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Metal-free Controlled Ring-Opening Polymerization of ε-Caprolactone in Bulk using Tris(pentafluorophenyl)borane as Catalyst

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Abstract

Narrowly distributed poly(ε-caprolactone) (PCL) was synthesized by the ring-opening polymerization (ROP) of ε-caprolactone (CL) using tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) as acidic catalyst and benzyl alcohol (BnOH) as the initiator in bulk at 80 °C. The use of functional initiators such as 2-hydroxyethyl methacrylate (HEMA), propargyl alcohol (PGA), 6-azido-1-hexanol (AHA) and methoxy poly(ethylene glycol) (mPEG) leads to end-functionalized PCLs. ^{1}H NMR, SEC and MALDI-TOF MS measurements clearly indicate the presence of the initiator residue at the chain end of the obtained PCL homopolymers. The study on polymerization kinetics confirm the controlled/living nature of the $B(C_6F_5)_3$-catalyzed ROP of CL. Accordingly, the block copolymerization of CL with δ-valerolactone (VL) and trimethylene carbonate (TMC) successfully proceeded to give PCL-*b*-PVL and PCL-*b*-PTMC copolymers. Macrocyclic PCL was also prepared by the intramolecular click reaction of the heterotelechelic α-azido,ω-enthynyl-PCL.

Keywords: ε-caprolactone; controlled/living ring-opening polymerization; end functionality; block and macrocyclic polymer

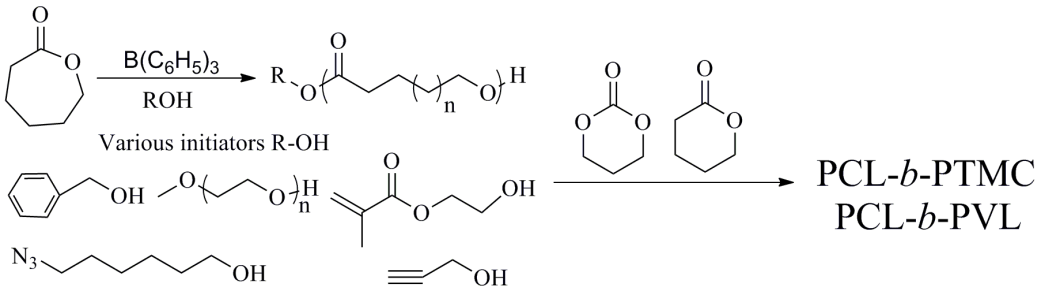
Introduction

Aliphatic polyesters, such as poly(lactide) (PLA), poly(ε-caprolactone) (PCL), poly(trimethylene carbonate) (PTMC) and their copolymers, possessing good biocompatibility and biodegradability are some of the fundamental polymers for utilization in biological and medical fields.[1-6] Over the past decades, great efforts have been made to develop functional materials based on aliphatic polyesters by controlling the composition, molecular weight, molecular weight distribution, chain end functionality and stereoregularity of macromolecules.[7-11] Most polyesters are generally produced by the ring-opening polymerization (ROP) of cyclic esters with metallic catalysts based on Al, Zn, Ti, Sn and Ca.[12,13] However, metal residues are very hard to remove from the synthesized polymers and appear as impurities that hinder application of the materials in biomedical and microelectronics fields. Although metal-free aliphatic polyesters can be prepared using enzymes as polymerization catalysts, the availability of enzymes is still limited and the polymerization is often slow, while the obtained polymer architecture is not well controlled.[14,15] Thus, it is of great interest to develop new alternatives based on metal-free catalysts.

In 2001, Hedrick and Waymouth first reported the organocatalytic living ROP of lactide (LA) using 4-dimethylaminopyridine (DMAP) as the catalyst.[16] Since then, many other organic compounds such as phosphine, carbenes, thioureas, guanidines, amidines, amido-indoles were utilized for the living/controlled ring-opening polymerization of different heterocyclic monomers.[17-25] However, in spite of the

significant advantage of the organocatalyzed ROP of cyclic esters from the viewpoint of material applications, this methodology still has been insufficiently utilized compared to the organometallic-catalyzed one.[12]

Tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) is a strong Lewis acid and is often used as activator or coinitiator in vinyl monomer polymerization.[26-29] To the best of our knowledge, there are only few reports on the use of $B(C_6F_5)_3$ as the catalyst in ROP except for the $B(C_6F_5)_3$ catalyzed vinyl-addition and ring-opening copolymerization.[30] In this work, we describe (a) the characterization of the polymers obtained by $B(C_6F_5)_3$-catalyzed ROP of ε-caprolactone (CL) utilizing various initiators (Scheme 1), (b) the synthesis of diblock copolymers consisting of PCL and PVL or PTMC (Scheme 1), (3) the synthesis of a macrocyclic poly(ε-caprolactone) (*cyclic*-PCL).



Scheme 1. General scheme for the ring-opening polymerization of ε-caprolactone (CL) using different alcohols as initiators and tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) as catalyst, as well as the synthesis of polyester block copolymers.

Experimental Section

Materials

ε-Caprolactone (CL), δ-valerolactone (VL) and propargyl alcohol (PGA) from Aldrich were dried over calcium hydride (CaH_2) and distilled under reduced pressure prior to use. Trimethylene carbonate (TMC) from JiNan GangDai was dissolved in THF at a concentration of 1 mg/mL and stirred over CaH_2 for 1 day before being filtered, recrystallized twice from cold THF and finally dried. Benzyl alcohol (BnOH) from Aladdin was dried over sodium with nitrogen protective atmosphere and distilled under vacuum after refluxing for hours. 2-Hydroxyethyl methacrylate (HEMA) from Aladdin was distilled under reduced pressure. 6-Azido-1-hexanol (AHA) was synthesized according to a previously reported procedure.[31] Methoxy poly(ethylene glycol) (mPEG, M_n = 2.0 × 10^3 g/mol) from Aldrich was purified by azeotropic distillation in toluene. Toluene (TOL) and tetrahydrofuran (THF) from Sinopharm were freshly distilled from sodium/benzophenone and stored under an argon atmosphere. Dichloromethane (DCM) from Sinopharm was freshly distilled from CaH_2 and stored under a nitrogen atmosphere. Tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) and Amberlyst A21 (a weak base anion exchange resin) from Aldrich were used as received. Other reagents from Sinopharm or Aldrich were used as received.

