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Articles

Activated Monomer Cationic Polymerization of Lactones and the Application to Well-Defined Block Copolymer Synthesis with Seven-Membered Cyclic Carbonate

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ABSTRACT: Activated monomer cationic ring-opening polymerization of ϵ-caprolactone (ϵ-CL) and δ-valerolactone (δ-VL) and the synthesis of di- and triblock copolymers of a seven-membered cyclic carbonate (7CC) and these lactones initiated with *n*-butyl alcohol/$HCl\cdot Et_2O$ and $H_2O/HCl\cdot Et_2O$ were carried out to obtain the corresponding homopolymers and block copolymers with narrow polydispersity ratios in one pot quantitatively. The molecular weights of the obtained polymers could be controlled with the feed ratio of the monomer and initiator.

Introduction

Ring-opening polymerization of lactones and cyclic carbonates attracts much attention because the resulting polymers are applicable to drug delivery and biodegradable materials.[1] Recent development of living ring-opening polymerization has enabled us to obtain the corresponding polymers with controlled molecular weights (M_n's) and polydispersity ratios (M_w/M_n's). One of the most powerful methods to control cationic ring-opening polymerization is "activated monomer cationic polymerization" reported by Penczek et al.,[2] which can suppress unfavorable reactions such as backbiting and deproportionation. This method has been applied to the polymerization of epichlorohydrin and propylene oxide to give the linear polymers free from cyclic oligomers.[3] Okamoto has reported that the combination of an alcohol and triethyloxonium hexafluorophosphate is effective for ring-opening polymerization of β-propiolactone, δ-valerolactone (δ-VL), and ϵ-caprolactone (ϵ-CL) to give the corresponding polymers with controlled M_n's (<3000), but the M_w/M_n's are relatively large (∼1.4).[4] These methods have been also applied to prepare the block copolymers using the hydroxy-terminated prepolymers such as poly(tetramethylene oxide).[5] We have recently reported that the ring-opening polymerization of 1,3-dioxepan-2-one (7CC) with an alcohol/$HCl\cdot Et_2O$ initiator gives the corresponding polycarbonate (M_n < 10 000) with narrow polydispersity ratios (∼1.15).[6] In this article, we describe the controlled ring-opening polymerization of ϵ-CL and δ-VL, along with di- and triblock copolymerization with 7CC by use of *n*-butyl alcohol/$HCl\cdot Et_2O$ and $H_2O/HCl\cdot Et_2O$ initiator systems.

Experimental Section

Materials. CH_2Cl_2 was distilled sequentially over P_2O_5 and CaH_2 under nitrogen. ϵ-CL and δ-VL were purchased from Aldrich and distilled over CaH_2 under nitrogen prior to use. 7CC was prepared according to the literature and stored at −20 °C under nitrogen.[7] *n*-Butyl alcohol was dried over CaH_2 and distilled under nitrogen. H_2O was distilled prior to use. A 2.0 mol/L HCl solution in diethyl ether (Et_2O) was purchased from Aldrich and used without further purification.

Measurements. ^1H NMR spectra were recorded with a JEOL Lambda-300 spectrometer. Number- and weight-average molecular weights (M_n and M_w) were measured by gel permeation chromatography (GPC) on a Tosoh HLC-8120 system equipped with two consecutive polystyrene gel columns (G2500HXL and G4000HXL) eluted with tetrahydrofuran (THF) at a flow rate of 1.0 mL/min calibrated by standard polystyrenes.

Polymerization of ϵ-CL and δ-VL. A typical procedure: All glass vessels were heated in vacuo before use and filled with and handled in a stream of dry nitrogen. To a solution of ϵ-CL (0.57 g, 5.0 mmol) in CH_2Cl_2 (4.5 mL) was added *n*-butyl alcohol (9.3 mg, 0.13 mmol). The polymerization was initiated by the addition of 65 μL (0.13 mmol) of HCl solution (2 mol/L) in Et_2O at 25 °C. After 4 h, the reaction mixture was poured into 300 mL of *n*-hexane to precipitate a polymer. The precipitate was filtered and dried at 25 °C for 5 h in vacuo to give 0.56 g of white powdery polymer (yield 99%).

