Graphical Abstracts

One-step enzymatic synthesis of poly(*p*-dioxanone-*co*-butylene-*co*-succinate) copolyesters with well-defined structure and enhanced degradability

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The copolyesters based on diethyl succinate, 1,4-butanediol and *p*-dioxanone (PDO) can be successfully synthesized in a mild one-step enzymatic-catalyzed copolymerization.

**One-step enzymatic synthesis of poly(*p*-dioxanone-*co*-butylene-*co*-succinate)
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Abstract

In this work, we present a mild one-step enzymatic-catalyzed copolymerization of diethyl succinate, 1,4-butanediol and *p*-dioxanone (PDO) to synthesize poly(*p*-dioxanone-*co*-butylene-*co*-succinate) copolyesters. Their chemical structure, triad distributions, and molecular weight of the copolyesters are characterized by ¹H-NMR, ¹³C-NMR and GPC. All copolyesters have narrow molecular weight polydispersity (1.3–1.5) and higher molecular weight (M_w) values (23700 to 33200 g mol⁻¹), which are well controlled by varying the amount of PDO units from 9–30 mol%. NMR, DSC, and XRD results show that copolyesters are semicrystalline random copolyesters and thermal properties depended on their composition. Furthermore, the degradation rate of the poly(*p*-dioxanone-*co*-butylene-*co*-succinate) are enhanced compared to PBS.

Keywords: enzymatic-catalyzed copolymerization; poly(butylene succinate); poly(*p*-dioxanone); triad distributions

1. Introduction

Since last century, aliphatic polyesters, such as poly(lactic acid) (PLA) [1], poly(ϵ -caprolactone) (PCL) [2], poly(butylene succinate) (PBS) [3] and poly(p-dioxanone) (PPDO) [4] et al., have been frequently explored as biomedical and environmental-friendly materials due to their excellent biocompatibility and biodegradability. Usually, these aliphatic polyesters are generally synthesized by ring-opening polymerization (ROP) of lactones with different ring sizes, or direct polycondensation of aliphatic diols and diacids/diesters.

To meet more application demands of different fields, copolymerization often need to be carried out. The most convenient way is to introduce third monomers to prepare copolyesters. For example, PBS-based copolyesters are often synthesized by incorporating comonomers such as diacids (adipic [5-7], terephthalic [8-11], 2,5-furandicarboxylic [12], azelaic [13, 14], alkynyl [15, 16], etc.) or diols (ethylene glycol [17-20], 1,3-propanediol [21-23], 1,6-hexanediol [24], cyclic alditol [25], etc.) into PBS's skeleton. PLA and PPDO-based copolyesters can be obtained by copolymerizing lactide (LA) and p-dioxanone (PDO) with ϵ -caprolactone or trimethylene carbonate (TMC), etc [26-29].

When to synthesize the copolyesters from lactones and diacids (or diols), multi-step synthesis procedures are generally involved because of the different mechanisms for polycondensation and ROP. The aliphatic polyester prepolymers are synthesized at first, and then connected by chain-extension reaction or click chemistry [30-33]. Other than the tedious processes, toxic organometallic catalysts and toxic coupling agents are needed.

In recent years, the work reported by Dr. Jiang and co-workers developed an one-step enzymatic synthesis of aliphatic lactone-diester-diol copolyesters [34-36]. However, Up to now, the approach has been successfully performed only on the lactones with high reactivity, such as ω -pentadecalactone and lactide. It is still unknown whether the method will work on stable six-membered ring monomers too [37], although the previous study revealed that Novozym-435 is a robust biocatalyst for PPDO synthesis [38, 39]. As an aliphatic polyester, PPDO has received the approval of the Food and Drug Administration (FDA) to be used as suture material [4]. Both ester bonds and the unique ether bonds exist in PPDO's polymer chain, which endows it with fast biodegradability and good flexibility. It is predictable that PDO is more effective than other lactone monomers with large ring size (e.g., ϵ -caprolactone, ω -pentadecalactone) in increasing PBS biodegradation rate.