Characterization techniques

NMR Measurements. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker AV400 NMR spectrometer by using deuterated chloroform

(*d*-$CDCl_3$), deuterated toluene (*d*-TOL) or deuterated dimethyl sulfoxide (*d*-DMSO) as the solvent and tetramethylsilane (TMS) as the internal standard.

Size Exclusion Chromatography (SEC). The number average molecular weight (M_n) and polydispersity index (PDI) were measured at 35 °C on a Waters size exclusion chromatography system (SEC) equipped with a model 510 pump, a differential refractive index detector model 410 (RI) and a Waters 2487 UV detector working at a wavelength of 254 nm. A series of monodisperse polystyrenes were used as the standards with THF as the eluent at a flow rate of 1.0 mL/min.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI−TOF MS). MALDI−TOF MS analysis of the obtained polymers was performed using a Bruker-Autoflex III Smartbeam. One hundred shots were accumulated for the spectra at a 25 kV acceleration voltage in the reflector mode and calibrated using polystyrene as the internal standard. Samples for the MALDI-TOF MS were prepared by mixing the polymer (10 mg/mL, 10 μL), the matrix (2,5-dihydroxybenzoic acid, 15 mg/mL, 50 μL) and the cationizing agent (sodium iodide, 4.0 mg/mL, 10 μL) in THF.[32]

Polymerization of ε-Caprolactone (CL)

A typical procedure for the polymerization of CL is as follows: CL (0.57 g, 5.0 mmol, 50 equiv), BnOH (10.40 μL, 0.1 mmol, 1.0 equiv) were placed in a flamed and nitrogen purged round-bottom flask equipped with a magnetic stirrer. The flask was placed in an oil bath at 80 °C and $B(C_6F_5)_3$ (51.2 mg, 0.1 mmol, 1.0 equiv) was added

under argon atmosphere to start the polymerization. The polymerization was quenched by the addition of Amberlyst A21 after 8 h. During polymerizations small portions of the polymerization mixture were withdrawn from the polymerization mixture and quenched with Amberlyst A21 in order to determine the monomer conversion by ^{1}H NMR measurements. The product was dissolved in DCM and precipitated into a large excess of cold methanol to give solid poly(*ε*-caprolactone) (PCL). The polymerizations of CL with other functional initiators and VL and TMC were performed following a similar process. PCL (Yield: 90%, $M_{n,GPC}$ = 5300 g/mol, PDI = 1.18, Table 1, Figure 1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 1.34 (2H, □CO(CH$_2$)$_2$C*H*$_2$(CH$_2$)$_2$O□), 1.64 (4H, □COCH$_2$C*H*$_2$CH$_2$*CH*$_2$CH$_2$O□), 2.29 (2H, □COC*H*$_2$(CH$_2$)$_4$O□), 3.65 (2H, □CO(CH$_2$)$_4$C*H*$_2$OH), 4.07 (2H, □CO(CH$_2$)$_4$C*H*$_2$O□), 5.10 (2H, PhC*H*$_2$O□), 7.32 (5H, aromatic); PVL (Yield: 97%, $M_{n,GPC}$ = 5200 g/mol, PDI = 1.28, Table 1, Figure S1), 1.66 (4H, □COCH$_2$(C*H*$_2$)$_2$CH$_2$O□), 2.32 (□COC*H*$_2$(CH$_2$)$_3$O□), 3.64 (2H, □CO(CH$_2$)$_3$C*H*$_2$OH), 4.05 (2H, □CO(CH$_2$)$_3$C*H*$_2$O□), 5.10 (2H, PhC*H*$_2$O□), 7.32 (5H, aromatic); PTMC (Yield: 90%, $M_{n,GPC}$ = 5700 g/mol, PDI = 1.16, Table 1, Figure S2), 2.04 (2H, □COOCH$_2$C*H*$_2$CH$_2$O□), 3.65 (2H, □COO(CH$_2$)$_2$C*H*$_2$OH), 4.23 (4H, □COOC*H*$_2$CH$_2$C*H*$_2$O□), 5.10 (2H, PhC*H*$_2$O□), 7.32 (5H, aromatic); poly(trimethylene carbonate-*co*-trimethylene oxide) (P(TMC-*co*-TMO)) (Yield 50%, $M_{n,GPC}$ = 5200 g/mol, PDI = 1.55, Table 1, Figure S3), 1.92 (2H, □CH$_2$C*H*$_2$CH$_2$O□), 2.04 (2H, □COOCH$_2$C*H*$_2$CH$_2$O□), 3.48 (4H, □C*H*$_2$CH$_2$C*H*$_2$O□), 3.65 (2H, □(CH$_2$)$_2$C*H*$_2$OH), 4.23 (4H, □COOC*H*$_2$CH$_2$C*H*$_2$O□), 5.10 (2H, PhC*H*$_2$O□), 7.32

(5H, aromatic).

Table 1. Ring-opening polymerization of ε-caprolactone (CL), δ-valerolactone (VL) and trimethylene carbonate (TMC) with tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) as the catalyst and benzyl alcohol (BnOH) as the initiator.[a]

Monomer	$[M]^0/[I]^{0b}$	Time(h)	Conv(%)[c]	$M_{n,NMR}\times10^{-4}$ (g/mol)[c]	$M_{n,theo}\times10^{-4}$ (g/mol)[d]	$M_{n,GPC}\times10^{-4}$ (g/mol)[e]	PDI[e]
CL	10	1	99	0.10	0.11	0.13	1.13
CL	30	4	97	0.30	0.33	0.30	1.16
CL[f]	--	8	80	--	--	2.82	1.23
CL	50	8	95	0.48	0.54	0.53	1.18
CL	100	10	94	1.10	1.04	1.22	1.19
CL	200	17	95	1.90	2.07	2.16	1.26
CL	500	24	85	3.52	4.85	4.32	1.30
VL	30	1	99	0.30	0.30	0.41	1.18
VL	50	2	98	0.42	0.51	0.52	1.20
VL	100	4	98	0.94	1.08	0.98	1.25
TMC	50	4	98	0.45	0.49	0.52	1.55
TMC[g]	50	4	95	0.49	0.49	0.57	1.16
TMC[g]	100	8	99	0.97	1.01	0.98	1.17

[a]Reaction temperature is 80 °C, bulk monomer; [b]Initial molar ratio of monomer to initiator; [c]Determined by ^{1}H NMR; [d]Calculated from $([M]^0/[I]^0) \times conv \times (MW\ of\ CL) + (MW\ of\ initiator)$; [e]Determined by SEC; [f]Initial molar ratio of monomer to catalyst is 50 without initiator; [g]Reaction temperature is 25°C, toluene as solvent.