Block Copolymerization. A typical procedure: To a solution of 7CC (0.58 g, 5.0 mmol) in CH_2Cl_2 (4.5 mL) was added *n*-butyl alcohol (13 mg, 0.17 mmol). The polymerization was initiated by the addition of 130 μL (0.26 mmol) of HCl solution (2 mol/L) in Et_2O at 25 °C. After confirming a quantitative conversion of 7CC by ^1H NMR, the copolymerization was conducted by charging 0.57 g (5.0 mmol) of ϵ-CL into the reaction mixture with vigorous stirring. After the polymerization, the mixture was poured into 300 mL of *n*-hexane to precipitate a polymer. The precipitate was filtered and dried at 25 °C for 5 h in vacuo to give 1.06 g of a white powdery block copolymer (yield 92%).

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Table 1. Ring-Opening Polymerization of ϵ-CL[a]

run	$[\epsilon\text{-CL}]_0/[\text{BuOH}]_0$	$[\text{HCl}]_0/[\text{BuOH}]_0$	conv[b] (%)	yield[c] (%)	M_n[b] (NMR)	M_n[d] (GPC)	M_w/M_n[d]
1	20	0	0	*e*	*e*	*e*	*e*
2	20	1	100	99	2600	3000	1.08
3	20	10	99	78	*e*	2700	1.17
4	40	1	100	99	*e*	6500	1.13
5	75	4	95	87	10700	7900	1.14
6	100	5	94	82	14300	10300	1.15

[a] Polymerization was carried out in CH_2Cl_2 at 25 °C for 24 h. $[M]_0 = 1$ mol/L. [b] Determined by ^1H NMR. The M_n was estimated from the integration of the terminal methyl proton signal and methylene proton signal of the main chain. [c] *n*-Hexane-insoluble part. [d] Determined by GPC (polystyrene standard, THF). [e] Not determined.

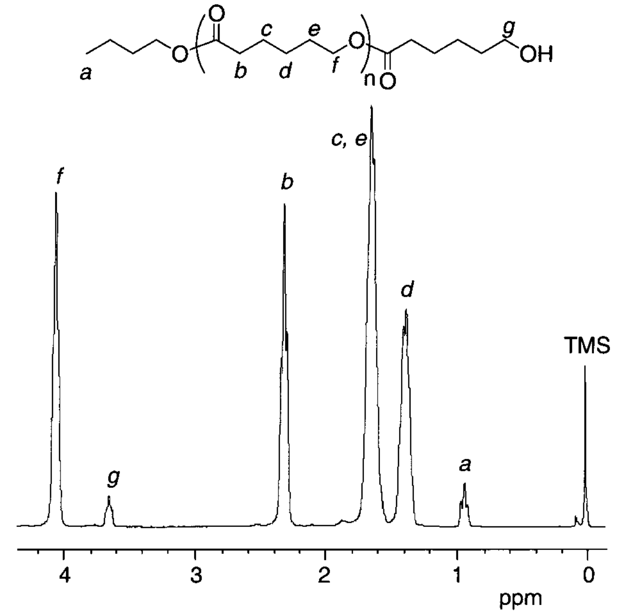
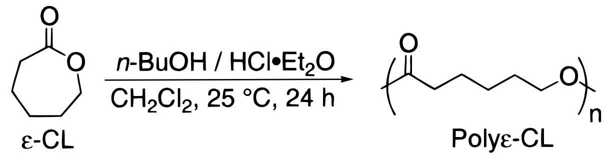


Figure 1. ^1H NMR spectrum (300 MHz, $CDCl_3$) of poly-ϵ-CL obtained by the polymerization of ϵ-CL with *n*-BuOH/HCl·Et_2O initiator system in CH_2Cl_2 at 25 °C. $[\epsilon\text{-CL}]_0 = 1$ mol/L, $[n\text{-BuOH}]_0 = [\text{HCl}]_0 = 0.1$ mol/L.

