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"Nonstrained" γ-Butyrolactone-Based Copolyesters: Copolymerization Characteristics and Composition-Dependent (Thermal, Eutectic, Cocrystallization, and Degradation) Properties

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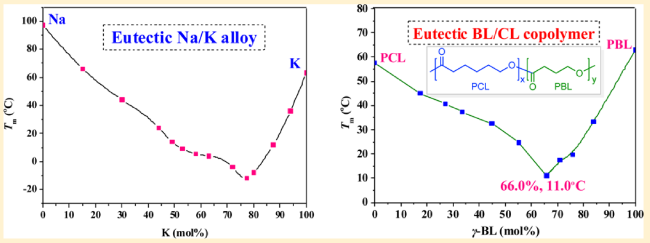
Supporting Information

ABSTRACT: Despite several anticipated advantages of the bioderived γ-butyrolactone (γ-BL) as an effective comonomer to modulate materials properties of its copolyesters, the currently unmet challenge hinders access to such copolyesters with high γ-BL incorporations due to unfavorable thermodynamics toward the ring-opening polymerization of the highly stable, typically referred to as "nonstrained", γ-BL. Here we report the effective copolymerization of γ-BL with two common cyclic esters with very different monomer thermodynamic polymerizability, ε-caprolactone (ε-CL) and δ-valerolactone (δ-VL), leading to a series of relatively high molecular weight (M_n up to 135 kg/mol) random copolyesters with unprecedented levels of γ-BL incorporations (up to 84.0 mol %) and thus providing access to γ-BL-based copolyesters in the entire composition range needed for comprehensive investigations into the composition-dependent physical properties and degradation behavior of the resulting copolyesters. This copolymerization was enabled by the judiciously chosen metal and organic catalysts that exhibit different kinetic behavior or monomer selectivity, designed to more effectively compete the "nonstrained" γ-BL against the relatively high-strained lactones toward ring-opening. The successful synthesis of the copolyesters with high γ-BL incorporations of >50 mol % led to the discovery of the eutectic phase of the γ-BL/ε-CL copolymer with a eutectic temperature T_{eu} of 11.0 °C and a eutectic composition X_{eu} of 66.0% γ-BL; thus, at this composition, the copolymer becomes a viscous liquid at room temperature, although the two constituent homopolymers are semicrystalline solids. Other important composition-dependent properties of γ-BL-based copolyesters, including thermal transitions, cocrystallization, as well as thermal and hydrolytic degradation behaviors, have also been examined.



INTRODUCTION

Aliphatic polyesters are a class of technologically important biodegradable and/or biocompatible polymers thanks to their large-scale accessibility by the ring-opening polymerization (ROP) of cyclic esters or lactones[1−10] and realized wide applications in medicine, absorbable sutures, temporary implants for tissue engineering, and food technologies (e.g., for packaging).[11,12] Although commercially available aliphatic polyesters, such as poly(ε-caprolactone) (PCL),[13] polylactide (PLA),[14−19] and polyglycolide [i.e., poly(glycolic acid), PGA],[20] prepared through the ROP of their respective monomers ε-CL, LA, and GA, exhibit certain desirable characteristics or materials properties, inherent defects significantly limit their many end uses. For example, on one hand, PCL has the specific applications in a diffusion-controlled drug delivery device and suture, thanks to its lack of toxicity and permeability of a low molecular weight drug (<400 Da).[13] On the other hand, high crystallinity and hydrophobicity of PCL lead to a slow degradation rate (1−2 years), making it only for long-term utilization and thus restricting its application.[21]

It is well-known that copolymerization is an effective strategy to obtain the materials with tailored properties by adjusting the chemical nature of the comonomers and the composition of the copolymers, often delivering improved or unattainable properties relative to those of the constituent homopolymers.[22−28] For example, poly(lactide-*co*-glycolide) (PLGA)[20] became one of the most suitable candidates for biomedical application as it possesses balanced crystallinity and processability with a relatively fast degradation rate (1−6 months),[21] although the degradation process of PLGA *in vivo* involves bulk hydrolysis that leads to an accumulation of the highly acidic degradation product that is suddenly released, resulting in a large decrease of the local pH, which induces inflammatory responses especially for large implants.[29,30] Compared with the commonly used cyclic esters or lactones for the synthesis of aliphatic copolyesters, γ-butyrolactone (γ-BL) is a very promising comonomer, thanks to its following benefits or advantages. First, γ-BL is commercially produced and bioderived from

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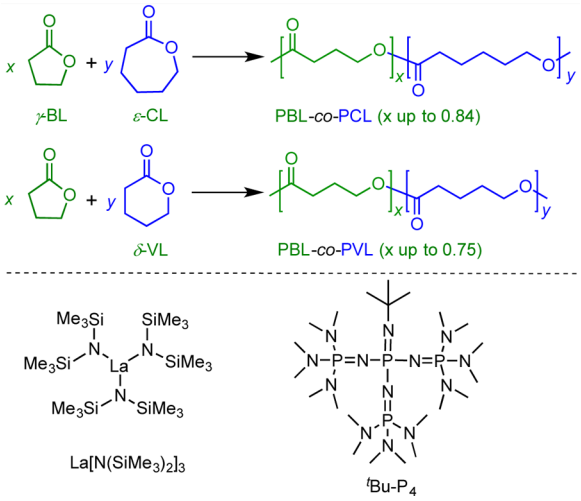
succinic acid, the top ranked chemical on the DOE's top 12 biomass-derived compounds best suited to replace petroleum-derived chemicals.[31,32] Second, the degradation rate of its corresponding polymer, poly(γ-butyrolactone) (PBL)—a structural equivalent of biomaterial poly(4-hydroxybutyrate) (P4HB) produced by bacterial fermentation—has been shown to be slower than PLGA but much faster than PLA, PCL, and other poly(hydroxyalkanoate)s such as poly(3-hydroxybutyrate) (P3HB).[33] Therefore, incorporation of γ-BL into other aliphatic polyesters can modify the degradation rate to meet the desired application demand. More importantly, the biocompatibility of P4HB is shown to be better than PGA and PLGA *in vivo* due to a slow release of well tolerated, less acidic degradation products.[29,33] Third, P4HB or PBL, as a flexible thermoplastic biomaterial, has more desirable mechanical properties.[29,33] Thus, γ-BL is a suitable comonomer for imparting flexibility to hard or brittle polymers such as PGA or PLA and improving degradation rates of common polyesters such as PCL, PLA, and P3HB.