Block Copolymerization of ε-Caprolactone (CL) and δ-Valerolactone (VL)

A typical procedure for the block copolymerization of CL and VL is as follows: CL (0.34 g, 3.0 mmol, 30 equiv), BnOH (10.40 μL, 0.1 mmol, 1.0 equiv) were placed in a flamed and nitrogen purged round-bottom flask equipped with a magnetic stirrer. The flask was placed in an oil bath at 80 °C and $B(C_6F_5)_3$ (51.20 mg, 0.1 mmol, 1.0 equiv) was added under argon atmosphere to start the polymerization. After CL polymerization was allowed to proceed for 4 h, an aliquot was taken out of the flask

and quenched in order to determine the molecular characteristics of the PCL block. The polymerization of the second block was started with addition of VL (0.50 g, 5.0 mmol, 50 equiv). Polymerization was quenched by the addition of Amberlyst A21 after an additional period of 4 h. During the polymerization small portions of the polymerization mixture were withdrawn and added to an amount of triethylamine in order to determine the monomer conversion by ^{1}H NMR measurements. The copolymer was dissolved in DCM and precipitated into a large excess of cold methanol to give solid poly(*ε*-caprolactone)-*block*-poly(*δ*-valerolactone) (PCL-*b*-PVL). (Yield 80%, $M_{n,GPC}$ = 8500 g/mol, PDI = 1.28). ^{1}H NMR (Table 2, Figure 6 (a), 400 MHz, $CDCl_3$, ppm): 1.35 (2H, □CO$(CH_2)_2$C*H*$_2(CH_2)_2$O□), 1.65 (4H, □COCH$_2$C*H*$_2$CH$_2$*CH*$_2$CH$_2$O□, 4H, □COCH$_2$ C*H*$_2$*CH*$_2$CH$_2$O□), 2.32 (2H, □COC*H*$_2(CH_2)_4$O□, 2H, □COC*H*$_2(CH_2)_3$O□), 3.63 (2H, □CO$(CH_2)_4$C*H*$_2$OH, 2H, □CO$(CH_2)_3$C*H*$_2$OH), 4.07 (2H, □CO$(CH_2)_4$C*H*$_2$O□, 2H, □COC*H*$_2(CH_2)_3$OH), 5.10 (2H, PhC*H*$_2$O□), 7.32 (5H, aromatic). The copolymerization of CL and TMC was performed in a similar process (PCL-*b*-PTMC). (Yield 68%, $M_{n,GPC}$ = 8700 g/mol, PDI = 1.40). ^{1}H NMR (Table2, Figure 6 (b), 400 MHz, $CDCl_3$, ppm): 1.34 (2H, □CO$(CH_2)_2$C*H*$_2(CH_2)_2$O□), 1.63 (4H, □COCH$_2$C*H*$_2$CH$_2$*CH*$_2$CH$_2$O□), 2.04 (2H, □COOCH$_2$C*H*$_2$CH$_2$O□), 2.30 (2H, □COC*H*$_2(CH_2)_4$O□), 3.65 (2H, □CO$(CH_2)_4$C*H*$_2$OH), 4.06 (2H, □CO$(CH_2)_4$C*H*$_2$O□), 4.12 (4H, □COOC*H*$_2$CH$_2$C*H*$_2$O□), 5.10 (2H, PhC*H*$_2$O□), 7.32 (5H, aromatic).

Synthesis of *α*-Azido, *ω*-Ethynyl Poly(*ε*-Caprolactone) (N$_3$□PCL□C≡CH)

N$_3$□PCL□OH ($M_{n,GPC}$ = 5900, PDI = 1.17, Table 2, 590 mg, 0.1 mmol) and

5-hexynoic acid (57.1mg, 0.5 mmol) were dissolved in degassed DCM. Then, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 95.0 mg, 0.5 mmol) and DMAP (64.1 mg, 0.5 mmol) were added to the degassed solution. After the reaction mixture was stirred for 60 h at 25 °C, most of the DCM was evaporated under vacuum and purified by precipitation in cold methanol to give N_3□PCL□C≡CH. The obtained polymer was dried in a vacuum oven overnight at room temperature. (Yield 72 %, $M_{n,GPC}$ = 6000, PDI = 1.17). ^{1}H NMR (400 MHz, DMSO, ppm): 1.30 (2H, □CO$(CH_2)_2$C$H_2$$(CH_2)_2$O□, 4H, $N_3(CH_2)_2CH_2CH_2(CH_2)_2$□), 1.55 (4H, $N_3CH_2CH_2(CH_2)_2CH_2CH_2$□, 4H, □COCH$_2CH_2CH_2CH_2CH_2$O□), 1.83 (2H, □CH$_2CH_2$ CH$_2$C≡CH), 1.95 (1H, □C≡CH), 2.25 (2H, □CH$_2$CH$_2$CH_2C≡CH, 2H, □COC$H_2$$(CH_2)_4$O□), 2.42 (2H, □C$H_2CH_2CH_2$C≡CH), 3.20 (2H, $N_3CH_2(CH_2)_5$□), 4.01 (2H, $N_3(CH_2)_5CH_2$□, 2H, □CO$(CH_2)_4CH_2$O□).