Scheme 1



Results and Discussion

Ring-Opening Polymerization of ϵ-CL with *n*-Butyl Alcohol/HCl·Et_2O Initiator System. As described in the Introduction, we have recently reported that the ring-opening polymerization of 1,3-dioxepan-2-one (7CC) by H_2O or a primary alcohol in the presence of HCl·Et_2O satisfactorily proceeds to give linear poly7CC with the controlled M_n (10^3−10^4) and narrow M_w/M_n (~1.15) without side reactions such as decarboxylation.[6] The key feature of this polymerization may be the acidity of the added protonic acid, which is not as large to polymerize the monomer by itself but is sufficient to activate the monomer. To extend this facile method to cyclic esters, we performed the ring-opening polymerization of ϵ-CL to examine the M_n and M_w/M_n of the polymer. Scheme 1 and Table 1 summarize the results of the polymerization of ϵ-CL with *n*-butyl alcohol (*n*-BuOH) in the presence of HCl·Et_2O. Although the polymerization did not proceed with *n*-butyl alcohol alone (run 1), the addition of HCl was quite effective to give polyϵ-CL quantitatively (runs 2−6). The increase of HCl amount did not affect the M_n of the obtained polymer seriously, and the M_w/M_n ratio was small (runs 2 and 3). These results suggest that HCl did not serve as an initiator, but an activator in this system, similar to the polymerization of 7CC. The M_n value agreed well with that calculated from the feed ratio of the monomer to initiator in every sample, keeping a narrow polydispersity ratio (runs 2 and 4−6).

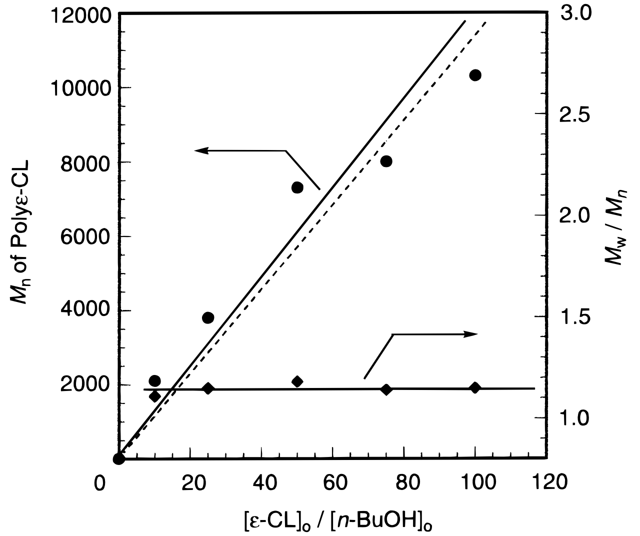


Figure 2. Dependence of $M_{n(GPC)}$ estimated by GPC (solid line), $M_{n(calc)}$ caluculated by the feed ratio of $[\epsilon\text{-CL}]_0/[n\text{-BuOH}]_0$ (broken line), and M_w/M_n of poly-ϵ-CL on $[\epsilon\text{-CL}]_0/[n\text{-BuOH}]_0$ obtained by the polymerization of ϵ-CL in CH_2Cl_2 at 25 °C for 24 h. $[\epsilon\text{-CL}]_0 = 1$ mol/L, $[\text{HCl}]_0/[n\text{-BuOH}]_0 = 1$.

Figure 1 illustrates the ^1H NMR spectrum of polyϵ-CL obtained by the polymerization of ϵ-CL with 1/10 equiv of *n*-BuOH/HCl initiator system in CH_2Cl_2 at 25 °C for 5 h (initial concentration of ϵ-CL, $[\epsilon\text{-CL}]_0 = 1$ mol/L). In addition to signals *b*−*f* assignable to α-, β-, γ-, δ-, and ϵ-methylene protons of the ester carbonyl moiety at 2.31, 1.65, 1.39, 1.65, and 4.06 ppm, signals *a* and *g* on the basis of terminal methyl and α-methylene proton signals of a hydroxyl group were observed at 0.94 and 3.65 ppm, respectively. The integration ratio of the signals *a* to *g* was exactly 3/2, which agreed with the expected value.

