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Alternating Copolymerization of Bicyclic Bis(γ-butyrolactone) and Epoxide through Zwitterion Process by Phosphines

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Aliphatic polyesters have attracted great interest as biocompatible and biodegradable materials in various fields such as biomedical and pharmaceutical industries.[1] One of the general methods to synthesize such polyesters is the ring-opening polymerization of lactones or lactides with metal alkoxides.[2] Meanwhile, as another synthetic approach to polyester, we have focused on anionic alternating copolymerizations of lactones and epoxides.[3−6] For example, bicyclic bis(γ-lactone) **1** and glycidyl phenyl ether (**2**) undergo the anionic alternating copolymerization with using potassium *tert*-butoxide (*t*-BuOK) as an initiator to give the corresponding polyester **3** (Table 1).[5] This copolymerization was facilitated by the double ring-opening reaction of **1** with forming a ketone moiety in the polymer side chain, which prevented the backward cyclization for reproducing the thermodynamically stable five-memberd lactone. In addition, the double ring-opening reactions of **1** resulted in another advantageous feature of the copolymerization, i.e., the small volume shrinkage upon the copolymerization. This feature allowed us to use **1** and its analogues as comonomers of the curing reactions of multifunctional epoxides in order to suppress volume shrinkage which leads to serious problems such as internal strain remained in materials, deterioration of adhesive properties, and occurrence of voids and cracks in materials.[5d,6]

On the other hand, metal-free ring-opening polymerizations by using organocatalysts,[7−11] organic initiators,[12] and enzymes[13] have attracted much attention because the obtained polymers are free from residual metal salts originated from the catalysts and initiators to permit their uses without bothersome purification processes. To date, a number of organocatalysts and initiators have been developed for the ring-opening polymerizations of lactones and lactides.[2] For example, *N*-heterocyclic carbenes were applied for the synthesis of the poly(lactic acid) with controlled molecular weight, narrow polydispersities,[8a,b] and high stereoregularity.[8c] Several nucleophilic compounds such as inidazole,[4,9b] pyridine,[9] amidine,[10] and guanidine derivatives[11] have been applied also to the ring-opening polymerization of lactones or lactides.

As described above, we have developed anionic alternating copolymerizations of lactones and epoxides as a new strategy for polyester synthesis. For the purpose of development of their metal-free versions, we focused on phosphine because of its high nuclophilicity, enough to initiate anionic polymerizations,[14] and its structural diversity. Herein, we demonstrate an alternating copolymerization of **1** and **2** using phosphines as a new metal-free system for polyester synthesis.[15]

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The copolymerization of **1** and **2** ($[\mathbf{1}]_0/[\mathbf{2}]_0$ = 50/50) was carried out in anhydrous tetrahydrofran (THF) at 120 °C for 72 h in the presence of phosphine (0.8 mol % to **1**) in a sealed tube (Table 1). When triphenylphosphine (PPh_3) was used as an initiator, the copolymerization proceeded to give the corresponding copolymer in a high yield (87%, run 1 in Table 1). The ^{1}H NMR spectrum of the obtained copolymer was identical to that of the 1:1 alternating copolymer **3** obtained by the *t*-BuOK-initiated copolymerization (Figure S1 in Supporting Information). The molecular weight of the obtained copolymer was comparable to the polyester synthesized by using *t*-BuOK. A remarkable feature of the PPh_3-initiated copolymerization was its much higher rate than that of the *t*-BuOK-initiated copolymerization; within 24 h, more than 70% of **1** was consumed, whereas only 20% of **1** was converted within 24 h in the *t*-BuOK-initiated copolymerization (Figure 1).

Other phosphines such as tri-*n*-butylphosphine (PBu_3) and tricyclohexylphosphine (PCy_3) also initiated the copolymerization to give the corresponding alternating copolymers in high yields (runs 2 and 3, respectively, in Table 1). The copolymerizations with using these phosphines were faster than that using PPh_3 (Figure 1). For example, bis(lactone) **1** was almost completely consumed within 24 h when PCy_3 was used as an initiator.