Synthesis of Macrocyclic Poly(ε-Caprolactone) (*cyclic*-PCL)

DMF (1 L) was placed in a three-neck flask and degassed by bubbling argon for 5 h. Copper (I) bromide (CuBr, 1.0 g, 6.9 mmol) and pentamethyldiethylenetriamine (PMDETA, 1.73 g, 10.0 mmol) were added to the degassed DMF. A solution of N_3□PCL□C≡CH (300 mg, 0.05 mmol) in degassed DMF (30 ml) was added to the solution via a syringe pump at a rate of 0.5 mL/h. The reaction was carried out at 60 °C for 70 h under an argon atmosphere. DMF was removed under reduced pressure after the mixture was cooled to room temperature. The residue was diluted with THF and passed through a short column of neutral alumina to remove the metal salt. After removing all the solvents by a rotary evaporator, the residue was dissolved in THF

and precipitated into a large excess of cold methanol. The obtained polymer was dried in a vacuum oven overnight at room temperature. (Yield 54 %, $M_{n,GPC}$ = 5900, PDI = 1.16). ^{1}H NMR (400 MHz, DMSO, ppm): 1.30 (2H, □CO(CH$_2$)$_2$C*H*$_2$(CH$_2$)$_2$O□, 4H, >N(CH$_2$)$_2$C*H*$_2$C*H*$_2$(CH$_2$)$_2$□), 1.55 (4H, >NCH$_2$C*H*$_2$(CH$_2$)$_2$C*H*$_2$CH$_2$□, 4H, □COCH$_2$C*H*$_2$CH$_2$*CH*$_2$CH$_2$O□), 1.88 (2H, □C*H*$_2$CH$_2$C=CH□), 2.26 (2H, □COC*H*$_2$(CH$_2$)$_4$O□, 2H, □C*H*$_2$CH$_2$CH$_2$C=CH□), 2.70 (2H, □CH$_2$CH$_2$C*H*$_2$C=CH□), 4.01 (2H, >N$_3$(CH$_2$)$_5$C*H*$_2$□, 2H, □CO(CH$_2$)$_4$C*H*$_2$O□), 4.25 (2H, >NC*H*$_2$(CH$_2$)$_5$□), 7.25 (1H, □CH$_2$CH$_2$CH$_2$C=C*H*□).

Results and Discussion

Ring-opening polymerization of CL using B(C$_6$F$_5$)$_3$ as the catalyst and BnOH as the initiator was first investigated in bulk at 80 °C (Scheme 1). Figure 1 shows the ^{1}H NMR spectrum of the prepared PCL. The peaks at 4.07, 2.29, 1.64 and 1.34 ppm are due to PCL and the peak due to the methylene protons adjacent to the *ω*-chain end of the hydroxyl group is clearly observed at 3.65 ppm. The peaks at 7.32, 5.10 ppm are due to the aromatic protons of BnO- moiety and the methylene protons adjacent to the ester linkage for BnOH, respectively. In addition, the number-average molecular weight ($M_{n,NMR}$) of the polymer estimated from ^{1}H NMR is in good agreement with that ($M_{n,theo}$) calculated from the initial monomer/initiator ratio and monomer conversions (Table 1). These results indicate that the obtained polymer should possess a BnOH residue at the initiating end. PVL was also prepared (Figure S1) with B(C$_6$F$_5$)$_3$ as the catalyst and BnOH as the initiator. The consumption rate of VL is

faster than that of CL (Table 1), which agrees with other catalytic systems utilized so far for the polymerization of VL and CL.[19,33] In order to demonstrate that $B(C_6F_5)_3$ is an efficient catalyst for ROP, the polymerization of another interesting monomer, TMC, was attempted. However, poly(trimethylene carbonate-*co*-trimethylene oxide) (P(TMC-*co*-TMO), Figure S3) copolymer with a relatively wide PDI (1.55, Table1) at 80°C was obtained, presumably due to the decarboxylation of the carbonate group. After polymerization of TMC at room temperature with toluene as the solvent, narrowly distributed PTMC (Figure S2) homopolymer was obtained. The results indicate that $B(C_6F_5)_3$ is an effective catalyst for the ROP of cyclic esters or carbonate.

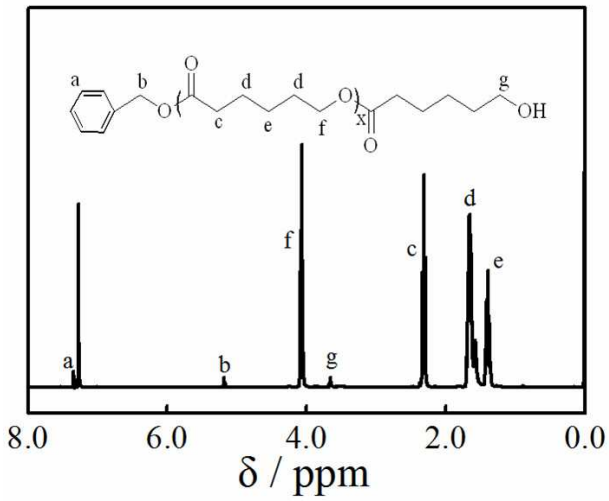


Figure 1. ^{1}H NMR spectrum of the obtained poly(ε-caprolactone) (PCL) initiated by benzyl alcohol (BnOH) in $CDCl_3$.

In order to provide direct evidence that the $B(C_6F_5)_3$-catalyzed ROP of CL was initiated by BnOH, a MALDI-TOF MS analysis was carried out, as shown in Figure 2. Only one series of peaks was observed from the MALDI-TOF MS analysis, which perfectly agrees with the molecular weight of PCL with the BnO-residue and the hydroxyl chain end. This result also confirms that the $B(C_6F_5)_3$-catalyzed ROP of CL

with BnOH as initiator proceeded in a controlled/living manner without any side reactions (e.g., backbiting, transesterification). To further confirm the polymerization proceeded in a controlled/living manner, we carried out the ROP of CL by varying initial monomer/initiator ratios from 10 to 100, as shown in Figure 3. The $M_{n,GPC}$ of the obtained PCL increases with increasing monomer/initiator ratio and fairly agrees with that of the calculated $M_{n,theo}$. These results clearly indicate the controlled/living nature of $B(C_6F_5)_3$-catalyzed ROP of CL with BnOH as the initiator.

