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Efficient “Living” and “Immortal” Polymerization of Lactones and Diblock Copolymer of ϵ-CL and δ-VL Catalyzed by Aluminum Alkoxides

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ABSTRACT: A novel aluminum alkoxide, which has demonstrated efficient catalytic activities in both “living” and “immortal” ROP of lactones, is prepared and characterized. The “living” character of the aluminum complex shown in the polymerization process enabled us to synthesize the P-ϵ-CL-b-P-δ-VL block polymer in a controlled manner. The structural determination and catalytic studies suggest that during the ROP of lactones, a lactone molecule coordinates to an aluminum center forming a pentacoordinated intermediate, followed by the attack of a benzylalkoxy group on lactone initiating the polymerization.

Introduction

The aliphatic polyesters, such as poly(ϵ-caprolactone) (PCL),[1] polylactide (PLA),[2] polycarbonate,[3] and their copolymers, are of great interest for their applications in the medical field as biodegradable surgical sutures or as a delivery medium for controlled release of drugs[4] due to their biodegradable, biocompatible, and permeable properties.[5] The major polymerization method used to synthesize these polymers has been the ring-opening polymerization (ROP) of lactones and functionally related compounds. In addition, “living” or “immortal” polymerization provides a particular powerful tool,[6] either through functionalized initiators or by the selective transformation of living polymer chain ends. For example, dialkylaluminum thiolates (R_2AlSR') initiate polymerization of lactones in a living fashion, leading to the formation of polyesters with a hydroxy functional end and an alkanethiolate ($-COSR'$) end group.

Though several aluminum derivatives of monodentate bulky phenol have demonstrate efficient catalytic activities toward the ROP of lactones,[7] these catalysts decrease activities in the presence of excess 2-propanol because metathesis occurs between aluminum phenolate and 2-propanol. We report herein the synthesis, characterization, and catalytic studies of a novel aluminum alkoxide. Preliminary results show that this aluminum alkoxide catalyzes the polymerization of lactons both in “living” and “immortal” fashions yielding polymers with very narrow polydispersity index (PDI $= M_w/M_n$) in a wide range of monomer-to-initiator ratios.

Results and Discussion

The initiator, $[(EDBP)Al(\mu\text{-}OBz)]_2$ (**1**),[8] was obtained from the reaction of $[(\mu\text{-}EDBP)AlMe]_2$[9] with benzyl alcohol at ambient temperature in high yield, followed by crystallization from toluene as white crystalline solids. Treatment of **1** with 2 molar equiv of PhCHO, yielded a neutral complex $[(PhCHO)Al(EDBP)(\mu\text{-}OBz)]_2$ (**2**). The ^{1}H NMR data of **1** and **2** reveal only one set of resonances for *tert*-butyl groups of phenyl ring in the EDBP^{2-} ligand. Similarly, one set of two resonances for the two hydrogens on both aryl moieties was observed. These observations suggest that these two aryl moieties are chemically equivalent and that requires that a σ plane of symmetry pass through the C-7 methine carbon and the aluminum atom. This is further verified by the crystal structure studies of **1** and **2**.

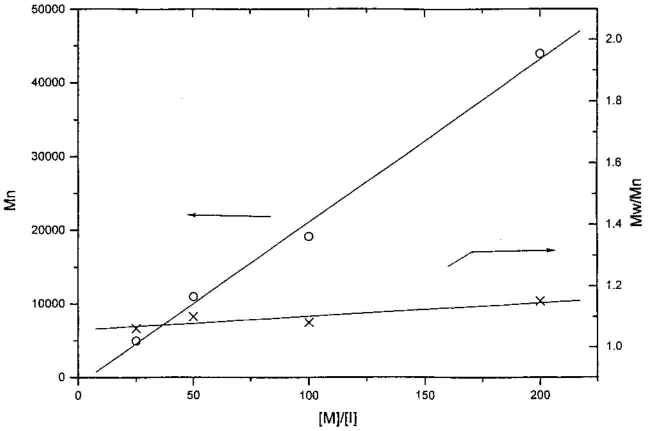

Figure 1. Polymerization of ϵ-CL catalyzed by 1 in toluene at 25 °C. The relationship between M_n (○) (M_w/M_n (×)) of the polymer and the initial mole ratio $[M]_0/[I]_0$ is shown.