Although the copolymerization behavior of γ-BL with ε-CL, GA, δ-valerolactone (δ-VL), and LA has been reported previously via both enzyme-catalyzed polymerization[34,35] and chemical ROP by acid (cationic) catalysts ($BF_3{\cdot}Et_2O$,[36] $FeCl_3$,[36] FSO_3H,[36] $SnPh_4$,[37,38] etc.) and coordination polymerization catalysts (rare-earth metal complexes[39,40] and $[Al(O^iPr)_3]_3$[41,42]), γ-BL incorporation was unfortunately limited below 43% for PBL-*co*-PCL and 15% for PBL-*co*-PVL. Furthermore, the polymer yield and molecular weight of the resulting copolyesters decreased significantly with increasing γ-BL incorporation. These limitations are a result of unfavorable thermodynamics toward the ROP of γ-BL, caused by its highly stable, commonly referred as "nonstrained" five-membered lactone ring.[43−46] Owing to the large difference in reactivity between "nonstrained" γ-BL and relatively high-strained lactones or cyclic esters, the synthesis of the copolyesters with high γ-BL incorporations and high molecular weight still *remained a challenge* to date. Accordingly, a comprehensive investigation into effects of the γ-BL incorporation over the entire composition range of copolyesters on their materials properties and degradation behavior has yet been reported, as all the previous studies were restricted to the copolyesters with only low γ-BL incorporations.[34,36,37]

Most recently, we disclosed the first successful chemical ROP of γ-BL into high molecular weight PBL under readily accessible conditions (i.e., 1 atm, −40 °C) by controlling the kinetic, thermodynamic, and processing conditions.[47,48] In that process, metal-based catalysts, $La[N(SiMe_3)_2]_3$, and a yttrium complex supported with tetradentate aminoalkoxy-bis-phenolate ligands and an organic catalyst, P_4-phosphazene superbase (^{t}Bu-P_4), were found to promote the most effective ROP to achieve relatively high molecular weight PBL (M_n up to 30 kg/mol) and high monomer conversion (up to 90%). On the basis of these findings, we hypothesized that the catalysts and conditions employed in such an effective γ-BL homopolymerization system should be the suitable candidates for synthesizing copolyesters with high γ-BL incorporations, thus addressing the current challenges in the γ-BL-based copolyesters, which was the central objective of this study. Accordingly, the present work has systematically investigated characteristics of the ring-opening copolymerization (ROC) of γ-BL with two common cyclic esters or lactones, ε-CL and δ-VL, which vary substantially in the monomer thermodynamic polymerizability. By employing commercially available metal-based catalyst $La[N(SiMe_3)_2]_3$ and organic catalyst ^{t}Bu-P_4, we have successfully synthesized, for the first time, a series of high molecular weight copolyesters with a very wide range of γ-BL incorporations (Scheme 1). This success provided the opportunity to investigate the effects of the γ-BL incorporation over the entire composition range on the physical properties and degradation behavior of the copolymers, which have been examined in detail by this study.

Scheme 1. Structures of Catalysts and ROCs of γ-BL with Two Cyclic Esters Employed in This Study



RESULTS AND DISCUSSION

Characteristics of γ-BL Copolymerizations with ε-CL and δ-VL. Two common strained cyclic esters, ε-CL and δ-VL, with their monomer thermodynamic polymerizability following the order of ε-CL > δ-VL (≫ γ-BL),[43,45] were employed for the study of γ-BL copolymerizations. Table 1 summarizes the copolymerization of γ-BL with ε-CL by both metal-based catalyst $La[N(SiMe_3)_2]_3$ and organic catalyst ^{t}Bu-P_4. As a control, homopolymerization of ε-CL was examined with $La[N(SiMe_3)_2]_3$ (0.2 mol % loading) at RT, which showed an extremely high activity by achieving 98% ε-CL conversion in 5 s, producing PCL with a M_n of 79.6 kg/mol and a relatively broad dispersity ($Đ$) of 2.46 (Table 1, run 1). Switching to ^{t}Bu-P_4 resulted in a lower activity (2 min, 68.1% ε-CL conversion, Table 1, run 2), but using BnOH as initiator enhanced the activity for the ^{t}Bu-P_4-promoted polymerization and rendered quantitative ε-CL conversion in 2 min (Table 1, run 3), producing PCL with similar M_n and $Đ$ values to those by the La catalyst.

Accordingly, for the γ-BL/ε-CL copolymerizations $La[N(SiMe_3)_2]_3$ was first utilized as the catalyst. At RT with THF as solvent, increasing the γ-BL/ε-CL feed ratio from 1/1 to 3/1 significantly enhanced γ-BL incorporation (mol %) from 17.5% to 31.0% (Table 1, runs 4 and 5). After that, however, the incorporation of γ-BL apparently reached a plateau as further increasing the γ-BL/ε-CL feed ratio to 5/1 only resulted in a slight increase of the γ-BL incorporation to 35.0% (Table 1, run 5 vs 7). Switching the solvent to relatively nonpolar toluene noticeably enhanced the γ-BL incorporation to 35.3% (vs 31.0% achieved in THF) but led to lower monomer conversion (Table 1, run 6 vs 5). Considering that the low polymerization temperature condition favors the ROP of the five-membered

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Table 1. Results of Copolymerizations of γ-BL with ε-CL[a]

run	Cat.	initiator (I)	M/Cat./I	temp (°C)	ε-CL/γ-BL[c]	time (min)	conv[d] (ε-CL%)	conv[d] (γ-BL%)	incorp[d] (γ-BL%)	M_n[e] (kg/mol)	$Đ$[e]
1[b]	La		500/1/−	25		5 (s)	98.3			79.6	2.46
2[b]	^{t}Bu-P$_4$		500/1/−	25		2	68.1			56.1	2.02
3[b]	^{t}Bu-P$_4$	BnOH	500/1/1	25		2	100			72.3	2.11
4	La		500/1/−	25	1/1	2	96.9	26.7	17.5	69.5	2.05
5	La		500/1/−	25	1/3	2	92.5	17.2	31.0	40.6	2.15
6[f]	La		500/1/−	25	1/3	2	68.8	11.4	35.3	30.2	1.91
7	La		500/1/−	25	1/5	2	82.3	10.0	35.0	32.1	1.98
8	La		500/1/−	−20	1/5	5	55.6	9.10	45.0	59.1	1.90
9	La		500/1/−	−20	1/10	180	51.6	6.00	53.8	58.0	1.92
10	La	BnOH	500/1/2	−40	1/10	5	91.5	23.4	70.0	20.0	2.13
11	La	Ph_2CHCH_2OH	500/1/2	−40	1/10	5	100	25.0	71.4	16.4	1.74
12[g]	La		2000/1/−	25	1/2	2	94.0	20.0	27.1	135	1.64
13[g]	La	Ph_2CHCH_2OH	2000/1/3	25	1/3	2	100	18.2	33.6	44.0	1.68
14[g]	La	Ph_2CHCH_2OH	2000/1/2	−40	1/5	10	92.4	38.5	55.2	48.8	1.53
15[g]	La	Ph_2CHCH_2OH	2000/1/2	−40	1/8	10	90.0	29.6	66.0	44.4	1.46
16[g]	La	Ph_2CHCH_2OH	2000/1/2	−40	1/10	10	87.2	20.8	71.0	42.3	1.60
17[g]	La	Ph_2CHCH_2OH	2000/1/2	−40	1/15	15	80.5	17.6	76.0	31.7	1.48
18[g]	La	Ph_2CHCH_2OH	1500/1/2	−40	1/20	30	83.3	22.0	84.0	22.9	1.41
19	^{t}Bu-P$_4$	BnOH	100/1/1	25	1/3	1440	72.7	22.0	42.4	5.25	1.59
20	^{t}Bu-P$_4$	BnOH	100/1/1	−20	1/3	5	100	50.0	51.8	8.90	1.91
21	^{t}Bu-P$_4$	BnOH	500/1/1	−40	1/4	30	32.1	20.0	74.0	16.0	1.35
22	^{t}Bu-P$_4$	BnOH	1000/1/1	−40	1/4	60	20.8	11.0	80.0	26.0	1.43