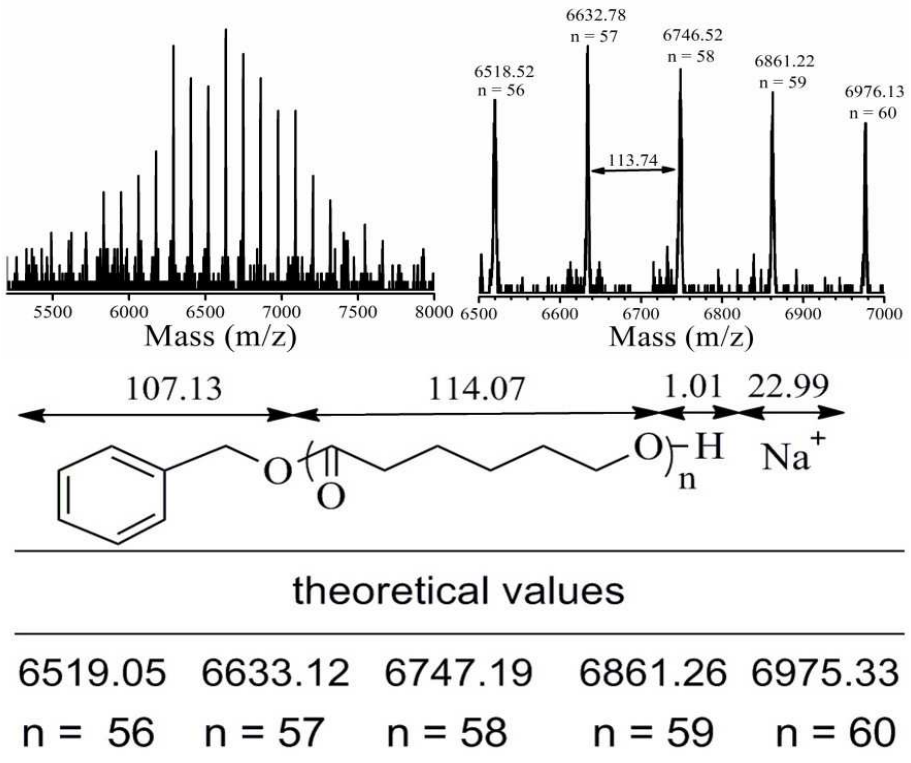


Figure 2. MALDI-TOF MS spectrum of the obtained poly(ε-caprolactone) (PCL). Theoretical values were calculated by the following equation: n × 114.07 + 107.13 + 1.01 + 22.99, where n is the degree of polymerization and the mass values correspond to the segments/end groups comprising the PCL chain as shown in the scheme.

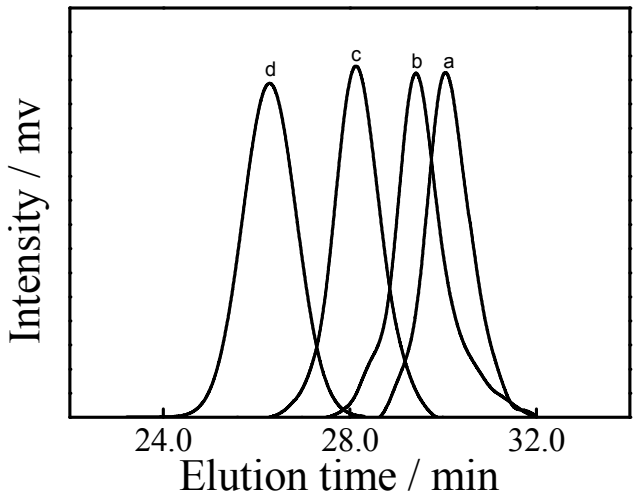


Figure 3. SEC curves of poly(ε-caprolactone) (PCL) obtained at various initial monomer/initiator ratios; a 10, b 30, c 50, d 100.

Kinetic and chain extension experiments were carried out to gather further evidence of the living nature of $B(C_6F_5)_3$-catalyzed ROP of CL. A distinct first-order kinetic relationship between the reaction time and the monomer conversion was observed in Figure 4 (b), indicating that the monomer consumption was constant during the polymerization, which further confirms the living character of the polymerization. Furthermore, the molecular weight $M_{n,GPC}$ of the obtained PCL increases linearly with monomer conversion, as shown in Figure 4 (a). In addition, the molecular weight $M_{n,GPC}$ closely agrees with the calculated values of $M_{n,theo}$. The PDI of the obtained PCL has low values ranging from 1.10 to 1.21.

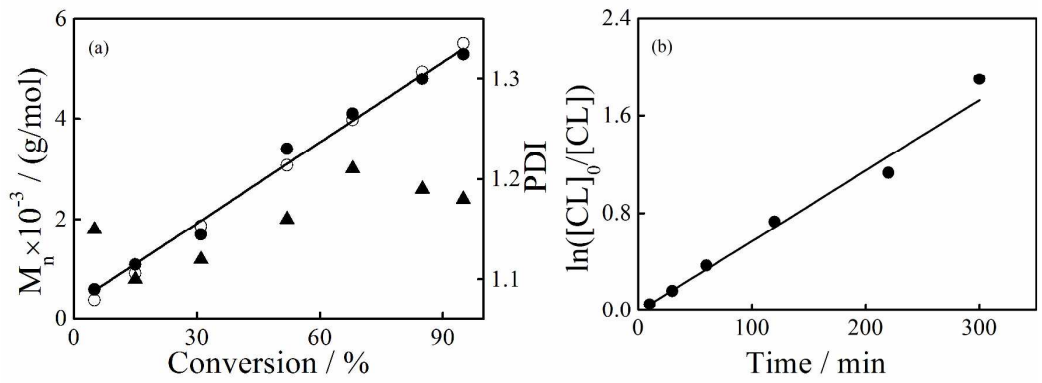


Figure 4. (a) Dependence of $M_{n,GPC}$ (○), $M_{n,theo}$ (●) and PDI (▲) of the obtained poly(ε-caprolactone) (PCL) on ε-caprolactone (CL) conversion, (b) Kinetic plot for the tris(pentafluorophenyl)borane ($B(C_6H_5)_3$) catalyzed ring-opening polymerization of ε-caprolactone (CL) initiated by benzyl alcohol (BnOH) ($[CL]_0$ = 50 mM, $[CL]_0/[BnOH]_0/[B(C_6H_5)_3]$ = 50/1/1).