Previously, we reported the detailed structural analysis of the alternating copolymer of **1** and **2** obtained by the *t*-BuOK-initiated copolymerization by MALDI-TOF mass spectroscopy.[16] The resulting spectrum revealed that there were three series of polymers having different terminal structures, i.e., (1) "series LC_n" polymers that were linear and have carboxyl groups at both the chain ends, (2) "series LA_n" polymers that were linear and have one carboxyl terminal and one hydroxyl terminal, and (3) "series CY_n" that were cyclic (Figure 2a).[16] On the basis of this experience, with using the same ionization conditions, the copolymer **3** obtained by the PPh_3-initiated copolymerization was analyzed. The resulting spectrum is shown in Figure 2b, and the corresponding m/z values of the signals are listed in Table S1 (see Supporting Information). In the spectrum, two sets of signals "series LC_n" and "series CY_n" were observed, and other unassignable signals were not detected at all, supporting that the copolymerization proceeded completely in a 1:1 alternating manner. The "series LC_n" signals were observed predominantly, while the intensities for the "series CY_n" signals were much weaker than those observed in Figure 2a, the spectrum of the copolymer obtained by the *t*-BuOK-initiated copolymerization. This implies that the backbiting reaction causing formation of cyclic copolymers was effectively suppressed in the PPh_3-initiated copolymerization. Figure 2c shows the MALDI-TOF mass spectrum of the copolymer obtained by the PBu_3-initiated copolymerization, where the "LC_n" series was the predominant one similarly to the spectrum for the copolymer obtained by the PPh_3-initiated copolymerization. On the other hand, in the spectrum of the copolymer prepared by using PCy_3, another series of signals (series "LA_n") was observed besides LC_n and CY_n.

Although the reason for the predominant formation of linear polyesters by the phosphine-initiated copolymerization is not clear at present, it can be attributable to the absence of potassium cation, which can act as a template for formation of cyclic copolymers in general.

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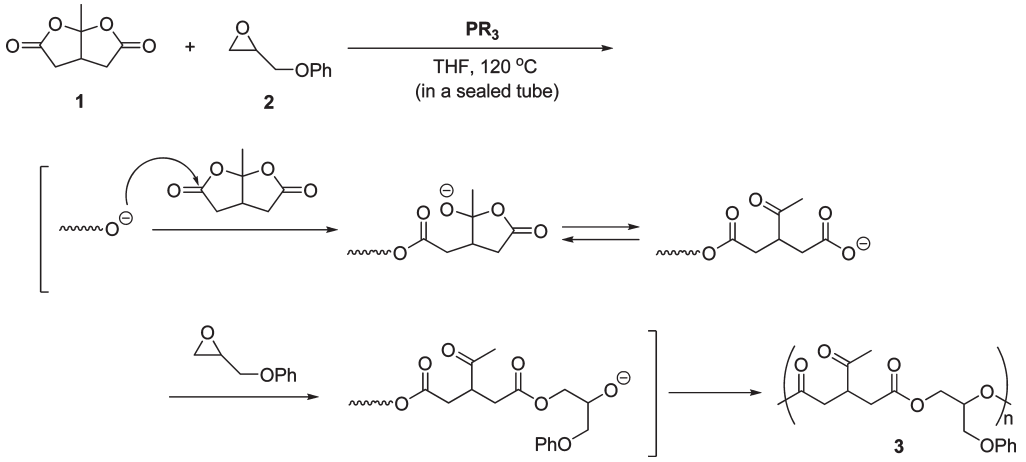
Table 1. Alternating Anionic Copolymerization of 1 with 2 Initiated by Phosphines[a]



run	initiator	conversion of **1** (%)[b]	yield (%)[c]	M_n (M_w/M_n)[d]
1	PPh_3	97	87	6.5×10^3 (1.32)
2	PBu_3	98	90	6.5×10^3 (1.31)
3	PCy_3	99	80	5.2×10^3 (1.41)
4	*t*-BuOK	76	72	6.7×10^3 (1.22)

[a] Polymerization conditions: $[initiator]_0/[\mathbf{1}]_0 = 0.008$, $[\mathbf{1}]_0 = [\mathbf{2}]_0 = 2.0$ M. The copolymerizations were carried out in THF at 120 °C for 72 h. [b] Determined by ^{1}H NMR. [c] Methanol-insoluble parts. [d] Estimated by GPC (eluent = THF, polystyrene standards).

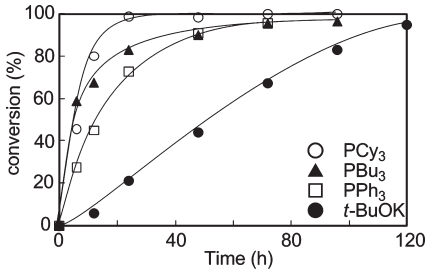


Figure 1. Time−conversion curves of the copolymerizations of **1** with **2** initiated by *t*-BuOK (●), PPh_3 (□), PBu_3 (▲), and PCy_3 (○).