The catalytic activities of **1** toward ϵ-caprolactone (ϵ-CL), δ-valerolactone (δ-VL), and their copolymers have been studied. In general, polymerization of lactones was carried out at 25 °C in toluene (30 mL) using **1** (0.25 mmol) as the initiator. Polymerizations of ϵ-CL and δ-VL under different reaction conditions have been systematically conducted as shown in Table 1. It was found that the PDI of polyesters are quite narrow, ranging from 1.06 to 1.15, and that a linear relationship between the number-average molecular weight (M_n) and the initial monomer-to-initiator ratio ($[M]_0/[I]_0$) existed (shown in Figure 1), implying the living character of the polymerization process (entry 1−4). This was further confirmed by the polymerization resumption experiment and by the sequential ROP of ϵ-CL and δ-VL. In the resumption experiment, excess ϵ-CL monomer was added after the polymerization effected by the first addition had gone to completion. Figure 2a shows that the molecular weight increased for the final polymer (peak B, $M_n = 20\,300$, PDI = 1.07), relative to the first (peak A, $M_n = 11\,000$, PDI = 1.10). In addition, the poly(ϵ-CL-*b*-δ-VL)(PCL-*b*-PVL) block polymer ($M_n = 25\,000$, $M_w/M_n = 1.11$, and WPCL = 53%, entry 7) was synthesized by the sequential ROP of ϵ-CL ($[M]_0/[I]_0 = 50$) and

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Table 1. Ring-Opening Polymerization of Lactones Catalyzed by Complexes 1 and 2 at 25 °C[a]

entry	monomer	catalyst	[M]/[Al]/[ROH]	time (h)	M_w/M_n	M_n(obsd)[d]	M_n(calcd)[e]	yield (%)
1	ε-CL	**1**	25:1:0	16	1.06	4900	2850	83
2	ε-CL	**1**	50:1:0	16	1.10	11000	5700	97
3	ε-CL	**1**	100:1:0	32	1.08	19100	11400	94
4	ε-CL	**1**	200:1:0	48	1.15	43900	22800	95
5	δ-VL	**1**	100:1:0	16	1.12	14200	10000	100
6[b]	CL(VL)	**1**	50(50):1:0	16(16)	1.10	16500	10700	95
7[b]	CL(VL)	**1**	50(100):1:0	16(16)	1.11	25000	15700	94
8	ε-CL	**1**	100:1:2	24	1.07	7100	5700	95
9	ε-CL	**1**	100:1:4	24	1.06	4500	2850	94
10	ε-CL	**1**	100:1:8	24	1.12	2800	1425	77
11	ε-CL	**1**	200:1:16	24	1.09	2800	1425	79
12	ε-CL	**2**	50:1:0	16	1.04	7900	5700	69
13[c]	CL(CL)	**1**	50(50):1	32	1.07	20300	11400	92

[a] For details of the polymerization procedure, see the Experimental Section. [b] Prepolymerization of CL with **1** for 16 h followed by the addition of VL. [c] Prepolymerization of CL with **1** for 16 h followed by the addition of another portion of CL. [d] Obtained from GPC analysis. [e] Calculated from the molecular weight of lactone times moles.