The chain extension experiments also supported the living nature of the $B(C_6F_5)_3$-catalyzed ROP of CL (Table 2). Figure 5 shows the SEC curves for chain extension experiments. A PCL with $M_{n,GPC}$ = 3400, PDI = 1.16 was first prepared. Then the chain extension was carried out by subsequent addition of 50 equiv VL to afford a PCL-*b*-PVL copolymer with $M_{n,GPC}$ = 8500 g/mol, PDI = 1.28 (Figure 5 (a)). The SEC curve of block copolymer shifts to a higher molecular weight region while keeping low PDI after the addition and polymerization of VL. PCL-*b*-PTMC was also prepared with a similar process by the chain extension experiment (Figure 5 (b)). The molecular weight increases from 3100 to 8700 g/mol and the PDI slightly increases from 1.18 to 1.40. The block copolymer nature of PCL-*b*-PVL and PCL-*b*-TMC was confirmed by ^{1}H NMR measurements (Figure S4). More importantly, these results indicate that PCL chain ends maintain their active/living character for further

polymerization. Thus, $B(C_6F_5)_3$-catalyzed ROP of CL was shown to proceed via a controlled/living mechanism and produced a molecularly controllable biodegradable PCL homopolymer or block copolymers.

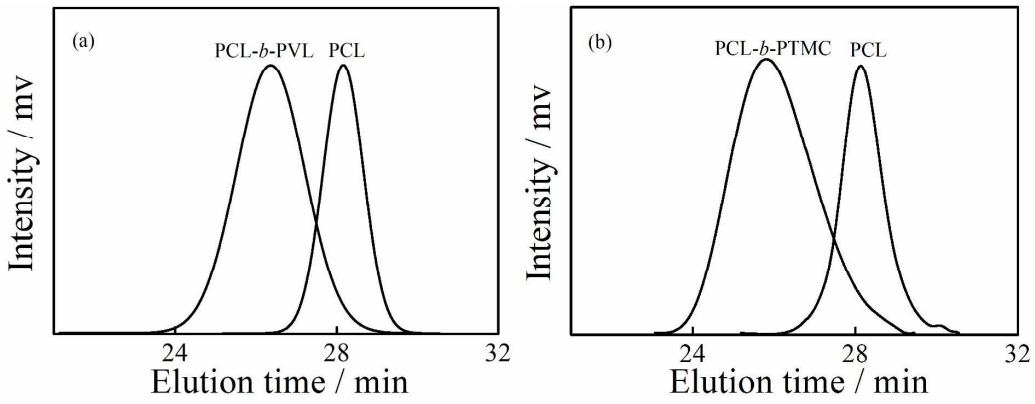
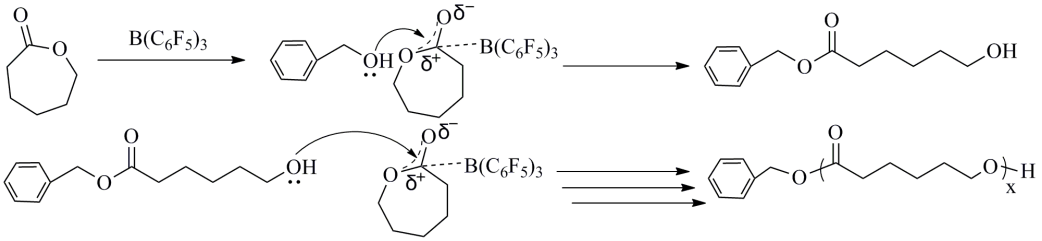


Figure 5. (a) SEC curve of poly(ε-caprolactone)-*b*-poly(δ-valerolactone) (PCL-*b*-PVL); (b) SEC curve of poly(ε-caprolactone)-*b*-poly(trimethylene carbonate) (PCL-*b*-PTMC) copolymer.



Scheme 2. A possible activated monomer mechanism for tris(pentafluorophenyl)borane ($B(C_6H_5)_3$) catalyzed ring-opening polymerization (ROP) of ε-caprolactone (CL).

We finally focus on the possible mechanism leading to the controlled/living nature of the $B(C_6F_5)_3$-catalyzed ROP of CL. A possible activated monomer mechanism is proposed based on the analogy of the principle for acid-catalyzed ROP of cyclic esters,

as shown in Scheme 2 (see also related works on the cationic polymerization of CL via the activated monomer mechanism[34,35]). The presence of initiator (alcohol) has a tremendous difference in the initiating step leading to an activated monomer polymerization path way, whereas in the absence of alcohol a conventional active chain end mechanism most probably is followed. The concentration of impurities is must lower than that of the initiator (alcohol) so any potential effects are screened leading to the formation of well defined macromolecular chains (essentially all chains are growing from initiator molecules). In order to elucidate the proposed mechanism, ^{13}C NMR spectrum analysis was performed. As shown in Figure 6, the peak of carbon adjacent to the oxygen and the peak of carbonyl carbon have a upfield shift for the 1:1 mixture of $B(C_6H_5)_3$ and CL when compared to the CL monomer in toluene-d_8. In addition, a downfield shift for other carbon peaks of CL is also observed in the 1:1 mixture of $B(C_6H_5)_3$ and CL. These results may demonstrate the interactions between the CL monomer and the catalyst in the proposed activated monomer mechanism of Scheme 2.