Figure 2 illustrates the dependence of M_n and M_w/M_n of polyϵ-CL on the feed ratio $[\epsilon\text{-CL}]_0/[n\text{-BuOH}]_0$ in the polymerization in CH_2Cl_2 at 25 °C. The M_n increased almost linearly with increasing the feed ratio of the monomer to initiator, keeping narrow polydispersity. The second-feed experiment to confirm the living nature of the polymerization was examined. First, ϵ-CL was polymerized with 1/40 equiv of *n*-BuOH/HCl·Et_2O initiator system in CH_2Cl_2 at 25 °C for 12 h. After confirming the quantitative monomer conversion, the same amount of monomer was fed into the polymerization

Scheme 2

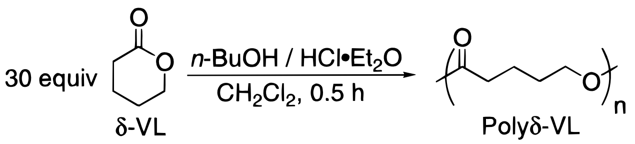


Table 2. Ring-Opening Polymerization of δ-VL[a]

run	temp (°C)	conv[b] (%)	yield[c] (%)	M_n[b] (NMR)	M_n[d] (GPC)	M_w/M_n[d]
1	25	92	77	2400	2700	1.27
2	0	95	86	3700	3200	1.17
3	−10	95	82	3000	2800	1.17
4	−40	94	85	3400	2700	1.10

[a] Polymerization was carried out in CH_2Cl_2 at 25 °C for 0.5 h. $[M]_0/[BuOH]_0 = 30$, $[H]_0/[BuOH]_0 = 1.5$ mol, $[M]_0 = 2$ mol/L. [b] Determined by ^1H NMR. The M_n was estimated from the integration of the terminal methyl proton signal and methylene proton signal of the main chain. [c] n-Hexane-insoluble part. [d] Determined by GPC (polystyrene standard, THF).

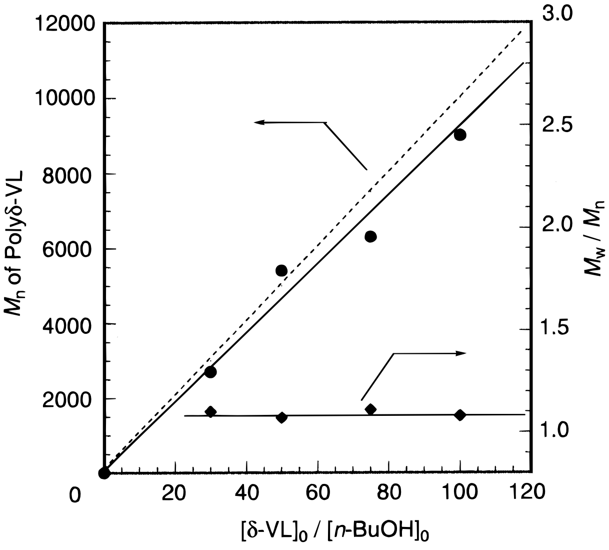
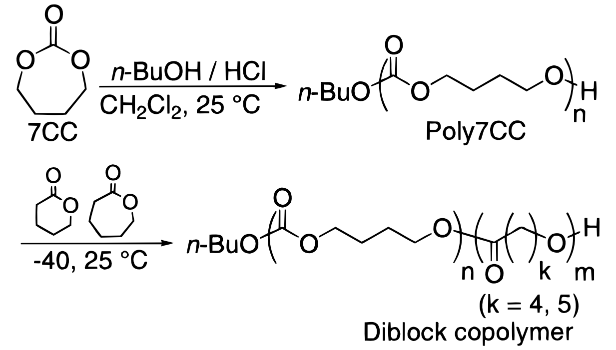


Figure 3. Dependence of $M_{n(GPC)}$ estimated by GPC (solid line), $M_{n(calc)}$ caluculated by the feed ratio of $[δ\text{-VL}]_0/[n\text{-BuOH}]_0$ (broken line), and M_w/M_n of poly-δ-VL on $[δ\text{-VL}]_0/[n\text{-BuOH}]_0$ in the polymerization of δ-VL in CH_2Cl_2 at −40 °C. $[δ\text{-VL}]_0 = 2$ mol/L, $[HCl]_0/[n\text{-BuOH}]_0 = 1.5$.

mixture to conduct postpolymerization. The GPC elution peak shifted to the higher M_n region, maintaining a narrow polydispersity. These results suggest that no termination or chain transfer reaction occurs; namely, this polymerization proceeds via *living* fashion.