[a]Conditions: La[N(SiMe$_3$)$_2$]$_3$ (La) = 10 μmol, ^{t}Bu-P$_4$ = 50 μmol, [ε-CL + γ-BL] = 6.67 M in THF for RT runs, [ε-CL + γ-BL] = 10.0 M in THF for the runs at −20 and −40 °C. [b]La = 10 μmol, ^{t}Bu-P$_4$ = 10 μmol, [ε-CL] = 2.0 M in THF. [c]Molar ratio of ε-CL/γ-BL in feed. [d]Monomer conversions and γ-BL incorporations of the copolymers measured by ^{1}H NMR spectra, γ-BL mol % = [$I_{2.38\ ppm}$/($I_{2.38\ ppm}$ + $I_{2.30\ ppm}$)] × 100%. [e]Number-average molecular weight (M_n) and dispersity ($Đ$ = M_w/M_n) determined by GPC at 40 °C in DMF relative to PMMA standards. [f]Toluene as solvent. [g]Copolymerizations performed in a multigram scale, La = 50 μmol.

Table 2. Results of Copolymerizations of γ-BL with δ-VL[a]

run	Cat.	initiator (I)	M/Cat./I	temp (°C)	δ-VL[b]/γ-BL	time (min)	conv[c] (δ-VL%)	conv[c] (γ-BL%)	incorp[c] (γ-BL %)	M_n[d] (kg/mol)	$Đ$[d]
1	La		1000/1/−	25		2	80.0			45.8	1.87
2	La		1000/1/−	25	1/0.5	2	83.2	18.2	8.00	47.4	1.90
3	La		1000/1/−	25	1/1	2	86.5	17.5	13.5	39.1	2.33
4	La		1000/1/−	25	1/10	5	60.0	3.50	40.0	34.5	1.38
5	La	Ph_2CHCH_2OH	1000/1/2	25	1/10	5	76.5	5.40	43.5	8.00	1.52
6	La	Ph_2CHCH_2OH	1000/1/2	−20	1/10	10	95.7	11.4	52.6	19.2	1.55
7	La	Ph_2CHCH_2OH	1000/1/2	−40	1/10	10	91.0	5.30	34.1	26.5	1.77
8	^{t}Bu-P$_4$	BnOH	100/1/1	25	1/1	5	94.6	26.6	19.8	10.2	1.71
9	^{t}Bu-P$_4$	BnOH	100/1/1	25	1/3	30	90.2	14.4	23.7	5.28	1.70
10	^{t}Bu-P$_4$	BnOH	100/1/1	−20	1/3	5	100	35.0	48.5	8.33	1.88
11	^{t}Bu-P$_4$	BnOH	100/1/1	−40	1/3	10	100	36.1	54.0	11.5	1.71
12	^{t}Bu-P$_4$	BnOH	100/1/1	−40	1/10	10	100	40.2	75.1	9.31	1.49
13	^{t}Bu-P$_4$	BnOH	400/1/1	−40	1/10	10	100	30.9	71.2	20.7	1.52

[a]Conditions: La[N(SiMe$_3$)$_2$]$_3$ (La) = 10 μmol, ^{t}Bu-P$_4$ = 50 μmol, THF used as the solvent, [δ-VL] = 2.0 M for homopolymerization, [δ-VL + γ-BL] = 6.67 M for RT runs, [δ-VL + γ-BL] = 10.0 M for the runs at −20 and −40 °C. [b]Molar ratio of δ-VL/γ-BL in feed. [c]Monomer conversions and γ-BL incorporations of the copolymers measured by ^{1}H NMR spectra, γ-BL mol % = ($I_{1.96\ ppm}$/$I_{2.32-2.40\ ppm}$) × 100%. [d]Number-average molecular weight (M_n) and dispersity ($Đ$ = M_w/M_n) determined by GPC at 40 °C in DMF relative to PMMA standards.

lactone because it overcomes the thermodynamic resistance of the five-membered lactone to ROP by reducing the positive contribution of the $-T\Delta S$ term (i.e., entropic penalty),[47−50] we next investigated the copolymerization behavior at lower temperatures. Indeed, fixing the γ-BL/ε-CL feed ratio of 5/1, lowering the temperature from RT to −20 °C not only increased the γ-BL incorporation from 35.0% to 45.0% but also significantly enhanced molecular weight of the resulted copolyester from M_n = 32.1 kg/mol to M_n = 59.1 kg/mol (Table 1, run 7 vs 8). When a large excess of γ-BL in feed (γ-BL/ε-CL = 10/1) was employed at −20 °C, the γ-BL incorporation further increased to 53.8% but with a decreased monomer conversion (Table 1, run 9). Notably, a high γ-BL incorporation up to 70% was achieved, also with enhanced ε-CL and γ-BL conversions (91.5% and 23.4%, respectively), from the copolymerization performed at −40 °C with BnOH as the initiator (Table 1, run 10), attributed to the *in situ* formed alkoxide initiating species being a stronger nucleophile than the corresponding amide analogue.[51,52] Using Ph_2CHCH_2OH as the initiator instead of BnOH, both γ-BL conversion and

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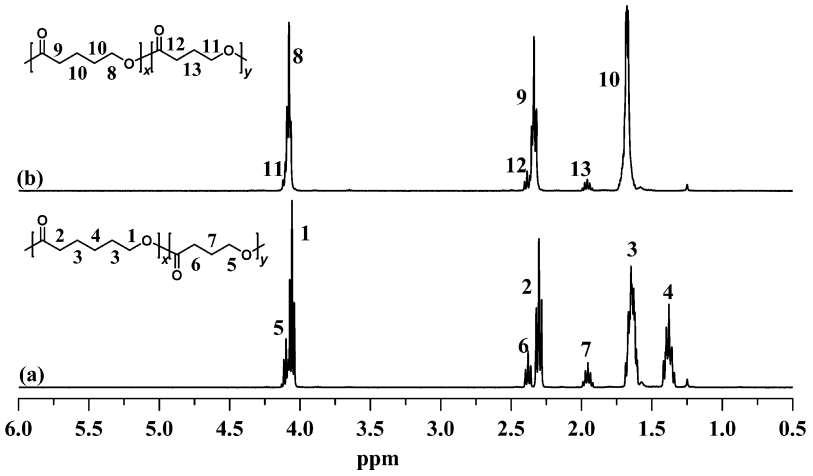

Figure 1. ^{1}H NMR spectra ($CDCl_3$): (a) PBL-*co*-PCL (17.5% γ-BL) (Table 1, run 4); (b) PBL-*co*-PVL (8.0% γ-BL) (Table 2, run 2).

incorporation were further increased (Table 1, run 11). Based on these results, copolymerizations in a larger scale under various conditions were also carried out, enabling the synthesis of PBL-*co*-PCL copolyester samples (2−5 g) with the γ-BL incorporation and copolymer molecular weight tuned in a very wide range, incorporation from low 27.1% to high 84.0% and molecular weight from low M_n = 22.9 kg/mol to high M_n = 135 kg/mol (Table 1, runs 12−18). In fact, a 21 g sample of PBL-*co*-PCL (M_n = 100 kg/mol, $Đ$ = 1.58, γ-BL mol % = 26.5%) was readily produced through this copolymerization with conditions [γ-BL + ε-CL]/[La] = 6000/1; γ-BL/ε-CL = 2/1; concentration = 6.67 M in THF; time = 400 min; ε-CL conversion% = 83.9%; γ-BL conversion% = 17.3%).