To address the question, the copolymerization of PDO, diethyl succinate, and 1, 4-butanediol is carried out in this study. The structure and molecular weights of the copolyesters are characterized by NMR and GPC. TGA, DSC, and WAXD are employed to investigate the composition of copolyesters on their thermal properties, crystallinity, and crystal structures. Furthermore, we also investigated the degradability of the representative PPBS copolyester.

2. Experimental

2.1. Materials.

Diethyl succinate (DES, AR grade) and 1,4-butanediol (BD, AR grade) were purchased from Alfa Co. PDO was provided by the Pilot Plant of the Center for

Degradable and Flame-Retardant Polymeric Materials (Chengdu, China) and was distilled twice in vacuum immediately before use. Novozym-435, *Candida Antarctica* lipase B (CALB) immobilized in methacrylate macroporous resin, was purchased from Novo Nordisk Bioindustrials Com. and dried in vacuum at 50°C for 24 h before use. Other reagents such as diphenyl ether, chloroform and methanol were purchased from Kelong Chemical Corporation (Chengdu, China) and used without further purification.

2.2. Synthesis of poly(*p*-dioxanone-*co*-butylene-*co*-succinate) (PPBS) copolyesters

PPBS copolyesters with varied components were synthesized by one-step enzymatic catalysis. Briefly, DES, BD and PDO with predetermined amounts were added into a 250 mL round-bottomed flask containing 5 wt% Novozym-435 (based on the total monomers) and 200 wt% diphenylether (based on the total monomers) as the catalyst and solvent. The mixture was stirred at 70 °C under argon atmosphere for 24 h, followed by treatment under 150 Pa pressure for 48 h. After that, the reaction mixture was dissolved in chloroform and filtrated to remove Novozym-435. Methanol was dropwise added to the filtrate to obtain white solid product, which was then washed with methanol three times and dried in vacuum at 50 °C for 48 h to remove low molecular weight oligomers or monomer. These copolyesters are labeled as PPBS- χ , where χ is the molar percentage of PDO units in the copolyesters. As controls, homopolymers of PBS and PPDO were also synthesized according to the previous reports [38, 40]. The purified procedures for PBS and PPDO were as same as PPBS.

2.3. Characterization

¹H and ¹³C-NMR spectra were recorded on a Bruker ADVANCE 500 spectrometer by using CDCl₃ as a solvent. Average molecular weights of samples were measured by a

Waters HPLC system equipped with a model 1515 pump and a 2414 refractive index (RI) detector. Chloroform was used as the eluent at a flowing rate of 1.0 mL min⁻¹, and sample concentration was 2.5 mg mL⁻¹. The average molecular weights (M_n and M_w) were calculated by using monodisperse polystyrenes as standards. DSC measurement was performed using a TADSC-Q200 instrument. Samples were heated to 140 °C quickly and maintained for 3 min to erase thermal history, followed by quenching to amorphous state. The amorphous samples were treated in the following procedures: heating from 70 °C to 140 °C at a rate of 10 °C min⁻¹; cooling to -70 °C at the same rate and finally heating to 140 °C. WAXD analysis was carried out at room temperature with an X-ray diffractometer (DX-1000 CSC, China). A Cu anode was used as the X-ray source ($K\alpha$ radiation: $\lambda = 0.15418$ nm). The degree of crystallinity (χ_c) was evaluated from scattering curves. TGA measurement was carried out using a TG 209 F1 (NETZSCH, Germany) thermogravimetric analyzer from 40 °C to 600 °C at a heating rate of 10 °C min⁻¹ under N₂ atmosphere.

2.4. In vitro degradation

To evaluate the degradation behavior of samples, samples were dissolved in 1,4-dioxane to form a 5 mg mL⁻¹ dilute solution. And then, 4 mL phosphate buffer solution (pH = 5.0, 1/15 M) was mixed with 1 mL of as-prepared polymer solution. The mixtures were placed in a shaker at 37 °C. At determined intervals, samples were taken out and freeze-dried to dry powder, whose molecular weights were determined by GPC.

3. Results and discussion

PPBS copolyesters were prepared by one-step enzymatic copolymerization of PDO, BD and DES (scheme 1). In the first stage, PDO, BD, and DES were subjected to oligomerize under argon atmosphere at 70 °C in the presence of Novozym-435 with the formation of ethanol. Then, the subsequent second stage polymerization of oligomers leading to PPBS copolyesters was performed under the reduced pressure with removing the byproduct (ethanol) at 70 °C for 48 h. For comparison, the homopolymers of PBS and PPDO were also prepared.