Scheme 3



Ring-Opening Polymerization of δ-VL with n-Butyl Alcohol/HCl·Et₂O Initiator System. Scheme 2 and Table 2 summarize the ring-opening polymerization of δ-VL with *n*-butyl alcohol in the presence of HCl·Et_2O at 25 to −40 °C. The polymerization of δ-VL at 25 °C provided the polymer in high yield, but the M_w/M_n was somewhat large (1.27) (run 1). At 0 °C, polyδ-VL with a small M_w/M_n was obtained in a high yield (run 2). The M_w/M_n became smaller at lower temperature (runs 2−4). Figure 3 depicts the dependence of the M_n and M_w/M_n of polyδ-VL on the feed ratio of $[δ\text{-VL}]_0/[n\text{-BuOH}]_0$ in the polymerization in CH_2Cl_2 at −40 °C. The M_n increased linearly with the monomer feed ratio, keeping a narrow polydispersity ($M_w/M_n \leq 1.11$). The experimental M_n values agreed well with theoretical ones calculated from the feed ratio of the monomer to initiator. The second-monomer-feed experiment was satisfactory, similar to ϵ-CL polymerization. These results may strongly support that δ-VL polymerization also proceeds via *living* fashion.

Synthesis of Diblock Copolymers of 7CC with Lactones. The combination of *n*-butyl alcohol and HCl·Et_2O could provide controlled polymers of ϵ-CL and δ-VL as described above. To develop this facile method to copolymer synthesis, we examined block copolymerization of these monomers with a seven-membered cyclic carbonate (7CC), undergoing controlled polymerization (Scheme 3). Table 3 summarizes the yield, M_n, M_w/M_n, and composition of a series of block copolymers obtained by the copolymerization. The second monomer conversion was almost quantitative in all cases. The polydispersities of the postpolymers were narrow ($M_w/M_n \leq 1.16$) with values similar to the prepolymers. Figure 4 depicts ^1H NMR spectra of the (A) prepolymer (poly7CC) and (B) diblock copoly7CC-*b*-ϵ-CL obtained in run 2 in Table 3. In addition to signals *h* and *i* assignable to α- and β-methylene protons of the carbonate moiety at 4.17 and 1.75 ppm, signals *a* and *k* assignable to terminal methyl and α-methylene proton signals of a hydroxyl group were observed at 0.94 and 3.70 ppm, respectively (Figure 4A). After the postpolymerization, new signals *b*, *c*, *d*, *e*, and *f* were observed at 2.31, 1.65, 1.39, 1.65,

Table 3. Synthesis of Diblock Copolymer of 7CC with Lactones

	homopolymerization[a]					block copolymerization								
run	$[7CC]_0/[BuOH]_0$	conv[b] (%)	M_n[b] (NMR)	M_n[c] (GPC)	M_w/M_n[c]	monomer	$[M]_0/[H_2O]_0$	time (h)	temp (°C)	yield[d] (%)	M_n[b] (NMR)	M_n[c] (GPC)	M_w/M_n[c]	unit ratio[b]
1	10	99	1900	1500	1.15	ϵ-CL	30	24	25	96	4800	6600	1.16	22:78
2	30	99	2800	3500	1.13	ϵ-CL	30	24	25	92	4800	6800	1.12	49:51
3	60	99	6500	6200	1.15	ϵ-CL	30	24	25	88	8600	9500	1.13	74:26
4	10	99	1500	1900	1.14	δ-VL	30	3	−40	99	5400	6900	1.14	22:78
5[e]	30	99	4300	4200	1.14	δ-VL	30	1.5	−40	99	5400	7200	1.14	48:52
6[e]	60	99	5800	6600	1.12	δ-VL	30	3	−40	84	7500	8600	1.14	70:30

[a] Conditions; in CH_2Cl_2 at 25 °C for 24 h, $[7CC]_0 = 1$ mol/L, $[HCl]_0/[BuOH]_0 = 1.5$. [b] Determined by ^1H NMR. The M_n was estimated from the integration of the terminal methyl proton signal and methylene proton signal of the main chain. [c] Determined by GPC (polystyrene standard, THF). [d] n-Hexane-insoluble part. [e] $[7CC]_0 = 2$ mol/L.