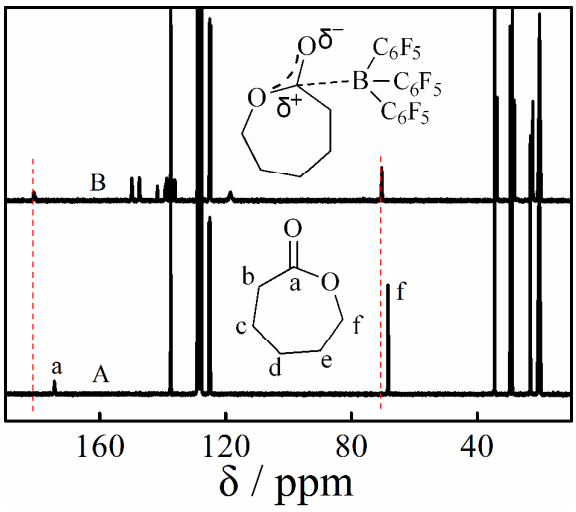


Figure 6. ^{13}C NMR spectra of (A) ε-caprolactone (CL) and (B) the 1:1 mixture of

tris(pentafluorophenyl)borane ($B(C_6H_5)_3$) and CL in toluene-d_8.

Table 2. Synthesis of end-functionalized poly(ε-caprolactone) (PCL) by the tris(pentafluorophenyl)borane ($B(C_6H_5)_3$) catalyzed ring-opening polymerization (ROP) with different functional initiators.[a]

Monomer	Initiator	Conv(%)[b]	$M_{n,NMR}$ (g/mol)[b]	$M_{n,theo}$ (g/mol)[c]	$M_{n,GPC}$ (g/mol)[d]	PDI[d]
CL	HEMA	96	5800	5602	5400	1.17
CL	AHA	97	5420	5654	5900	1.17
CL	PGA	94	5020	5414	4600	1.15
CL	PEG	98	6900	7586	6900	1.20
VL	PCL[e]	99	--	--	8500	1.28
TMC	PCL[f]	90	--	--	8700	1.40

[a]Reaction temperature is 80 °C, bulk CL monomer and reaction time is 8 h, initial $[M]^0/[I]^0$ = 50/1; [b]Determined by ^{1}H NMR; [c]Calculated from ($[M]^0/[I]^0$) × conv × (MW of CL) + (MW of initiator); [d]Determined by SEC; [e]For the PCL block, $M_{n,GPC}$=3400 g/mol, PDI= 1.16; [f]For the PCL block, $M_{n,GPC}$=3100 g/mol, PDI= 1.18 (reaction temperature is 25 °C, toluene as solvent).

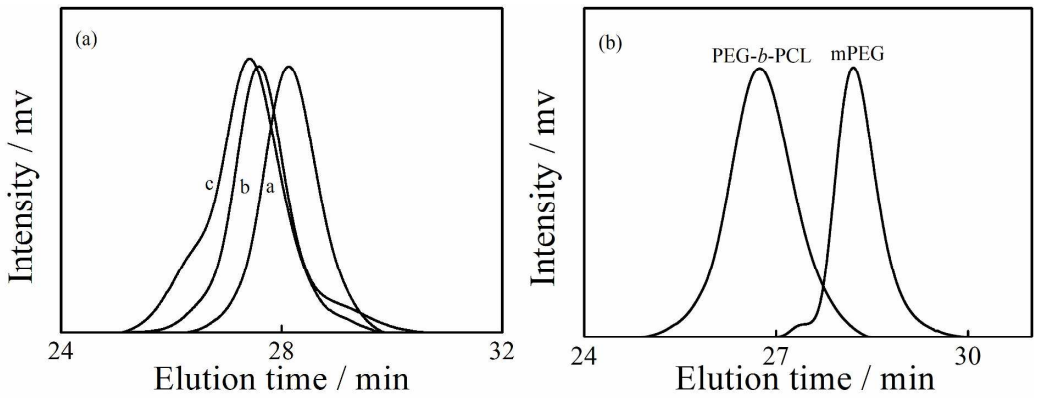
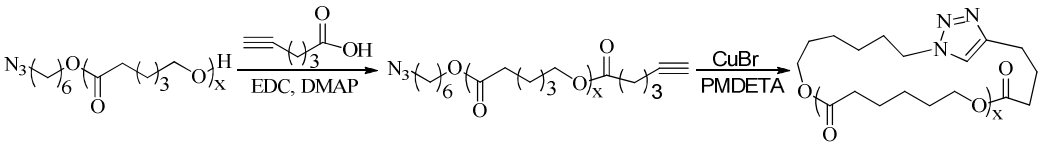


Figure 7. (a) SEC curves of poly(ε-caprolactone) (PCL) with different end functionality; a propargyl alcohol (PGA), b 2-hydroxyethyl methacrylate (HEMA), c 6-azido-1-hexanol (AHA); (b) SEC curve of poly(ethylene glycol)-*b*-poly(ε-caprolactone) (PEG-*b*-PCL) copolymer.

To further demonstrate the distinct advantages of the $B(C_6F_5)_3$-catalyzed ROP of CL, we selected 2-hydroxyethyl methacrylate (HEMA), propargyl alcohol (PGA),

6-azido-1-hexanol (AHA) and methoxy poly(ethylene glycol) (mPEG) in order to synthesize end-functional PCLs and an amphiphilic block copolymer (Table 2). The use of such functional initiators allows the preparation of end-functionalized polymers that can be further utilized in polymer and materials synthesis. Also the use of the PEG macroinitiator allows for the synthesis of amphiphilic biocompatible block copolymers. A controlled molecular weight and narrow polydispersity was achieved with HEMA, PGA, AHA or mPEG as initiators by the $B(C_6F_5)_3$-catalyzed ROP of CL, as shown in Figure 7. A shoulder in the SEC trace of azido-PCL is observed, presumably from intermolecular coupling of some azido groups at 80 °C in bulk. In addition, the polymer structures were confirmed as ^{1}H NMR measurements proved the end-functionalization of PCL with vinyl, ethynyl, azido and ethylene oxide groups (Figure S5). The peaks due to initiator residue appear at 6.12, 5.59, 1.97 ppm (HEMA), 4.70, 2.47 ppm (PGA), 3.28 ppm for the methylene adjacent to azido group and the peak at 3.60 ppm is typical for PEG.



Scheme 3. Synthesis of macrocyclic poly(ε-caprolactone) (*cyclic*-PCL) by intramolecular click reaction of α, ω-end-functionalized PCL.