Scheme 1. Synthesis route to PPBS copolyester.

As a following investigation, we synthesized a series of PPBS copolyesters with different PDO contents by adjusting the feeding ratio of BD/DES/PDO. The obtained molecular weights for PPBS copolyesters and relative homopolymers are listed in Table 1. GPC traces of PPBS copolyesters and relative homopolymers are provided in Figure S1. From Table 1, we can see that the M_w values of PPBS were in the range from 23700 to 33200 g mol⁻¹. Importantly, their PDI values were below 1.5, suggesting the enzymatic approach was effective to control the molecular structure.

Table 1. PPBS copolyesters obtained by one-step in the presence of Novozym-435

sample	PDO/BD/DE ^a (feed)	PDO unit content (mol%)	¹ H-NMR	GPC			Yield ^c (%)
			P: B: S ^b unit ratio	M_n (g mol ⁻¹)	M_w (g mol ⁻¹)	PDI	
PBS	0/1/1	0	0/1/1	13050	18400	1.41	88
PPBS-9	0.4/1/1	9	0.10/1/1	16600	23700	1.43	78
PPBS-16	0.6/1/1	16	0.19/1/1	18800	27500	1.46	64
PPBS-26	0.8/1/1	26	0.35/1/1	19000	26000	1.37	61
PPBS-30	1/1/1	30	0.43/1/1	25500	33200	1.30	55
PPDO	1/0/0	100	1/0/0	22000	62900	2.86	86

^a Molar ratio.

^b Unit abbreviations: P for PDO unit; B for butylene unit; S for succinate unit.

^c Yield was calculated on the basis of theoretical amount of polymer formed.

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132 The chemical structure of PPBS copolyesters was determined by ¹H-NMR (Figure
133 1). The assignments of the NMR resonance absorptions were facilitated by comparing
134 signals of the copolyesters to those of two relative homopolymers, PPDO [38] and PBS
135 [40]. The H_c and H_b peaks at 1.71 and 4.15 ppm were attributed to butylene units, while
136 the H_a peak at 2.61 ppm was belonged to succinate units (Figure 1). In addition, the H_e,
137 H_f, and H_d peaks at 3.80, 4.17, 4.35 ppm originated from PDO units. It should be noted
138 that some small splitting peaks were observed at 2.61 ppm (Figure S2); the phenomenon
139 was caused by the existence of different structural units in PPBS (Figure S2).The molar
140 percentage of PDO unit was tuned from 0 to 30% by changing the feeding ratio of
141 BD/DES/PDO from 0:1:1 to 1:1:1. However, the actual PDO contents in copolyesters
142 were lower than feeding, which was resulted from the lower activity of PDO. The similar
143 phenomenon was also observed in the synthesis of poly(ω -pentadecalactone-co-*p*-
144 dioxanone) [29].

145

Figure 1. ^1H -NMR spectra of PPDO, PPBS copolyesters, and PBS.

In order to obtain more information about the microstructure of PPBS copolyesters, ^{13}C -NMR measurement was performed. Figure 2 shows the resonances of carbonyl and methoxy groups, respectively. The ^{13}C chemical shifts at 172.24, 172.18, 171.00 ppm were ascribed to the carbonyls of succinate units in butylene-succinate*-butylene [B-S*-B], butylene-succinate*-PDO [B-S*-P+P-S*-B] and PDO-succinate*-PDO [P-S*-P]. Besides, the peaks at 170.02 and 170.10 ppm were ascribed to the carbonyls of PDO units in butylene-PDO*-PDO [B-P-P*] and PDO-PDO*-PDO [P-P*-P]. The peaks in the range of 63.65-69.43 ppm were attributed to methoxy groups in both PDO and butylene units. The three peaks at 63.65, 68.36 and 69.42 ppm belonged to the methylene groups in PDO-PDO*-PDO [P-P*-P]. The absorption at 68.26 and 69.27 ppm appeared substantially weak for the copolyester, which were ascribable to methylene groups of PDO units in succinate-butylene-PDO* [S-B-P*] structure. The three peaks at 64.31,

64.05 and 64.14 ppm were ascribed to methylene groups of butylene units in succinate-butylene*-PDO [S-B*-P] and succinate-butylene*-succinate [S-B*-S].