Compared to the metal (La)-based system, the ROC by ^{t}Bu-P$_4$ (catalyst)/BnOH (initiator) at RT displayed a much lower activity and also produced the copolymer with much lower molecular weight (Table 1, run 19 vs 5). In sharp contrast, once the polymerization temperature was decreased to −20 °C, the activity of the ^{t}Bu-P$_4$/BnOH system was enhanced significantly so that quantitative conversion of ε-CL and 50.0% conversion of γ-BL were achieved in just 5 min (Table 1, run 20). Further lowering the temperature to −40 °C and decreasing the catalyst/initiator loading to 0.2% and 0.1% yielded the copolyester with a high γ-BL incorporation of 74% (M_n = 16.0 kg/mol and $Đ$ = 1.35) and 80% (M_n = 26.0 kg/mol and $Đ$ = 1.43), respectively (Table 1, runs 21 and 22). Hence, it is noteworthy that behaving rather differently from the metal-based system where copolyesters with high γ-BL incorporations (γ-BL% > 50%) were realized only when a large excess of γ-BL in feed was employed (γ-BL/ε-CL ≥ 10), the organic catalyst system based on ^{t}Bu-P$_4$/BnOH afforded the copolyesters with high γ-BL incorporations at a relatively low γ-BL/ε-CL feed ratio of 3/1−4/1. It is noted here that the atom efficiency of γ-BL used in the copolymerization study is low to moderate due to its relatively low conversions (6−50%), especially in those copolymerizations using γ-BL in large excess in feed to achieve high γ-BL incorporations, but it can be easily recycled.

Switching to the less strained, six-membered δ-VL comonomer, the γ-BL copolymerization behavior by La[N(SiMe$_3$)$_2$]$_3$ at RT was rather similar to that observed for the γ-BL copolymerization with ε-CL (Table 2, runs 1−5). However, lowering the polymerization temperature did not further enhance the γ-BL incorporation in the resulting copolyester PBL-*co*-PVL, which is in sharp contrast to the γ-BL/ε-CL copolymerization. For example, the γ-BL incorporation in PBL-*co*-PVL produced at −40 °C (34.1%) was even lower than that obtained at −20 °C (52.6%, Table 2, run 7 vs 6). Even though a large excess of γ-BL in feed was employed, it was still difficult to synthesize a copolyester with γ-BL incorporation higher than 52.6%. However, this problem was readily solved by employing the ^{t}Bu-P$_4$/BnOH system that afforded PBL-*co*-PVL copolyesters with a wide range of γ-BL incorporations from low 19.8% to high 75.1%, simply by varying the reaction temperature and the γ-BL/δ-VL ratio in feed (Table 2, runs 8−12). For example, PBL-*co*-PVL with a high γ-BL incorporation of 71.2% and M_n of 20.7 kg/mol ($Đ$ = 1.52) was produced with γ-BL/^{t}Bu-P$_4$/BnOH = 400/1/1 and γ-BL/δ-VL = 10/1 at −40 °C (Table 2, run 13). These results showed again the different kinetic behavior (toward monomer selectivity) between the metal (La)-based and organic ^{t}Bu-P$_4$/BnOH systems.

To verify the monomer sequence of the resultant copolymers, kinetic studies were carried out. In the case of the copolymerization of γ-BL with ε-CL in a γ-BL/ε-CL feed ratio of 3/1 at 25 °C, γ-BL and ε-CL conversions increased gradually with increasing the polymerization time from 1 to 15 min, while γ-BL incorporation decreased slightly from 37.6% to 33.4% in the first 10 min and maintained at about 33.6% at the late stage of the copolymerization (Table S1, runs 1−6, Figures S1 and S2). Even under the conditions (γ-BL/ε-CL = 15/1 in feed, −40 °C) that produced the copolymers with a high level of γ-BL incorporation (>70%), no obvious variations in γ-BL incorporations were observed when the polymerization time was extended from 4 to 15 min (72% vs 78%, Table S1, runs 7 and 8). Hence, both results demonstrated that the resultant PBL-*co*-PCL copolymers are the statistical random copolymers rather than the possible tapered ones. Kinetic studies of the copolymerization of γ-BL with δ-VL also yielded similar results (Table S1, runs 9−15).

Microstructures of γ-BL-Based Copolyesters. The microstructures of the copolymers of γ-BL with ε-CL and δ-VL were investigated by ^{1}H and ^{13}C NMR methods. Figure 1 depicts ^{1}H NMR spectra of typical γ-BL/ε-CL and γ-BL/δ-VL copolymers, where the peaks were assigned based on the previous literature methods[37,39] as well as by comparing peak positions between homopolymers and copolymers with different γ-BL contents. The monomer incorporation was calculated by ^{1}H NMR spectra while ^{13}C NMR spectra provided more detailed information about the microstructure. Taking the ^{13}C

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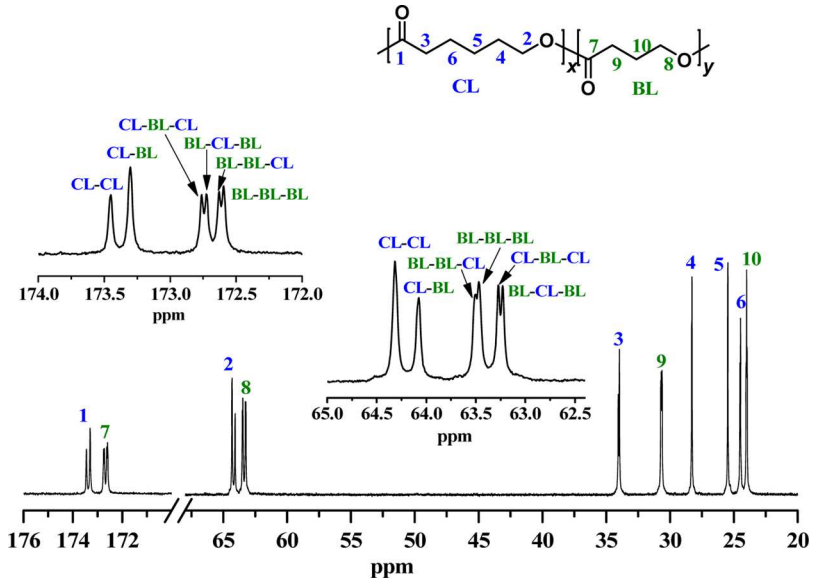

Figure 2. ^{13}C NMR spectrum ($CDCl_3$) of PBL-*co*-PCL copolymer (γ-BL mol % = 55.2%, Table 1, run 14).