In order to clarify the initiation step of the copolymerization, we carried out some model reactions. First, an equimolar mixture of bis(lactone) **1** and PPh_3 was heated in THF at 120 °C, with expecting that the corresponding zwitterionic species would be obtained (Scheme 1, in "mechanism A"). As the MALDI-TOF mass analysis revealed, most of the copolymers had carboxyl groups at both the chain ends (= series "LC$_n$"). This made us to postulate that the reaction of phosphine with bis(lactone) **1** could have taken place at first to give the corresponding zwitterionic species **4**, of which carboxylate could have reacted with epoxide. This mechanism allows the incorporation of the acylphosphonium moiety at the initiating end of the copolymer, of which hydrolysis during the isolation of the copolymer would give the carboxyl group. Against this postulation, the ring-opening reaction of **1** by PPh_3 was not detected at all by ^{1}H NMR or ^{31}P NMR, implying that this reaction may not govern the initiation step.

Mechanism B would involve the nucleophilic attack of PPh_3 to epoxide, which gives the corresponding zwitterionic species **5** (Scheme 1). When an equimolar mixture of glycidyl phenyl ether **2** and PPh_3 was heated in THF at 120 °C, the resulting products were allyl phenyl ether and triphenylphosphine oxide.[17] These compounds can be formed via 1,2-oxaphosphetane (**6**), which would be in an equilibrium with the zwitterionic intermediate **5**. In the presence of bis(lactone) **1**, the alkoxide moiety of **5** would react with **1** to generate the corresponding adduct having carboxylate moiety, which can then react with epoxide. We also attempted copolymerization with using triphenylphosphine oxide as an initiator; however, no reaction took place.

In the both mechanisms, regeneration of phosphine may be possible: The initiating end of the copolymer is acylphosphonium (in mechanism A) or alkylphosphonium (in mechanism B), which are both highly elecrophilic to react with nucleophilic species efficiently, and these reactions would be accompanied by release of phosphines having intrinsically high leaving ability.

Mechanism A is favorable to explain the terminal structure of the copolymer, but the experimental results did not support it. Meanwhile, mechanism B was supported by the model reaction, but it is not in good accordance with the terminal structure. Then, we postulated another idea that supports mechanism A again: The reaction of bis(lactone) and phosphine would be reversible, where the concentration of the zwitterionic intermediate **4** would be negligibly low. However, because of the presence of epoxide in the copolymerization system, **4** can be immediately transformed into the corresponding phosphine−bis(lactone)−epoxide three-component adduct. To prove this assumption, we also heated a mixture of **1**, **2**, and PPh_3 ($[\mathbf{1}]_0/[\mathbf{2}]_0/[PPh_3]_0 = 1/1/1$). As a result, some reaction proceeded to give several phosphine-containing compounds, of which structures were analyzed by ^{31}P NMR; however, formation of the three-component adduct was not proven due to the complexity of the spectrum.

In summary, phosphines worked effectively as initiators for the anionic alternating copolymerization of bis(lactone) **1** and epoxide **2**. The copolymerization proceeded much faster than the previously reported *t*-BuOK-initiated one. In addition, MALDI-TOF mass analysis of the resulting copolymers revealed that the backbiting reaction that accompanied the *t*-BuOK-initiated copolymerization was effectively suppressed to permit the selective formation of linear polyesters. Further detailed investigation on these favorable aspects and mechanism for them is currently ongoing. Application of the present phosphine-initiated copolymerization to metal-free curing system of multifunctional epoxides to develop high-performance materials is currently under investigation.