Figure 2. Expanded ^{13}C -NMR spectra showing carbonyl resonance absorptions (A) and methoxy group resonance absorptions (B).

The ^{13}C -NMR is very sensitive to small differences in the chemical environment, which enabled us to determine the different triad structures of copolyesters [41]. For comparison, the experimental triad distribution values were measured from NMR spectra of the copolyesters at same compositions, and their results are listed in Table 2. As seen from Table 2, the experimental ratios of triad sequence distribution in the copolyesters chains were not completely agreed with the theoretical triad distributions. Unlike the

previous report [34, 42], our results suggested that the repeat unit sequence distributions in the PPBS copolyester chains are not completely random. Among all triad distributions, the triads (P-S*-P, S-P*-B, S-P*-P) were highly lower than the values of the triads in theoretical random copolymer chains; meanwhile conversely, the triads (S-B*-S, P-B*-P, P-P*-P) were substantially higher than the values of the triads in theoretical random copolymer chains. Thus, these results suggested that PDO units prefer to link with a butylene unit or be adjacent to each other, i.e. they have a low tendency to link with a succinate unit in the copolyester chain.

Table 2. Relative distributions of selected triads for PPBS copolyesters

		sample				Calc. Formula
		PPBS-9	PPBS-16	PPBS-26	PPBS-30	
P/(P+S) (mol% P units),%		9	16	26	30	
Triads						
S-B*-S	theoretical	0.4319	0.3808	0.3081	0.2787	2f(S)×f(B)×2f(S)
	experimental	0.5963	0.5339	0.4701	0.4357	
S-B*-P+P-B*-S	theoretical	0.0432	0.0724	0.1080	0.1198	2f(S)×f(B)×f(P)+f(P)×f(B)×2f(S)
	experimental	0.0808	0.1150	0.1602	0.1988	
P-B*-P	theoretical	0.0011	0.0034	0.0094	0.0130	f(P)×f(B)×f(P)
	experimental	0.0043	0.0067	0.0158	0.0136	
B-S*-B	theoretical	0.4319	0.3808	0.3081	0.2787	2f(B)×f(S)×2f(B)
	experimental	0.2894	0.2889	0.2689	0.2343	
B-S*-P+P-S*-B	theoretical	0.0432	0.0724	0.1080	0.0599	2f(B)×f(S)×f(P)+f(P)×f(S)×2f(B)
	experimental	0.0151	0.0254	0.0374	0.0548	
P-S*-P	theoretical	0.0011	0.0034	0.0094	0.0130	f(P)×f(S)×f(P)
	experimental	0.0000	0.0000	0.0000	0.0009	
S-P*-B	theoretical	0.0432	0.0724	0.1079	0.1199	2f(S)×f(P)×2f(B)

	experimental	0.0000	0.0000	0.0000	0.0000	
S-P*-P	theoretical	0.0022	0.0069	0.0189	0.0258	$2f(S) \times f(P) \times f(P)$
	experimental	0.0000	0.0000	0.0000	0.0000	
P-P*-B	theoretical	0.0022	0.0069	0.0189	0.0258	$f(P) \times f(P) \times 2f(B)$
	experimental	0.0030	0.0095	0.0204	0.0280	
P-P*-P	theoretical	0.0000	0.0006	0.0033	0.0055	$f(P) \times f(P) \times f(P)$
	experimental	0.0111	0.0206	0.0272	0.0340	

180

181 Based on the above results, we can propose the possible copolymerization
182 mechanism of PPBS copolyester (Scheme 2). At the first stage, 1,4-butanediol was not
183 only as a diol to react with diethyl succinate to form the low molecular weight PBS
184 oligomers with ethyl succinate terminal group, but also as an initiator for the enzymatic
185 ring-opening polymerization of PDO to form PPDO oligomers with hydroxyl end group.
186 During the second stage of copolymerization, the transesterification of PPDO oligomers
187 with PBS oligomers was occurred to form longer copolyester chains with random
188 structures, accompanied with ethanol as a byproduct. Besides, because of the relatively
189 low activity of PPDO oligomers, it would be less reactive than PBS oligomers giving the
190 copolyesters less PDO units.