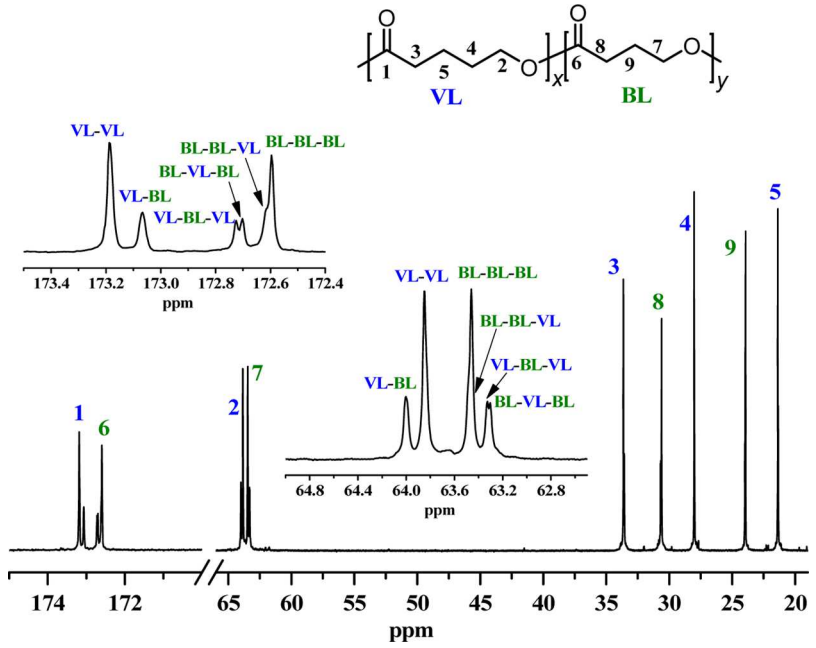

Figure 3. ^{13}C NMR spectrum ($CDCl_3$) of PBL-*co*-PVL (γ-BL mol % = 54.0%, Table 2, run 11).

Table 3. Molar Ratios of Different Sequence Linkages Determined by ^{13}C NMR

		M ring-opened unit		γ-BL (B) ring-opened unit			
copolymer	incorp (γ-BL%)	M−M (mol %)	M−B (mol %)	M−B−M (mol %)	B−M−B (mol %)	B−B−M (mol %)	B−B−B (mol %)
PBL-*co*-PCL	17.5	66.7	15.8	11.5	4.25	1.75	0
	33.6	44.2	22.2	18.6	6.52	6.15	2.33
	55.2	17.7	27.2	13.0	13.0	11.0	18.1
	76.0	4.63	19.3	4.71	14.4	14.5	42.5
PBL-*co*-PVL	8.00	84.6	7.36	5.76	2.28	0	0
	23.7	57.3	19.0	14.1	4.00	3.65	1.95
	54.0	32.5	13.5	8.70	8.37	15.3	21.63
	71.2	17.6	11.2	3.10	9.47	58.63	

NMR spectrum (Figure 2) of PBL-*co*-PCL (γ-BL% = 55.2%) as an example, the signal of the carbonyl carbon of the ε-CL ring-opened unit is split into two peaks attributed to the CL−CL continuous sequence and CL−BL alternating sequence. For the γ-BL ring-opened unit, the triad sequence can be revealed by ^{13}C NMR spectra, including CL−BL−CL and BL−CL−BL

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Table 4. Thermal Properties of γ-BL-Based Copolyesters and Control Homopolymers[a]

entry	copolyester	incorp (γ-BL %)	M_n (kg/mol)	T_m (°C)	T_g (°C)	T_c (°C)	ΔH_f (J/g)	T_d (°C)
1	PCL	0	79.6	57.6	−59.4	32.5	54.3	360
2	poly(BL-*co*-CL)	17.5	69.5	45.1	−63.0	19.0	50.0	n.d.
3	poly(BL-*co*-CL)	27.1	134.8	40.8	−59.6	10.5	47.1	312
4	poly(BL-*co*-CL)	33.6	44.0	36.4	−59.4	8.36	55.1	302
5	poly(BL-*co*-CL)	45.0	59.1	32.5	−58.7	7.21	50.4	n.d.
6	poly(BL-*co*-CL)	55.2	48.8	24.8	−56.4	−4.87	51.2	281
7	poly(BL-*co*-CL)	66.0	44.4	11.0	−65.0	−26.2	38.1	n.d.
8	poly(BL-*co*-CL)	71.0	42.3	17.5	−59.3	−20.4	39.5	n.d.
9	poly(BL-*co*-CL)	76.0	31.7	20.0	−54.4	−21.0	40.9	267
10	poly(BL-*co*-CL)	84.0	22.8	33.3[b]	−48.1	11.9	46.0	231
11	PBL	100	12.0	63.5	−45.6	32.7	33.2	201
12	PVL	0	45.8	58.6	−54.6	33.8	68.2	264
13	poly(BL-*co*-VL)	13.5	39.1	43.0	−60.9	17.4	55.6	n.d.
14	poly(BL-*co*-VL)	34.1	26.5	19.2	−61.0	−14.3	35.4	283
15	poly(BL-*co*-VL)	54.0	11.5	14.0	−55.7	−26.1	26.1	n.d.
16	poly(BL-*co*-VL)	72.0	15.0	53.1	−51.6	3.68	33.8	270

[a]All T_m and T_g values were obtained from the second scan after the thermal history was removed from the first scan. The first heating rate was 20 °C/min while the second heating rate was 10 °C/min and cooling rate was 5 °C/min. [b]Cooling rate is 2 °C/min.

