE3). (A) Number distribution and (B) scattering intensity-based distribution. The same sample as that shown in Figure 3 (entry 9 in Table 2).

Note for Figure S18: A small amount of aggregates with a diameter of >10^2 nm was detected even at low temperature as indicated by the scattering intensity-based distribution data (Figure S18B). These aggregates are likely derived from copolymer chains with low MOVE ratios (high SOE ratios) due to composition distribution among chains. The result is likely consistent with transmittance of 50–60% in the transmittance measurement even at low temperature (Figure 3B).

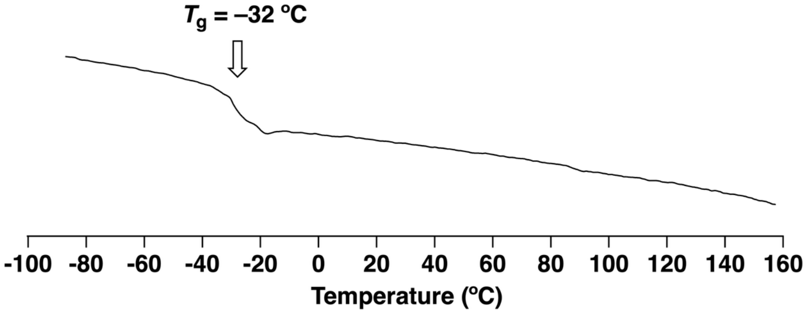


Figure S19. DSC analysis of poly(IBVE-*co*-SOE1) (entry 9 in Table 1; after purification by reprecipitation in methanol). The 2nd heating scan, 10 ºC min^{-1}.

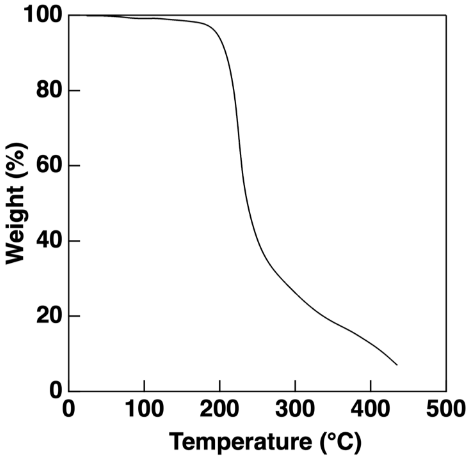


Figure S20. TGA analysis of poly(IBVE-*co*-SOE1) (entry 9 in Table 1; after purification by reprecipitation in methanol).