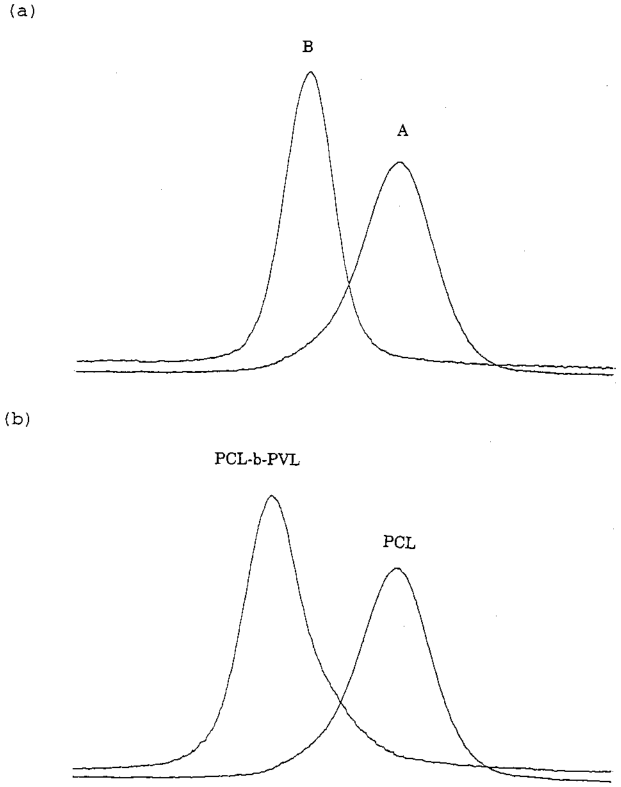
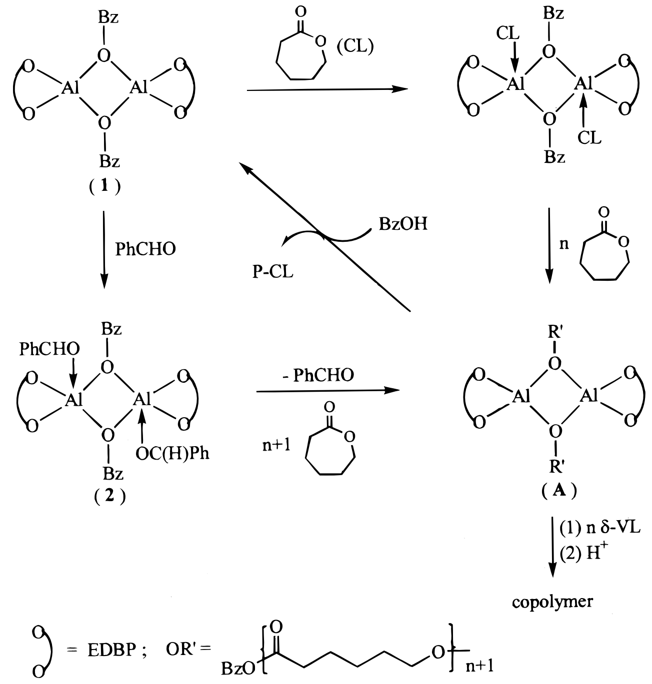


Figure 2. (a) GPC profiles of polymerization resumption experiment: (peak A) after prepolymerization of ε-CL (50 equiv to **1**, 16 h), M_n = 11 000 (PDI = 1.10); (peak B) after polymerization of 50 equiv more ε-CL (16 h), M_n = 20 300 (PDI = 1.07). (b) GPC profiles of copolymerization of ε-CL-*b*-δ-VL: (peak A) after prepolymerization of ε-CL (50 equiv to **1**, M_n = 11 000); (peak B) after block copolymerization of ε-CL-*b*-δ-VL ($[CL]_0/[I]_0/[VL]_0$ = 50/1/100, M_n = 25 000, entry 7).

δ-VL ($[M]_0/[I]_0$ = 100) monomer in the presence of $[(EDBP)Al(\mu\text{-}OBz)]_2$ as shown in Figure 2b.

To establish the chemical nature of the structure chain ends, ^1H NMR studies were carried out as shown in Figure 3. The ^1H NMR spectrum of PCL-100 (the number 100 indicates the designed $[M]_0/[I]_0$) gave an integral ratio close to 1 between H_b ($-CH_2$ from ε-CL at the benzylester chain end) and H_g ($-CH_2$ from ε-CL at the hydroxy end) which is in agreement, as expected, with the theory that the polymer chain should be capped with one benzyl ester and one hydroxy end. This result indicates that the initiation occurs through the insertion of the benzylalkoxy group from compound **1** to lactone. More importantly, compound **1** catalyzes the ROP of lactones not only in a living manner but also in an immortal manner in which a narrow PDI polymer is obtained with a number of polymer molecules exceeding the number of initiator molecules (entries 8–11). The polymerization of ε-CL was initiated with **1** in the presence of benzyl alcohol as the chain transfer agent. The exchange between the growing alkoxide species and alcohol leads to a chain transfer reaction, since the resulting aluminum alkoxide is able to reinitiate the polymerization. Preliminary results show that as much as 16 folds of BzOH can be added resulting in a narrow PDI polymer with a M_n of only $^1/_{16}$th of that without the addition of BzOH. In these experiments, the experimental value of M_n (M_n(obsd)) obtained from the GPC analysis is always higher than the theoretical M_n value (M_n(calcd)). There are two possible reasons for the unexpected high value of M_n(obsd). First, the activity of intermediate **A** (as shown in Scheme 1) is higher than catalyst **1**; therefore only part of compound **1** participates in the catalytic cycle. Second, the inter- or intratransesterification reaction occurs during the polymerization process.