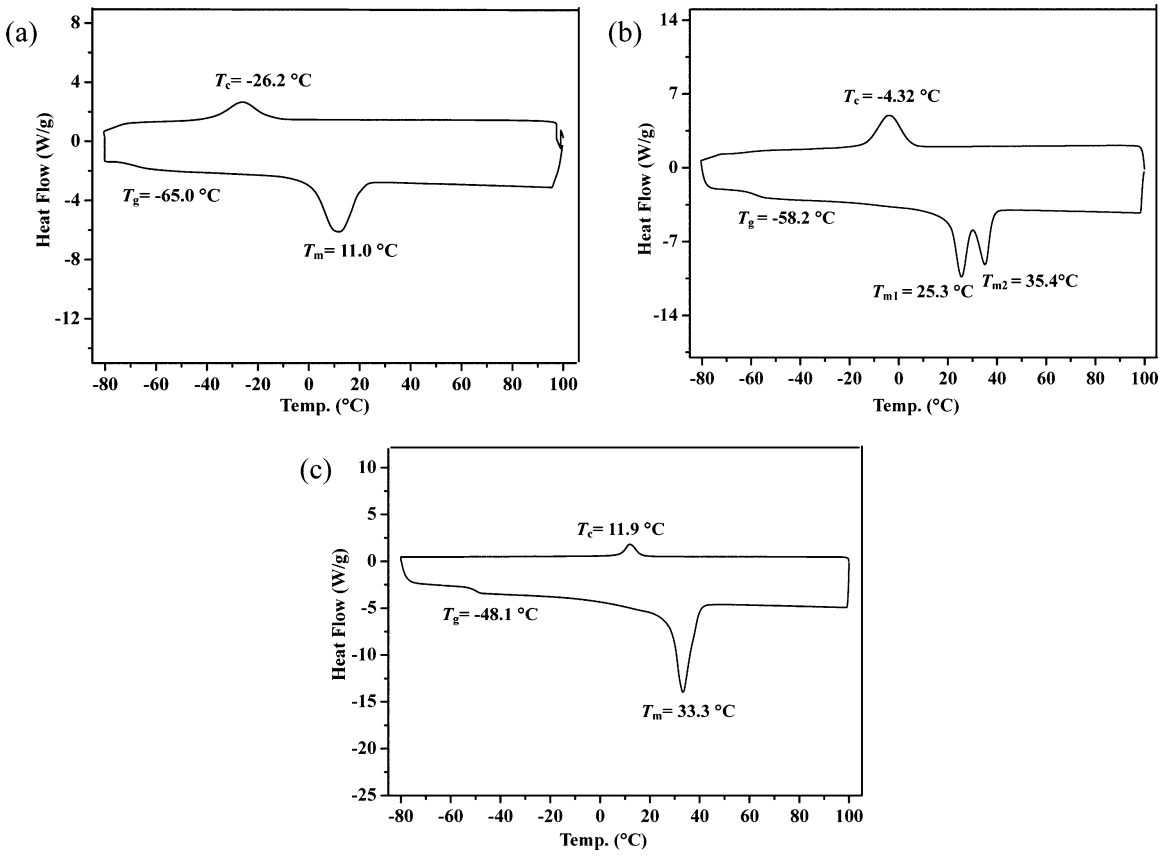

Figure 4. DSC curves: (a) PBL-*co*-PCL (γ-BL mol % = 66.0%, Table 4, entry 7); (b) PBL-*co*-PCL (cooling rate: 5 °C/min, γ-BL mol % = 84.0%, Table 4, entry 10); (c) PBL-*co*-PCL (cooling rate: 2 °C/min, γ-BL mol % = 84.0%, Table 4, entry 10).

alternating sequences as well as BL−BL−CL and BL−BL−BL continuous sequences. Similar sequence structures can also detected in the methylene carbon adjacent to the oxygen atom in both ε-CL and γ-BL ring-opened units. Figure 3 depicts ^{13}C NMR spectrum of PBL-*co*-PVL (γ-BL mol % = 54.0%), which also shows similar dyad δ-VL ring-opened units and triad γ-BL ring-opened units. The results of quantitative analysis of sequence distributions of both PBL-*co*-PCL and PBL-*co*-PVL copolymers with different γ-BL incorporations by ^{13}C NMR spectra are provided in Table 3 (Figures S3−S10). ^{13}C NMR analysis of both PBL-*co*-PCL and PBL-*co*-PVL copolymers (Figures 2 and 3 and Figures S3−S10) indicated that with an increase of γ-BL incorporation, M−M (M = ε-CL, δ-VL) continuous sequence and M−B−M (B = γ-BL) alternating sequence decreased, while B−M−B alternating sequence, B−B−M sequence, and B−B−B continuous sequence increased

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(Table 3). Comparing the copolymers with ε-CL and δ-VL at the similar level of γ-BL incorporation (PBL-*co*-PCL with 55.2% and 76.0% γ-BL% vs PBL-*co*-PVL with 54.0% and 71.2% γ-BL%), PBL-*co*-PCL copolymers contain a lower content of M−M continuous sequences in the M ring-opened unit as well as B−B−M and B−B−B continuous sequences in the B ring-opened units, but with a higher amount of M−B alternating sequences in the M ring-opened units as well as M−B−M and B−M−B alternating sequences in the B ring-opened unit, relative to PBL-*co*-PVL copolymers (Table 3); these results indicate that PBL-*co*-PCL has a more random structure than PBL-*co*-PVL.

The reactivity ratios for both copolymerizations, $r_M = k_M/k_B$ and $r_B = k_B/k_M$, were evaluated by the Fineman−Ross plots (Figure S11). The graphical plots, together with the copolymerization data used to make the plots, as well as the resulting reactivity ratios, are provided in Table S2. Specifically, the kinetic study of the copolymerization of γ-BL with ε-CL by $La[N(SiMe_3)_2]_3/Ph_2CHCH_2OH$ gave $r_M = 1.41$ and $r_B = 0.076$, while the kinetic study of the copolymerization of γ-BL with δ-VL by $^tBu\text{-}P_4/Ph_2CHCH_2OH$ gave $r_M = 0.86$ and $r_B = 0.16$. Thus, the product of the two reactivity ratios ($r_M r_B \approx 0.11$ for the copolymerization of γ-BL with ε-CL and $r_M r_B \approx 0.14$ for the copolymerization of γ-BL with δ-VL) indicates a tendency of monomers to form random copolymers containing considerable alternating monomer sequences, which is in agreement with the microstructure determined by ^{13}C NMR analysis.

Thermal Properties and Cocrystallization Behavior of γ-BL-Based Copolyesters. The thermal properties of the PBL-*co*-PCL and PBL-*co*-PVL copolymers with different γ-BL incorporations synthesized herein were analyzed by DSC and TGA, the results of which are summarized in Table 4. Representative DSC curves of γ-BL/ε-CL copolymers are depicted in Figures 4, showing a single endothermic T_m peak in the second heating scan for all the PBL-*co*-PCL copolymers, except for the copolymer with the γ-BL incorporation of 84.0% that exhibited two melting-transition peaks, presumably caused by the insufficient/slow crystallization due to the relatively fast cooling rate. Indeed, decreasing the cooling rate from 5 to 2 min/°C in the cooling cycle led to mergence of the two melting peaks into a single melting peak (Figure 4b vs 4c). Notably, γ-BL/ε-CL copolymers maintain *high crystallinity over the entire compositional range*, which is different from the common cases for semicrystalline random A−B copolymers that their crystallinity substantially decreases with increasing the content of the comonomer units (T_m depression) and finally completely disappears.[54] Another common scenario for a semicrystalline random A−B copolymer is that the copolymer remains its high crystallinity over the whole composition range as a result of cocrystallization of the two comonomer units (i.e., isomorphic crystallization); for such an isomorphic copolymer system, there typically exhibits a linear relationship between the molar composition and T_m that spans in between the T_m's of the two constituent homopolymers.[55−57] However, an *isodimorphic cocrystallization* behavior was observed for PBL-*co*-PCL from the plot of the dependence of the T_m value on the composition or γ-BL incorporation provided in Figure 5. Thus, the T_m value of the copolymer decreased first with increasing the γ-BL incorporation in the copolymer, but after reaching the lowest temperature of 11.0 °C (which is considerably lower than the T_m of either homopolymer, 63.5 °C for PBL and 57.6 °C for PCL), then it started to rise with further increasing the γ-BL

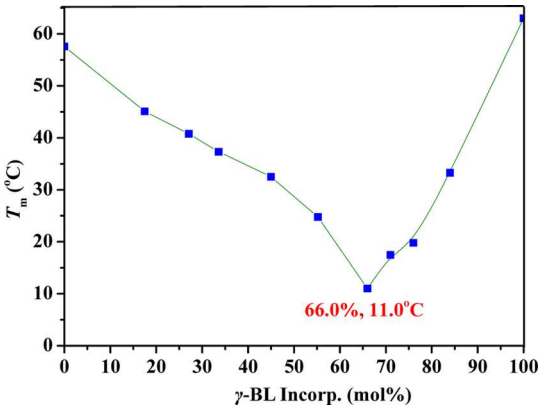

Figure 5. Plot of T_m values of PBL-*co*-PCL as a function of γ-BL incorporation (Table 4, entries 1−11), showing an isodimorphic cocrystallization behavior with a discrete eutectic temperature of T_{eu} = 11.0 °C and composition of X_{eu} = 66.0% γ-BL.

incorporation, revealing a unique eutectic phase behavior. Hence, PBL-*co*-PCL exhibits a eutectic temperature (T_{eu}) of 11.0 °C, at which temperature the eutectic composition (X_{eu}) is with 66.0% γ-BL. Therefore, at this composition, $(PBL)_{0.66}$-*co*-PCL becomes a viscous liquid at RT, although the two constituent homopolymers are semicrystalline solids at RT.