191

Scheme 2. Proposed copolymerization mechanism of PDO, DES, and BD.

In general, it can be expected that the random copolymers will have their thermal properties and crystallinity as a function of chemical composition between those of the neat homopolymers. Therefore, we employed DSC, and WAXD to investigate the effect of composition on the thermal transition and crystallization of PPBS copolyesters.

The DSC scans of PPDO, PPBS, PBS are shown in Figure 3, and the detail results are summarized in Table 3. The glass transition temperature (T_g) was obtained from the first DSC heating scans of the melt-quenched sample (Figure 3A), and the crystallization temperature (T_c), crystallization enthalpy (ΔH_c), melting temperature (T_m), as well as fusion enthalpy (ΔH_m) were obtained from the first cooling and second heating scans (Figure 3B, C).

Figure 3. DSC thermograms of PPBS and relative homopolymers, the first heating scans from melt-quenched state (A), the first cooling scans (B) and the second heating scans (C) at a rate of $10\text{ }^{\circ}\text{C min}^{-1}$.

It can be seen that the thermal behavior of PPBS copolyesters depended on composition. PPBS copolyesters containing up to 30 mol% of PDO units are semicrystalline, as evidenced by the melting endotherm. However, both T_m (Figure 3B) and T_c (Figure 3C) decreased clearly with increasing the PDO content. The corresponding endotherm and exotherm regions broadened considerably with the presence of high PDO amounts. This revealed that the presence of PDO units in the copolyester chains hindered the chain movement and packing, which depressed its crystallization. In Figure S3, both T_m and ΔH_m are displayed as a function of the PDO content in the copolyesters. The values of them decreased linearly with increasing PDO content. This trend suggested that PDO segment was excluded from the crystal of PBS, showing diluent effect on the crystallization of PPBS.

The change in T_g of the copolyesters was represented in Figure 3A. Concerning the homopolymers, PBS showed a glass-transition temperature (T_g) at $-42.2\text{ }^{\circ}\text{C}$; PPDO was characterized by a T_g at $-10.8\text{ }^{\circ}\text{C}$ (Figure S4). For all copolyesters, only one T_g was

224 detected in the DSC curves and the values of T_g steadily increased from -39.5 to -37.0 °C
 225 with the increase in PDO content ranging from 9 to 30%, which indicated that the
 226 incorporation of PDO units would slightly hinder the chain mobility of PBS segment and
 227 form a single amorphous phase without microscale separation. The above results
 228 confirmed the random PPBS structure, which was in agreement with the random
 229 sequence structure validated by NMR.

230

231 **Table 3.** Thermal properties and χ_c of PBS, PPDO and PPBS

sample	DSC									$\chi_{c,WAXD}$ (%)
	TGA		First heating	First cooling		Second heating				
	$T_{5\%}$ (°C)	T_{max} (°C))	T_g (°C)	T_c (°C)	ΔH_c (J/g)	T_{cc} (°C))	ΔH_{cc} (J/g)	T_m (°C)	ΔH_m (J/g)	
PBS	359.4	396.1	-42.2	80.4	73.9	-	-	114.7	74.1	49.4
PPBS-9	351.1	398.3	-40.9	67.3	64.6	-	-	108.1	72.6	48.0
PPBS-16	350.5	393.2	-39.5	51.1	60.1	-	-	99.0	70.2	45.5
PPBS-26	354.1	397.3	-37.2	25.7	54.6	-	-	86.3	61.8	29.1
PPBS-30	320.9	390.3	-37.0	23.8	47.9	-	-	83.1	57.9	26.0
PPDO	274.8	334.7	-10.8	43.7	10.7	34.3	40.3	105.7	77.0	40.4