Scheme 1



Encouraged by the excellent catalytic activities of **1**, we were prompted to figure out the crystal structure of

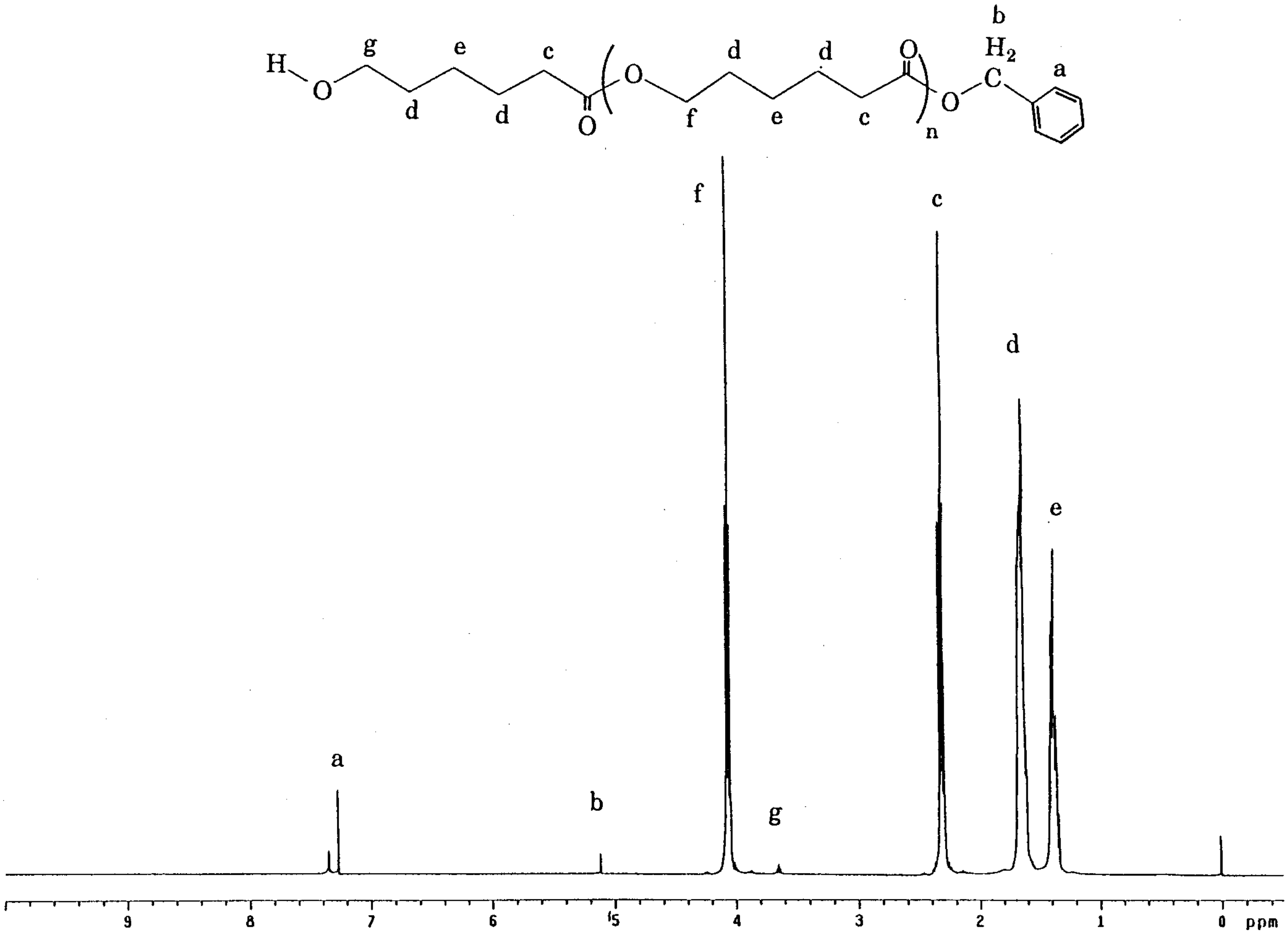


Figure 3. ^{1}H NMR spectrum of PCL-100 in $CDCl_3$.