Table 4. Synthesis of Triblock Copolymer of 7CC with Lactones

homopolymerization[a]						triblock copolymerization								
run	$[7CC]_0/[H_2OH]_0$	$[M]_0$ (mol/L)	M_n[b] (NMR)	M_n[c] (GPC)	M_w/M_n[c]	comonomer	$[M]_0/[H_2O]_0$	time (h)	temp (°C)	yield[d] (%)	M_n[b] (NMR)	M_n[c] (GPC)	M_w/M_n[c]	7CC:ϵ-CL[b] or δ-CL
1	30	1	2400	3100	1.14	ϵ-CL	30	24	25	92	5700	5900	1.10	46:54
2	30	2	2100	3500	1.13	δ-VL	30	1.5	−40	85	5500	6300	1.08	54:46

[a] Conditions; in CH_2Cl_2 at 25 °C for 24 h, $[HCl]_0/[H_2O]_0 = 1.5$. [b] Determined by ^1H NMR. The M_n was estimated from the integration of the terminal methyl proton signal and methylene proton signal of the main chain. [c] Determined by GPC (polystyrene standard, THF). [d] *n*-Hexane-insoluble part.

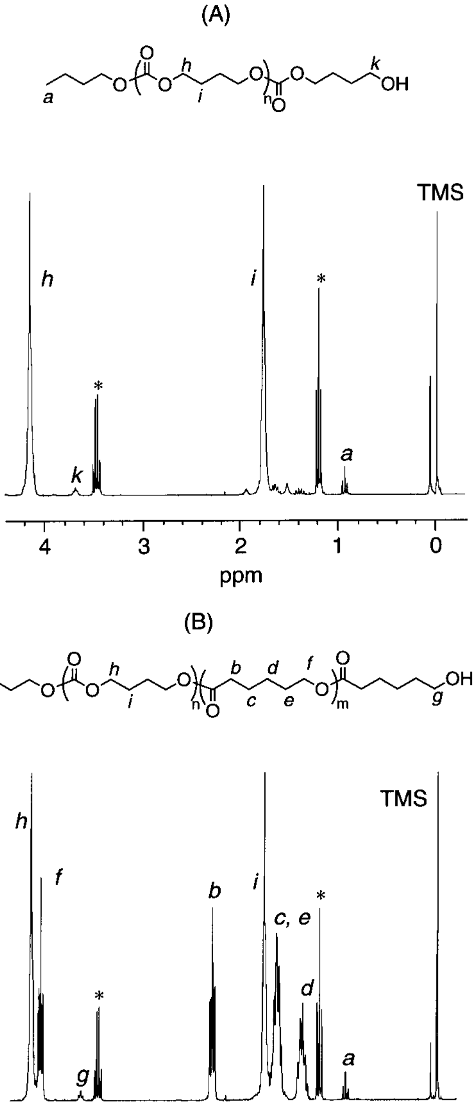


Figure 4. ^1H NMR spectra (300 MHz, $CDCl_3$) of (A) homo-poly-7CC obtained by the polymerization of 7CC (30 equiv) with *n*-BuOH/HCl·Et_2O initiator system in CH_2Cl_2 at 25 °C ($[7CC]_0$ = 1 mol/L, $[HCl]_0/[n\text{-}BuOH]_0 = 1$) and (B) diblock copolymer obtained by the further addition of ϵ-CL (30 equiv) into the polymer mixture (A). Asterisks indicate signals due to diethyl ether.

and 4.06 ppm (Figure 4B), which corresponded completely to polyϵ-CL as shown in Figure 1. The terminal methylene signal *k* disappeared, and a new signal *g* assignable to α-methylene protons of a hydroxyl moiety at the polyϵ-CL terminal unit appeared at 3.65 ppm, supporting the formation of a diblock copolymer free from homo-poly7CC. The unit ratio of 7CC and the comonomer in the resulting polymer was calculated by the ^1H NMR integration ratio of signals *h* and *b* in Figure 4B, which agreed well with the feed ratio. The GPC traces of the resulted copolymer before precipitation with *n*-hexane showed unimodal, maintaining a narrow polydispersity. These results strongly support the formation of block copolymer free from homopolymer.