232

233 In order to elucidate how PDO units affect the crystal structure of PBS, WAXD has
 234 been performed. The WAXD patterns of copolyester and homopolymers are presented in
 235 Figure 4. In agreement with previous reports, PBS showed three diffraction peaks at 2θ
 236 = 19.9, 22.2, 22.9°, ascribed to (020), (021), and (110) planes [22]. PPDO presented two
 237 diffraction peaks at 2θ = 22, 24°, as shown by Zhang et al [32]. Regarding the PPBS
 238 copolyesters, all copolyesters showed the same diffraction peaks with neat PBS, while

their peak intensities decreased with the increase of PDO content. The result suggested that the crystal structure of the PPBS was consistent with neat PBS, however, the reduction in the crystallinity (χ_c) was caused by the incorporation of PDO content into PBS segment. The detail χ_c values were further calculated on the basis of deconvolution of crystalline and amorphous peaks in the WAXD pattern using the peak separation software [43]. The results are showed in Table 3. The χ_c value decreased from 49.4% to 26.0% with increasing PPDO content from 0 to 30%. In conclusion, the incorporation of PPDO into PBS did not change its crystal structure, but reduced the degree of crystallinity of the copolyesters.

Figure 4. WAXD of PBS, PPDO, and PPBS copolyesters.

The thermal stability of polymers is an important factor that can limit their application. Therefore, the thermal stability of PPDO, PBS, and PPBS was studied by TGA under nitrogen atmosphere. TGA curves are shown in Figure 5, and the decomposition temperature at 5% weight loss, $T_{d,5\%}$, and decomposition temperature at the maximum rate, $T_{d,max}$, are summarized in Table 3. As it might be seen, all PPBS

copolyesters had good thermal stability and clearly showed one degradation step with the maximal decomposition rates at approximately 395 °C. For PBS, its $T_{5\%}$ was observed at 359.4 °C. The thermal stability of PPBS copolyesters did not have a strong relationship with PDO content. It was found that when PDO content was less than 26%, all $T_{5\%}$ almost remained unchanged. With a further increase in PDO content, $T_{5\%}$ of PPBS-30 decreased to 320.9 °C, while its $T_{d,max}$ stayed unchanged. These results clearly indicated that PPBS copolyesters had good thermal stability and the incorporation of PDO units into PBS chain did not have a significant effect on their thermal stability.

Figure 5. TGA thermograms of neat PBS, PPDO, and PPBS copolyesters.

The synthesized PPBS copolymers were aliphatic copolyesters containing PDO repeat units in the polymer chains, which were expected to have faster biodegradation rate than neat PBS. In order to estimate this, PPBS-30 was chosen as the representative sample for the degradation behavior. The degradation behavior was evaluated via in vitro hydrolysis at 37 °C. GPC was used to monitor the change in the molecular weight of polymers with the hydrolysis time. As it was expected, PPBS-30 copolyester degraded

fast in the buffer solution. After 14 days, the M_w value of PPBS-30 copolyester decreased from 33200 to 28320 g mol⁻¹ (Figure 6A). As for as homopolymers are concerned, neat PPDO show fast degradation rate than PBS, it quickly reduced from 62900 to 51300 g mol⁻¹ (Figure S5) after 14 days in vitro hydrolysis. However, the M_w of neat PBS almost unchanged over the 14 days (Figure S6), even it had lower M_w value than that of PPDO. Meanwhile, to better understand the degradation mechanism, ¹H-NMR spectra for PPBS were recorded at various hydrolysis time at 37 °C (Figure 6B). The proton signal at 3.68 ppm, belonged to the end group of copolyesters (HOCH₂CH₂CH₂CH₂O-), didn't change with the hydrolysis time. At the same time, a new proton signal appeared at 4.36 ppm, which was ascribed to the end group of PPDO oligomers (-CO-CH₂-O-CH₂CH₂-OH) [44], and it increased gradually with hydrolysis time. This illustrated that PPDO units in PPBS were apt to be attacked by water in weak acid buffer and the principal point of weakness in PPDO units was ester bond. Based on the above results, we proposed the degradation mechanism of PPBS (Scheme 3). During the hydrolysis process, the ester bonds of PPDO units were mainly attacked, and produced low molecular weight polymers with carboxylic and hydroxyl end groups. The formed carboxylic acid end group will catalyze further hydrolysis into low molecular weight water-soluble oligomers, which has been well demonstrated by the previous literatures [45-46].