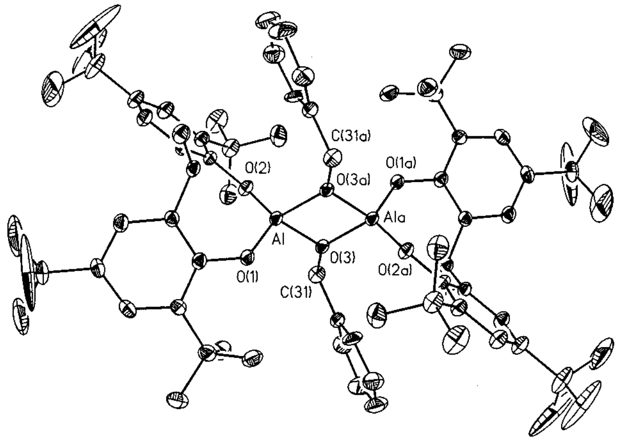


Figure 4. Molecular structure of 1 as 20% ellipsoids. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Al−O(1) = 1.689(2), Al−O(2) = 1.683(2), Al−O(3) = 1.812(2), Al−O(3a) = 1.816(2), and O(3)−C(31) = 1.452(4).

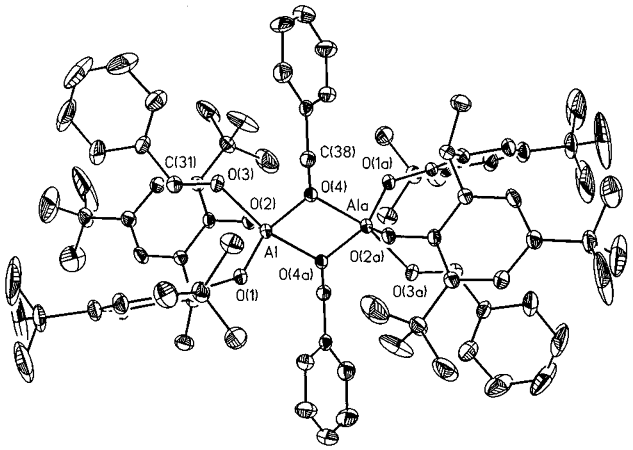


Figure 5. Molecular structure of **2** as 20% ellipsoids. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Al−O(1) = 1.753(4), Al−O(2) = 1.745(6), Al−O(3) = 2.030(3), Al−O(4) = 1.809(3), Al−O(4A) = 1.900(3), O(3)−C(31) = 1.241(8), O(4)−C(38) = 1.442(5).

catalyst **1** and the intermediate of the ROP process. Suitable crystals for structure determination of **1** are obtained from slowly cooling a hot toluene solution, and its ORTEP is shown in Figure 4. The structure of **1** shows a dimeric structure that contains a four coordinated aluminum bridging through the oxygen atom from the benzylalkoxy group. Attempts to obtain a single crystal of the intermediate **A** for structure determination were in vain. However, the reaction of **1** with PhCHO gives a five-coordinate compound, [(PhCHO)-Al(EDBP)(μ-OBz)]$_2$ (**2**). The X-ray diffraction analyses of compound **2** revealed the dimeric feature in which each aluminum is coordinated by two terminal phenoxides, two bridging η^2-alkoxides, and one benzaldehyde as shown in Figure 5. Though **2** also shows great catalytic activity toward the ROP of ϵ-CL, the reaction rate is, however, much slower compared to that of compound **1**, probably due to the existence of PhCHO inhibiting the coordination of lactone to the Al atom, thereby retarding the polymerization. The structural determination and catalytic studies of pentacoordinated compound **2** suggest that during the ROP of lactones, a lactone molecule coordinates to an aluminum center, forming a pentacoordinated intermediate, followed by the attack of a benzylalkoxy group on lactone, initiating the polymerization as depicted in Scheme 1. It is further verified by the experiment in which the ROP of ϵ-CL in the presence of PhCHO with **1** ($[\mathrm{PhCHO}]_0/[\mathrm{CL}]_0/[\mathrm{I}]_0 = 50/50/1$) gives only a low molecular weight polyester ($M_n = 4400$, PDI = 1.34) in low yield.

Conclusion

In conclusion, we have discovered a novel aluminum alkoxide that has demonstrated efficient catalytic activities in both "living" and "immortal" ROP of lactones. The "living" character of the aluminum complex shown in the polymerization process enabled us to synthesize P-ϵ-CL-*b*-P-δ-VL block polymer in a controlled manner. More importantly, the combined "living" and "immortal" character of this complex paved the way to synthesize as much as 16-fold polymer chains of polymer with narrow PDI in the presence of a small amount of catalyst. Further studies of this catalyst in a higher $[\mathrm{M}]_0/[\mathrm{I}]_0$ ratio and in other oxiranes are being currently undertaken.