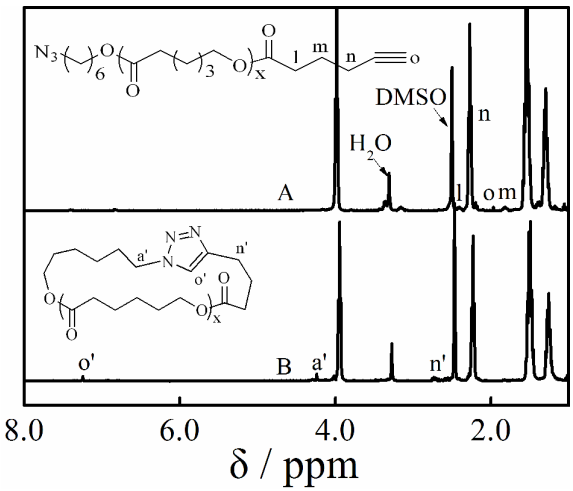


Figure 8. ^{1}H NMR spectra of (A) N_3−PCL−C≡CH and (B) *cyclic*-PCL in *d*-DMSO.

The hetero end-functionalized N_3−PCL−C≡CH prepared by the $B(C_6F_5)_3$-catalyzed ROP of CL, was utilized in the synthesis of macrocyclic PCL (*cyclic*-PCL) by the intramolecular click reaction of the *α*-*ω*-end-groups (Scheme 3). First, CL polymerization was initiated with AHA and then the esterification of N_3-PCL-OH by 5-hexynoic acid was carried out using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and DMAP to produce the hetero *α*-*ω*-end-functionalized N_3-PCL-C≡CH. In addition, the intramolecular click reaction of N_3-PCL-C≡CH was carried out in the presence of copper (I) bromide (CuBr) and pentamethyldiethylenetriamine (PMDETA) in DMF at 60 °C for 70 h. We confirmed these structures by ^{1}H NMR. The signal for ethynyl proton in Figure 8 (A) confirmed the synthesized N_3-PCL-C≡CH. The signal due to ethynyl at 1.95 ppm disappeared and a new signal due to triazole proton appeared at 7.25 ppm, confirming the successful click reaction, as shown in Figure 8 (B).

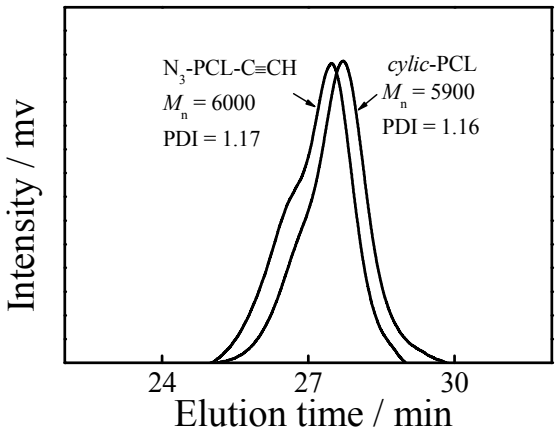


Figure 9. SEC curves of N_3−PCL−C≡CH and *cyclic*-PCL.

Although the data from ^{1}H NMR analyses confirmed that the click reaction proceeded smoothly, these results are not sufficient to demonstrate that click reaction was intramolecular. In other words, the click reaction between the azido α-chain-end and the ethynyl ω-chain-end might take place in an intermolecular pathway and might cause dissociation. To exclude the possibility for intermolecular reaction and dissociation, SEC measurements were performed. Figure 9 shows the SEC traces of N_3−PCL−C≡CH and *cyclic*-PCL. The SEC trace for *cyclic*-PCL displays a sharp and monodisperse peak in the lower molecular weight region of the chromatograms when compared to the linear N_3−PCL−C≡CH. Furthermore, there is no peak in the higher molecular weight region compared to that of N_3−PCL−C≡CH, strongly supporting the fact that the intermolecular click reaction did not occur and the intramolecular cyclic reaction proceeded selectively to form *cyclic*-PCL. Thus, we successfully synthesized the *cyclic*-PCL by esterification of the hetero azido, ethynyl-functionalized PCL and subsequent intramolecular click reaction.

Conclusions

In this study, we successfully synthesized well-defined poly(ε-caprolactone) (PCL) by ring-opening (ROP) polymerization of ε-caprolactone (CL) using $B(C_6F_5)_3$ as the metal-free catalyst and benzyl alcohol (BnOH) as the initiator. The molecular weights of the polymers were well controlled with narrow PDIs. Well-defined poly(ε-caprolactone)-*b*-poly(δ-valerolactone) (PCL-*b*-PVL), poly(ε-caprolactone)-*b*-poly(trimethylene carbonate) (PCL-*b*-TMC), were also synthesized by chain extension polymerization of CL with VL and TMC monomers. The activated monomer mechanism was supported by NMR experiments. In addition, end-functionalized PCLs with vinyl, propargyl and azido groups, as well as a PEG-*b*-PCL copolymer were synthesized by using functional initiators, such as 2-hydroxyethyl methacrylate (HEMA), propargyl alcohol (PGA), 6-azido-1-hexanol (AHA), and methoxy poly(ethylene glycol) (mPEG) macroinitiator. We also synthesized a macrocyclic poly(ε-caprolactone) (*cyclic*-PCL) by intramolecular click reaction of hetero α, ω-end-functionalized PCL. In conclusion, we have demonstrated that $B(C_6F_5)_3$ is a novel acidic catalyst which can be used to catalyze ROP of CL in a controlled/living manner.

Acknowledgments

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TOC graphic

Metal-free Controlled Ring-Opening Polymerization of ε-Caprolactone in Bulk using Tris(pentafluorophenyl)borane as Catalyst

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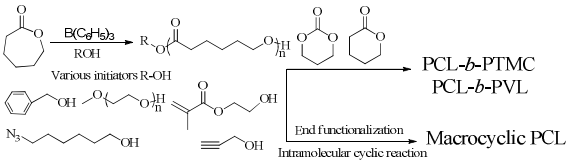

Controlled/living ring-opening polymerization of ε-caprolactone utilizing tris(pentafluorophenyl)borane as the metal-free catalyst was demonstrated, leading to block, end-functionalized and macrocyclic poly(ε-caprolactone) containing macromolecules.