Figure 6. (A) Change in M_w of PPBS-30 incubated in PBS solution at 37 °C, and (B) ^1H -NMR spectra of PPBS-30 as a function of hydrolysis time.

Scheme 3. Hydrolytic degradation mechanisms of PPBS copolyesters.

4. Conclusions

In summary, PPBS copolyesters with the PDO content ranging from 9 to 30 mol% were enzymatically synthesized via the copolymerization of DES, BD, and PDO. The structure and sequence distribution were tested by ¹H and ¹³C-NMR, and the results suggested that the copolyesters presented nearly random microstructure. DSC analyses showed that the copolyesters have one *T_g* shifting to higher temperatures upon increasing the PDO content. Meanwhile, *T_c* and *T_m* shifted to lower temperatures with increasing the PDO content, and the corresponding enthalpies are lower than the value of PBS homopolymer, which is a typical phenomenon for random copolymers. The WAXD results revealed no influence of the PDO content on the copolyesters crystalline phase, indicating the PDO content exists in the amorphous region and is excluded from crystal region of PBS. The copolyesters present one weight loss stage and are thermally stable up to at least 320 °C. Additionally, the degradation studies revealed that PPBS can rapidly degrade, suggesting its potential biomedical application.

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References

- [1] Raquez JM, Habibi Y, Murariu M, Dubois P. Prog Polym Sci 2013; 38 (10–11): 1504-1542.
- [2] Woodruff MA, Hutmacher DW. Prog Polym Sci 2010;35(10):1217-1256.
- [3] Xu J, Guo BH. Biotechnol J 2010;5(11):1149-1163.
- [4] Yang KK, Wang XL, Wang YZ. J Macromol Sci Part C 2002;42(3):373-398.
- [5] Nikolic MS, Djonlagic J. Polym Degrad Stab 2001;74(2):263-270.
- [6] Tserki V, Matzinos P, Pavlidou E, Vachliotis D, Panayiotou C. Polym Degrad Stab 2006;91(2):367-376.
- [7] Zhu C, Zhang Z, Liu Q, Wang Z, Jin J. J Appl Polym Sci 2003;90(4):982-990.
- [8] Nagata M, Goto H, Sakai W, Tsutsumi N. Polymer 2000;41(11):4373-4376.
- [9] Honda N, Taniguchi I, Miyamoto M, Kimura Y. Macromol Biosci 2003;3(3-4):189-197.
- [10] Li F, Xu X, Li Q, Li Y, Zhang H, Yu J, Cao A. Polym Degrad Stab 2006;91(8):1685-1693.
- [11] Deng LM, Wang YZ, Yang KK, Wang XL, Zhou Q, Ding SD. Acta Mater 2004;52(20):5871-5878.

- 335 [12] Wu L, Mincheva R, Xu Y, Raquez JM, Dubois P. *Biomacromolecules*
336 2012;13(9):2973-2981.
- 337 [13] Ravi RN A, Karunanidhi M, Jaisankar V. *Asian J Chem* 2011;23(2):556-560.
- 338 [14] Mincheva R, Delangre A, Raquez JM, Narayan R, Dubois P. *Biomacromolecules*
339 2013;14(3):890-899.
- 340 [15] Liu GC, Zhang WQ, Wang XL, Wang YZ. *Chinese Chem Lett.*
341 <http://dx.doi.org/10.1016/j.ccllet.2016.10.014>
- 342 [16] Liu GC, Zhang WQ, Zhou SL, Wang XL, Wang YZ. *Rsc Adv* 2016;6(73):68942-
343 68951.
- 344 [17] Cao A, Okamura T, Nakayama K, Inoue Y, Masuda T. *Polym Degrad Stab*
345 2002;78(1):107-117.
- 346 [18] Zeng JB, Huang CL, Jiao L, Lu X, Wang YZ, Wang XL. *Ind Eng Chem Res*
347 2012;51(38):12258-12265.
- 348 [19] Pepic D, Zagar E, Zigon M, Krzan A, Kunaver M, Djonlagic J. *Eur Polym J*
349 2008;44(3):904-917.
- 350 [20] Huang CL, Jiao L, Zhang JJ, Zeng JB, Yang KK, Wang YZ. *Polym Chem*
351 2012;3(3):800-808.
- 352 [21] Papageorgiou GZ, Bikiaris DN. *Biomacromolecules* 2007;8(8):2437-2449.
- 353 [22] Xu Y, Xu J, Guo B, Xie X. *J Polym Sci Part B: Polym phys* 2007;45(4):420-428.
- 354 [23] Xu Y, Xu J, Liu D, Guo B, Xie X. *J Appl Polym Sci* 2008; 109(3):1881-1889.
- 355 [24] Wang G, Qiu Z. *Ind Eng Chem Res* 2012;51(50):16369-16376.
- 356 [25] Duan RT, He QX, Dong X, Li DF, Wang XL, Wang YZ. *Acs Sustain Chem Eng*
357 2016;4(1):350-362.