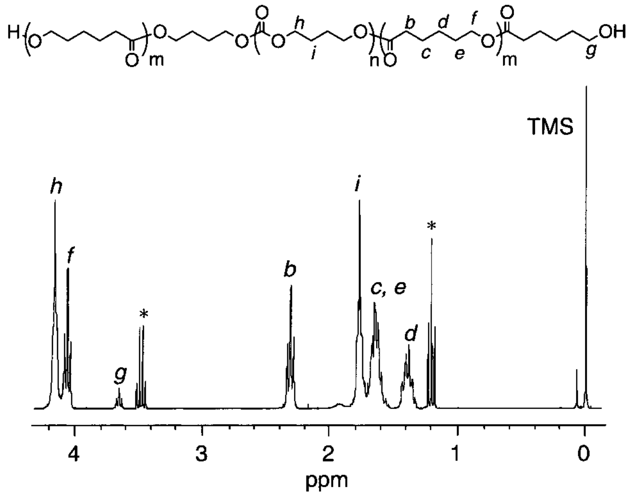


Figure 5. ^1H NMR spectrum (300 MHz, $CDCl_3$) of triblock copolymer obtained by the polymerization of 7CC (30 equiv) with H_2O/HCl·Et_2O initiator system in CH_2Cl_2 at 25 °C ($[7CC]_0$ = 1 mol/L, $[HCl]_0/[H_2O]_0 = 1$), followed by the further addition of ϵ-CL (30 equiv). Asterisks indicate signals due to diethyl ether.

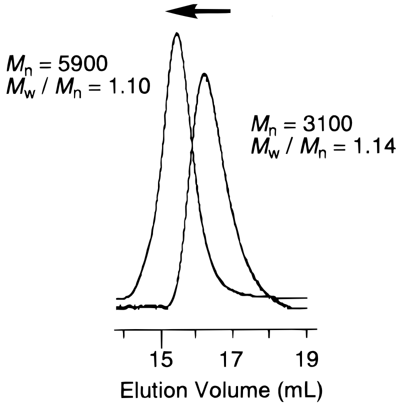


Figure 6. GPC traces of homo-poly7CC obtained by the polymerization of 7CC (30 equiv) with H_2O/HCl·Et_2O in CH_2Cl_2 at 25 °C ($[7CC]_0$ = 1 mol/L, $[HCl]_0/[H_2O]_0 = 1$) and the triblock copolymer obtained by further addition of ϵ-CL (30 equiv).

Synthesis of Triblock Copolymers. When H_2O was employed instead of *n*-butyl alcohol as the initiator in 7CC polymerization in the presence of HCl, the initiating carbonic acid polymer end smoothly changed into a hydroxyl group by rapid decarboxylation to form a polycarbonate containing hydroxyl groups at the polymer ends.[6] We attempted to obtain triblock copolymers utilizing this prepolymer. Table 4 summarizes the results of triblock copolymerization of 7CC, ϵ-CL, and δ-VL with $H_2O/HCl \cdot Et_2O$ initiator system. The corresponding triblock copolymers with narrow polydispersities were obtained in good yields. The copolymer composition determined by ^1H NMR spectroscopy agreed well with the expected value. The ^1H NMR spectrum of the triblock copolymer obtained in run 2 in Table 4 showed no signal corresponding to α-methylene protons of a hydroxyl group of poly7CC end at 3.70 ppm but a signal *g* assignable to α-methylene protons of a hydroxyl group of polyϵ-CL end at 3.65 ppm. The molecular weights of the triblock copolymers calculated by the integration ratio of signal *g* and the other signals *h* and *b* in Figure 5 showed good agreement with the value estimated by GPC ($M_{n(NMR)}/M_{n(GPC)}$ = 5700/5900 and 5500/6300, respectively). The GPC curve of the copolymer showed complete participation of homo-poly7CC to the initiation of ϵ-CL (Figure 6).

Summary

In this article, the controlled ring-opening polymerizations of ϵ-CL and δ-VL and block copolymerization of 7CC with these lactones by n-BuOH/$HCl \cdot Et_2O$ and $H_2O/HCl \cdot Et_2O$ initiator systems were investigated to obtain the corresponding homopolymers, and copolymers with narrow polydispersities were obtained quantitatively. As far as we know, these results may be the first example as the most convenient and successful block copolymer synthesis, by common and cheap reagents: *n*-butyl alcohol, H_2O, and $HCl \cdot Et_2O$.

Supporting Information Available: The GPC profiles in the second-feed experiment for the polymerization of ϵ-CL with n-BuOH/$HCl \cdot Et_2O$ (Figure S1) and in the diblock copolymerization of 7CC with ϵ-CL (Figure S2). This material is available free of charge via the Internet at http://pubs.acs.org.

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