Overall, the dependence of the copolymer T_m value on the γ-BL incorporation depicted in Figure 5 can be explained as follows. Generally, at the eutectic composition, the A−B copolymer can crystallize in both A *and* B lattices so that two kinds of crystalline lattices coexist which are compatible on the scale of a crystallite (but incompatible on the scale of a monomer unit), indicative of isodimorphic cocrystallization.[57−62] When outside of the eutectic region, the A−B copolymer crystallizes either in A lattice or in B lattice depending on the copolymer composition, leading to one crystalline lattice. Thus, with gradually increasing the B (γ-BL) unit content, the structure of the crystal lattice shifts from the A type crystal to the isodimorphic phase and then to the B type crystal.[57−62]

PBL-*co*-PCL copolymers with different γ-BL incorporations were also characterized by XRD and SAXS analyses of the annealed samples (by heating the samples from RT to 80 °C at 10 °C/min and then cooling to RT (for XRD) or −10 °C (for SAXS) with at 5 °C/min). As shown in Figure 6, PCL exhibited the two characteristic semicrystalline diffraction peaks at 2θ of 21.6° and 23.3° (orange line), while the two peaks of PBL were noticeably less separated (i.e., moved closer) from each other at 2θ of 21.9° and 23.1° (black line). For PBL-*co*-PCL copolymers, the diffraction pattern remained similar, but the two characteristic diffraction peaks were shifted further apart from each other and separated more than either PBL or PCL homopolymer, now appearing in the 2θ range from 21.4°−21.5° to 23.6°−23.8°, with the largest separation of 2.4° (blue curve) observed for the copolymer with the lowest γ-BL incorporation of the series. In addition, a small broad shoulder peak appeared at ~22.4° for the copolymer samples. Interestingly, microcrystalline domains of ca. 384, 84.2, 72.7, and 135 nm, calculated from the q value at the maximum intensity in SAXS analysis[63] (Figure 7), can be observed for the PBL-*co*-PCL copolymers with the γ-BL incorporation of 33.6%, 55.2%, 66.0%, and 76.0%, respectively, which decreased first with increasing the γ-BL incorporation and then enhanced after reaching the smallest the domain size of 72.7 nm at the eutectic

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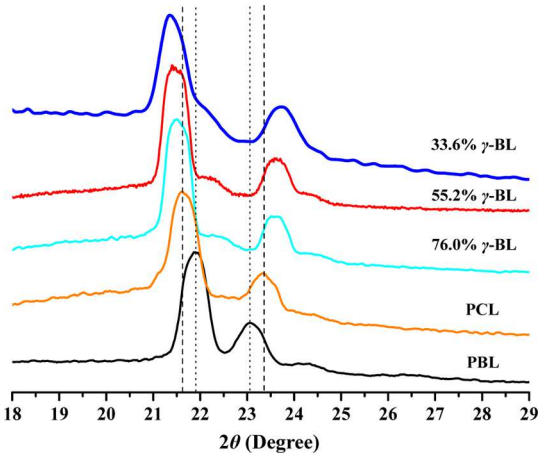

Figure 6. XRD diffraction patterns of PBL-*co*-PCL with various compositions and their homopolymer controls.

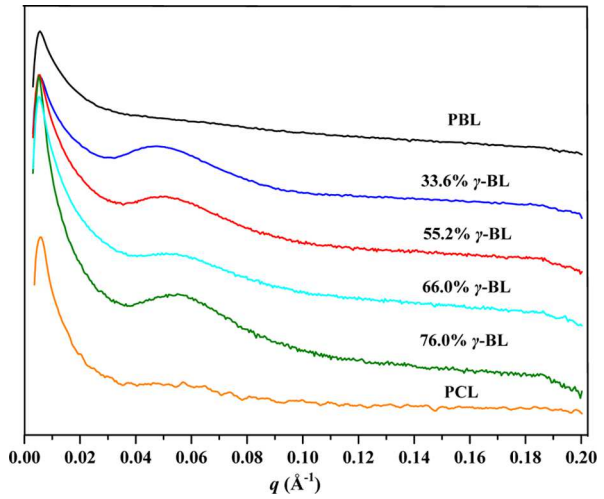

Figure 7. SAXS patterns of PBL-*co*-PCL and their homopolymer controls. Data collected at −10 °C.

composition. In sharp contrast, no significant peaks were detected in the SAXS profile of PCL and PBL homopolymers. In the case of PBL-*co*-PVL copolymers, a similar dependence of the T_m value on the comonomer composition was also observed (Table 4, entries 13−16), indicative of an eutectic behavior.

Typical TGA curves of PBL-*co*-PCL copolymers, together with PCL and PBL homopolymer controls, are shown in Figure 8. PCL (M_n = 79.6 kg/mol) exhibits higher thermal stability than the relatively low molecular weight PBL (M_n = 12.0 kg/mol). Accordingly, the thermal stability, as defined by the degradation temperature (T_d), of PBL-*co*-PCL is dependent on the γ-BL incorporation, which decreased with increasing the γ-BL incorporation, indicating that the incorporation of γ-BL into PCL facilities thermal degradation of the resulting copolymer. Different from PBL-*co*-PCL copolymers, the T_d values of copolymers PBL-*co*-PVL (T_d = 269.8−282.7 °C, Table 4, entries 14 and 16) are slightly above, or similar to, homopolymer PVL (T_d = 264.0 °C, Table 4, entry 12).

Hydrolytic Degradation Profiles of γ-BL/ε-CL Copolymers. The hydrolytic degradation behavior of ε-CL/γ-BL copolymers with different levels of γ-BL incorporation as well as the control PCL and PBL homopolymers was studied by

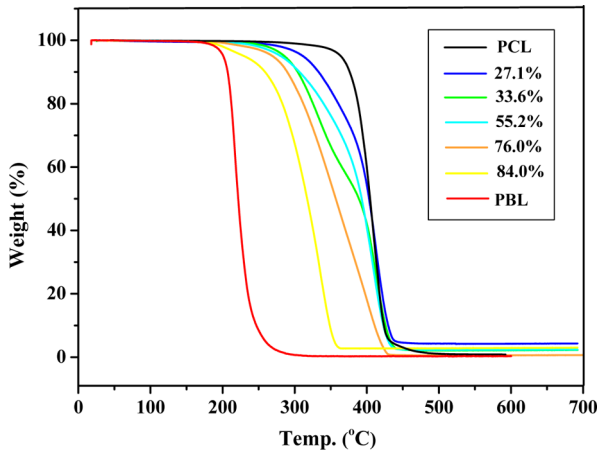

Figure 8. TGA curves of PBL-*co*-PCL with different γ-BL incorporations, in comparison to homopolymers PBL and PCL.