Experimental Section

General Data. All manipulations were carried out under a dry nitrogen atmosphere. Solvents were dried by refluxing them for at least 24 h over sodium/benzophenone (toluene, hexane, tetrahydrofuran) or phosphorus pentaoxide (CH_2Cl_2), and they were freshly distilled prior to use. Deuterated solvents were dried over molecular sieves. $AlMe_3$ (2.0 M in toluene) and 2,2′-ethylidenebis(4,6-di-*tert*-butylphenol) were purchased and used without further purification. Benzyl alcohol, δ-valerolactone, and ϵ-caprolactone were dried over molecular sieves. Melting points were determined with a Buchi 535 digital melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury-400 (400 MHz) or a VXR-300 (300 MHz) spectrometer with chemical shifts given in ppm from the internal TMS. Microanalyses were performed using a Heraeus CHN-O-RAPID instrument. Infrared spectra were obtained from a Brucker Equnox 55 spectrometer. The GPC measurements were performed on a Hitachi 7100 system equipped with a differential Bischoff model 8120 RI detector using THF (HPLC grade) as an eluent. The molecular weights and polydispersity index were calculated according to a modified universal calibration curve derived from polystyrene standards and the Mark−Houwink equations for both polystyrene and PCL.

[Al(EDBP)(μ-OBz)]$_2$ (1) To a rapidly stirring solution of [Al(μ-EDBP)Me]$_2$ (0.96 g, 1.0 mmol) in toluene (30 mL) was added benzyl alcohol (0.21 mL, 2.0 mmol), and the reaction mixture was stirred at 25 °C for 10 h during which a white precipitate formed. The volatile materials were removed under vacuum, and the residue was redissolved in hot toluene (30 mL) and was allowed to cool to room temperature affording colorless crystalline solid after 12 h. Yield: 0.98 g (86%). Anal. Calcd for $C_{37}H_{51}AlO_3$: C, 77.86; H, 9.01%. Found: C: 77.26; H: 9.46%. ^{1}H NMR (CDCl$_3$, ppm): δ 7.09−7.45 (m, 9H, Ph), 5.50 (s, 2H, OCH$_2$), 3.55 (q, 1H, CH(CH$_3$), $J = 6.8$ Hz), 0.99 (d, 3H, CH(CH$_3$), $J = 6.8$ Hz), 1.36 (s, 18H, C(CH$_3$)$_3$), 1.26 (s, 18H, C(CH$_3$)$_3$). ^{13}C NMR (CDCl$_3$, ppm): δ 150.57, 141.06, 137.03, 135.26, 132.73, 128.78, 128.23, 125.55, 121.53, 120.82 (Ph); δ 68.39 (OCH$_2$); δ 35.25, 34.32, 31.62, 30.29 (*t*-Bu); δ 33.41 (**C**H(CH$_3$)); 21.59 (CH(**C**H$_3$)). IR (KBr, cm^{-1}): 2959 (s), 2871 (m), 1475 (s), 1445 (s), 1302 (m), 1268 (s), 1239 (m), 1010 (m), 879 (m), 677 (m). Mp: 234−236 °C dec.

[(PhCHO)Al(EDBP)(μ-OBz)]$_2$ (2). Benzaldehyde (0.20 mL, 2.0 mmol) was added to a rapidly stirring solution of [Al(EDBP)(μ-OBz)]$_2$ (1.14 g, 1.0 mmol) in hexane (40 mL), and the reaction mixture was stirred at 25 °C for 2 h, during which an orange precipitate formed. Volatile materials were removed under vacuum, and the residue was redissolved in hot hexane (80 mL) and was then allowed to cool to room temperature affording red crystals after 24 h. Yield: 1.15 g (85%). Anal. Calcd for $C_{44}H_{57}AlO_4$: C, 78.07; H, 8.49%. Found: C, 77.81; H, 8.55%. ^{1}H NMR (CDCl$_3$, ppm): δ 8.57 (s, 1H, PhCHO), 6.98−7.58 (m, 14H, Ph), 5.61 (s, 2H, OCH$_2$), 4.25 (q, 1H, CH(CH$_3$), $J = 6.8$ Hz), 1.04 (d, 3H, CH(CH$_3$), $J = 6.8$ Hz), 1.36 (s, 18H, C(CH$_3$)$_3$), 1.24 (s, 18H, C(CH$_3$)$_3$). ^{13}C NMR (CDCl$_3$, ppm): δ 195.13 (C=O); δ 151.86, 140.18, 137.77, 137.05, 135.86, 134.63, 134.05, 130.77, 128.77, 120.25, 127.12, 125.86, 120.99, 120.87 (Ph); δ 67.40 (OCH$_2$); δ 35.42, 34.36, 31.83, 30.73 (*t*-Bu); δ 31.07 (**C**H(CH$_3$)); δ 22.00 (CH(**C**H$_3$)). IR (KBr, cm^{-1}): 2954 (s), 2904 (m), 2870 (m), 1639 (s), 1476 (s), 1456 (m), 1441 (s), 1268 (m), 1238 (m), 855 (m), 670 (m). Mp: 224−226 °C dec.