- 358 [26] Zhang X, Pichora D, Goosen MFA. *J Macromol Sci Part A* 1993;30(12):933-947.
- 359 [27] Plikk P, Målberg S, Albertsson AC. *Biomacromolecules* 2009;10(5):1259-1264.
- 360 [28] Hong JT, Cho NS, Yoon HS, Kim TH, Lee DH, Kim WG. *J Polym Sci Part A:*
361 *Polym Chem* 2005;43(13):2790-2799.
- 362 [29] Jiang Z, Azim H, Gross RA, Focarete ML, Scandola M. *Biomacromolecules*
363 2007;8(7):2262-2269.
- 364 [30] Li WD, Zeng JB, Li YD, Wang XL, Wang YZ. *J Polym Sci Part A: Polym Chem*
365 2009;47(21):5898-5907.
- 366 [31] Tuominen J, Kylmä J, Seppälä J. *Polymer* 2002;43(1):3-10.
- 367 [32] Zhang YH, Wang XL, Wang YZ, Yang KK, Li J. *Polym Degrad Stab*
368 2005;88(2):294-299.
- 369 [33] Ding SD, Zheng GC, Zeng JB, Zhang L, Li YD, Wang YZ. *Eur Polym J*
370 2009;45(11):3043-3057.
- 371 [34] Jiang Z. *Biomacromolecules* 2008;9(11):3246-3251.
- 372 [35] Zhou J, Liu J, Cheng CJ, Patel TR, Weller CE, Piepmeier JM, Jiang Z, Saltzman
373 WM. *Nat Mater* 2012;11(1):82-90.
- 374 [36] Jiang Z, Zhang J. *Polymer* 2013;54(22):6105-6113.
- 375 [37] Dong FX, Xu C, Tong XZ, Wang XL, Song F, Wang YZ. *J Mol Catal B-Enzym*
376 2013;96:40-45.
- 377 [38] Nishida H, Yamashita M, Nagashima M, Endo T, Tokiwa Y. *J Polym Sci Part A:*
378 *Polym Chem* 2000;38(9):1560-1567.
- 379 [39] Dong FX, Zhang L, Tong XZ, Chen HB, Wang XL, Wang YZ. *J Mol Catal B-*
380 *Enzym* 2012;77:46-52.

- [40] Azim H, Dekhterman A, Jiang Z, Gross RA. *Biomacromolecules* 2006;7(11):3093-3097.
- [41] Yang Z, Zhang X, Luo X, Jiang Q, Liu J, Jiang Z. *Macromolecules* 2013;46(5):1743-1753.
- [42] Mazzocchi L, Scandola M, Jiang Z. *Macromolecules* 2009;42(20):7811-7819.
- [43] Zhu QY, He YS, Zeng JB, Huang Q, Wang YZ. *Mater Chem Phys* 2011;130(3):943-949.
- [44] Jin C, Liang B, Li J, Li F. *J Polym Environ* 2013;21(4):1088-1099.
- [45] Li XY, Zhou Q, Wen ZB, Hui Y, Yang KK, Wang YZ. *J Appl Polym Sci* 2016, DOI: 10.1002/APP.43483
- [46] Ando Y, Yoshikawa K, Yoshikawa T, Nishioka M, Ishioka R, Yakabe Y. *Polym Degrad Stab* 1998; 61(1):129-137.