monitoring the weight variation of the polymer film samples immersed in neutral, acidic, and basic aqueous solutions. Figure 9 shows the weight remaining profiles of the polymer samples with different times (days). As can be seen from the profiles depicted in Figure 9, the degradation rates of the polymer samples in different aqueous solutions are substantially different, which follow the degradation rate order of $OH^-/H_2O > H^+/H_2O > H_2O$. Compared with PCL and PBL-*co*-PCL copolymers, the hydrolytic degradation of PBL is relatively fast, especially in the basic aqueous solution. For example, only 4.7% of weight remained for PBL after 1 month while PCL still had 87% weight remained. It is noteworthy that incorporation of γ-BL into PCL can accelerate the hydrolytic degradation rate of PCL, which increases with the γ-BL incorporation. For instance, the PBL-*co*-PCL copolymer with 76 mol % of γ-BL incorporation had 77% weight remaining after 1 month in the basic aqueous solution decreased from 87% for PCL. Worth noting here is the observation that the copolymer even with a high level of γ-BL incorporation (76 mol %) still exhibited relatively strong resistance toward hydrolytic degradation, rendering its degradation behavior resembling more closely to PCL than to PBL. The same phenomenon was also observed in other types of copolymers such as such as PLGA,[64] which is presumably caused by the relatively random distribution of γ-BL and ε-CL ring-opened units of this copolymer as indicated by ^{13}C NMR analysis (Table 3).

CONCLUSIONS

In summary, toward the goal of addressing the current challenge in the synthesis of the bioderived γ-BL-based copolyesters with a wide range of γ-BL incorporations across the entire composition range needed for comprehensive investigations into the composition-dependent physical properties and degradation behavior of the resulting copolyesters, we successfully developed the effective copolymerization of the nonstrained γ-BL with two common strained cyclic esters (ε-CL and δ-VL) with very different monomer thermodynamic polymerizability, which yielded a series of relatively high MW copolyesters with unprecedented levels of γ-BL incorporations. The key to this success is attributable to the carefully designed kinetic and thermodynamic conditions: To increase the γ-BL incorporation, on one hand, we need to enhance the polymerizability γ-BL by performing the copolymerization under low temperatures at −20 and −40 °C (to lessen the

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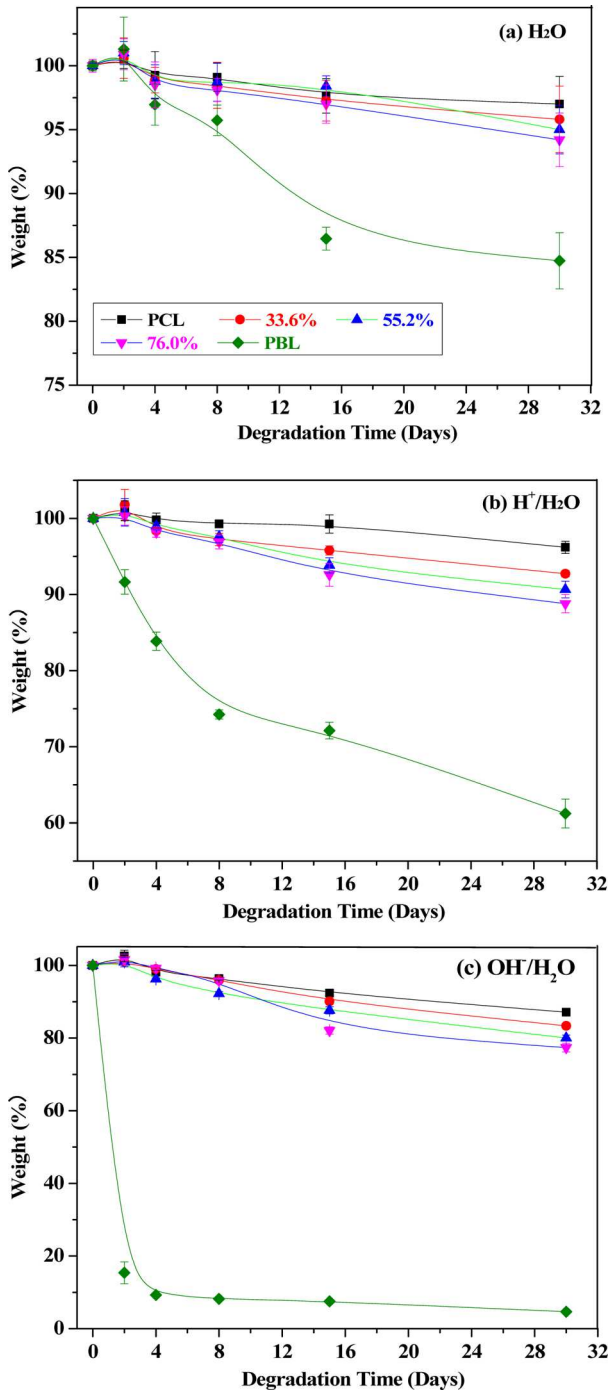

Figure 9. Hydrolytic degradation profiles with error bar of PBL-*co*-PCL copolymers in comparison with PCL and PBL homopolymers: (a) in deionized water, (b) in acidic aqueous solution ($[H^+]$ = 1.0 M), and (c) in basic aqueous solution ($[OH^-]$ = 1.0 M).

entropic penalty of its ROP) and high initial monomer concentrations (by adjusting the feed ratio); on the other hand, we also need effective catalysts and initiators that exhibit not only good activity, especially at low temperatures, but also monomer selectivity for incorporating γ-BL into the copolymer. In this context, two catalyst/initiator systems, metal-based catalyst $La[N(SiMe_3)_2]_3$ and organic catalyst ^{t}Bu-P$_4$, which showed different kinetic behavior or monomer selectivity, coupled with judiciously selected reaction conditions, were found to effectively compete the relatively inert "nonstrained" γ-BL against the relatively high-strained (more reactive) lactones toward ring-opening polymerization. As a result, this synthetic capability enabled access to γ-BL-based aliphatic copolyesters with their compositions tuned in a wide range: from low to 84.0 mol % γ-BL for PBL-*co*-PCL and up to 75.1 mol % γ-BL for PBL-*co*-PVL. The copolymerization of γ-BL and ε-CL in a multigram scale (>20 g) readily led to the synthesis of high-MW PBL-*co*-PCL copolyesters with M_n up to 135 kg/mol. All of the copolyesters exhibit random copolymer structures with considerable alternating monomer sequences, as established by microstructure analysis with ^{1}H and ^{13}C NMR.

Analysis of the copolyesters across the wide composition range revealed several intriguing or interesting thermal, cocrystallization, and degradation properties, which can be controlled and regulated by the copolymer composition. Such composition-dependent properties revealed in this study included chiefly: (a) The copolymer of γ-BL/ε-CL (and γ-BL/δ-VL) displays the unique eutectic phase behavior with high crystallinity maintained over the entire composition range of PBL-*co*-PCL, with the eutectic temperature of 11.0 °C at the unique composition of 66.0% γ-BL. (b) Incorporation of γ-BL into the copolymers facilitates thermal degradation of the PCL chain. (c) The study of hydrolytic stability showed that incorporation of γ-BL into PCL accelerates the hydrolytic degradation rate of PCL, which can be modulated by changing the copolyester composition.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.7b02174.

Experimental details; Figures S1−S11; Tables S1 and S2 (PDF)

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Notes

The authors declare no competing financial interest.

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