Synthesis of Benzyl Ester End-Functionalized PCLs. A typical polymerization procedure was exemplified by the synthesis of PCL-100 (the number 100 indicates the designed $[\mathrm{M}]_0/[\mathrm{I}]_0$). To a rapidly stirring solution of [Al(EDBP)(μ-OBz)]$_2$ (0.143 g, 0.25 mmol) in toluene (30 mL) was added ϵ-CL (2.63 mL, 25 mmol). The reaction mixture was stirred at 25 °C for 32 h during which an increase in viscosity was observed. After the reaction was quenched by adding excess 0.35 N acetic acid solution, the polymer was precipitated into *n*-heptane. The white precipitate was washed with hexane three times and dried under vacuum giving a white solid. Yield: 2.67 g (94%).

Synthesis of Diblock Copolymer PCL-*b*-PVL. The living prepolymer PCL-50 was synthesized by a similar approach as described above, but ϵ-CL (1.31 mL, 12.5 mmol) was used. After prepolymerization for 16 h, δ-VL (2.4 mL, 25 mmol) was added. After another 16 h, the reaction was quenched using the procedures described previously. Yield: 3.77 g (94%).

Synthesis of Benzyl Ester End-Functionalized PCLs in the Presence of Benzyl Alcohol. A typical polymerization was exemplified by the synthesis of PCL-100 in the presence of 4 molar equiv of BzOH. ϵ-CL (2.63 mL, 25 mmol) and BzOH (0.105 mL, 1.0 mmol) were dissolved in 30 mL of toluene, and then the mixture was added to a rapidly stirring solution of [Al(EDBP)(μ-OBz)]$_2$ (0.145 g, 0.25 mmol) in toluene (20 mL). The reaction mixture was stirred at 25 °C for 24 h. After the reaction was quenched by adding 0.35 N acetic acid solution, the polymer was precipitated into *n*-heptane. The white precipitate was washed with hexane three times and dried under vacuum giving white solids. Yield: 2.66 g (94%).

X-ray Crystallographic Studies. Suitable crystals of **1** and **2** were sealed in thin-walled glass capillaries under nitrogen atmosphere and mounted on a Bruker AXS SMART 1000 or a Siemens P4 diffractometer. The crystallographic data were collected using a ω-2θ scan mode with Mo Kα radiation. Cell constants were obtained by least-squares analysis on positions of 35 randomly selected reflections in the 2θ range 4−28°. The space group determination was based on a check of the Laue symmetry and systematic absences and was confirmed using the structure solution. The structure was solved by direct methods using a Siemens SHELXTL PLUS package. All non-H atoms were located from successive Fourier maps and all hydrogen atoms were refined using a riding model. Anisotropic thermal parameters were used for all non-H atoms, and fixed isotropic parameters were used for H atoms.

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Supporting Information Available: Tables giving further details of the crystal structure determination, atomic coordinates and isotropic thermal parameters, bond lengths and angles, and anisotropic displacement parameters for **1** and **2** and text giving synthetic procedures and characterization data for [(EDBP)AlMe]$_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) EDBP−H_2 is the abbreviation of 2,2′-ethylidenebis(4,6-di-*tert*-butylphenol).

(9) B.-T Ko 1998, MS thesis. (b) [Al(μ-EDBP)Me]$_2$ was prepared from the reaction of 2,2′-ethylidenebis(2,4-di-*tert*-butylphenol) (EDBP−H_2) with 1 molar equiv of $AlMe_3$ in hexane.

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