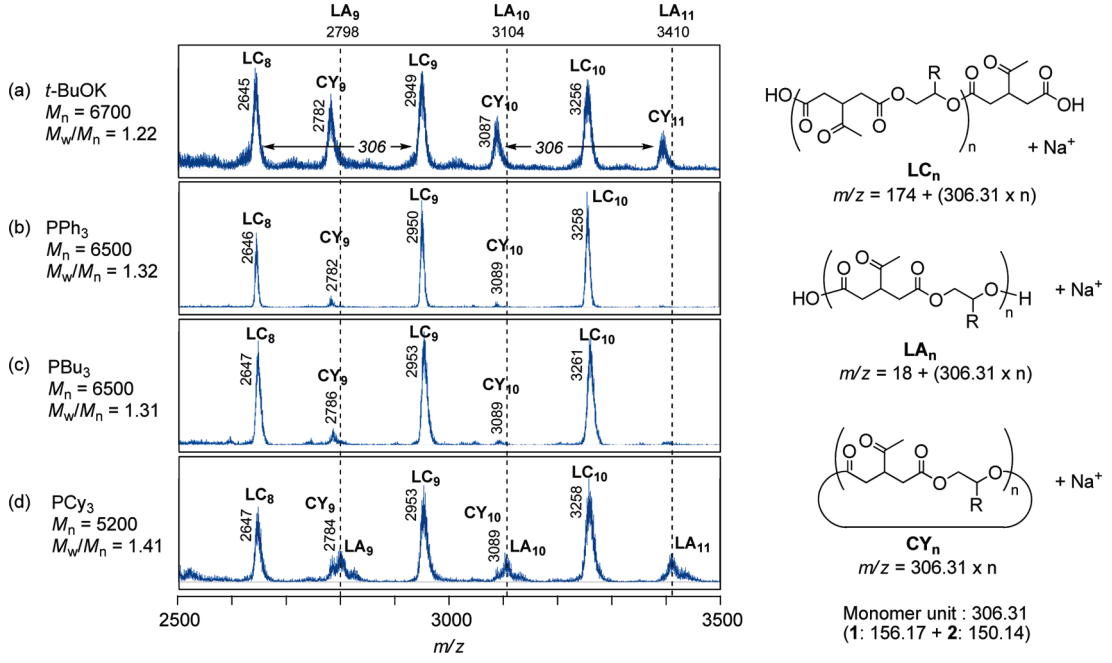
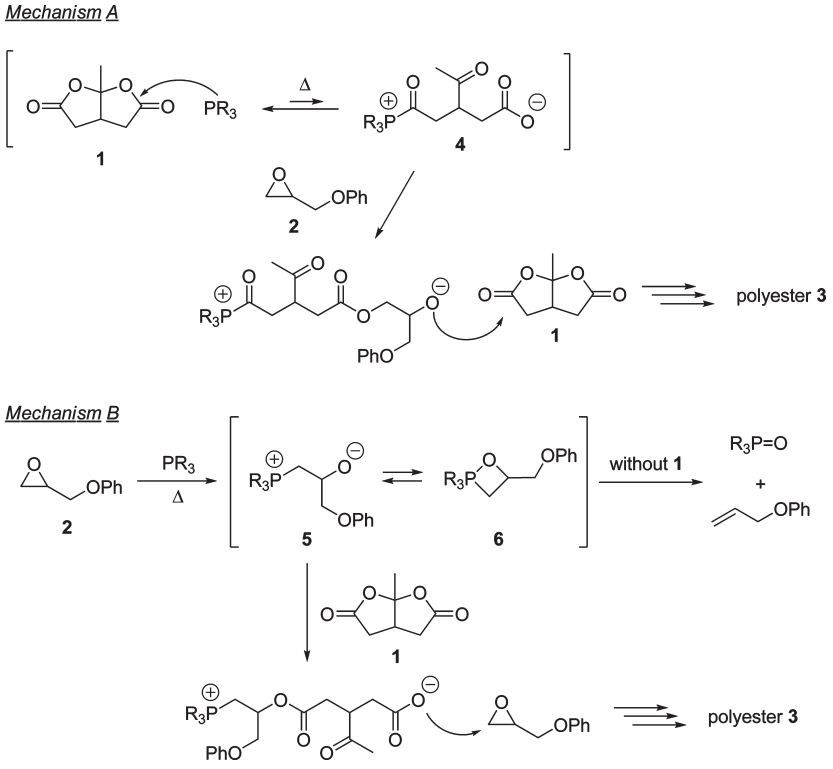


Figure 2. MALDI-TOF mass spectra of the obtained alternating copolymers synthesized by the copolymerization of **1** with **2** using *t*-BuOK (a), PPh_3 (b), PBu_3 (c), and PCy_3 (d).

Scheme 1. Possible Initiation Mechanisms of Alternating Copolymerization of 1 with 2 with Using Phosphines



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Supporting Information Available: Experimental procedures, ^1H NMR spectra of the copolymers prepared by PPh_3 and *t*-BuOK, and calculated *m*/*z* values of possible copolymer structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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